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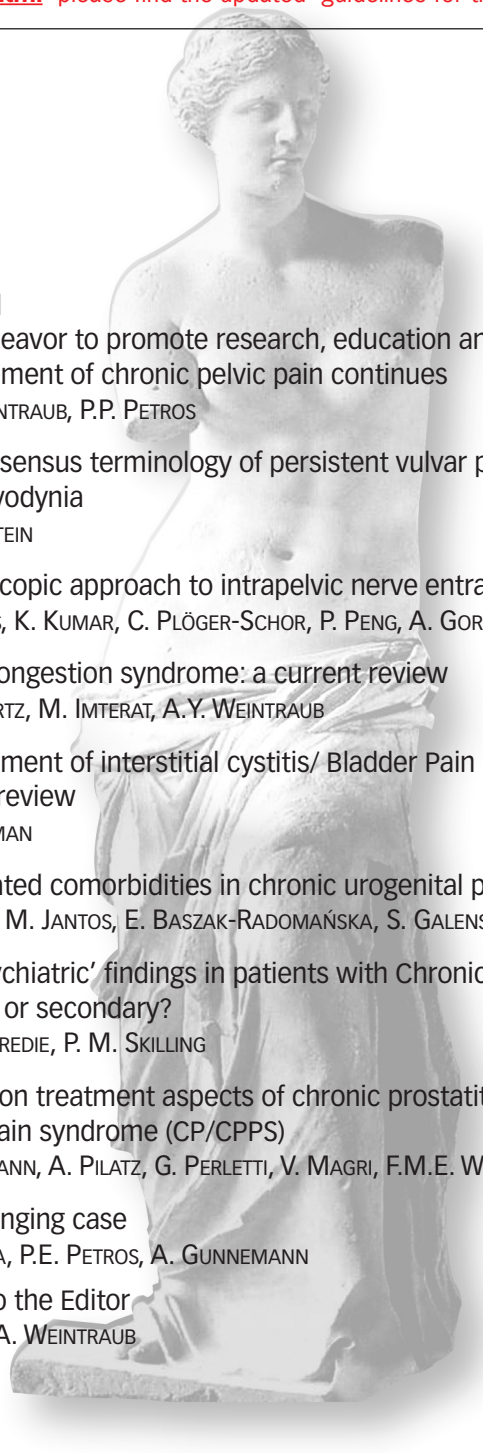

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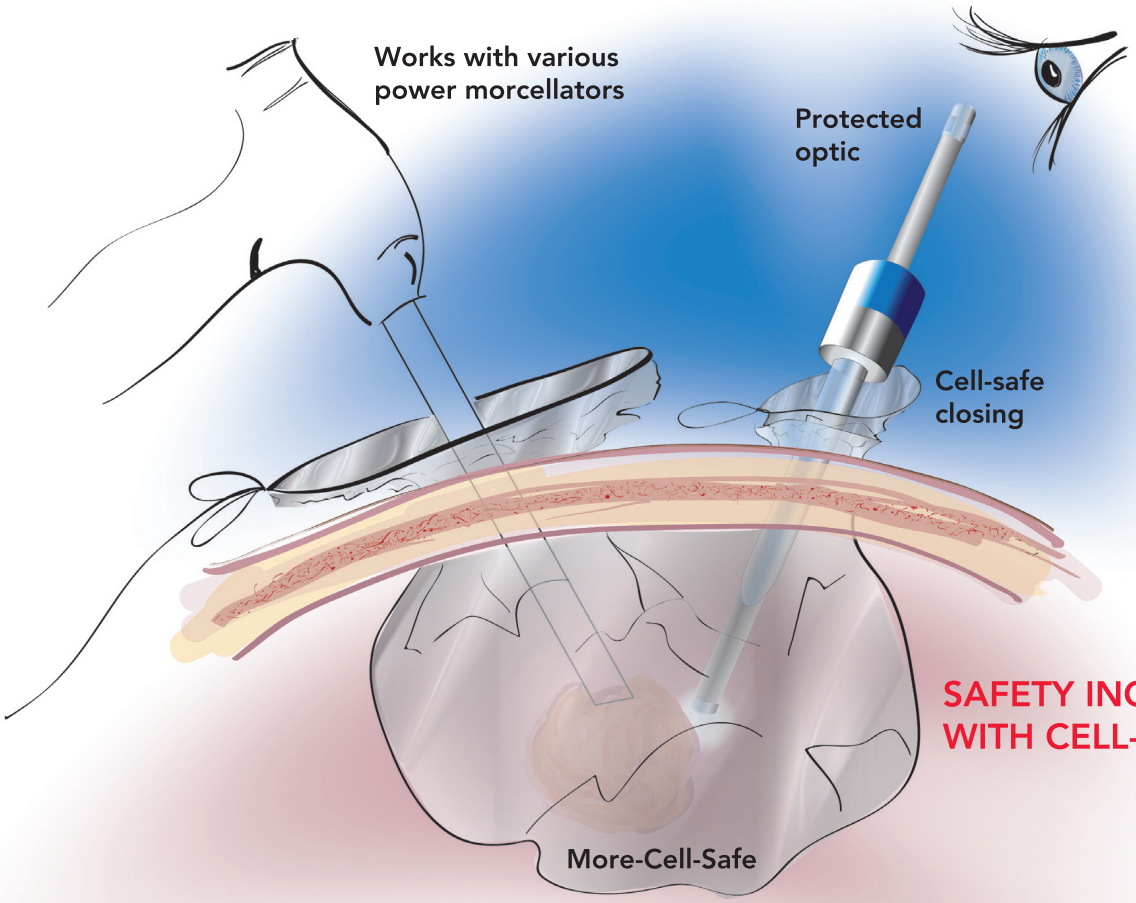

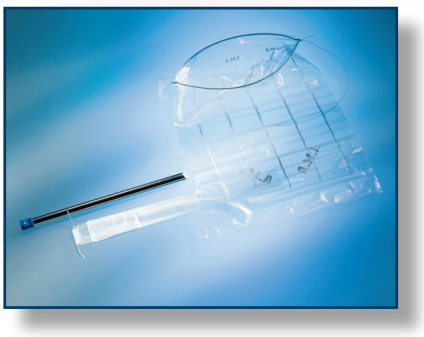

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Editorial

The endeavor to promote research, education and the clinical management of chronic pelvic pain continues

CARL MORANDI, MONICA ZANICHELLI, GIUSEPPE DI CHIACCHIO, ANNA PARMIGIANI

Even today, chronic pelvic pain (CPP) is not considered curable by learned bodies. This is not the opinion of this journal. The September 2017 issue of Pelviperineology Journal published evidence that not only can CPP be caused by the inability of lax uterosacral ligaments to support nerve plexuses contained within, it can be cured by reconstruction of these ligaments. This has been known for some years.

This 2nd Chronic Pelvic Pain issue continues the journal's exploration of peripheral neurological causation of CPP. The role of pudendal nerve damage in the causation of CPP was raised by Ahmed Shafik in 1998. Drs Lemos and Beco elaborate and expand this direction with two important works.

The initial paper in this 2nd Pain issue is presented by Professor Bornstein. It summarizes the 2015 consensus statement on vulvar pain terminology made on behalf of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS), of which he was Chairman. This is followed by the Lemos and Beco papers. Dr Friedman summarizes another 'deeply unknown' condition, Interstitial Cystitis. Johns and Jantos compare age related comorbidities in vulvodynia and bladder pain syndrome. Joan McCredie and Patricia Skilling's anecdotal descriptions of almost immediate psychological improvement in patients cured of severe chronic pelvic pain by uterosacral ligament reconstruction question the generally accepted concept that much of CPP is caused by psychiatric conditions. Hoffman and Wagenlehner give a State of the Art review of Chronic Prostatitis, a major cause of CPP in the male, another condition with 'unknown etiology'.

The issue concludes with an important ongoing educational initiative from Pelviperineology, presentation and discussion of challenging clinical cases under the editorship of Dr Leanza.

ADI Y. WEINTRAUB, PETER P. PETROS
Editors, 2nd pain Issue, Pelviperineology Journal

The International Society of Pelviperineology Congress - 2018 Bucharest, Romania

We are pleased to invite you to the International Society of Pelviperineology Congress, which will be held in 2018 in Bucharest, between the 4th and the 6th of October.

BUCHAREST is situated between the Carpathians Mountains and the Danube, also known as the City of Joy.

In the period between the two World Wars, the city has thrived, under the careful watch of the Monarchy, the intellectual elite and the French architects, becoming known as "The Small Paris" or "The Paris of the East".

The Old Town is one of the most animated and lively places in Bucharest. Near the center of the city there is an area with small streets and a big variety of interwar buildings where you can find more than 200 pubs, clubs and terraces.

In this part of the city one can find, among others, the National Bank (the first bank ever built in Romania), The Royal Court of Vlad Dracul (Dracula), an old famous street called Lipscani and many buildings that imitate the French style from the beginning of the 20th century. There are also many restaurants, some of them with a clear theme, with traditional food and architecture, and others with elements that bring back to life the interwar atmosphere.

The Old Town symbolizes quite well the mixture of the Romanian Culture, the great mosaic that was created here. The Latin spirit, the oriental (Ottoman Empire) influences and some elements from Western Europe (French architecture, a little bit of Italian fashion style, international music) are quite visible.

This year's edition of the Congress will reunite prominent professionals in the field of pelviperineology, joining specialties such as obstetrics-gynecology, urology, urogynecology, colorectal surgery.

Interesting topics will be debated during the sessions, with multidisciplinary round-table sessions with interactive participation from the audience.

We invite you to enhance your surgical and clinical knowledge with a diversified scientific program and a line up of speakers who are not only opinion leaders but also willing to teach.

We look forward to seeing you in Bucharest!

Prof. Dr. Akin Sivaslioglu
President of the International Society of Pelviperineology

Professor Dr. Elvira Bratila
President of the Romanian Society of Urogynecology

Review

The consensus terminology of persistent vulvar pain and vulvodynia

JACOB BORNSTEIN

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INTRODUCTION

Vulvar pain is an enigma. Its etiology, pathophysiology and treatment have not yet been elucidated. This condition is presented with pain during intercourse.

Around the enigma of vulvar pain, myths about its causes and treatments that have not been proved to be effective emerged. However, in 2015, an evidence based consensus terminology has been introduced ("2015 terminology") [1,2,3], with a clear definition and understanding of vulvar pain. Consequently, a new paradigm to the treatment of vulvar pain was developed making it etiology-based.

"VULVAR PAIN", "VULVODYNIA" OR "DYSPAREUNIA"?

For years, the International Society of Vulvovaginal Disease (ISSVD) discussed "vulvar pain", but this is somewhat misleading. In fact, the most common and disturbing presenting symptom is introital pain during intercourse, i.e. superficial dyspareunia. Dyspareunia is one of the most common complaints associated with sexual dysfunction. Why has the ISSVD chosen to focus on "vulvar pain" and not on "Dyspareunia"? There are several reasons to this. One is an attempt of the ISSVD to broaden the terminology so that it involves pain in general and not only pain during intercourse. An additional reason may be to move away from the limited psycho-sexual connotation of dyspareunia that prevailed years ago.

THE 2015 TERMINOLOGY

The 2015 consensus terminology of "persistent vulvar pain and vulvodynia" (table 1) has been created by three international societies: the ISSVD, the International Society for The Study of Women's Sexual Health (ISSWSH) and the International Pelvic Pain Society (IPPS). The new terminology was achieved in four steps. The first involved a terminology consensus conference with representatives of the three societies, held in April 2015. Then, an analysis of the relevant published studies was used to establish a level of evidence for each factor associated with vulvodynia. The terminology was amended based on feedback from members of the societies. Finally, each society's board accepted the new terminology.

The final terminology was simultaneously published by three journals[1,2,3].

CATEGORIES OF PERSISTENT VULVAR PAIN

The 2015 terminology divides 'persistent vulvar pain' into two categories: vulvar pain that its cause is known, so that it is related to a specific disorder (e.g., inflammatory, neoplastic, traumatic, infection-related, neurologic, traumatic, iatrogenic, and hormonal) and 'vulvodynia'.

DEFINITION OF VULVODYNIA

The new definition of Vulvodynia is "vulvar pain of at least three months' duration, without clear identifiable cause, which may have potential associated factors".

DESCRIPTORS OF VULVODYNIA

The 2015 terminology further characterizes vulvodynia based on location (vestibulodynia, Cliterodynia, generalized, mixed), provocation (upon contact or spontaneous), temporal pattern (intermittent or constant), and onset (primary or secondary).

Of the various descriptors that are included in the 2015 terminology, the most important is its localization (localized or generalized) and relation to provocation (provoked and spontaneous) of vulvodynia. Generalized vulvodynia (formerly termed 'essential' or 'dysesthetic' vulvodynia affects the whole vulva and is usually spontaneous. It is regarded as a neuropathic pain and affects postmenopausal women mainly.

In addition, the onset of vulvodynia significantly matters to treatment outcome[4]. LPV that has been present since the first attempt of vaginal penetration is termed primary. If LPV started after a period of pain-free intercourse it is named "secondary" LPV. Several researchers believe that primary LPV is difficult to treat than secondary.

The severity of LPV is determined by the patient's level of pain during vaginal intercourse (dyspareunia), using the Marinoff criteria[5]: Level 1 – dyspareunia causes discomfort but does not prevent sexual intercourse; Level 2: dyspareunia sometimes prevents sexual intercourse; Level 3: dyspareunia completely prevents sexual intercourse. However, when intercourse is not practiced, a tampon insertion may be used to determine severity of LPV and evaluate the success of therapy.[6]

The significance of determining severity of LPV is that the approach to treatment should be determined according to the severity of the condition, e.g. In level 1 cases, treatment should not involve surgery. In many cases there is deterioration of LPV severity with time, and LPV that was level 1 may become level 3. Less frequently, a level 3 LPV will spontaneously resolve or become a level 1 in severity. In other cases, treatment will reduce the level of sensitivity, rather than leading to a complete resolution of the pain.

FACTORS ASSOCIATED WITH VULVODYNIA

The most important innovation of the 2015 terminology is an appendix table (Table 2) with a list of potential associated factors (musculoskeletal, neuroproliferation, associated co-morbidities, psychosocial factors, etc) acknowledging that vulvodynia likely is not one disease, but several disease processes. Only few recognize the significance of that "appendix" to the consensus terminology, but these "potential associated factors" are helpful in identifying pos-

sible etiologies of vulvodynia. So far, no etiology of vulvodynia has been recognized by the ISSVD. Hence, the new terminology revolutionized the approach to the study and management of vulvodynia, which now need to be individualized, according to the associated factor. The data on each associated factor is detailed in a recent review[7], and presented below:

Neuroproliferation or hyperinnervation

An increase in the density of nerve endings in the vestibular endoderm of women with LPV as compared to controls has been repeatedly documented. These nerve endings have been shown to be nociceptors and have an increased density of the vanilloid receptor VR1. We have shown that the increased density of nerve fibers in women with LPV was 10 times greater than in non-affected women, and was associated with significant increase in the number of mast cells and degranulated mast cells within the vestibular mucosa. We then demonstrated an increased subepithelial heparanase activity (degranulated from the aforementioned mast cells) in the vestibular mucosa. We further postulated that histamine, leukotrienes, and nerve growth factor – which are released from the degranulated mast cell – can cause nociceptor proliferation and sensitization. In addition, the heparanase, which can degrade the vestibular stroma, allows these activated and proliferating nociceptors to penetrate through the degraded basement membrane into the superficial mucosal epithelium of the vestibule. It has been theorized by many groups that certain genetic polymorphisms may predispose affected women with LPV to have an exaggerated inflammatory response or chronic infection, which leads to mast cell activation and subsequent nociceptor proliferation.

Central nervous system involvement in vulvodynia

Central nervous system alterations as a cause of vulvodynia has been suspected. Several mechanisms have been proposed:
- Altered central nervous system processing;
- Activation of the hypothalamic pituitary adrenal (HPA) axis via chronic stress;
- Visceromotor responses to vaginal distension;
- Global sensitization of nociceptive transmission.

TABLE 1. 2015 Consensus terminology and classification of persistent vulvar pain and vulvodynia

A. Vulvar pain caused by a specific disorder*
- Infectious (e.g. recurrent candidiasis, herpes)
- Inflammatory (e.g. lichen sclerosus, lichen planus, immunobullous disorders)
- Neoplastic (e.g. Paget disease, squamous cell carcinoma)
- Neurologic (e.g. post-herpetic neuralgia, nerve compression or injury, neuroma)
- Trauma (e.g. female genital cutting, obstetrical)
- Iatrogenic (e.g. post-operative, chemotherapy, radiation)
- Hormonal deficiencies (e.g. genito-urinary syndrome of menopause [vulvo-vaginal atrophy], lactational amenorrhea)

B. Vulvodynia – Vulvar pain of at least 3 months' duration, without clear identifiable cause, which may have potential associated factors

Descriptors:
- Localized (e.g. vestibulodynia, clitorodynia) or Generalized or Mixed (localized and generalized)
- Provoked (e.g. insertional, contact) or Spontaneous or Mixed (provoked and spontaneous)
- Onset (primary or secondary)
- Temporal pattern (intermittent, persistent, constant, immediate, delayed)

* Women may have both a specific disorder (e.g. lichen sclerosus) and vulvodynia.

Genetic predisposition of vulvodynia

Genetic studies have focused on two mechanisms:
– An inability to end a local incident of infection or inflammation;
– An increased susceptibility to hormonal changes caused by oral contraceptive pills.

Women with LPV were likely to have the less effective polymorphism of Mannose-binding lectin (MBL). MBL is major component of antimicrobial innate immunity, thus leading to an increased rate of infections.

Furthermore, a loss-of-function mutation in the melanocortin-1 receptor (MC1R)—which carries anti-inflammatory effects, in women with LPV. Addition risk may be caused by a loss-of-function mutation in the MC1R gene with a variant allele of the IL-1B receptor antagonist gene.

Musculoskeletal factors

The association between the pain associated with LPV and the pelvic floor muscle overactivity may work both ways. The dyspareunia frequently results in reflex pelvic muscles contractions and subsequently a permanent increased muscle tone. On the other hand, , increased muscle tension may press on fibers of the pudendal nerve and pelvic trauma may lead to nerve damage and myofascial trigger points. Furthermore, it was hypothesized that myofascial tissues reflexes activate nociceptive and visceral neurons.

Hormonal factors

A controversy exists as to whether combined oral hormonal contraceptives pills (HCP) play a role in the development of LPV. Against that association is that of the millions of women taking HCP, only a slight fraction suffers from LPV.

Indeed, three studies have failed to show an association between HCPs and vulvodynia. A case control study even showed that HCPs actually decreased the risk of vestibulodynia.

On the other hand, some women with LPV describe an improvement with cessation of the HCP, and other studies depicted association of vestibulodynia with HCP and identified a polymorphism in the androgen receptor that significantly increased the risk of developing HCP-induced LPV in affected women.

With prolonged use of HCP, the net effect is progestogenic, so that the estrogen influence on the vestibule and vagina is reduced. This leads to diminished lubrication and decreased elasticity, causing increased friability and epithelial damage with vaginal intercourse. Later, allodynia and burning may occur.

Embryological/Congenital Factors

Vulvodynia is sometimes associated with painful bladder syndrome (interstitial cystitis) and with periumbilical hypersensitivity. This association dates back to the embryo development period; the vestibule develops from the urogenital sinus, which is contiguous with the allantois, which later differentiates to the urachus and the umbilicus.

Inflammatory factors

Women with vulvodynia are more likely to have a history of allergic rashes. This may clarify the excess of mast cells, found in cases with LPV compared to controls. Mast cell produced tumor necrosis factor (TNF) which has been as-

TABLE 2. 2015 Consensus terminology and classification of persistent vulvar pain and vulvodynia

Appendix: Potential factors associated with Vulvodynia*
- Co-morbidities and other pain syndromes (e.g. painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder) [Level of evidence 2]
- Genetics [Level of evidence 2]
- Hormonal factors (e.g. pharmacologically induced) [Level of evidence 2]
- Inflammation [Level of evidence 2]
- Musculoskeletal (e.g. pelvic muscle overactivity, myofascial, biomechanical) [Level of evidence 2]
- Neurologic mechanisms:
  - Central (spine, brain) [Level of evidence 2]
  - Peripheral – Neuroproliferation [Level of evidence 2]
- Psychosocial factors (e.g. mood, interpersonal, coping, role, sexual function) [Level of evidence 2]
- Structural defects (e.g. perineal descent) [Level of evidence 3]

* The factors are ranked by alphabetical order.

sociated with nerve fiber elongation in animal models of contact hypersensitivity.

Psychological factors

The prevailing belief that dyspareunia whether mood changes precede LPV, or develop in response to the extreme inconvenience and difficulties of LPV, is controversial.

Another controversial issue is whether childhood victimization may be a risk factor for the development of sexual pain. In addition, women with vulvodynia report significantly less sexual desire, arousal and satisfaction, difficulty in reaching orgasm, a lower frequency of intercourse, more negative attitudes toward sexuality and more sexual distress than pain-free controls. Although this may be consequent to the pain associated with vaginal penetration, it may be an initiating factor

Many women with vulvar pain report feelings of shame and low self-esteem.

Structural defects

Pelvic organ prolapse has been associated with vulvodynia[8,9]. A test consisting of locally anesthetizing the nerve plexuses at the uterosacral ligaments can depict whether the origin of the vulvodynia results for laxity of the uterosacral ligaments[10].

CONCLUSION

The terminology of vulvar pain and vulvodynia was prepared by the ISSVD, ISSWSH, and IPPS. It acknowledges the complexity of the clinical presentation and pathophysiology involved in vulvar pain and vulvodynia, and incorporates data from evidence-based studies conducted during the last decade. The inclusion of factors associated with vulvodynia enables novel approach to research, diagnosis and treatment.

REFERENCES

1. Bornstein J, Goldstein AT, Stockdale CK, Bergeron S, Pukall C, Zolnoun D, Coady D; 2015 ISSVD, ISSWSH, and IPPS Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia. consensus vulvar pain terminology committee of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS). J Low Genit Tract Dis. 2016; 20 (2), 126-30.
2. Bornstein J, Goldstein AT, Stockdale CK, Bergeron S, Pukall C, Zolnoun D, Coady D; 2015 ISSVD, ISSWSH, and IPPS Consensus terminology and classification of persistent vulvar pain and vulvodynia. Consensus vulvar pain terminology committee of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS). J Sex Med. 2016, 13 (4), 607-12.
3. Bornstein J, Goldstein AT, Stockdale CK, Bergeron S, Pukall C, Zolnoun D, Coady D; 2015 ISSVD, ISSWSH, and IPPS Consensus terminology and classification of persistent vulvar pain and vulvodynia. Consensus vulvar pain terminology committee of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS). Obstet Gynecol. 2016, 127 (4), 745-51.
4. Bornstein J, Maman M, Abramovici H. Primary versus secondary vestibulitis - one disease, two variants. Am J Obstet Gynecol 2001, 184, 28-31.
5. Marinoff, SC, Turner ML. Vulvar vestibulitis syndrome: an overview. Am J Obstet Gynecol. 1991, 165, 1228-33.
6. Foster DC, Kotok MB, Huang LS, Watts A, Oakes D, Howard FM, Stodgell CJ, Dworkin RH. The tampon test for vulvodynia treatment outcomes research: reliability, construct validity, and responsiveness. Obstet Gynecol. 2009, 113 (4), 825-32.
7. Pukall CF, Goldstein AT, Bergeron S, Foster D, Stein A, Kellogg-Spadt S, Bachmann G. Vulvodynia: definition, prevalence, impact, and pathophysiological factors. J Sex Med. 2016, 13 (3), 291-304.
8. Petros P, Bornstein J. Re: vulvar vestibulitis may be a referred pain arising from laxity in the uterosacral ligaments: a hypothesis based on three prospective case reports. Aust N Z J Obstet Gynaecol 2004, 44, 484-85.28.
9. Beco J. Interest of retro-anal levator plate myorrhaphy in selected cases of descending perineum syndrome with positive anti-sagging test. BMC Surg 2008, 8, 13.
10. Zarfati Z, Petros PPE. The Bornstein's test – a local anesthetic technique for testing uterosacral nerve plexus origins for chronic pelvic pain. Pelviperineology, 2017, 36, 89-91.

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Original article

Laparoscopic approach to intrapelvic nerve entrapments

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Abstract: It has been well-established that a large portion of the lumbosacral plexus is located intra-abdominally, in the retroperitoneal space. However, most of the literature descriptions of lesions on this plexus refer to its extra-abdominal parts whereas its intra-abdominal portions are often neglected.The objective of this review paper is to describe the laparoscopic anatomy of intrapelvic nerve bundles, as well as the findings and advances already achieved by Neuropelveology practitioners.

Abreviations:
- LANN – Laparoscopic Neuronavigation
- LION – Laparoscopic Implantation of Neuroprosthesis

Keywords: Sciatic; Nerve Entrapment; Gluteal Pain; Neuromodulation; Laparoscopy.

INTRODUCTION

It is well established that a large portion of the lumbosacral plexus is located intra-abdominally in the retroperitoneal space[1]. However, descriptions of lesions on this plexus in most of the literature refer to its extra-abdominal course. The intra-abdominal location and the potential entrapment of nerves from lumbosacral plexus at these sites are often neglected in the literature[2].

In 2007, Possover et al.[3] described the Laparoscopic Neuronavigation (LANN) technique, opening the doors to accessing the retroperitoneal portion of the lumbosacral plexus through a safe, minimally invasive, and objective way. Since then, multiple causes of intrapelvic nerve entrapments have been described and a new field in Medicine – Neuropelveology – was created.

In this paper, we will review the laparoscopic anatomy of the intrapelvic nerve bundles, describe the symptoms and signs associated with intrapelvic neuropathies, as well as the diagnosis and treatment rationale of these conditions.

LAPAROSCOPIC ANATOMY OF THE INTRAPELVIC NERVES

Ilio-Hypogastric, Ilio-Inguinal And Genito-Femoral Nerves

These nerves are sensitive branches of the lumbar plexus. The ilio-hypogastric and ilio-inguinal nerves enter the retroperitoneal space emerging on the lateral border of the psoas muscle and follow anteriorly and distally to pierce the internal abdominal oblique muscle close to the antero-superior iliac spine[4]. The genito-femoral nerve emerges from the anterior border of the psoas muscle and its two branches leave the abdomen through the femoral (femoral branch) and inguinal (genital branch) canals. Their fibrotic entrapment is related to post-herniorhaphy inguinodynia[5] (Figure 1).

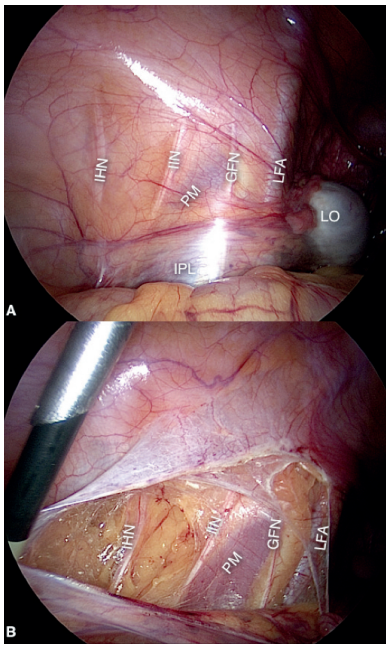

Figure 1. – Laparoscopic view the left abdominal wall exhibiting the Ilio-Hypogastric (IHN), Ilio-Inguinalis (IIN) and Genito-Femoralis (GFN) Nerves, with the overlying peritoneal intact (A) and exposed (B) [PM – Psoas Muscle; LO – Left Ovary; IPL – Infundibulopelvic Ligament; LFA – Left Femoral Artery

Femoral nerve

The femoral nerve is the largest motor and sensory nerve of the lumbar plexus. It emerges from the postero-lateral aspect of the psoas muscle and leaves the abdomen through the femoral canal (Figure 2) to innervate the quadriceps muscle and the skin covering the anterior thigh and medial aspect of the leg.

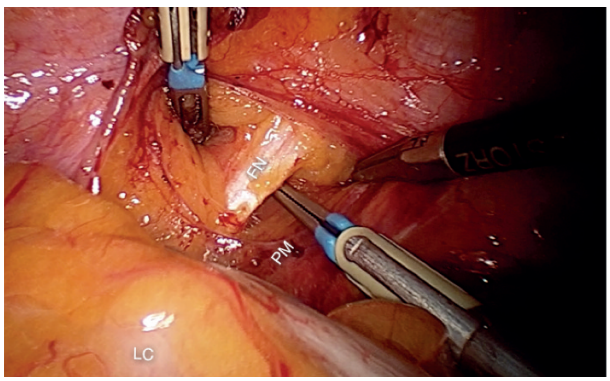

Figure 2. – The Left Femoral Nerve (FN) entering the retroperitoneal space on the posterolateral aspect of the Psoas Muscle (PM). (LC – Left Colon)

Nerves of the Obturator Space

The obturator nerve enters the obturator space at the level of the pelvic brim and leaves the pelvis through the obturator canal. It gives sensory branches to the skin of the medial thigh and motor branches to the hip adductors (Figure 3-A).

The lumbosacral trunk and the distal portions of the S1, S2, S3 and S4 nerve roots merge into the obturator space and form the sciatic and pudendal nerves (Figure 3-B).

The sciatic nerve is formed by the L4 and L5 fibers of the lumbosacral trunk and fibers from the S1, S2 and S3 nerve roots and leaves the pelvis through the greater sciatic notch. It gives out sensory branches to the upper gluteal region, postero-lateral thigh, leg, ankle and foot. It also controls the hip extensors, abductors and rotators, knee flexors, and all the muscles for the ankle and foot.

The pudendal nerve is formed by fibers of the 2nd, 3rd and 4th nerve roots and leaves the pelvis in the interligamentous plane between the sacrospinous and sacrotuberous ligament. It then enter the pudendal (Alcock's) canal. It provides sensory branches to the the perineal skin. It also sends motor branches to the perineal muscles and the anterior fibers of the levator ani muscles. Finally, there are direct motor and sensory branches from the S3 and S4 nerve roots to the posterior fibers of the levator ani muscle[6-8].

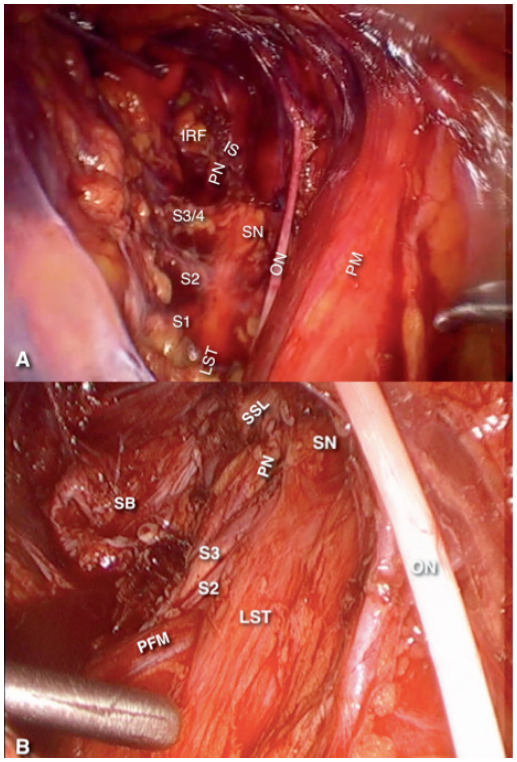

Figure 3. – Nerves of the obturator space (right side). Picture (A) is the final aspect of a laparoscopic approach to Alcock's Canal Syndrome, where the sacrospinous ligament has been transected to expose the pudendal nerve (PN). In picture B, the sacrospinous ligament (SSL) is intact. In both pictures, the internal and external iliac vessels are retracted medially. (ON – Obturator Nerve; PM – Psoas Muscle; SN – Sciativ Nerve; LST – Lumbosacral Trunk; PN – Pudendal Nerve; IRF – Ischiorectal Fossa; IS – Ischial Spine; SB – Sacral Bone; PFM – Piriformis Muscle)

Nerves of the Presacral and Pararectal Spaces

The superior hypogastric plexus, which is formed by fibers from para-aortic sympathetic trunk and gives rise to the hypogastric nerves. The hypogastric nerves run over the hypogastric fascia in an anterior and distal direction. After crossing about two thirds of the distance between the sacrum and the uterine cervix or the prostate, its fibers spread to join the pelvic splanchnic nerves (described below) to form the inferior hypogastric plexus (Figure 4). The hypogastric nerves carry the sympathetic signals to the internal urethral and anal sphincters, rectum and bladder, which cause detrusor relaxation and bladder contraction, thus promoting continence. They also carry proprioceptive and nociceptive afferent signals from the pelvic viscera[9].

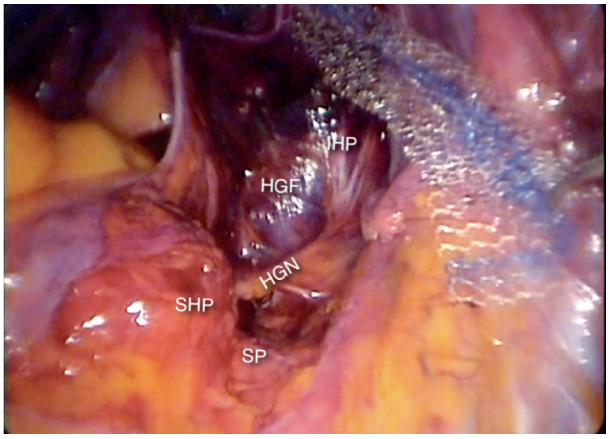

Figure 4. – The hypogastric nerve (HN) emerges from the Superior Hypogastric Plexus (SHP) at the level of the Sacral Promontory (SP) and runs anteriorly and distally, juxta-laterally to the Hypogastric Fascia (HF), to merge with the Pelvic Splanchnic Nerves to form the Inferior Hypogastric Plexus (IHP)

The lateral limit of the presacral space is the hypogastric fascia, which is the formed by the medial most fibers of the endopelvic fascia. The sacral nerve roots can be found juxta-laterally to this fascia (Figure 5). They leave the sacral foramina and run anteriorly and distally, lying over the piriformis muscle and crossing the internal iliac vessels laterally to them, to merge and form the nerves of the sacral plexus[10]. Before crossing the internal iliac vessels, they give out the thin parasympathetic branches called pelvic splanchnic nerves, which promote detrusor contraction and provide extrinsic parasympathetic innervation to the descending colon, sigmoid and rectum. They also carry nociceptive afferent signals from the pelvic viscera[9]. The pelvic splanchnic nerves join the hypogastric nerves to form the inferior hypogastric plexus in the pararectal fossae[10].

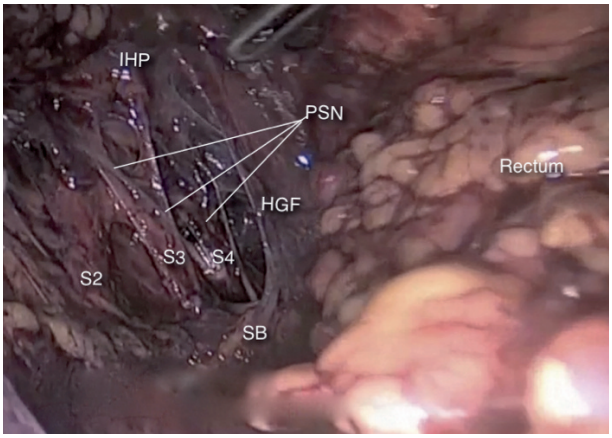

Figure 5. – The Sacral Nerve Roots (S2-S4) can be found juxta-laterally to the Hypogastric Fascia (HGF) and give origin to the Pelvic Splanchnic Nerves (PSN), which run anteriorly and distally to merge the Hypogastric Nerve and form the Inferior Hypogastric Plexus (IHP).

INTRAPELVIC NERVE ENTRAPMENT SYNDROME

Definition and Clinical Features

Nerve entrapment syndrome, or compression neuropathy, is a clinical condition caused by compression on a single nerve or nerve root. The symptoms and signs include pain, tingling, numbness, and muscle weakness on the affected nerve's dermatome and myotome[11]. Intrapelvic nerve entrapments are, therefore, entrapments of the intrapelvic portions of the nerves described in the previous sessions and will produce clinical features related to the affected nerves.

The above definition refers to the entrapment of somatic nerves. Autonomic nerve entrapment will produce visceral and vegetative symptoms, such as urinary frequency or urgency, dysuria, rectal pain, suprapubic and/or abdominal cramps and chills. However, as described, above, the sacral nerve roots give origin to both somatic and parasympathetic nerves. Therefore, entrapments of these roots will produce somatic (such as pain along the dermatome) and visceral (such as urinary and bowel dysfunction) clinical pictures.

In a concise manner, the main symptoms of intrapelvic nerve entrapments are:

- Sciatica associated with urinary symptoms (urgency, frequency, dysuria) without any clear orthopedic cause (spinal or deep gluteal nerve entrapment);
- Gluteal pain associated with perineal, vaginal or penile pain;
- Dysuria and/or painful ejaculation;
- Refractory urinary symptoms;
- Refractory pelvic and perineal pain.

It is important to emphasize that, due to the distance between both plexuses, intrapelvic nerve entrapments will usually cause unilateral symptoms.

Diagnostic Workup

Once the hypothesis of an intrapelvic entrapment is raised, it is mandatory to perform the topographic diagnosis, which is the determination of the exact point of entrapment. So far, careful neuropelveological evaluation, combined with a detailed medical history and neurological examination is the most reliable method for this.

To increase objectivity and accuracy of the diagnosis, we have been examining the use of high definition pelvic MRI and sacral plexus tractography, which is a technique for functional MRI of peripheral nerves[12]. Asymmetries and structures that could entrap the plexus are identified at MRI and those specific portions are investigated on tractography for any gaps in neural activity (Figure 6).

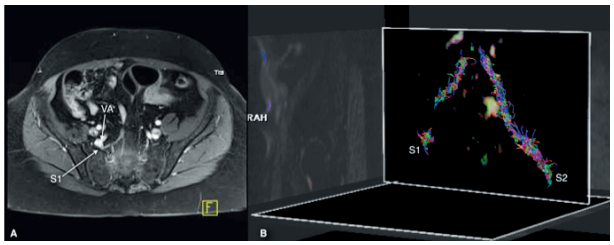

Figure 6. – A: contrasted MRI showing enlarged vessels (VA) in direct contact with S1 nerve root. B: Tractography showing a signal gap in S1.(Courtesy of Dr. Suzan M. Goldman, MD, PhD & Homero Faria)

Our results so far are very promising, but the accuracy of this method still needs to be investigated. Therefore, for further assurance, our next step is a diagnostic block, guided by ultrasound or fluoroscopy and performed by an intervention pain specialist; the exact point where a signal gap is identified at the tractography is infiltrated with 0.5mL to 1mL of lidocaine 0.5%. If a reduction of 50% or more in pain (VAS) is observed, the test is considered positive (Figure 7).

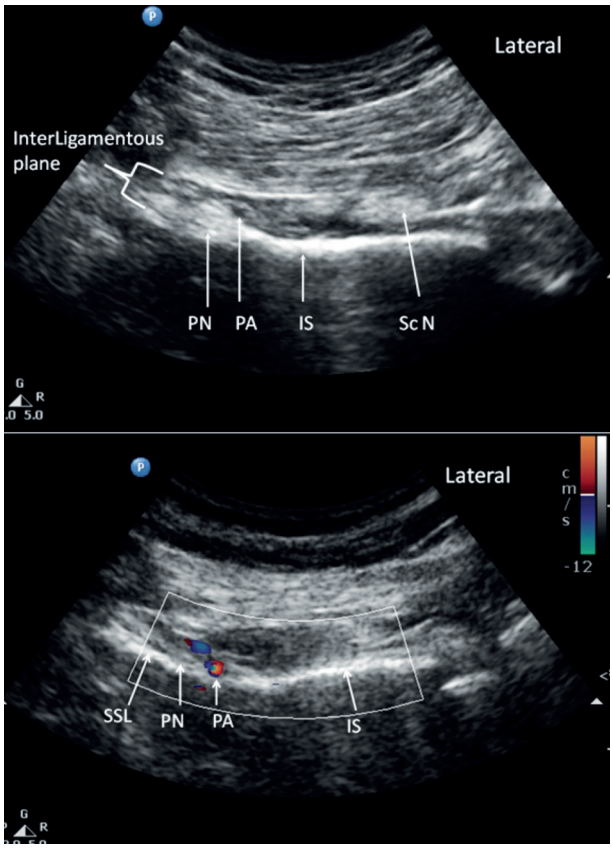

Figure 7. – (A) Ultrasound image of the interligamentous plane at the ischial spine where the pudendal artery and nerve are located between the sacrospinous and sacrotuberous ligaments. (B) Color Doppler of the same picture showed the pudendal artery. Reprinted with permission from Philip Peng Educational Series

Etiology of intrapelvic entrapments

Endometriosis

The first report of intrapelvic nerve entrapment was made by Denton and Sherill[13], who described a case of cyclic sciatica due to endometriosis in 1955. After that, some other case reports and small series were published, until 2011, when Possover et al[2] described the largest series so far, with 175 patients, all treated laparoscopically.

In endometriotic entrapments, the symptoms tend to be cyclic, worsening during the premenstrual and menstrual days and ameliorating or even disappearing during the post-menstrual period[2,14-15].

Evaluation consists of preoperative identification of the symptoms and determination of the topographical localization of the lesions mainly by clinical evaluation, although radiological examination (MRI) is sometimes required. Treatment is achieved by exploring all suspect segments of the plexus through laparoscopic approach, with radical removal of all endometriotic foci and fibrosis[2,14-15] (Figure 8).

The true incidence of endometriosis involving the sacral plexus is unknown, as this presentation of the disease is often neglected. On average, patients undergo four surgical procedures seeking to treat the pain before receiving the right diagnosis[2]. Moreover, about 40% of women with endometriosis refer unilateral pain on the inferior limb[16] and,

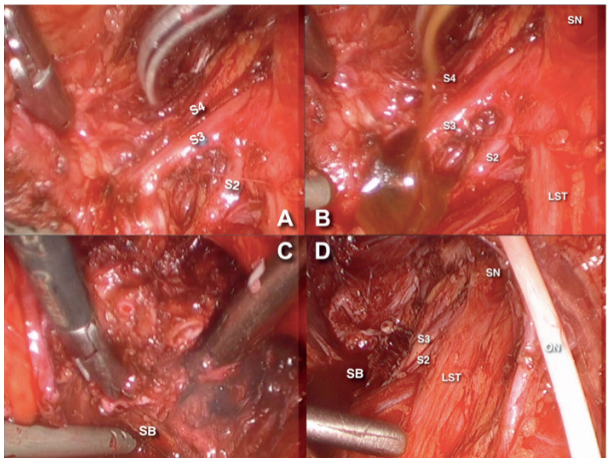

Figure 8. – A – after partial detachment of the nodule, allowing for visualization of S2, S3 and S4 nerve roots, S3 was found to be dilated on its proximal part; B – opening of the S3 nerve root sheath revealed an endometrioma inside the nerve; C – the nodule was detached from the sacral bone (SB); D – final aspect of the right pelvic sidewall; ON – obturator nerve; SN – sciatic nerve.

in 30% of patients with endometriosis, leg pain was demonstrated to be neuropathic[17], which leads to the conclusion that endometriotic involvement of the lumbosacral plexus is probably underdiagnosed and much more frequent than reported.

Fibrosis

This is one of the most frequent causes of intrapelvic nerve entrapments and possibly the most well-known etiology, since Amarenco[18] described the pudendal neuralgia in cyclists, in whom the pain is a consequence of fibrotic entrapment due to continued trauma.

Despite the historical aspect, however, surgical manipulation seems to be the most frequent cause of fibrosis over the sacral plexus (Figure 9). Among the surgeries with higher risks of inducing such kinds of entrapments are the pelvic reconstructive procedures[19].

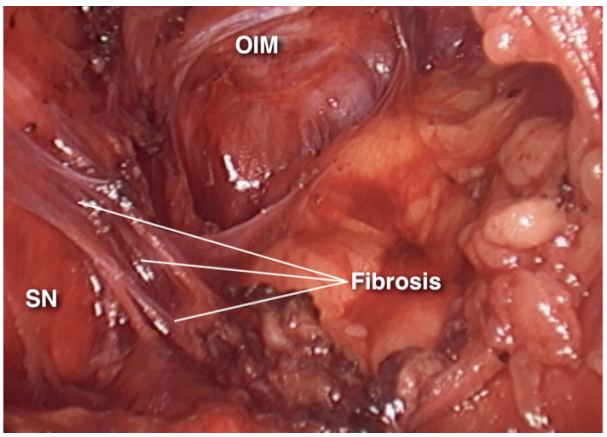

Figure 9. – Fibrotic entrapment of the left sciatic nerve

Vascular Entrapment

Pelvic congestion syndrome is a well-known cause of cyclic pelvic pain. Patients commonly present with pelvic pain without evidence of inflammatory disease. The pain is worse during the premenstrual period and pregnancy, and is exacerbated by fatigue and standing[20].

However, what is much less known is the fact that dilated or malformed branches of the internal or external iliac vessels can entrap the nerves of the sacral plexus against the pelvic sidewalls, producing symptoms such as sciatica, or refractory urinary and anorectal dysfunction[2,21] (Figure 10).

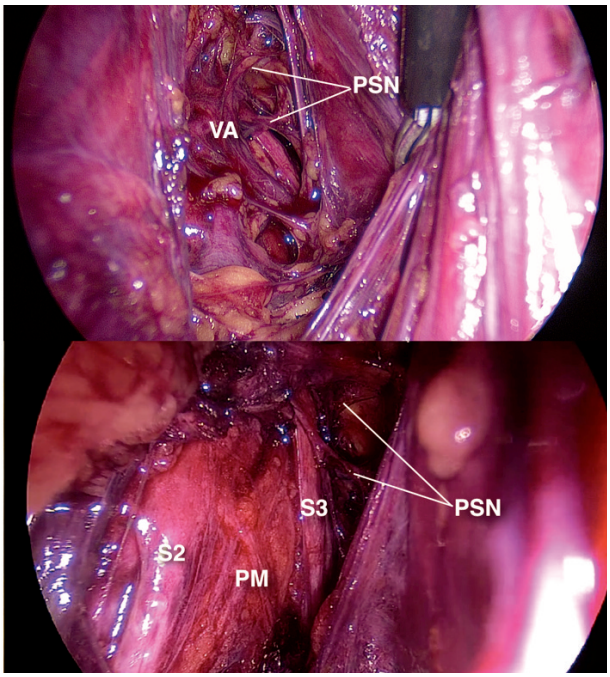

Figure 10. – Varicose tributary (VA) of the left internal iliac vein entrapping the S2 and S3 nerve roots against the left piriformis muscle (PM)

Piriformis Syndrome

Numerous malformations of the piriformis muscle have been described in the deep gluteal space that can entrap branches of the sciatic nerve. The laparoscopic approach has revealed that the intrapelvic fibers of this muscle can also entrap the sacral nerve roots[22]. Usually, these fibers originate from the sacral bone, laterally to the sacral foramina. However, part of the piriformis fibers may originate medially to the sacral foramina and the corresponding nerve roots in some individuals (Figure 11). Differentiating intrapelvic from extrapelvic piriformis syndrome can be very challenging. Bowel and urinary symptoms are a good indication that the entrapment is intrapelvic, but these are not always present.

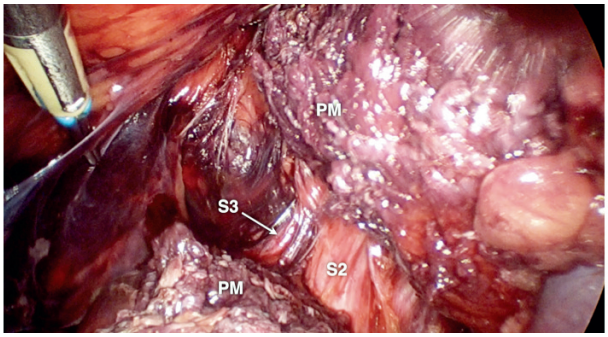

Figure 11. – Muscular entrapment of the right S2 and S3 nerve roots. Observe the transected piriformis muscle bundle (PM) originating from the sacral bone medially from the sacral nerve roots and, therefore, crushing the nerves every time the muscle contracts.

Neoplasms

Tumors can also entrap the nerves or nerve roots. Tumors can be primary neural tumors, such as Schwanomas, or

metastatic tumors, such as pelvic lymph nodes, entrapping the nerves in pelvic malignancies (Figure 12).

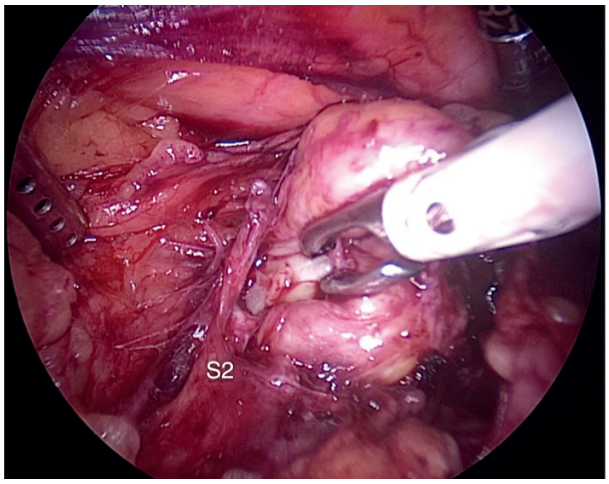

Figure 12. – Schwannoma in S2 (left)

Primary Neuropathic Pain, Nerve Transection and Secondary Neuropathic Pain

All the previously described causes of intrapelvic neuropathies have extrinsic entrapment as the etiology of pain. Intrapelvic radiculopathies can also result from nerve transections and or degenerations or intrinsic dysfunctions of the nerves themselves.

Nerve transections can occur during surgery or trauma and can induce neuroma formation, resulting in phantom pain and anesthesia of the affected nerve dermatome. An example of this is the phantom pain secondary to amputations, where branches of the sciatic and femoral nerves are transected. In the same fashion, pudendal transection will induce perineal pain and perineal anesthesia, as well as unilateral atrophy of perineal muscles, frequently resulting in urinary and fecal incontinence.

In entrapment syndromes, chronic ischemia induces cytoarchitectural changes to the neuron, which do not heal properly after the detrapment, resulting in neuropathic pain. The later the detrapment is performed, the higher the risk of neuropathic pain[23].

Neuropathic pain can also result from metabolic disturbances of the neuron, infectious agents, chronic exposure to neurotoxic substances, or a myriad of other causes.

In cases where there is no suspicion of entrapment as the primary cause of symptoms, extensive neurological investigation must be performed, preferably by a neurologist trained in assessing peripheral nerve pain. The symptoms must be clinically treated by an interprofessional pain team composed of a pain physician (usually an anesthesiologist or neurologist), a physiotherapy team (pelvic and motor), and a mental healthcare team (psychologist and psychiatrist). The pain specialist will prescribe and adjust the pharmacological treatment and, in cases where poor response to medical treatment is observed, perform the appropriate intervention (e.g. anesthetic blocks, pulsed radiofrequency).

Etiology of intrapelvic entrapments

As a rule, once a nerve entrapment has been diagnosed, decompression (usually surgical) is mandatory, since chronic ischemia can lead to endoneurial degeneration[23]. Therefore, the longer the time between the beginning of symptoms and detrapment, the lower the chance of success.

Surgical decompression will lead to complete resolution of pain and other symptoms in about 30% of the patients; around 50% will experience more than 50% reduction in pain and about 20% will not improve or, in some cases, experience worsening of their pain. Approximately 25% of patients will present with post-decompression neuropathic pain and 17% will present neuropathic strength loss, both of which tend to be transient; the former will last, on average, 5.5 months and the latter will last 2.5 months[24].

Patients who present with transient post-decompression pain, persistent post-neuropathic pain or worsening of symptoms, should be treated like patients with primary neuropathic pain, as described in the following session.

Pharmacological Treatment

There are no specific recommendations for the treatment of neuropathic pain of intra-pelvic origin. Management of this group of patient will follow the recommendation of neuropathic pain in general. Antidepressants, anticonvulsants, local anesthetics, N-methyl-D-aspartate (NMDA) antagonists, opioids, cannabinoids, botulinum toxin, capsaicin, and others may be used[25-27]. Most of these drugs were originally developed for other indications (e.g. depression and epilepsy), and their effectiveness for controlling neuropathic pain was later verified. The following tables outline commonly used drugs used for neuropathic pain control:

TABLES

Anticonvulsants	
Carbamazepine	400 to 1600 mg / day
Oxcarbazepine	600 to 1200 mg / day
Diphenylhydantoin	300 to 400 mg / day
Valproate Sodium	500 to 1500 mg / day
Lamotrigine	50 to 400 mg / day
Topiramate	50 to 200 mg / day
Gabapentin	900 at 2400 mg / day
Pregabalin	150 to 300 mg / day
Amitriptyline	50 to 150 mg / day
Nortriptyline	50 to 150 mg / day
Maprotiline	50 to 150 mg / day
Duloxetine	60 mg / day
Antidepressants Neuroleptics	
Fluphenazine	2 to 20 mg / day
Levomepromazine	25 to 500 mg / day
Chlorpromazine	50 at 600 mg / day
Antiarrhythmics	
Lidocaine	5 mg/kg/h/6h
Mexiletine	600 mg / day
Central Acting Muscle Relaxants	
Baclofen	10 to 30 mg / day
Opioids	
Tramadol	100 to 300 mg / day
Oxycodone	20 to 60 mg / day
Morphine Sulfate	20 to 90 mg / day
Methadone	150 to 400 mg / day
Transdermal Fentanyl	Up to 75 mg / day
Local anesthetics	
Capsaicin	
Anti-inflammatories	

Physiotherapy

In pelvic dysfunction resulting from nerve compression, the main goals of physical therapy are to reduce pain, train the pelvic floor muscles, and provide education about dysfunction and lifestyle interventions. This includes teaching awareness of the pelvic muscle group, the correct way to contract the pelvic muscles, coordination, motor control, strength, endurance, and relaxation of the musculature[28,29,30].

In order to reduce the patient's pain after surgical nerve decompression, cryotherapy has proven to be an effective therapeutic resource when applied to the vaginal canal. It is recommended to fill a non-sterile glove finger (or a condom) with ice and insert it into the patient's vagina for less than 20 minutes.

Electrical stimulation is also an important resource in the treatment of pain. It stimulates the rapidly conducting myelinated gross nerve fibers, triggering at the central level the descending inhibitory analgesic systems on the nociceptive transmission conducted by the non-myelinated fibers of small caliber, thus generating pain reduction[31,32].

Manual therapy techniques for myofascial release should be applied when there are signs of muscular tension of the pelvic floor, with the presence of trigger points, due to pain caused by nerve compression. The technique involves firm massage on the levator anus muscle with sliding movements towards the origin and insertion, punctual pressure at the trigger points at the limit of the patient's pain, in addition to perpendicular movements to the muscle fiber[33].

The techniques described for strengthening and awareness of pelvic floor musculature include biofeedback, and electrostimulation. These represent an important form of prevention and treatment for pelvic floor dysfunction.

Biofeedback is one of the most used resources for urogynecological physiotherapy, since it has no side effects. This technique allows the objective awareness of the physiological function that is unconscious in the individual, facilitating the correct learning of the pelvic floor muscle contraction. It can also be used for training and hypertrophy of the muscles. In addition, biofeedback assists in patient motivation during treatment, improving adherence to the physiotherapy program[34,35].

Electrical stimulation, when applied in the vaginal canal acts passively, and has an important effect on the proprioceptive awakening along with stimulating the correct learning of the perineal contraction. In addition, it has shown effective therapeutic results in patients with pelvic floor dysfunction, contributing to training of strength and muscular endurance, increasing the number of activated motor units and generating hypertrophy of the fibers. These benefits promote a strong and rapid contraction of the muscles, increasing urethral pressure and preventing urine loss during an abrupt increase in intra-abdominal pressure[36].

Interventional Treatments

Interventional procedures are an important option for the treatment of pelvic and perineal neuropathic pain. This is true especially for patients in whom conservative treatment did not bring the expected relief from pain, or for those whom the adverse effects of medications are intolerable.

The percutaneous blockade of specific nerves serves both diagnostic and therapeutic roles. In addition to the local anesthetic, it is quite common to add depot steroid for the anti-inflammatory and membrane-stabilizing effect. Imaged guidance with ultrasound[37,38], computed tomography, or fluoroscopy[39] enhanced the accuracy, reduce the volume of injectate and potentially minimize the complication rates.

If the pain relief is temporary, it is possible to apply more lasting techniques, such as radiofrequency, cryoablation, or neurolysis by chemical agents, such as phenol.

In the case of neuralgia caused by nervous incarceration by a muscle, there is the possibility of infiltration of this muscle with local anesthetic at first, followed by specific physiotherapy[40,41]. If this muscle contracts again, resulting again in nervous compression, it is possible to inject botulinum toxin, for a more prolonged relaxation. These techniques are best described in the myofascial pain chapter.

Pulsed Radio Frequency (RFP) is an alternative technique to conventional radiofrequency, and its advantage would be a longer pain relief without neural damage. During RFP application, a high frequency, pulsed current is generated and this allows the heat generated in the tissue to dissipate during the latency periods, not exceeding 45°C, which would be a neurodestructive temperature[42]. Thus, by maintaining the temperature only up to 42°C, there is no neural destruction, and, therefore, can be applied even in mixed nerves (i.e. both sensory and motor). The mechanism of action of the RFP is related to the electric field formed, which would alter painful signaling in a neuromodulatory form, but has not yet been fully elucidated[42,43]. The RFP can be applied distally to the nerve responsible for the patient's pain, or proximal, at its exit in the intervertebral foramen.

The Dorsal Root Ganglia (DRG) block corresponding to the nerve responsible for the pain can be performed with local anesthetic, guided by fluoroscopy. If the blockage alleviates at least 50% of the pain, it is possible to apply RFP thereafter[38].

Phenol Neurolysis has been described in several targets, especially to treat cancer pain, but also for non-cancer pain, and may bring prolonged pain relief. Care must be taken not to inject near motor nerves, because of the risk of flaccid paralysis. Chemical neuritis is another possible complication, although uncommon[44].

Cryoablation is a technique that promotes prolonged analgesia. The application of tissue cold blocks nerve conduction is similar to the local anesthetic. Long-term analgesia is due to freezing, which damages the nerve structure and causes Wallerian degeneration. However, since the myelin sheath and endoneurium remain intact, the nerve can regenerate after a period of time. One of its advantages over other neurolysis techniques, such as phenol for example, is the absence of post-procedure neuritis[39].

The main complications described with these procedures are similar to those experienced with any injection, including hematoma, infection and nerve damage.

Neuromodulation

In cases where medical and intervention pain treatment has failed or in cases where, although the topography of the lesion is determined, its etiology cannot be identified intraoperatively, the laparoscopic implantation of neuromodulation electrodes can be used to specifically modulate the af-

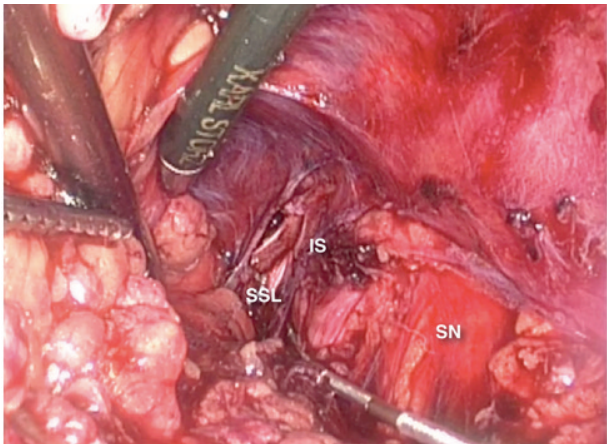

Figure 13. – LION Electrode placed on right sciatic and pudendal nerves (PM – Psoas Muscle; IS – Ischial Spine; SN – Sciatic Nerve; SSL – Sacrospinous Ligament)

fected nerve, producing very encouraging results when compared to the more commonly available epidural neuromodulation[5,45].

The laparoscopic implantation of neuroprosthesis – the LION procedure – was first reported by Possover in 2009 as a rescue procedure in patients with local complications of a Brindley procedure[45]. Due to its successful results and decreased invasiveness, it was then used as a primary procedure in spinal cord-injured patients, aiming to improve locomotion and bladder function[46]. Long term data has shown improvement in voluntary motor function and sensitivity, suggesting positive effects on neuroplasticity[47] (Figure 13).

CONCLUSION

Laparoscopy provides minimally invasive access with optimal visualization to virtually all abdominal portions of the lumbosacral plexus, which are also subject to entrapment neuropathies. Therefore. when facing sciatica, gluteal or perineal pain without any obvious spinal or deep gluteal causes, the examiner should always remember that the entrapment could be in the intrapelvic portions, especially when urinary or anorectal symptoms are present.

The laparoscopic approach to the intrapelvic bundles of the lumbosacral nerves opened a myriad of possibilities to assess and treat this neglected portion of the plexus, by means of nerve decompression or selective neuromodulation.

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REFERENCES

1. Gray, Henry. 1918. Anatomy of the Human Body. IX. Neurology. 6d. The Lumbosacral Plexus.
2. Possover M, Schneider T, Henle KP (2011) Laparoscopic therapy for endometriosis and vascular entrapment of sacral plexus. Fertil Steril, 95 (2), 756-8.
3. Possover M, Chiantera V, Baekelandt J (2007) Anatomy of the Sacral Roots and the Pelvic Splanchnic Nerves in Women Using the LANN Technique. Surg Laparosc Endosc Percutan Tech, 17 (6), 508-10.
4. Whiteside JL, Barber MD, Walters MD, Falcone TA (2003) Anatomy of ilioinguinal and iliohypogastric nerves in relation to trocar placement and low transverse incisions. Am J Obstet Gynecol, 180 (6), 1574-8.
5. Possover M. Use of the LION procedure on the sensitive branches of the lumbar plexus for the treatment of intractable postherniorrhaphy neuropathic inguinodynia. Hernia. 2013 Jun; 17 (3), 333-7. doi: 10.1007/s10029-011-0894-x.
6. Grigorescu BA, Lazarou G, Olson TR, Downie SA, Powers K, Greston WM, Mikhail MS. Innervation of the levator ani muscles: description of the nerve branches to the pubococcygeus, iliococcygeus, and puborectalis muscles. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Jan, 19 (1), 107-16.
7. Barber MD, Bremer RE, Thor KB, Dolber PC, Kuehl TJ, Coates KW. Innervation of the female levator ani muscles. Am J Obstet Gynecol., 2002 Jul, 187 (1), 64-71.
8. Wallner C, van Wissen J, Maas CP, Dabhoiwala NF, DeRuiter MC, Lamers WH. The contribution of the levator ani nerve and the pudendal nerve to the innervation of the levator ani muscles; a study in human fetuses. Eur Urol. 2008 Nov, 54 (5), 1136-42.
9. DeGroat WC, Yoshimura N. Anatomy and Physiology of the Lower Urinary Tract. In: Handbook of Clinical Neurology 3rd Series. Ed. Elsevier. Oxford, UK, 2015.
10. Possover M, Baekelandt J, Flaskamp C, Li D, Chiantera V. Laparoscopic neurolysis of the sacral plexus and the sciatic nerve for extensive endometriosis of the pelvic wall. *Minim Invasive Neurosurg*. 2007 Feb; 50 (1), 33-6.
11. Bouche P. Compression and entrapment neuropathies. *Handb Clin Neurol*. 2013, 115, 311-66.
12. van der Jagt PK, Dik P, Froeling M, Kwee TC, Nievelstein RA, ten Haken B, Leemans A. Architectural configuration and microstructural properties of the sacral plexus: a diffusion tensor MRI and fiber tractography study. Neuroimage. 2012 62 (3), 1792-9. doi:10.1016/j.neuroimage.2012.06.001.
13. Denton RO, Sherrill JD. Sciatic syndrome due to endometriosis of sciatic nerve. South Med J. 1955 Oct; 48 (10), 1027-31.
14. Lemos N, Kamergorodsky G, Ploger C, Castro R, Schor E, Girão M. Sacral nerve infiltrative endometriosis presenting as perimenstrual right-sided sciatica and bladder atonia: case report and description of surgical technique. J Minim Invasive Gynecol. 2012 May-Jun; 19 (3), 396-400. doi: 10.1016/j.jmig.2012.02.001.
15. Lemos N, D'Amico N, Marques R, Kamergorodsky G, Schor E, Girão MJ. Recognition and treatment of endometriosis involving the sacral nerve roots. Int Urogynecol J. 2016 Jan, 27 (1), 147-50.
16. Missmer SA, Bove GM. A pilot study of the prevalence of leg pain among women with endometriosis. J Body Mov Ther. 2011 Jul, 15 (3), 304-8. doi: 10.1016/j.jbmt.2011.02.001.
17. Pacchiarotti A, Milazzo GN, Biasiotta A, Truini A, Antonini G, Frati P, Gentile V, Caserta D, Moscarini M. Pain in the upper anterior-lateral part of the thigh in women affected by endometriosis: study of sensitive neuropathy. Fertil Steril. 2013 Jul; 100 (1), 122-6. doi: 10.1016/j.fertnstert.2013.02.045.
18. Amarenco G, Lanoe Y, Perrigot M, Goudal H. [A new canal syndrome: compression of the pudendal nerve in Alcock's canal or perinal paralysis of cyclists]. Presse Med., 1987 Mar 7, 16 (8), 399.
19. Possover M, Lemos N. Risks, symptoms, and management of pelvic nerve damage secondary to surgery for pelvic organ prolapse: a report of 95 cases. Int Urogynecol J. 2011 Dec, 22 (12), 1485-90. doi: 10.1007/s00192-011-1539-4.
20. Ganeshan A, Upponi S, Hon LQ, Uthappa MC, Warakaulle DR, Uberoi R. Chronic pelvic pain due to pelvic congestion syndrome: the role of diagnostic and interventional radiology. Cardiovasc Intervent Radiol. 2007 Nov-Dec, 30 (6), 1105-11.
21. Lemos N, Marques RM, Kamergorodsky G, Ploger C, Schor E, Girão M. Vascular entrapment of the sciatic plexus causing catamenial sciatica and urinary symptoms. In: 44th Annual Meeting of the International Continence Society (ICS), 2014, Rio de Janeiro. Neurourology and Urodynamics. Hoboken, NJ: Willey, 2014, v. 33. p. 999-1000. doi: 10.1016/j.jbmt.2011.02.001.
22. Possover M. The sacral LION procedure for recovery of bladder/rectum/sexual functions in paraplegic patients after explantation of a previous Finetech-Brindley controller. J Minim Invasive Gynecol. 2009, Jan-Feb, 16 (1), 98-101.
23. Rempel D, Dahlin L. Pathophysiology of Nerve Compression Syndromes: Response of Peripheral Nerves to Loading. *J Bone Joint Surg Am*., 1999 Nov, 81 (11), 1600-10 .
24. Lemos et al. Intrapelvic nerve entrapments – a neglected cause of perineal pain and urinary symptoms. In: "Scientific Programme, 45th Annual Meeting of the International Continence Society (ICS), 6-9 October 2015, Montreal, Canada." Neurourol Urodyn. 2015 Aug, 34 Suppl 3: S53-S55. doi: 10.1002/nau.22830.
25. Finnerup N, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin R et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. The Lancet Neurology. 2015, 14 (2), 162-173.
26. Haanpää M, Attal N, Backonja M, Baron R, Bennett M, Bouhassira D et al. NeuPSIG guidelines on neuropathic pain assessment. Pain. 2011, 152 (1), 14-27.

27. Attal N, Cruccu G, Baron R, Haanpää M, Hansson P, Jensen T et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. European Journal of Neurology. 2010, 17 (9), 1113-e88.
28. Bo K, Berghmans B, Morkved S, Van Kampen M. *Evidence-Based Physical Therapy for the Pelvic Floor*. 2nd Ed. China: Elsevier; 2007.
29. Weiss JM. Pelvic floor miofascial trigger points: manual therapy for interstitial cystitis and the urgency-frequency syndrome. *J Urol*. 2001, Dec, 166: 2226-2231.
30. Stockdale CK, Lawson HW. 2013 Vulvodynia Guideline update. J Low Genit Tract Dis. 2014 Apr, 18 (2), 93-100. doi: 10.1097/LGT.0000000000000021.
31. Robinson AJ, Snyder-Mackler L. *Eletrofisiologia clínica: eletroterapia e teste fisiológico*. 3 ed. Porto Alegre: Artmed; 2010.
32. Fitzwater JB, Kuehl TJ, Schrier JJ. Electrical stimulation in the treatment of pelvic pain due to levanto rani spasm. *J Reprod Med*. 2003, 48, 573-577.
33. Srinivasan AK, Kaye JD, Moldwin R. Myofascial dysfunction associated with chronic pelvic pain: management strategies. *Curr Pain Headache Rep*. 2007, Oct, 11 (5), 359-64
34. Fitz FF, Resende APM, Stüpp L, Costa TF, Sartori MGF, Girão MJBC, Castro RA. Efeito da adição do biofeedback ao treinamento dos músculos do assoalho pélvico para tratamento da incontinência urinária de esforço. *Rev Bras Ginecol Obstet*. 2012, 34 (11), 505-10.
35. Moreno, AL. *Fisioterapia em Uroginecologia*. São Paulo: Manole, 2004.
36. Palma, P (ed). Urofisioterapia aplicações clínicas das técnicas fisioterapêuticas nas disfunções miccionais e do assoalho pélvico. Campinas/SP: Personal Link Comunicações; 2009.
37. Bendtsen TF, Lönnqvist PA, Jepsen KV, Petersen M, Knudsen L, Børglum J. Preliminary results of a new ultrasound-guided approach to block the sacral plexus: the parasacral parallel shift. Br J Anaesth. 2011 Aug, 107 (2), 278-80. doi: 10.1093/bja/aer216.
38. Peng PWH, Tumber PS. Ultrasound-Guided Interventional Procedures for Patients with Chronic Pelvic Pain – A Description of Techniques and Review of Literature. *Pain Physician*. 2008, 11, 215-224.
39. Trescot AM. Cryoanalgesia in Interventional Pain Management. *Pain Physician*. 2003, 6, 345-360.
40. Ingber RS. Iliopsoas myofascial dysfunction: a treatable cause of "failed" low back syndrome. *Arch Phys Med Rehabil*. 1989, 70 (5), 382-6.
41. Lewit K. Manipulative Therapy in Rehabilitation of the Motor System. In: John P. Butler (ed). *Myofascial Pain and Dysfunction*. Volume 2. The Trigger Point Manual Butterworths, London. Lippincott Williams & Wilkins, 1985. p. 138, 276, 315.
42. Rozen D, Parvez U. Pulsed radiofrequency of lumbar nerve roots for treatment of chronic inguinal herniorraphy pain. *Pain Physician*. 2006, 9 (2), 153-6.
43. Cahana A, Zundert JV, Macrea L, van Kleef M, Sluijter M. Pulsed Radiofrequency: Current Clinical and Biological Literature Available. *Pain Medicine*. 2006, 7 (5), 411-23.
44. Weksler N, Klein M, Gurevitch B, Rozentsveig V, Rudich Z, Brill S, et al. Phenol neurolysis for severe chronic nonmalignant pain: is the old also obsolete? *Pain Med*. 2007, 8 (4), 332-7.
45. Possover M. Laparoscopic management of endopelvic etiologies of pudendal pain in 134 consecutive patients. J Urol. 2009 Apr; 181 (4), 1732-6. doi: 10.1016/j.juro.2008.11.096.
46. Possover M, Schurch B, Henle K. New strategies of pelvic nerves stimulation for recovery of pelvic visceral functions and locomotion in paraplegics. *Neurourol Urodyn*. 2010, 29, 1433-1438.
47. Possover M. Recovery of sensory and supraspinal control of leg movement in people with chronic paraplegia: a case series. *Arch Phys Med Rehabil*. 2014 Apr, 95 (4), 610-4.

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CORRIGENDUM

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All patients signed informed consent and the principles of the Helsinki Declaration were followed.

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ETHICS. This was a prospective case study audit. Prior to undertaking this study, each unit obtained EC approval for use of the TFS instrument in prolapse and incontinence surgery as standard hospital practice. All patients signed informed consent and the principles of the Helsinki Declaration were followed.

Review

Pelvic congestion syndrome: a current review

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Abstract: Pelvic congestion syndrome (PCS) is an obscure diagnosis thought to cause chronic pelvic pain (CPP) in premenopausal women. It is believed to be caused by pelvic vein insufficiency but its etiology is still being investigated. Diagnostic criteria have yet to be determined making its prevalence unclear. Moreover, its clinical presentation mimics that of other common conditions causing chronic abdominal and pelvic pain[1,2]. In this review we will attempt to summarize the key elements of the clinical features, diagnostic work-up and treatment options of this enigmatic and complex entity.

Keywords: Pelvic pain, Congestion, Incompetence, Reflux, Embolization, Chronic

EPIDEMIOLOGY OF PCS

Having no definite diagnostic criteria, the incidence of PCS is difficult to determine. According to current literature, up to 10% of women have ovarian varices, and 60% of them may develop PCS[3-5]. PCS is to be considered in the differential diagnosis of CPP which affects approximately 4-16% of women, and up to 30% of them are thought to have PCS if no other obvious pathology can be found[6-9].

ETIOLOGY OF PCS

The exact etiology of PCS is unclear. Multiple investigations have observed that insufficiency of the pelvic veins originates mainly from the ovarian veins, but may also originate from the internal iliac veins or other communicating branches found in the pelvis[5,10,11].

The pathophysiology of congestion is believed to be multifactorial as a result of valvular insufficiency, vein obstruction or hormonal changes[12]. Valvular insufficiency can be caused by congenital absence of the ovarian veins' valves, which is relatively common, reported in 13-15% of patients[13]. Alternatively, it may be caused by valvular incompetence seen more frequently in multiparous women as a result of the 50% increase in pelvic vein capacity during pregnancy, which may in turn lead to venous incompetence and reflux in the non-pregnant state[10].

The absence of PCS in post-menopausal women suggests the role of estrogen in premenopausal women as a venous dilator, an observation supported by the symptom relief or resolution that is observed following the initiation of a hypo-estrogenic state in these women[14,15].

Extrinsic compression of the left renal vein ("Nutcracker syndrome") which receives inflow from the left ovarian vein or compression of the left common iliac vein can also account for pelvic vein congestion (May-Thurner Syndrome)[16,17]. Whatever may be the cause for reflux and congestion, the clinical symptoms are probably attributed to the abnormal dilatation of the pelvic venous system, as stretch and stasis of the engorged ovarian and pelvic veins may activate selective pain receptors and cause release of neurotransmitters from the walls of the dilated vessel[2,18-20].

A genetic basis has not been established but some studies suggest certain genetic traits to be involved in venous pathology[21-23].

CLINICAL PRESENTATION

PCS is characterized by symptoms of CPP, such as intermittent or constant abdominal or pelvic pain, not limited to any period of the menstrual cycle or intercourse and not associated with pregnancy. It typically affects multiparous women of reproductive age. The pain is usually described as a dull ache or fullness that persists for more than six months, and is often exacerbated with prolonged standing, coitus, menstruation and pregnancy. Symptoms are most severe at the end of the day and diminish with supine positioning. The presence of vulvovaginal, perineal or limb varices is suggestive[24,25].

The physical examination may reveal ovarian point tenderness, cervical motion tenderness and uterine tenderness with direct palpation. One study by Beard et al.[26] reported that the combination of these symptoms with post-coital pain are 94% sensitive and 77% specific for PCS.

After excluding other possible causes for CPP including gynecological, urinary, gastrointestinal, musculoskeletal, neurological and even mental health disorders, the key finding in PCS is documentation of pelvic vein dilation or incompetence on imaging studies. Congested pelvic veins can be very painful and account for approximately one third of cases of CPP[27]. Even so, the hallmark feature of enlarged pelvic veins can also be found in asymptomatic women[28,29], emphasizing the challenging diagnosis.

DIAGNOSTIC WORKUP

Although documentation of pelvic vein dilation is necessary for accurate diagnosis, pelvic imaging supports the diagnosis but does not define it, as pelvic congested veins are a common and non-specific finding that can bae seen in many asymptomatic women as well[29]. In addition, to date, there are no validated measures to determine venous congestion or tortuosity[30].

Ultrasound

Pelvic ultrasound is usually the first line of imaging study in patients with suspected PCS. It is easy of perform, non-invasive and relatively low cost. Sonography is also used to exclude other potential causes for pelvic pain such as pelvic masses or uterine pathologies. With regard to PCS, ultrasound can evaluate dilation of pelvic veins and morphology of other pelvic structures such as the uterus or the ovaries that might suggest the diagnosis of PCS. The transvaginal approach (TVS) with Doppler is generally preferred due to better visualization of pelvic venous system[31]. Common findings in sonography of PCS are dilated left ovarian vein or pelvic venous plexuses, stasis (slow blood flow) or reversed blood flow and variable duplex waveforms in the varicoceles during the Valsalva's maneuver (implying valve incompetence)[6,7,32-34]. It is recommended to perform the transabdominal or transvaginal sonography in semi-supine or upright position since veins are flaccid when the patient is supine, and venous changes may not be detected. Another maneuver that can improve sensitivity is the Valsalva maneuver, but even with these techniques employed, imaging is still operator dependent and may render false results[10].

Venography

Catheter-directed venography is the diagnostic gold standard test for pelvic congestion[35,36]. A percutaneous jugular, brachial or femoral catheter is used to visualize the ovarian or internal iliac veins and assess for incompetence, congestion and retrograde filling[37]. It is more sensitive than ultrasound scan and thus, the Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) guidelines recommend it as the test of choice for pelvic venous disorders[38]. Its main disadvantage is being an invasive procedure that carries potential risks and complications, however, using catheter venography provides a therapeutic opportunity for intervention (embolization or sclerotherapy) if indicated.

CT (Computed tomography) and MR (Magnetic resonance) Imaging

CT and MRI scans provide better imaging of pelvic congestion but are more expensive and do not allow therapeutic intervention[4,6,28,39]. Moreover, CT scan requires radiation and should be avoided when possible, especially in premenopausal women[36]. Specificity is also considered low for both modalities; however, both scans provide a good anatomical overview of the pelvic vasculature and surrounding tissues and can identify coexisting pathologies.

Contrast-enhanced MRI may become a leading imaging study for pelvic venous incompetence due to its superior imaging and, in contrast to CT, does not involve radiation exposure. Velocity-encoded phase contrast imaging and time-resolved MR angiography have significantly improved detection of venous reflux[40-42].

Laparoscopy

Diagnostic laparoscopy is often preformed as part of a CPP investigation[43]. Although it is useful for detecting conditions such as endometriosis or adhesions which are otherwise undetected, its role in PCS detection is less established. Characteristic pelvic venous changes can sometimes be visualized at laparoscopy[44], but since the procedure is performed with the patient in the supine position and requires insufflation of carbon dioxide gas, the pelvic varicosities are often drained or compressed and ultimately remain undetected[27,45].

MANAGEMENT OF PCS

Several treatment modalities have been proposed and evaluated, including medical, invasive or surgical approaches. All modalities have shown effective relief of symptoms, but no standard approach to treat PCS exists, and it is not clear which could be considered the best option[46]. Therefore, therapy is individualized based on the clinical presentation and symptoms.

Medical therapy can be considered for first line treatment as risks are low compared with invasive procedures. However, limited data exists from only few small randomized trials. These trials reported that treatment with medroxyprogesterone acetate, GnRH agonist (goserelin) and subcutaneous etonogestrel implant improved pain scores and venography scores[8,15,47]. Presumably, the hypo-estrogenic state causes venous constriction that alleviates congestion and offers symptomatic relief. However, this symptomatic relief typically lasts for several weeks and benefits are rarely sustained. For example, women treated with medroxyprogesterone acetate reported rapid return of pain after treatment cessation[15]. Some systemic side-effects and need for regular follow up also reduces compliance of the medical therapy. Patients refractory or non-compliant to medical treatment should be considered for invasive treatment.

Surgical treatment such as ovarian vein or pelvic vasculature ligation (whether using laparoscopic or laparotomy approaches) have shown symptomatic relief of PCS in up to 75% of symptomatic women[30]. Nevertheless, this evidence is supported only by observational data and case series, therefore the value of these treatments has not been established in clinical practice. Hysterectomy and bilateral salpingo-oophorectomy have also been performed to treat this condition, but are limited only to women who have completed childbearing. This radical approach does not always provide relief of symptoms and is only indicated in cases where less invasive techniques are unavailable or have failed[38]. The surgical approaches are accompanied by the potential for several complications such as high rates of residual or recurrent pelvic pain, esthetic damage and longer hospitalizations[48-50]. A randomized controlled trial showed that embolization was superior to hysterectomy and oophorectomy in providing symptomatic relief for PCS[51]. Finally, the most important risk related to gonadal vein ligation and oophorectomy remains the post-procedural loss of gonadal function and the need for hormonal replacement[52].

Radiological treatments are now being used more often for PCS as they provide good technical success rates and a minimally invasive approach. **Percutaneous embolization procedures** can be performed in an outpatient or day hospital setting, thus reducing patient's discomfort and costs[53,54]. A trans-catheter embolization of the ovarian veins can be achieved through femoral, jugular, subclavian and brachial routes, all with good technical success and low complication rates[33]. Regardless of the embolization agent used (coils, foams, glue or liquid sclerosants), clinical and technical success rates remain high for all. Complications are rare but may be variable and most commonly include coil migration, vessel perforation and local thrombophlebitis[55-57]. These complications can be reduced by using a combination of embolization agents and techniques. Additional complications related to drug administration for sedation, venous puncture such as hematoma or pneumothorax and those related to radiation exposure are noteworthy[35,58,59]. Long term symptom relief with embolization therapy has been suggested in several studies since the 1990s[48,51,55,60-62] with 60-100% of patients reporting significant relief lasting up to 72 months[55]. No gynecological complications, such as menstrual cycle changes or changes in hormonal levels, were noticed[60,61].

Specific treatments for pelvic vein compression syndromes ("Nutcracker" or "May-Thurner" syndromes) are available with the use of percutaneous stent placement or in combination with ligation or embolization[63-65].

SUMMARY

PCS is a common condition that negatively impacts women's daily life, with significant physical, psychological and sexual consequences. It must be considered in the differential diagnosis of CPP and if overlooked it may cause delay in correct diagnosis and treatment. Although PCS is multifactorial and still poorly understood, treatment modalities exist with encouraging success rates. The clinical practice guidelines of the society for vascular surgery (SVS) and the American venous forum (AVF) conclude that ovarian and pelvic vein embolization has become the standard of treatment for this condition with a grade 2B recommendation[38]. Nevertheless, to date, limited evidence for long-term efficacy of these treatments is available and further studies are required and called for to optimize treatment for this complex condition.

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REFERENCES

1. Borghi C, Dell'Atti L. Pelvic congestion syndrome: the current state of the literature. Arch Gynecol Obstet. 2016 Feb;293(2):291-301. PubMed PMID: 26404449. Epub 2015/09/24. eng.
2. Phillips D, Deipolyi AR, Hesketh RL, Midia M, Oklu R. Pelvic congestion syndrome: etiology of pain, diagnosis, and clinical management. J Vasc Interv Radiol. 2014 May;25(5):725-33. PubMed PMID: 24745902. eng.
3. Belenky A, Bartal G, Atar E, Cohen M, Bachar GN. Ovarian varices in healthy female kidney donors: incidence, morbidity, and clinical outcome. AJR Am J Roentgenol. 2002 Sep;179(3):625-7. PubMed PMID: 12185031. eng.
4. Meneses LQ, Uribe S, Tejos C, Andía ME, Fava M, Irarrazaval P. Using magnetic resonance phase-contrast velocity mapping for diagnosing pelvic congestion syndrome. Phlebology. 2011 Jun;26(4):157-61. PubMed PMID: 21690172. eng.
5. Liddle AD, Davies AH. Pelvic congestion syndrome: chronic pelvic pain caused by ovarian and internal iliac varices. Phlebology. 2007;22(3):100-4. PubMed PMID: 18268860. eng.
6. Beard RW, Highman JH, Pearce S, Reginald PW. Diagnosis of pelvic varicosities in women with chronic pelvic pain. Lancet. 1984 Oct;2(8409):946-9. PubMed PMID: 6149342. eng.
7. O'Brien MT, Gillespie DL. Diagnosis and treatment of the pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord. 2015 Jan;3(1):96-106. PubMed PMID: 26993690. Epub 2014/06/25. eng.
8. Soysal ME, Soysal S, Vicdan K, Ozer S. A randomized controlled trial of goserelin and medroxyprogesterone acetate in the treatment of pelvic congestion. Hum Reprod. 2001 May;16(5):931-9. PubMed PMID: 11331640. eng.
9. Fassiadis N. Treatment for pelvic congestion syndrome causing pelvic and vulvar varices. Int Angiol. 2006 Mar;25(1):1-3. PubMed PMID: 16520716. eng.
10. Hobbs JT. The pelvic congestion syndrome. Br J Hosp Med. 1990 Mar;43(3):200-6. PubMed PMID: 2180521. eng.
11. Koo S, Fan CM. Pelvic congestion syndrome and pelvic varicosities. Tech Vasc Interv Radiol. 2014 Jun;17(2):90-5. PubMed PMID: 24840963. eng.
12. Asciutto G, Mumme A, Asciutto KC, Geier B. Oestradiol levels in varicose vein blood of patients with and without pelvic vein incompetence (PVI): diagnostic implications. Eur J Vasc Endovasc Surg. 2010 Jul;40(1):117-21. PubMed PMID: 20202867. Epub 2010/03/03. eng.
13. Ahlberg NE, Bartley O, Chidekel N. Right and left gonadal veins. An anatomical and statistical study. Acta Radiol Diagn (Stockh). 1966 Nov;4(6):593-601. PubMed PMID: 5929114. eng.
14. Ashour MA, Soliman HE, Khougeer GA. Role of descending venography and endovenous embolization in treatment of females with lower extremity varicose veins, vulvar and posterior thigh varices. Saudi Med J. 2007 Feb;28(2):206-12. PubMed PMID: 17268690. eng.
15. Farquhar CM, Rogers V, Franks S, Pearce S, Wadsworth J, Beard RW. A randomized controlled trial of medroxyprogesterone acetate and psychotherapy for the treatment of pelvic congestion. Br J Obstet Gynaecol. 1989 Oct;96(10):1153-62. PubMed PMID: 2531611. eng.
16. Gulleroglu K, Gulleroglu B, Baskin E. Nutcracker syndrome. World J Nephrol. 2014 Nov;3(4):277-81. PubMed PMID: 25374822. PMCID: PMC4220361. eng.
17. Birn J, Vedantham S. May-Thurner syndrome and other obstructive iliac vein lesions: meaning, myth, and mystery. Vasc Med. 2015 Feb;20(1):74-83. PubMed PMID: 25502563. Epub 2014/12/10. eng.

18. Kindgen-Milles D, Arndt JO. Nitric oxide as a chemical link in the generation of pain from veins in humans. Pain. 1996 Jan;64(1):139-42. PubMed PMID: 8867256. eng.
19. Stones RW, Thomas DC, Beard RW. Suprasensitivity to calcitonin gene-related peptide but not vasoactive intestinal peptide in women with chronic pelvic pain. Clin Auton Res. 1992 Oct;2(5):343-8. PubMed PMID: 1422102. eng.
20. Stones RW, Vials A, Milner P, Beard RW, Burnstock G. Release of vasoactive agents from the isolated perfused human ovary. Eur J Obstet Gynecol Reprod Biol. 1996 Aug;67(2):191-6. PubMed PMID: 8841811. eng.
21. Hauge M, Gundersen J. Genetics of varicose veins of the lower extremities. Hum Hered. 1969;19(5):573-80. PubMed PMID: 5365895. eng.
22. Matousek V, Prerovský I. A contribution to the problem of the inheritance of primary varicose veins. Hum Hered. 1974;24(3):225-35. PubMed PMID: 4435791. eng.
23. Oklu R, Habito R, Mayr M, Deipolyi AR, Albadawi H, Hesketh R, et al. Pathogenesis of varicose veins. J Vasc Interv Radiol. 2012 Jan;23(1):33-9; quiz 40. PubMed PMID: 22030459. Epub 2011/10/26. eng.
24. Jung SC, Lee W, Chung JW, Jae HJ, Park EA, Jin KN, et al. Unusual causes of varicose veins in the lower extremities: CT venographic and Doppler US findings. Radiographics. 2009 2009 Mar-Apr;29(2):525-36. PubMed PMID: 19325063. eng.
25. Scultetus AH, Villavicencio JL, Gillespie DL, Kao TC, Rich NM. The pelvic venous syndromes: analysis of our experience with 57 patients. J Vasc Surg. 2002 Nov;36(5):881-8. PubMed PMID: 12422096. eng.
26. Beard RW, Reginald PW, Wadsworth J. Clinical features of women with chronic lower abdominal pain and pelvic congestion. Br J Obstet Gynaecol. 1988 Feb;95(2):153-61. PubMed PMID: 3349005. eng.
27. Ignacio EA, Dua R, Sarin S, Harper AS, Yim D, Mathur V, et al. Pelvic congestion syndrome: diagnosis and treatment. Semin Intervent Radiol. 2008 Dec;25(4):361-8. PubMed PMID: 21326577. PMCID: PMC3036528. eng.
28. Nascimento AB, Mitchell DG, Holland G. Ovarian veins: magnetic resonance imaging findings in an asymptomatic population. J Magn Reson Imaging. 2002 May;15(5):551-6. PubMed PMID: 11997896. eng.
29. Rozenblit AM, Ricci ZJ, Tuvia J, Amis ES. Incompetent and dilated ovarian veins: a common CT finding in asymptomatic parous women. AJR Am J Roentgenol. 2001 Jan;176(1):119-22. PubMed PMID: 11133549. eng.
30. Tu FF, Hahn D, Steege JF. Pelvic congestion syndrome-associated pelvic pain: a systematic review of diagnosis and management. Obstet Gynecol Surv. 2010 May;65(5):332-40. PubMed PMID: 20591203. eng.
31. Sharma K, Bora MK, Varghese J, Malik G, Kuruvilla R. Role of trans vaginal ultrasound and Doppler in diagnosis of pelvic congestion syndrome. J Clin Diagn Res. 2014 Jul;8(7):OD05-7. PubMed PMID: 25177607. PMCID: PMC4149113. Epub 2014/07/20. eng.
32. Park SJ, Lim JW, Ko YT, Lee DH, Yoon Y, Oh JH, et al. Diagnosis of pelvic congestion syndrome using transabdominal and transvaginal sonography. AJR Am J Roentgenol. 2004 Mar;182(3):683-8. PubMed PMID: 14975970. eng.
33. Freedman J, Ganeshan A, Crowe PM. Pelvic congestion syndrome: the role of interventional radiology in the treatment of chronic pelvic pain. Postgrad Med J. 2010 Dec;86(1022):704-10. PubMed PMID: 21106807. eng.
34. Asciutto G, Mumme A, Marpe B, Köster O, Asciutto KC, Geier B. MR venography in the detection of pelvic venous congestion. Eur J Vasc Endovasc Surg. 2008 Oct;36(4):491-6. PubMed PMID: 18718774. Epub 2008/08/20. eng.
35. Bittles MA, Hoffer EK. Gonadal vein embolization: treatment of varicocele and pelvic congestion syndrome. Semin Intervent Radiol. 2008 Sep;25(3):261-70. PubMed PMID: 21326516. PMCID: PMC3036435. eng.
36. Arnoldussen CW, de Wolf MA, Wittens CH. Diagnostic imaging of pelvic congestive syndrome. Phlebology. 2015 Mar;30(1 Suppl):67-72. PubMed PMID: 25729070. eng.
37. Geier B, Barbera L, Mumme A, Köster O, Marpea B, Kaminsky C, et al. Reflux patterns in the ovarian and hypogastric veins in patients with varicose veins and signs of pelvic venous incompetence. Chir Ital. 2007 2007 Jul-Aug;59(4):481-8. PubMed PMID: 17966768. eng.
38. Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2011 May;53(5 Suppl):2S-48S. PubMed PMID: 21536172. eng.
39. Desimpelaere JH, Seynaeve PC, Hagers YM, Appel BJ, Mortelmans LL. Pelvic congestion syndrome: demonstration and diagnosis by helical CT. Abdom Imaging. 1999 1999 Jan-Feb;24(1):100-2. PubMed PMID: 9933685. eng.
40. Yang DM, Kim HC, Nam DH, Jahng GH, Huh CY, Lim JW. Time-resolved MR angiography for detecting and grading ovarian venous reflux: comparison with conventional venography. Br J Radiol. 2012 Jun;85(1014):e117-22. PubMed PMID: 21385913. PMCID: PMC3474099. Epub 2011/03/08. eng.
41. Dick EA, Burnett C, Anstee A, Hamady M, Black D, Gedroyc WM. Time-resolved imaging of contrast kinetics three-dimensional (3D) magnetic resonance venography in patients with pelvic congestion syndrome. Br J Radiol. 2010 Oct;83(994):882-7. PubMed PMID: 20846985. PMCID: PMC3473747. eng.
42. Pandey T, Shaikh R, Viswamitra S, Jambhekar K. Use of time resolved magnetic resonance imaging in the diagnosis of pelvic congestion syndrome. J Magn Reson Imaging. 2010 Sep;32(3):700-4. PubMed PMID: 20815070. eng.
43. Howard FM. The role of laparoscopy in the chronic pelvic pain patient. Clin Obstet Gynecol. 2003 Dec;46(4):749-66. PubMed PMID: 14595216. eng.
44. Sharma D, Dahiya K, Duhan N, Bansal R. Diagnostic laparoscopy in chronic pelvic pain. Arch Gynecol Obstet. 2011 Feb;283(2):295-7. PubMed PMID: 20072784. Epub 2010/01/14. eng.
45. Osman MI, Din Shafeek MA, Abdall MI, Khattar NY, Bayad MA, Mohamed HM, et al. Chronic pelvic pain in Lippes IUD users. Laparoscopic and venographic evaluation. Contracept Deliv Syst. 1981 Jan;2(1):41-51. PubMed PMID: 12278588. eng.
46. Nicholson T, Basile A. Pelvic congestion syndrome, who should we treat and how? Tech Vasc Interv Radiol. 2006 Mar;9(1):19-23. PubMed PMID: 17145481. eng.
47. Shokeir T, Amr M, Abdelshaheed M. The efficacy of Implanon for the treatment of chronic pelvic pain associated with pelvic congestion: 1-year randomized controlled pilot study. Arch Gynecol Obstet. 2009 Sep;280(3):437-43. PubMed PMID: 19190927. Epub 2009/02/04. eng.
48. Monedero JL, Ezpeleta SZ, Perrin M. Pelvic congestion syndrome can be treated operatively with good long-term results. Phlebology. 2012 Mar;27 Suppl 1:65-73. PubMed PMID: 22312070. eng.
49. Meissner MH, Gibson K. Clinical outcome after treatment of pelvic congestion syndrome: sense and nonsense. Phlebology. 2015 Mar;30(1 Suppl):73-80. PubMed PMID: 25729071. eng.
50. Smith PC. The outcome of treatment for pelvic congestion syndrome. Phlebology. 2012 Mar;27 Suppl 1:74-7. PubMed PMID: 22312071. eng.
51. Chung MH, Huh CY. Comparison of treatments for pelvic congestion syndrome. Tohoku J Exp Med. 2003 Nov;201(3):131-8. PubMed PMID: 14649734. eng.
52. Beard RW, Kennedy RG, Gangar KF, Stones RW, Rogers V, Reginald PW, et al. Bilateral oophorectomy and hysterectomy in the treatment of intractable pelvic pain associated with pelvic congestion. Br J Obstet Gynaecol. 1991 Oct;98(10):988-92. PubMed PMID: 1751445. eng.
53. Gandini R, Chiocchi M, Konda D, Pampana E, Fabiano S, Simonetti G. Transcatheter foam sclerotherapy of symptomatic female varicocele with sodium-tetradecyl-sulfate foam. Cardiovasc Intervent Radiol. 2008 2008 Jul-Aug;31(4):778-84. PubMed PMID: 18172712. Epub 2008/01/03. eng.
54. Gandini R, Konda D, Abrignani S, Chiocchi M, Da Ros V, Morosetti D, et al. Treatment of symptomatic high-flow female varicoceles with stop-flow foam sclerotherapy. Cardiovasc Intervent Radiol. 2014 Oct;37(5):1259-67. PubMed PMID: 24190634. Epub 2013/11/05. eng.
55. Kwon SH, Oh JH, Ko KR, Park HC, Huh JY. Transcatheter ovarian vein embolization using coils for the treatment of pelvic congestion syndrome. Cardiovasc Intervent Radiol. 2007 2007 Jul-Aug;30(4):655-61. PubMed PMID: 17468903. Epub 2007/04/28. eng.
56. Nasser F, Cavalcante RN, Affonso BB, Messina ML, Carnevale FC, de Gregorio MA. Safety, efficacy, and prognostic factors in endovascular treatment of pelvic congestion syndrome. Int J Gynaecol Obstet. 2014 Apr;125(1):65-8. PubMed PMID: 24486124. Epub 2014/01/07. eng.
57. Asciutto G, Asciutto KC, Mumme A, Geier B. Pelvic venous incompetence: reflux patterns and treatment results. Eur J Vasc Endovasc Surg. 2009 Sep;38(3):381-6. PubMed PMID: 19574069. Epub 2009/07/01. eng.
58. Hansrani V, Abbas A, Bhandari S, Caress AL, Seif M, McCollum CN. Trans-venous occlusion of incompetent pelvic veins for chronic pelvic pain in women: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2015 Feb;185:156-63. PubMed PMID: 25590499. Epub 2014/12/19. eng.
59. van der Vleuten CJ, van Kempen JA, Schultze-Kool LJ. Embolization to treat pelvic congestion syndrome and vulval varicose veins. Int J Gynaecol Obstet. 2012 Sep;118(3):227-30. PubMed PMID: 22727416. Epub 2012/06/22. eng.
60. Kim HS, Malhotra AD, Rowe PC, Lee JM, Venbrux AC. Embolotherapy for pelvic congestion syndrome: long-term results. J Vasc Interv Radiol. 2006 Feb;17(2 Pt 1):289-97. PubMed PMID: 16517774. eng.
61. Venbrux AC, Chang AH, Kim HS, Montague BJ, Hebert JB, Arepally A, et al. Pelvic congestion syndrome (pelvic venous incompetence): impact of ovarian and internal iliac vein embolotherapy on menstrual cycle and chronic pelvic pain. J Vasc Interv Radiol. 2002 Feb;13(2 Pt 1):171-8. PubMed PMID: 11830623. eng.
62. Laborda A, Medrano J, de Blas I, Urtiaga I, Carnevale FC, de Gregorio MA. Endovascular treatment of pelvic congestion syndrome: visual analog scale (VAS) long-term follow-up clinical evaluation in 202 patients. Cardiovasc Intervent Radiol. 2013 Aug;36(4):1006-14. PubMed PMID: 23456353. Epub 2013/03/02. eng.
63. d'Archambeau O, Maes M, De Schepper AM. The pelvic congestion syndrome: role of the "nutcracker phenomenon" and results of endovascular treatment. JBR-BTR. 2004 2004 Jan-Feb;87(1):1-8. PubMed PMID: 15055326. eng.
64. Jeanneret C, Beier K, von Weymarn A, Traber J. Pelvic congestion syndrome and left renal compression syndrome - clinical features and therapeutic approaches. Vasa. 2016;45(4):275-82. PubMed PMID: 27428495. eng.
65. Rogers A, Beech A, Braithwaite B. Transperitoneal laparoscopic left gonadal vein ligation can be the right treatment option for pelvic congestion symptoms secondary to nutcracker syndrome. Vascular. 2007 2007 Jul-Aug;15(4):238-40. PubMed PMID: 17714643. eng.

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Review

Management of interstitial cystitis/ Bladder Pain Syndrome: a short review

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INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder condition which is characterized by bladder pain, urinary frequency, and nocturia. IC/BPS had been considered a progressive disease that may evolve from early to late stages[1]. According to the American Urological Association (AUA) guidelines, IC/BPS is diagnosed if symptoms are present for a period of more than 6 weeks[2]. The underlying etiology of IC/BPS is not well understood and it is likely that a number of mechanisms are involved in the development of the condition. The urothelium/transitional epithelium is thought to play a fundamental role in the pathogenesis of IC/BPS[3]. The protective layer of glycosaminoglycans (GAG) on the surface of the urothelial cells provides a barrier against solutes in the urine. Components of this layer include hyaluronic acid, chondroitin sulfate, heparin sulfate, dermatan sulfate and keratin sulfate[4]. GAG layer has been shown to be defective in some patients with IC/BPS[5].

Since other medical conditions may mimic IC/BPS symptoms, careful multi-disciplinary evaluation of the pelvic organs should be needed in order to rule out other conditions, including urological (infections, stone disease, malignancy), gynecological (endometriosis, painful menstrual periods), gastrointestinal (diverticulitis, irritable bowel syndrome, inflammatory bowel disease) and others.

Treatment of IC/BPS often depends upon clinician's preferences and experience rather than upon scientific studies mainly because the cause of IC/BPS is not clear. Most patients will need several treatments to improve their symptoms[6]. The need to reduce the pain may be significant only during flares, when symptoms are bothersome or even severe. It is not always clear why flares develop and some triggers we suggested as promoting exacerbations: beverages such as alcohol and coffee, spicy foods, certain body positions and medical conditions including gastrointestinal problems and infections[7].

Management of IC/BPS is staged and includes several steps[8].

TREATMENT

General measures

Reassurance – Often the patients wander between different care providers and seek help for years before diagnosis is made. Acknowledging patients distress and the effects on their quality of life, encourage many of them to advance to next step of seeking relief. On-line support groups such as the Interstitial Cystitis Network (www.ic-network.com) give the patients a valuable information.

Changing life habits – stressful way of life may exacerbate the flares of IC/BPS. A relaxing activity including Pilates or Yoga may reduce amount and severity of the flares[9]. Changing body positioning from sitting to working at standing desk may also give some relief.

Diet changes – There are reports that spicy, acidic and caffeine enriched diet may worsen the pain among IC/BPS patients[7]. There is a controversy whether to reduce aggravating foods only during flares or to recommend a regular restrictive diet.

Psychological guidance – since pain can be worsened by anxiety and stress[10], and it has been suggested that unsolved events from the past may promote chronic pain, psychosocial support can be helpful in dealing with IC/BPS[11]. In addition, living with pain can cause difficulties in day to day life such as at work and personal relationships, which could be ameliorated by psychological guidance. Psychotherapy may include participation in support groups for sharing difficulties or private meetings with a social worker, a psychologist or a psychiatrist[12].

Physiotherapy – IC/BPS patients suffer from groin and perineal muscle spasms. Pelvic floor physiotherapies include training the muscles to relax and decrease the tone, pressing on trigger points, and controlling movements of the connective tissues and related muscles[13,14].

Bladder hydrodistention – hydrodistending the bladder through a cystoscope under epidural or general anesthesia to the maximal bladder capacity, is a combination of diagnostic and treatment procedure[15]. Diffused glomerulations over the bladder endothelium that may be seen, would be strengthening the diagnosis of IC/PBS. Some patients report pain relief after the procedure[16,17] including a prolong relief up to 12 months[18].

Oral medications

Pentosan polysulfate sodium (Elmiron) is the only oral medication that has been approved by the US Food and Drug Administration (FDA) to treat interstitial cystitis/bladder pain syndrome (IC/BPS). It affects by repairing the lining of the bladder[19]. It reduces symptoms in some patients with IC/BPS, although mostly the symptoms do not totally disappear. Studies reported promising results as a single therapy or combined with other oral medications[20,21,22]. The side effects include abnormality of liver function tests, gastrointestinal symptoms, and hair loss that reduce the compliance among patients.

Cimetidine (Tagamet) have been used to treat IC/BPS, with variable results[23,24]. This medication can cause diarrhea, fatigue and muscle pain that reduce the compliance among patients.

Amitriptyline (Elavil) is an antidepressant that is used to treat chronic pain as well as mood disorders. The drug reduces pain perception when used in low doses, but the exact mechanism of its benefit is unknown. The results reported are quite conflicting[25]. Side effects include decrease in blood pressure, fatigue, dry mouth or weight gain that reduce the compliance among patients.

Other medications – include narcotics and NSAIDS medications as part of the pain management. Different anecdotal drugs were used including Sildenafil[26], Cyclosporine A[27] and others without any promising results.

Bladder Instillations

Dimethylsulfoxide (DMSO) – is the only bladder liquid instillation that has been approved by the US FDA to treat IC/BPS. It probably acts by promoting repair of the lining of the bladder[28]. The induction is for 6-8 weeks on a weekly basis and if it proves to be beneficial, it may be followed by a monthly instillation. The liquid is held in place for approximately 20-60 minutes. Studies show that DMSO can temporarily improve bladder pain[29,30]. Side effect is a garlic-like odor of the compound that reduces the compliance among patients.

Other bladder instillations – Several "cocktail" combination instillations were suggested to improve the effect on IC/BPS. These include among others: DMSO, lidocaine, heparin, sodium bicarbonate and antibiotics (mostly Garamycin)[31]. The aim of the combined instillations is to decrease nerve sensitivity in the bladder with improving the bladder lining. The treatment is offered either as a series twice to three times a week or a single treatment to reduce a severe flare[32]. The patient is instructed to hold as much as possible, up to two hours before urinating. The duration of pain reduction is very heterogenic and lasts up to several weeks.

In one small study, approximately 80 percent of patients had decreased pain for at least four hours after one treatment with heparin, sodium bicarbonate, and lidocaine. In other series patients experienced reduced pain for days or weeks after bladder installations[31].

Intravesical botulinum toxin type A (Botox) injections – Injecting botulinum toxin type A to the detrusor muscle is well-established routine in the overactive bladder management guidelines. A cystoscope with a special needle is used intravesically to inject in 10-20 spots along the detrusor using 100-200 units of Botox. Studies using the same technique for IC/BPS patients showed promising results after single treatment[33,34,35,36] as well as after repeated applications of injections[37,38].

Electrical Stimulation

Electrical Stimulation offers an alternative option of treatment for IC/BPS. The less invasive mode is by evoking the tibial nerve passing next to the lateral calcaneus transcoutaneously either with delicate needle or plug connected to a battery and sending electrical signals[39]. This wire sends a mild electrical pulse which ascends up to the sacral nerve. This pulse is thought to interrupt signals from the brain that trigger pain, urgency, and frequency in people with IC/BPS.

A different approach is a direct stimulation of the sacral nerve by placing a small wire under the skin just above the tailbone. It is first attached externally by a wire that is placed next to the nerve in the low back, then tunneled out of the skin and connected to a small battery (about the size of a pager) that is worn on the waist. The wires are taped securely to the skin. If it shows benefit in reducing pain, a permanent battery is attached to the wire, and the battery and wire are then surgically implanted under the skin of the upper buttock. This trademark instrument, called Interstim, is FDA approved for overactive bladder, but can be used in the arsenal treatments for IC/BPS patients as well[40,41]. The side effects reported included local dermal symptoms, bleeding, pain as well as battery exhausting needed additional surgery to replace it. There are numerous trials showing improvement of symptoms among IC/BPS patients.

Surgery

Most patients with IC/BPS are not good candidates for major surgery. Surgical options of cystectomy with ileal conduit or neobladder for a non-respondant patients are quite unusual since it is not guaranteed the pelvic pain may be relieved and the morbidity of the procedure is high[42].

CONCLUSION

In summary, IC/BPS is a pain disorder that affects the quality of life of the patients and since no treatment proved a dominant effect, a combined behavioral, psychological and pharmacological treatment is needed to reduce the flares exacerbations.

REFERENCES

1. Jhang JF, Kuo HC. Pathomechanism of Interstitial Cystitis/Bladder Pain Syndrome and Mapping the Heterogeneity of Disease. Int Neurourol J 2016; 20 Suppl 2:S95.
2. Hanno PM, Burks DA, Clemens JQ et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. J Urol, 2011, 185, 2162.
3. Cvach K, Rosamilia A. Review of intravesical therapies for bladder pain syndrome/ interstitial cystitis. *Transl Androl Urol,* 2015, 4 (6), 629.
4. Hurst RE. Structure, function, and pathology of proteoglycans and glycosaminoglycans in the urinary tract. World J Urol, 1994, 12, 3.
5. Slobodov G, Feloney M, Gran C et al. Abnormal expression of molecular markers for bladder impermeability and differentiation in the urothelium of patients with interstitial cystitis. J Urol, 2004, 171, 1554.
6. Koziol JA. Epidemiology of interstitial cystitis. Urol Clin North Am, 1994, 21, 7.
7. Atchley MD, Shah NM, whitmore KE. Complementary and alternative medical therapies for interstitial cystitis: an update from the United States. Transl Androl Urol, 2015, 4 (6), 662.
8. Pazin C, de Souza Mitidieri AM, Silva AP et al. Treatment of bladder pain syndrome and interstitial cystitis: a systematic review. Int Urogynecol J, 2016, 27, 697.
9. Rovner E, Propert KJ, Brensinger C et al. Treatments used in women with interstitial cystitis: the interstitial cystitis data base (ICDB) study experience. The Interstitial Cystitis Data Base Study Group. Urology, 2000, 56, 940.
10. Rothrock NE, Lutgendorf SK, Kreder KJ et al. Stress and symptoms in patients with interstitial cystitis: a life stress model. Urology, 2001, 57, 422.
11. Clemens JQ, Brown SO, Calhoun EA. Mental health diagnoses in patients with interstitial cystitis/painful bladder syndrome and chronic prostatitis/chronic pelvic pain syndrome: a case/control study. J Urol, 2008, 180, 1378.
12. Watkins KE, Eberhart N, Hilton L et al. Depressive disorders and panic attacks in women with bladder pain syndrome/interstitial cystitis: a population-based sample. Gen Hosp Psychiatry, 2011, 33, 143.
13. Bassaly R, Tidwell N, Bertolino S et al. Myofascial pain and pelvic floor dysfunction in patients with interstitial cystitis. Int Urogynecol J, 2011, 22, 413.
14. FitzGerald MP, Payne CK, Lukacz ES et al. Randomized multicenter clinical trial of myofascial physical therapy in women with interstitial cystitis/painful bladder syndrome and pelvic floor tenderness. J Urol, 2012, 187, 2113.
15. Cole EE, Scarpero HM, Dmochowski RR. Are patient symptoms predictive of the diagnostic and/or therapeutic value of hydrodistention? Neurourol Urodyn, 2005, 24, 638.
16. Yamada T, Murayama T, Andoh M. Adjuvant hydrodistension under epidural anesthesia for interstitial cystitis. Int J Urol, 2003, 10:463.
17. Hsieh CH, Chang ST, Hsieh CJ et al. Treatment of interstitial cystitis with hydrodistention and bladder training. Int Urogynecol J Pelvic Floor Dysfunct, 2008, 19, 1379.
18. McCahy PJ, Styles RA. Prolonged bladder distension: experience in the treatment of detrusor overactivity and interstitial cystitis. Eur Urol, 1995, 28, 325.

19. Hurst RE, Roy JB, Min KW et al. A deficit of chondroitin sulfate proteoglycans on the bladder uroepithelium in interstitial cystitis. Urology, 1996, 48, 817.
20. Davis EL, El Khoudary SR, Talbott EO et al. Safety and efficacy of the use of intravesical and oral pentosan polysulfate sodium for interstitial cystitis: a randomized double-blind clinical trial. J Urol, 2008, 179, 177.
21. Sairanen J, Tammela TL, Leppilahti M et al. Cyclosporine A and pentosan polysulfate sodium for the treatment of interstitial cystitis: a randomized comparative study. J Urol, 2005, 174, 2235.
22. Sant GR, Propert KJ, Hanno PM et al. A pilot clinical trial of oral pentosan polysulfate and oral hydroxyzine in patients with interstitial cystitis. J Urol, 2003, 170, 810.
23. Thilagarajah R, Witherow RO, Walker MM. Oral cimetidine gives effective symptom relief in painful bladder disease: a prospective, randomized, double-blind placebo-controlled trial. BJU Int, 2001, 87, 207.
24. Dasgupta P, Sharma SD, Womack C et al. Cimetidine in painful bladder syndrome: a histopathological study. BJU Int 2001, 88, 183.
25. van Ophoven A, Pokupic S, Heinecke A, Hertle L. A prospective, randomized, placebo controlled, double-blind study of amitriptyline for the treatment of interstitial cystitis. J Urol 2004, 172, 533.
26. Chen H, Wang F, Chen W et al. Efficacy of daily low-dose sildenafil for treating interstitial cystitis: results of a randomized, double-blind, placebo-controlled trial – treatment of interstitial cystitis/painful bladder syndrome with low-dose sildenafil. Urology, 2014, 84, 51.
27. Forrest JB, Payne CK, Erickson DR. Cyclosporine A for refractory interstitial cystitis/bladder pain syndrome: experience of 3 tertiary centers. J Urol, 2012.
28. Daha LK, Riedl CR, Lazar D et al. Effect of intravesical glycosaminoglycan substitution therapy on bladder pain syndrome/interstitial cystitis, bladder capacity and potassium sensitivity. Scand J Urol Nephrol, 2008, 42, 369.
29. Perez-Marrero R, Emerson LE, Feltis JT. A controlled study of dimethyl sulfoxide in interstitial cystitis. J Urol, 1988, 140, 36.
30. Peeker R, Haghsheno MA, Holmäng S, Fall M. Intravesical bacillus Calmette-Guerin and dimethyl sulfoxide for treatment of classic and nonulcer interstitial cystitis: a prospective, randomized double-blind study. J Urol, 2000, 164, 1912.
31. Barua JM, Arance I, Angulo JC, Riedl CR. A systematic review and meta-analysis on the efficacy of intravesical therapy for bladder pain syndrome/interstitial cystitis. Int Urogynecol J, 2016, 27, 1137.
32. www.ichelp.org/TreatmentAndSelfHelp/ICAandDiet.html.
33. Pinto R, Lopes T, Frias B et al. Trigonal injection of botulinum toxin A in patients with refractory bladder pain syndrome/interstitial cystitis. Eur Urol, 2010, 58, 360.
34. Kuo HC, Chancellor MB. Comparison of intravesical botulinum toxin type A injections plus hydrodistention with hydrodistention alone for the treatment of refractory interstitial cystitis/painful bladder syndrome. BJU Int, 2009, 104, 657.
35. Giannantoni A, Porena M, Costantini E et al. Botulinum A toxin intravesical injection in patients with painful bladder syndrome: 1-year followup. J Urol, 2008, 179, 1031.
36. Liu HT, Kuo HC. Intravesical botulinum toxin A injections plus hydrodistension can reduce nerve growth factor production and control bladder pain in interstitial cystitis. Urology, 2007, 70, 463.
37. Shie JH, Liu HT, Wang YS, Kuo HC. Immunohistochemical evidence suggests repeated intravesical application of botulinum toxin A injections may improve treatment efficacy of interstitial cystitis/bladder pain syndrome. BJU Int, 2013, 111, 638.
38. Pinto R, Lopes T, Silva J et al. Persistent therapeutic effect of repeated injections of onabotulinum toxin a in refractory bladder pain syndrome/interstitial cystitis. J Urol, 2013, 189, 548.
39. Ragab MM, Tawfik AM, Abo El-enem M et al. Evaluation of Percutaneous Tibial Nerve Stimulation for Treatment of Refractory Painful Bladder Syndrome. Urology, 2015, 86, 707.
40. Zabihi N, Mourtzinos A, Maher MG et al. Short-term results of bilateral S2-S4 sacral neuromodulation for the treatment of refractory interstitial cystitis, painful bladder syndrome, and chronic pelvic pain. Int Urogynecol J Pelvic Floor Dysfunct, 2008, 19, 553.
41. Peters KM, Feber KM, Bennett RC. A prospective, single-blind, randomized crossover trial of sacral vs pudendal nerve stimulation for interstitial cystitis. BJU Int, 2007, 100, 835.
42. Rössberger J, Fall M, Jonsson O, Peeker R. Long-term results of reconstructive surgery in patients with bladder pain syndrome/interstitial cystitis: subtyping is imperative. Urology 2007, 70, 638.

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Original article

Age related comorbidities in chronic urogenital pain

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Abstract: Chronic urogenital pain affects women of all ages. Its prevalence peaks at age 25, however the incidence of comorbidities varies significantly between women of reproductive age and post-reproductive age. Gynecological, urological, gastroenterological and neuromuscular comorbidities increase significantly in the post-reproductive age group. Understanding the increased prevalence of comorbidities with increased age will enhance the management of CUP in post-reproductive age women.

Keywords: Chronic urogenital pain (CUP); Vulvodynia, Bladder Pain Syndrome (BPS); Comorbidities; Post-reproductive age (PRA).

INTRODUCTION

Chronic urogenital pain (CUP) is associated with a number of comorbidities, including irritable bowel syndrome (IBS), pelvic floor dysfunction (PFD), headaches, fibromyalgia, allergies and musculoskeletal changes all of which have been well documented in literature[1-3]. Reports indicate that prevalence of CUP is comparable to lower back pain, asthma and migraines[4].

The two most common CUP conditions in women are vulvodynia and bladder pain syndrome (BPS). According to current estimates, vulvodynia affects up to 8.3% of women[5] and BPS up to 6.5% of women[6], though lifetime prevalence of these conditions may be much higher[7]. It is estimated that 10%-28% of women report experiencing chronic vulvar pain symptoms consistent with the diagnostic criteria for vulvodynia[8-11] and a similar pattern appears to exist in BPS[12-15]. CUP conditions expose the sufferers and health care systems to significant costs of management[16]. In the United States it is estimated that the economic impact of vulvodynia alone may be in the range of $31-72 billion dollars in direct and indirect costs[17]. The actual cost to the health care system would be even greater if all women were to disclose their symptoms, however most suffer in silence[18].

Reliable profile data on women with CUP is essential for improved understanding of CUP disorders and for the development of management guidelines. To date, there have been no studies specifically comparing age related profiles of women with CUP. This study, based on a large sample of women, examines the differences between women of reproductive age (RA) and those of post reproductive age (PRA). Women with CUP who are of PRA are understudied, and only recently are researchers paying more attention to the relationship between CUP and menopause[19].

Ageing in women is linked with anatomic and physiological changes that affect the urogenital, digestive, and musculoskeletal systems[20]. This is exemplified by reduction in muscle strength and fascial support[21], accelerated bone turnover, decreased gastric function, diminished colonic motility[22], reduced vaginal secretions and urethral closing pressure[20]. Postural changes such as kyphosis place a greater load on the pelvic structures that may predispose menopausal women to dyspareunia[21]. Vulvovaginal atrophy and genitourinary syndrome of menopause, IBS symptoms, back pain, urinary incontinence and a host of other neuromuscular changes create challenges for the management of CUP in PRA women[23,24].

MATERIALS AND METHODS

This is a retrospective study based on data derived from questionnaires completed by women diagnosed with vulvodynia and BPS. The questionnaires were completed post diagnosis and prior to the commencement of therapy. The sample originated from an existing database consisting of 1143 de-identified questionnaire responses by women attending a network of private CUP clinics in Australia between the years of 2006-2016. The questionnaire contained 83 questions focusing on demographic information, birthing and health history, pain symptoms and sexual function. The response rate to specific questions varied between subjects depending on their personal relevance. All women over the age of 18 who suffered from CUP and provided written assent for their data to be used were entered into the database. The database was used in its entirety with no exclusions, thereby minimizing potential bias.

The clinics guidelines required all women to undergo screening by the referring doctor prior to the commencement of physical therapy. The specialists consisted of gynecologists, urologists, dermatologists, sexual health physicians and GP's who had a special interest in the management of CUP and women's health issues. All of the women attended the clinics for the purpose of conservative therapy that consisted of education, counseling, biofeedback and myofascial therapy. Subjects were divided into two groups for statistical analysis; those of RA and PRA. In Australia, women's reproductive years are considered to begin at age 15 and end at age 50[25] and this formed the basis for defining the RA group as age 18-49 and PRA group as 50 and above[24].

This subgrouping of women forms the basis of subsequent statistical comparison. A range of statistical analyses were used, including Pearson correlation coefficient, analysis of variance, t-test for comparison of two means, chi-square test for independence between categorical variables. Institutional review board approval was obtained from the University of South Australia's Human Research Ethics Committee.

RESULTS

Age

The age of all subjects in the study ranged from 18-70, with a mean age of 30.6 years (±10.3). The 1143 subjects were subdivided into two groups consisting of 1048 (92%) subjects in the RA group and 95 (8%) subjects in the PRA group.

Due to the policy of the private clinics from which the database was obtained, the analysis focused only on wom-

en over the age of 18, thus the age range of this study was 18-70 years. An analysis of the age distribution of the sample showed that prevalence of CUP peaks at age 25, with women in the 21-30 age bracket constituting over half of the sample (56.8%). Three-quarters of the group (76.6%) were under the age of 35 years. By age 36, prevalence decreased noticeably and plateaued from age 37 onwards, dropping to less than 1% per each age group from 60 years onwards.

Associated factors & comorbidities

Candidiasis in CUP women was reported by 76.6% (*n*=914) and 90.3% in RA and PRA women respectively. A total of 68.1% of these women's symptoms were confirmed via swab test.

Candidiasis Symptoms	RA (*n*=914)	PRA (*n*=72)	Significance
Candidiasis Dx	76.6%	90.3%	p = 0.006
Frequency of Symptoms	Total Group (RA + PRA)		
Occasional	54.3%		
Frequent	25.3%		
Chronic	20.4%		

Figure 1. – Frequency of candidiasis reported by RA and PRA women

Thrush diagnoses showed a statistically significant increase with age (p=0.006), however there was no statistically significant difference between the RA and PRA groups in relation to frequency or treatment methods (p = 0.656).

Treatment of Candidiasis	RA (*n*=519) + PRA (*n*= 52)
Topical meds	38.7%
Oral meds	10.3%
Both	51%

Figure 2. – Frequency of candidiasis treatments reported by total sample of women (RA + PRA)

Prevalence of the PRA group's gynecological symptoms was double that of the RA group. Ovarian cysts and adhesions were reported by 26.2% and 57.5% of RA (*n*=915) and PRA (*n*=73) subjects respectively. The frequency with which subjects reported such diagnoses is summarized in Figure 3. Cysts were present in 17.7% of RA women, increasing to 48% in PRA women (p<0.001). Adhesions increased from 3.7% in RA women to 21.9% of PRA women (p<0.001). Significant differences between RA and PRA groups were established using the chai-squared test.

Gynecological Symptom	RA (n=913)	PRA (n=73)	p
Adhesions	3.7%	21.9%	<0.001
Cysts	17.7%	48%	<0.001

Figure 3.- Frequency of gynecological symptoms reported by RA and PRA women

Urological history

Women answered questions regarding urological diagnoses and symptoms of dysuria, urge, frequency, incontinence and BPS. In the RA group 33.8% reported at least one of these symptoms compared with 69.3% in the PRA women. The results are statistically significant for all variables as the frequency with which the PRA group reported symptoms was more than double that of the RA women. Incontinence was an exception as it was five times higher in the PRA than RA women. The results are summarized in Figure 4.

Urological Symptom	RA (n=913)	PRA (n=73)	p
Dysuria	6.6%	14.7%	0.009
Urinary Urge	4.9%	14.7%	<0.001
BPS	24.1%	52.0%	<0.001
Urinary Frequency	9.9%	24.0%	<0.001
Incontinence	4.8%	26.7%	<0.001

Figure 4.- Frequency of urological symptoms reported by RA and PRA women

Gastroenterological history

A total of 31.3% of RA (n=281) women reported at least one GI symptom, with incidence rising to 52.8% in PRA women (n=38) (p<0.001). Results were statistically significant for differences in the frequency of reported abdominal pain, distension and bloating between RA and PRA groups. There was no statistically significant difference between the groups in relation to constipation and diarrhea. Prevalence of specific GI symptoms in RA and PRA groups is summarized in Figure 5.

Gastroenterological Symptom	RA (n=897)	PRA (n=72)	p
Abdominal pain	13.7%	29.2%	<0.001
Distension and bloating	14.6%	38.7%	<0.001
Constipation and/or diarrhoea	21.8%	27.8%	0.238
Passage of mucus	4.0%	4.2%	0.951

Figure 5.- Frequency of gastroenterological symptoms reported by RA and PRA women

A summary of the frequency of gynecological, urological, and gastroenterological symptoms is provided in table 6. Prevalence for most of the conditions listed doubled for the PRA group.

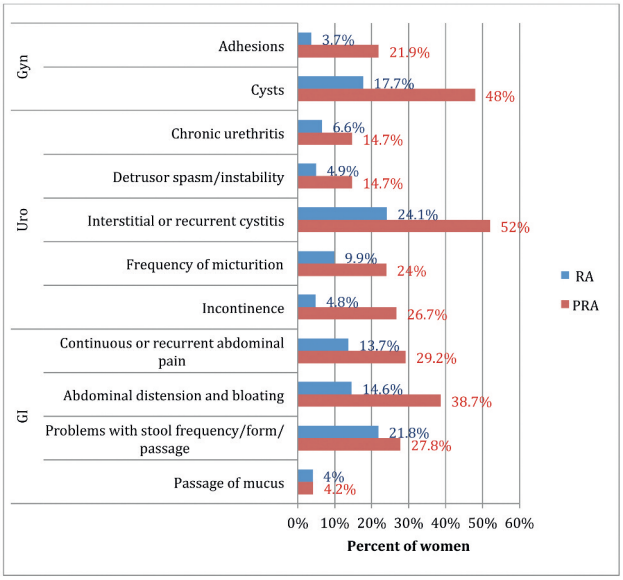

Figure 6.- Frequency of all symptoms reported by RA and PRA women

Neuromuscular changes

Muscle, joint and bone conditions are three times more prevalent in the PRA group (59%, n=70) when compared with the RA group (17%, n=865). There was no significant difference between the RA and PRA groups in prevalence of headaches (35%, n=329), anxiety (32.4%, n=305) and depression (26.5%, n=250).

Sexual activity and pain

Due to a lack of statistically significant differences between the two groups, the combined sexual difficulties re-

ported included pain (87.1%), muscle spasm/tension (56.9%) and lack of lubrication (39.6%). A higher percentage of RA women responded affirmatively to the question, "Is sex still enjoyable?' than PRA women (p= 0.008) as summarized in Figure 7.

Is Sex Still Enjoyable?	RA (*n*=796)	PRA (*n*=64)
No	41.3%	56.3%
Yes	24.4%	28.1%
Sometimes	34.3%	15.6%

Figure 7. – Enjoyment of sexual activity reported by women of RA and PRA

DISCUSSION

Chronic urogenital pain disorders such as vulvodynia and BPS are common among women. Recent publications have focused on the prevalence of these disorders and the potential influence of genetics, physiological and sensory characteristics as well as immunological factors[26-28]. Nonetheless, there has been a lack of studies examining the role of aging in relation to symptoms and comorbidities in CUP. This study contributes unique insights into age related changes in a population of women diagnosed with CUP. The outcomes of this study may assist with the development of age appropriate management strategies.

This study is based on a retrospective review of data derived from a questionnaire specifically designed for pretherapy screening of women who had been diagnosed with vulvodynia and/or BPS. Given that a complete database of 1143 was used without exclusions, risk of bias was reduced however the results should not be generalized to other pain population groups. Numbers varied significantly between the two groups with 92% of the women forming the RA group and only 8% in the PRA group. However, the numbers of participants were sufficient to complete several statistically significant comparisons.

From the analysis of age distribution it is evident that women of all ages are affected by CUP. As has been highlighted in previous studies, the prevalence peaks among younger women of RA as reflected in the mean age of 30.6 years. This differs from earlier reports that suggested that prevalence of CUP increased with age[29-31].

The role of comorbidities in CUP is acknowledged in some classification systems and guidelines[3]. Conditions such asfibromyalgia, chronic fatigue syndrome, temporomandibular joint pain, headaches, anxiety, depression and IBS are frequently mentioned[3,32,33]. Some have suggested that these comorbidities are manifestations of different levels of centrally mediated sensitization[1,8,5]. However, it has been argued that most of the changes are mediated by peripheral mechanisms that in time give rise to centrally mediated sensitization[34].

This study, using a large sample of women, shows a significant connection between gynecological, urological and gastrointestinal symptoms in CUP patients. In the case of vulvodynia, the most common comorbidity was BPS and IBS. In the case of BPS the most common comorbidity was vulvodynia and IBS. The prevalence with which BPS and vulvodynia coexist may have significant implication for understanding the underlying mechanisms of these two CUP disorders[35]. The coexistence of these disorders may be linked on account of common embryological origins of the bladder and vulva, but in the case of the IBS, it may be due to the close proximity of the gastrointestinal tract to the reproductive and urinary systems and neural cross-talk[36].

Gastroenterological symptoms are also prevalent in women with CUP, with a third of women reporting IBS symptoms, including increased abdominal distension and bloating. The presence of gastroenterological symptoms more than doubled in the PRA group, a trend consistent with other research[37]. Urological indicators like dysuria, urge, frequency and BPS are common but show a significant rise in the PRA group and positively correlate with increased age. Functional changes are more prevalent in the PRA group, this may be due to morphological changes and to weakening structural supports for pelvic viscera, well illustrated by increased prevalence of stress incontinence.

Candidiasis is commonly reported as a chronic and recurrent problem for a large percentage of women[35,38].The incidence of candidiasis was significantly higher among women in the PRA group. However, the high number of associated gynecological variables reported raised some uncertainty as to whether they were confirmed by pathology tests or considered potential alternative causes of CUP. One of the shortcomings of this study was that there was no way of identifying whether the increase in reported candidiasis in the PRA group reflected a lifetime or point prevalence. Caution needs to be exercised in interpreting these findings.

CUP is also associated with a number of musculoskeletal comorbidities such as back pain and temporomandibular joint pain. PRA women report more than three times as many muscle, joint and bone conditions. The presence of headaches, anxiety and depression is common in the PRA group but not significantly different to the RA group. It is uncertain if neuromuscular disorders have a causal relationship or are secondary to CUP[39-42]. This study did not find the incidence of comorbid fibromyalgia and chronic fatigue to be as common as reported elsewhere[32,35,43].

Given the increased incidence of comorbidities in the PRA group, it is not surprising that older women reported sexual activity to be less enjoyable.

CONCLUSION

This study provides insight into two age differentiated profiles of women with CUP. The variables identified between groups may assist health care providers to develop better management strategies for women with CUP with their age and common comorbidities in mind[40,44,45]. An individualised approach involving gerontologists and urogynecologists with a special interest in age related changes and chronic pain special is recommended for women of PRA.

REFERENCES

1. Reed BD, Harlow SD, Sen A, Edwards RM, Chen D, Haefner HK. Relationship between vulvodynia and chronic comorbid pain conditions. Obstetrics and Gynecology. 2012, 120 (1), 145.
2. Peters KM, Carrico DJ, Kalinowski SE, A II. Prevalence of pelvic floor dysfunction in patients with interstitial cystitis. Urology. 2007, 70 (1), 16-8.
3. Bornstein J, Goldstein AT, Stockdale CK, Bergeron S, Pukall C, Zolnoun D et al. 2015 ISSVD, ISSWSH, and IPPS consensus terminology and classification of persistent vulvar pain and vulvodynia. Journal of Lower Genital Tract Disease. 2016, 20 (2), 126-30.
4. Jamieson DJ, Steege JF. The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. Obstetrics & Gynecology. 1996, 87 (1), 55-8.
5. Reed BD, Harlow SD, Sen A, Legocki LJ, Edwards RM, Arato N. Prevalence and demographic characteristics of vulvodynia in a population-based sample. Amer J Obstet Gynecol. 2012, 206.
6. Berry SH, Elliot MN, Suttorp M, Bogart LM, Stoto MA, Eggars P et al. Prevalence of symptoms of bladder pain syndrome/interstitial cystitis among adult females in the United States. Journal of Urology. 2011, 186 (2), 540-4.

7. Harlow BL, Kunitz CG, Nguyen RH, Rydell SA, Turner RM, MacLehose RF. Prevalence of symptoms consistent with a diagnosis of vulvodynia: population-based estimates from 2 geographic regions. American Journal of Obstetrics and Gynecology. 2014, 210 (1), 40. e1-. e8.
8. Arnold LD, Backmann GA, Rosen R, Rhoads GG. Assessment of vulvodynia symptoms in a sample of U.S. women: a prevalence survey with a nested case control study. American Journal of Obstetrics and Gynecology. 2007, 196 (2), 128-e1 - -e6.
9. Harlow BL, Stewart EG. A population-based assessment of chronic unexplained vulvar pain: have we underestimated the prevalence of vulvodynia? Journal of the American Medical Women's Association. 2003, 58 (2), 82-8.
10. Reed BD, Crawford S, Couper M, Cave C, Haefner HK. Pain at the vulvar vestibule: A web-based survey. Journal of lower genital tract disease. 2004, 8 (1), 48-57.
11. Reed BD, Haefner HK, Edwards L. A survey on diagnosis and treatment of vulvodynia among vulvodynia researchers and members of the International Society for the Study of Vulvovaginal Disease. The Journal of Reproductive Medicine. 2008, 53 (12), 921-9.
12. Rosenberg MT, Page S, Hazzard MA. Prevalence of interstitial cystitis in a primary care setting. Urology. 2007, 69 (4, Supplement), S48-S52.
13. Bachmann G, Rosen R, Kelly S, Rhoads G, Arnold L. Vulvodynia: characteristics and associations with co-morbidities and quality of life. Obstetrics and Gynecology. 2006, 107 (3), 617-24.
14. Tripp DA, Nickel JC, Wong J, Pontari M, Moldwin R, Mayer R et al. Mapping of pain phenotypes in female patients with bladder pain syndrome/interstitial cystitis and controls. European Urology. 2012, 62 (6), 1188-94.
15. Nguyen RH, Veasley C, Smolenski D. Latent class analysis of comorbidity patterns among women with generalized and localized vulvodynia: preliminary findings. Journal of Pain Research. 2013, 6, 303.
16. Clemens JQ, Markossian T, Calhoun EA. Comparison of economic impact of chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis/painful bladder syndrome. Urology. 2009, 73 (4), 743-6.
17. Xie Y, Shi L, Xiong X, Wu E, Veasley C, Dade C. Economic burden and quality of life of vulvodynia in the United States. Current Medical Research and Opinion. 2012, 28 (4), 601-8.
18. Nguyen RH, Turner RM, Rydell SA, Maclehose RF, Harlow BL. Perceived stereotyping and seeking care for chronic vulvar pain. Pain Med. 2013, 14.
19. Reissing ED, VanZuylen H. Psychosocial management of the overactive pelvic floor. In: Padoa A, Rosenbaum T, editors. The overactive pelvic floor: Springer; 2015, p. 321-33.
20. Sherburn M, Guthrie JR, Dudley EC, O'connell HE, Dennerstein L. Is incontinence associated with menopause? Obstetrics & Gynecology. 2001, 98 (4), 628-33.
21. Morse LR, Battaglino RA, Widrick JJ. Menopause and the musculoskeletal system. Pain in women: Springer, 2013, p. 255-75.
22. Chila AG, Association AO. Foundations of osteopathic medicine. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2010.
23. Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical practice guidelines on menopause: An executive summary and recommendations. Journal of Mid-Life Health. 2013, 4 (2), 77.
24. Edwards D, Panay N. Treating vulvovaginal atrophy/genitourinary syndrome of menopause: how important is vaginal lubricant and moisturizer composition? Climacteric. 2016, 19 (2), 151-61.
25. Australian Bureau of Statistics. Australian social trends. Canberra, ABS, 2005.
26. Vehof J, Zavos HM, Lachance G, Hammond CJ, Williams FM. Shared genetic factors underlie chronic pain syndromes. PAIN®. 2014, 155 (8), 1562-8.
27. Harlow BL, He W, Nguyen RH. Allergic reactions and risk of vulvodynia. Annals of Epidemiology. 2009, 19 (11), 771-7.
28. Hampson JP, Reed BD, Clauw DJ, Bhavsar R, Gracely RH, Haefner HK et al. Augmented central pain processing in vulvodynia. The Journal of Pain, 2013, 14 (6), 579-89.
29. Arnold LD, Bachmann GA, Kelly S, Rosen R, Rhoads GG. Vulvodynia: characteristics and associations with co-morbidities and quality of life. Obstetrics and Gynecology. 2006, 107 (3), 617.
30. Reed BD, Haefner HK, Punch MR, Roth RS, Gorenflo DW, Gillespie BW. Psychosocial and sexual functioning in women with vulvodynia and chronic pelvic pain. A comparative evaluation. The Journal of Reproductive Medicine. 2000, 45 (8), 624-32.
31. Sandownik LA. Clinical profile of vulvodynia patients: a prospective study of 300 patients. The Journal of Reproductive Medicine. 2000, 45, 679-84.
32. Nickel JC, Tripp DA, Pontari M, Moldwin R, Mayer R, Carr LK et al. Interstitial cystitis/painful bladder syndrome and associated medical conditions with an emphasis on irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome. The Journal of urology. 2010, 184 (4), 1358-63.
33. Hanno PM, Erickson D, Moldwin R, Faraday MM. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome: AUA guideline amendment. The Journal of Urology. 2015, 193 (5), 1545-53.
34. Jantos M. Fascia, the new frontier in anatomy. Pelviperineology. 2016, 35 (1), 2.
35. Mullins C, Bavendam T, Kirkali Z, Kusek JW. Novel research approaches for interstitial cystitis/bladder pain syndrome: thinking beyond the bladder. Translational Andrology and Urology. 2015, 4 (5), 524-33.
36. Cuckow PM. Embryology of the urogenital tract. In: Mouriquand JP, GearhartRichard C, RinkPierre DE, editors. Pediatric urology 2nd ed. Philadelphia: W.B. Saunders, 2010. p. 1-10.
37. Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. The American Journal of Gastroenterology. 2011, 106 (9), 1582-91.
38. Sobel JD. Vulvovaginitis. In: Goldstein AT, Pukall CF, Goldstein I, editors. Female sexual pain disorders: evaluation and management. West Sussex: Wiley-Blackwell, 2009, p. 95-104.
39. Romão AP, Gorayeb R, Romao GS, Poli-Neto OB, Dos Reis FJ, Rosa-e-Silva JC et al. High levels of anxiety and depression have a negative effect on quality of life of women with chronic pelvic pain. International Journal of Clinical Practice. 2009, 63 (5), 707-11.
40. Sadownik LA. Etiology, diagnosis, and clinical management of vulvodynia. International Journal of Women's Health. 2014, 6, 437-49.
41. Chuang Y-C, Weng S-F, Hsu Y-W, Huang CL-C, Wu M-P. Increased risks of healthcare-seeking behaviors of anxiety, depression and insomnia among patients with bladder pain syndrome/interstitial cystitis: a nationwide population-based study. International Urology and Nephrology. 2015, 47 (2), 275-81.
42. American Psychiatric Association. Somatic symptom and related disorders. Diagnostic and statistical manual of mental disorders. Arlington, VA: American Psychiatric Publishing; 2013, p. 309-28.
43. Lee J, Ellis B, Price C, Baranowski A. Chronic widespread pain, including fibromyalgia: a pathway for care developed by the British Pain Society. British journal of anaesthesia. 2014, 112 (1), 16-24.
44. Engeler DS, Baranowski AP, Dinis-Oliveira P, Elneil S, Hughes J, Messelink EJ et al. The 2013 EAU Guidelines on Chronic Pelvic Pain: Is Management of Chronic Pelvic Pain a Habit, a Philosophy, or a Science? 10 Years of Development. European Urology. 2013, 64 (3), 431-9.
45. Shah N, Ginzburg N, Morrissey D, Whitmore K. Update in diagnosis and treatment of chronic pelvic pain syndromes. Curr Bladder Dysfunct Rep. 2015, 10 (3), 198-206.

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Opinion

Are 'psychiatric' findings in patients with Chronic Pelvic Pain primary or secondary?

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Abstract: The often accepted view that CPP is not curable, may be psychological, is the background to the patient histories which form the main body of this paper. These are taken from a book for patients "Unlocking the Female Pelvic Floor" by Peter Petros, Joan McCredie and Patricia Skilling. As such, the descriptions are simplified, but clear. The theme of the book is "A conspiracy of Silence"

Key words: Chronic pelvic pain; Psychiatric; TFS ligament repair; Posterior fornix syndrome.

INTRODUCTION

The 2005 Cochrane Review summarizes Chronic Pelvic Pain as follows "*Chronic pelvic pain (CPP) is common in women in the reproductive and older age groups and causes disability and distress. Often investigation by laparoscopy reveals no obvious cause for the pain. As the pathophysiology of chronic pelvic pain is not well understood its treatment is often unsatisfactory and limited to symptom relief. Currently the main approaches to treatment include counselling or psychotherapy, attempts to provide reassurance by using laparoscopy to exclude serious pathology, progestogen therapy such as medroxyprogesterone acetate, and surgery to interrupt nerve pathways*"[1].

The association between pain, depression and psychological disturbance is well described[2,3].

Traditionally hysterectomy has been recommended as a cure for chronic pelvic pain by a significant body of specialist opinion[4]. The present trend to psychiatric evaluation and treatment appears to have arisen as a consequence of previous studies which showed a high correlation between CPP and psychiatric disturbances[5,6].

No mention is made by Cochrane[1] of Integral Theory related concepts for pain[7], that CPP frequently co-occurs with urgency, nocturia, abnormal emptying and anorectal dysfunctions as part of the 'Posterior Fornix Syndrome". This was first reported in 1993[7]. Nor is there any mention of the substantial cure rates achieved with posterior sling surgery for pain, bladder and bowel dysfunctions[8-15].

This often accepted view that CPP is psychological and not curable, is the background to the patient histories which follow. These are taken from a book for patients "Unlocking the Female Pelvic Floor" by Peter Petros, Joan McCredie and Patricia Skilling. As such, the descriptions are simplified, but clear. The theme of the book is "A conspiracy of Silence"[16].

Excerpts from the patient book "Unlocking the Female Pelvic Floor" by Peter Petros, Joan McCredie and Patricia Skilling.

The Back Ligaments (uterosacral).

The back ligaments when damaged can cause prolapse of the uterus, which descends down the vagina as a firm "lump". If the tissue damage is in the middle or lower part of the vagina, the patient may complain of a soft "lump" called a rectocoele. However, not all prolapses have symptoms. The main symptoms of back ligament looseness are urgency, getting up at night to pass urine more than twice 'nocturia', low dragging pain in the lower abdomen, pain on deep penetration with intercourse, "vulvodynia, (hypersensitivity or "burning" at the entrance of vagina), inability to empty the bladder properly, constipation and sometimes faecal incontinence. However, quite major symptoms can occur with only minimal prolapse of the uterus.

Characteristics of pelvic pain caused by back ligament (uterosacral) looseness

- Almost invariably occurs with other symptoms, specifically urgency, nocturia, abnormal emptying.
- Low abdominal 'dragging' pain, usually one side, often right-sided.
- Low sacral pain (pain near the tailbone)- present in 50% of cases.
- Pain on deep penetration with intercourse.
- Low abdominal ache the next day after intercourse.
- Pain worsens during the day and is relieved by lying down.
- Pain is reproduced on pressing the cervix or the back wall of the vagina if a patient has had a hysterectomy.
- Tiredness- worsening during the day.
- Irritability- worsening during the day

CASE REPORTS

Nocturia, urgency, abnormal emptying and pelvic pain caused by looseness in the back ligaments

Mrs LM was 53 years old. She stated, *"get up 4-5 times a night. I find this very tiring as I have to work next day. I have a dragging pain on the right side which can be quite distracting by the end of the day. I am always going to the toilet at work. My urine dribbles away after I stand up and I often wet the toilet seat. I have problems with bladder infections. My first GP did a whole lot of xrays, a CT scan, blood tests for the pain. I went to a gynaecologist who put a tube into my tummy and found nothing. She said that she couldn't find anything wrong and she sent me to a psychiatrist, because she thought the pain was in my head. She said there was nothing wrong psychologically. I saw many GPs and several specialists about the bladder. They gave me tablets to stop the bladder from working so frequently but these made my emptying worse and they gave me a dry mouth as well, so I had to stop taking them. They said they couldn't do anything else for me. One even said it might all be in my head. Mostly they said I had to learn to put up*

with these symptoms, because they were incurable. I came here because I felt a lump coming out." Mrs LM had symptoms typical of looseness in the back ligaments. When we examined her, we noted that her uterus was protruding outside the vagina. We inserted a TFS "minisling" (Tissue Fixation System, Adelaide, South Australia) to repair her back ligaments (cardinal/uterosacral). This repaired the prolapse and tightened the vaginal membrane. It was minimal surgery performed entirely from the vagina. Mrs LM required only an overnight stay in hospital and she returned to work in 7 days. When reviewed at 9 months, she was getting up only once per night to empty her bladder. She said that her low abdominal pain was still present but was 90% better and it rarely bothered her now. Her bladder emptying also was not entirely cured but had improved significantly and she had not had any bladder infections since the operation.

Pain during intercourse and bowel problems caused by back ligament looseness

Mrs RM was a hard-working 47 year old mother of 2 who worked in a Nursing Home. She stated:

"I always have urgency to empty my bowel but I am also frequently constipated. I get up 3-4 times a night to pass urine. I have problems emptying my bladder. My worst problem is that I can't have sex any more. Almost every time I have intercourse, my bowels open. It is so horrible. My husband is very understanding but I am sure he is as distressed as I am. I always have pain on deep penetration. Often I have a dragging pain low down on my right side which seems to get worse by the end of the day".

She had 2 teenage sons and helped her husband in his business in her spare time. At one stage she had sought medical advice, was told she could not be helped and that maybe a psychiatrist could help her learn how to deal with the pain. After confiding her problem to a close a friend who had been to the clinic, she was persuaded to make an appointment. Many patients came to the clinic in this way.

Her symptoms of nocturia and abnormal emptying indicated damage in the back ligaments. When we examined her, there was very minimal prolapse. As Mrs RM's problems were complex, we recommended that we repair only the back ligaments and then we would re-assess her. We advised her that she could expect a cure rate of 80% for some of her symptoms. As for the urge to empty her bowel and constipation, these could be due to many other causes, so we were reluctant to predict a cure for these symptoms.

We inserted a TFS "minisling" to repair the back ligaments. Mrs RM was discharged the next day with very little pain and she went back to work the following week. She attended with her husband for the post-operative visit. She was smiling and confident. She could not contain her excitement and said to the secretary, *"I'm cured. It's all gone"*. In the privacy of the consulting room, she reported cure of all her bowel symptoms and a major improvement in her other symptoms. Her husband said, " you don't know what a burden has been lifted from our lives". Mrs RM remained cured at last review 4 years later. Mrs RM is a good example of the passive "Conspiracy of Silence", a reticence to discuss this condition, even between man and wife. Without input from her friend, Mrs RM is unlikely to have sought assistance. Even with patients who do come to see us, faecal soiling is rarely volunteered in a face to face situation, another "Conspiracy of Silence", this time, even with her doctor. This is why it is important for patients to take the questionnaire (a series of printed questions) home and to answer the questions in their own time. It is so much easier to write it down, than to say it as it becomes almost anonymous.

Severe Pelvic Pain Caused by Back ligament looseness

Mrs D was a 34 year old science teacher from London, UK. She attended with severe pain in the right side of her abdomen. Some years previously, she had attended a London hospital where the Professor had created an international reputation using psychological tests to prove that such pain was psychological in origin. Mrs D had read widely on the subject of pain. Her facial expression indicated a person who was guarded. Her face lit up after she answered positively to the following questions because she suddenly became aware that we knew what her problem was.

- Do you have pain on deep penetration with intercourse?
- Do you get up more than twice per night to pass urine?
- Do you have problems emptying your bladder?
- Do you have urgency?"

Positive answers to at least some symptoms other than pain are required before we can predict that the pain is caused by damage to the back ligaments. There are, after all, many other causes of chronic pelvic pain in the 30 plus age group, for example, endometriosis, infection in the Fallopian tubes, problems with large intestine, to name just a few. This is what she said one week after her pain was cured by a small operation which tightened her back ligaments. *"I was almost suicidal after interminable attacks of pain on my right side. It has now been a week since the operation and I feel like a rabbit that has been released from a trap. My mind keeps scanning up and down my body searching for the pain which for so long has been my centre and my focus."*

Postscript. Mrs D. wrote to the Professor in England and told him her story. She sent him some published scientific articles which described cure of urgency, frequency, nocturia, and pelvic pain.

He could not understand the relationship between all these symptoms, or that her pelvic pain could be cured in such a simple way. He wrote back and said "but these articles are about bladder problems".

He just did not understand the ramifications of the "Integral System" which our clinic was applying. It is difficult even for the most learned person to associate lower abdominal pain with apparently unrelated symptoms such as urge and frequency which are thought to arise from the bladder.

Vulvodynia – Pain and Burning at the Entrance to the Vagina ("Vulvodynia") Caused by Back Ligament Looseness

- There are many causes of "vulvodynia", including skin conditions. The type we are describing is associated with low abdominal pain, urgency, nocturia and abnormal bladder emptying.

Mrs P was 49 years old. She had chronic pelvic pain and she requested referral to the clinic because she had heard that we were achieving good results in patients with pelvic pain. Her General Practitioner, an empathetic and caring man, rang the doctor before she arrived and asked that *we "handle her very carefully"* as she was severely disturbed psychologically, that this was the reason for her pain and there was nothing anyone could do for her. The first impression we had of this lady did indeed fit the description of her GP. Her face was contorted, she spoke rapidly and with obvious anxiety. She had visited many specialists over the years for her pain. She had undergone several diagnostic laparoscopies (a type of telescope inserted into the abdomen to view the uterus and ovaries), even a hysterectomy and had attended a pain clinic. None of these treatments had helped her pain. The consensus

from other specialists as reported to the GP was that her problem was psychological. Her replies to the questionnaire gave the first hint that this woman may have a physical cause for her problem, damage to her back ligaments. She woke 6 times per night to empty her bladder (nocturia), wore pads continually as she wet 6 times per day (urge incontinence) and had difficulties emptying her bladder. She also had faecal incontinence. We asked her if she had told her GP about her bladder and bowel problems. She said she had only consulted him about the burning pain around her vagina and anus. She said that her vagina was so tender that she couldn't have sexual intercourse and sometimes had problems sitting. Examination revealed a moderate prolapse of the back part of her vagina (apex). The entrance to the vagina was hypersensitive- she recoiled when gently tested with a cotton bud, the classical test for "vulvodynia" (pain at the entrance of the vagina). We did not claim that we could cure this lady's pain, as there are many other causes for pelvic pain. Nevertheless, it was explained that her vaginal prolapse needed to be fixed and that there was a strong possibility that some of her symptoms would also improve with a sling inserted into the back part of her vagina, a fairly minor day-care procedure. The first thing we noticed at the 6 week post-operative visit was the absence of tension in her face. She was smiling and calm. Her pain was gone, as was her urgency and faecal incontinence. Her nocturia had reduced to 2 per night and her bladder emptying was "60% improved".

Pelvic Pain Commencing Soon After the First Period Caused by Back Ligament Looseness.

Miss PN was 23 years old. She complained of severe pelvic pain which began some months after her first period at the age of 15. The pain was worse at period time. She had already undergone two laparoscopies where nothing was found. The doctor thought her problem was psychological and she had been referred to a psychiatrist. She came to the clinic with her mother, who was certain that her daughter was not only psychologically normal but there was some physical reason for the pain. On assessment, it was clear to us that Miss PN had looseness in her back ligaments dating from birth, a looseness exacerbated by hormones from her periods. The ligaments were just not strong enough. She had symptoms of urge and nocturia. These symptoms were all worse at period time. We explained that at period time, the brain secretes a hormone which relaxes the collagen fibres in the cervix sufficiently for the menstrual blood to exit the uterus. This relaxation also loosens the ligaments which are attached to the uterus, causing her symptoms of pain and urge to worsen. Miss PN did not respond to the pelvic floor exercises which were prescribed prior to surgery but had a very good result when the back ligaments were surgically tightened with a minor day-care operation. No tapes were used and this did not affect her ability to have children in any way.

Hysterectomy for Lower Backache and Pelvic Pain Caused by Back Ligament Looseness

Mrs JMK developed chronic lower back pain and pain with intercourse after a difficult forceps delivery of her second child 50 years ago when she was 27 years old. The pain as described earlier was constant and debilitating. At age 35, a specialist gynaecologist advised hysterectomy. This caused a major emotional shock, as she wished to have more children. She was persuaded to proceed with the operation. The operation did not go so well initially. She needed a blood transfusion during the surgery. Because of continuing anaemia, she remained weak for another 6 months. Although the physical pain had improved, Mrs JMK was mentally traumatized by the hysterectomy for some time afterwards. By the time she was 65 years old, the chronic pelvic pain and lower backache had returned, along with urgency, nocturia and prolapse of the vagina and bladder. We attributed all this to age-related loss of collagen and weakening of the back ligaments, a long-term problem in many patients who have had hysterectomy. Ligament reconstruction cured the prolapse and greatly improved the symptoms.

DISCUSSION

In the patient book, we discussed the issues raised by these cases as 'comments".

Comment on hysterectomy. Removal of the uterus is a major operation. It is not always complication-free and may have long-term physical and psychological consequences for some women. Fortunately, minor treatments for uterine haemorrhage, for example, intrauterine devices which slowly leach progesterone-type hormones, are now available.

Comment on pain with intercourse. The back ligaments form an important support for the pain nerves contained inside them. Earlier we discussed how a loose ligament will not support nerve fibres. As the penis thrusts into the back part of the vagina, it will cause pain if it stretches the unsupported nerve fibres.

Comment on psychiatric treatment of pain. Like the case of Mrs D, this lady's problem raises many issues about the attitudes of doctors, patients, even modern medicine itself. Many doctors, including this lady's General Practitioner, were not aware that this type of pelvic pain is associated with loose ligaments. Because of the scientific nature of medicine, if an obvious cause cannot be found, the doctor seeks another cause, usually "psychological".

The concept of psychological disturbance as the root cause of a medical condition can be traced back to Sigmund Freud himself. However, any type of chronic pain is sufficient to unsettle even the most rational person and such patients do become psychologically disturbed, often severely, as we saw in several of the histories. According to our experience, it is the pain which causes the psychological disturbance, not the other way round. Whether it be Freud's influence, or exhaustion of all known physical causes, attributing these difficult problems to a psychological cause is an important contributor to the "Conspiracy of Silence". No woman wishes to be labelled a "nut case". As soon as a psychological causation has been hinted at, she becomes silent. She remains so for all subsequent medical consultations, another contributor to the "Conspiracy of Silence". Our experience is that modern women are far too busy to complain about symptoms they do not have.

Comment on whether it be Freud's influence, or exhaustion of all known physical causes... There is another possibility, a new discovery which can address these so-called "incurable" problems of incontinence and pelvic pain. That is why we wrote this book, to inform women that a cure for these conditions already exists and to use this knowledge, especially the patient histories, to empower them when they choose to seek treatment for such problems.

Comment on the characteristics of 'Vulvodynia'. Vulvodynia which has no apparent local cause (such as a skin condition) is often expressed by a burning pain over the entrance of the vagina and anus with extreme sensitivity on touching, often associated with dragging lower abdominal pain and sometimes, painful bladder conditions.

Comment on causes of vulvodynia. We do not claim that all vulvodynia patients have this cause. However, if other symptoms of back ligament looseness such as nocturia, abnormal bladder emptying, and urgency are grouped with the vulvodynia, there is a strong possibility that this pain can be improved in many patients with a posterior sling for repair of the back ligaments.

Tampon test. A simple test to see if the back ligaments are causing the problem. We have found that a large tampon inserted into the back part of the vagina as a test can often instantaneously relieve the sensitivity and pain in the vulva. Generally such women also have other back ligament symptoms.

Conflicts. None

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REFERENCES

1. Stones W, Cheong YC, Howard FM. Interventions for treating chronic pelvic pain in women. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD000387. DOI: 10.1002/14651858.CD000387. From the Cochrane Menstrual Disorders and Subfertility Group
2. Latthe P, Luciano, L, Gray R, Hills R, Khan K: Factors predisposing women to chronic pelvic pain: systematic review BMJ, doi:10.1136/bmj.38748.697465.55 (published 16 February 2006)
3. Walker E, Katon W, Harrop-Griffiths J, Holm L, Russo J, Hickok LR. Relationship of chronic pelvic pain to psychiatric diagnoses and childhood sexual abuse. Am J Psychiatry. 1988 Jan; 145 (1): 75-80.
4. Te Linde RW, Mattingly RF. Operative Gynecology. 4th Ed, Eds Te Linde RW. Mattingly RF JP Lippincott Company, Phil 1970; 469-533.
5. Beard R, Reginald P, Wadswoxth 1. Clinical features of women with chronic lower abdominal pain and pelvic congestion. Br J Obstet Gynaecol 1988 95: 153-161.
6. Beard R. Reginald P, Pearce S. Psychological and somatic factors in women with pain due to pelvic congestion. Br J. Obstet Gynaecol 1988: 245: 413-421.
7. Petros PE & Ulmsten U. An Integral Theory and its Method, for the Diagnosis and Management of female urinary incontinence. Scand J Urolo Nephrol 1993; 27 (153): 1-93.
8. Petros PE, Ulmsten U. The posterior fornix syndrome: a multiple symptom complex of pelvic pain and abnormal urinary symptoms deriving from laxity in the posterior fornix. Scand J Urol Nephrol 1993; 27 (153): 89-93.
9. Farnsworth BN. Posterior intravaginal slingplasty (infracoccygeal sacropexy) for severe posthysterectomy vaginal vault prolapse – a preliminary report on efficacy and safety. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13: 4-8.
10. Goeschen K, Gent HJ. Das posteriore Fornixsyndrom. Frauenarzt 2004; 45: 104-112.
11. Müller-Funogea A. Posterior fornix syndrome: a new urogynecologic entity. Ethiopathogenesis and proposal for surgical therapy. Thesis, Medical University of Bucharest, Romania 2014.
12. Caliskan A, Goeschen K, Zumrutbas AE. Long term results of modified posterior intravaginal slingplasty (P-IVS) in patients with pelvic organ prolapse. Pelviperineology 2015; 34: 94-100.
13. Goeschen K. Posterior Fornix Syndrome: Comparison of original (2004) and modified (2015) post-PIVS anatomic and symptomatic results - a personal journey. Pelviperineology 2015; 34: 85-91.
14. Inoue H, Kohata Y, Sekiguchi Y, Kusaka T, Fukuda T, Monnma M. The TFS minisling restores major pelvic organ prolapse and symptoms in aged Japanese women by repairing damaged suspensory ligaments 12-48 month data, Pelviperineology 2015; 34: 79-83.
15. Liedl B, Goeschen K, Durner L. Current treatment of pelvic organ prolapse correlated with chronic pelvic pain, bladder and bowel dysfunction. Curr Opin Urol 2016; 12: (in press).
16. Petros PE, McCredie JP, Skilling PM Chapter 6, "Back Ligaments" from "Unlocking the Female Pelvic Floor" Amazon.com pp 47-63.

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INVITED COMMENT
Persuasive medical tools to mitigate against patients psychologization

The field of cognitive sciences is affirming the approach of "embodied cognition" which proposes that our mental states are shaped by the characteristics and the state of our physical body. This perspective, besides inflicting a further blow to Cartesian dualism, contributes to consolidating the view of the chain of causality going from the body to the mind at the expense of the chain of events going from the mind to the body. This conception is in line with the implicit warning in Petros and colleagues' work: it is likely to fall into the trap of fundamentalist psychology if we neglect that a sick and suffering body (especially a chronically sick one), is more likely to produce a debilitated, confused and sick mind, rather than vice versa. Why then, as in Mrs D's report, are there some professors that persist in seeking psychological explanations of pain before excluding any possible physiological variables? And what could be an antidote to this (causal) "perversion"?

Our hypothesis is that the most fascinating and insidious psychologization is of the Freudian type, because with its sexual and anal conceptualization of psychopathology, it easily convinces women suffering from pelvic floor disorders. The concepts of dirtiness, feces, incontinence and vaginal penetration pain, find an easy and misleading resonance with psychoanalytic language and representations. If this resonance is then combined with the sense of impotence and despair caused by doctors who claim to have excluded all the possible physiological causes of pain, and the feelings of guilt and embarrassment that the women associate with these problems, then the temptation to "psychologize" becomes irresistible. Any antidote to this view must exploit the same mechanisms that make the Freudian conceptualization so fascinating. It is therefore necessary to create and disseminate (capitalizing on social media), evidence-based metaphors, for example, the uterus represented as a "lump" (that clings to the vagina) and other short and engaging clinical narratives that can attract through resonance women who otherwise would risk falling victim to the "conspiracy of silence."

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Review

Update on treatment aspects of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)

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Abstract: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a frequent disease affecting men of all ages. Chronic prostatitis can significantly impair quality of life. Symptoms attributed to CP/CPPS are heterogenous. Patients with CP/CPPS present an individual etiological and symptomatology profile resulting in an unique clinical phenotype. Research efforts were made to define multimodal therapeutic strategies addressing the wide array of signs and symptoms. A clinical phenotyping system has been suggested clinically directive to focus on the symptoms of the patients. This system contains six major complain domains of CP/CPPS patients: urinary, psychosocial, organ specific, infection, neurologic and tenderness of skeletal muscles (UPOINT). Recently, the system was modified by adding the sexual dysfunction as a domain to create UPOINTS. Promising results have currently been reported from multimodal approaches of CP/CPPS therapy as it aims to offer a personalized combination therapy.

Key words: Prostatitis; Chronic pelvic pain syndrome; UPOINTS; Phenotype; Treatment.

INTRODUCTION

According to the National Institutes of Health (NIH) 1995 classification Chronic Prostatitis/ Chronic Pelvic Pain Syndrome (CP/CPPS) represents category III of prostatitis with no bacteria detectable in urine or expressed prostatic secretion. CP/CPPS can be inflammatory with an elevated white cell count in prostatic secretion (NIH IIIa) or non-inflammatory with no white cells in the prostatic secretion (NIH IIIb)[1]. The leucocyte count does not correlate with the severity of symptoms[2]. The worldwide prevalence of CP/CPPS is between 2.7 and up to 16%[3,4]. CP/CPPS has a significant negative impact on quality of life[5]. In a large European study 21 % of patients with chronic pain syndrome had a depression. 19% of patients lost and 13% changed their occupation because of pain[6]. CP/CPPS is likely to have different causal determinants and different disease progression pathways[7]. It has been suggested that the cause may be infectious, autoimmunal, hormonal, psychological or associated with an intraprostatic urinary reflux. CP/CPPS may cause anxiety, impair emotional function, and cause insomnia and fatigue[5,8]. Genetic components are evident as family clusters and an accumulation of pain syndromes in twins have been observed[9,10]. An upregulation of the corticotropin-releasing hormone has been suggested as a hormonal risk factor. Chlamydia trachomatis[11], Ureaplasma urealyticum[12], Mycoplasma hominis[13], Trichomonas vaginalis[14], Viruses[15], Candida[16] and parasites have been described to be associated with the infectious forms of CP/CPPS. Monotherapy strategies for CP/CPPS have been shown to be ineffective[17]. These discouraging results show that the complex symptom array of CP/CPPS patients cannot be targeted by a single therapeutic agent. The UPOINT/UPOINTS system has been proposed in order to classify patients with CP/CPPS clinically and to offer patients a symptom related therapy.

Recently a possible etiological pathway has been described that was recognized by many experts. According to this mechanism, an unfavorable event (trauma, infection etc.) leads to an injury-response of the tissue. Inflammation and the upregulation of cytokines may lead to additional organ damage involving nerves, blood vessels, smooth muscles and the loss of bladder epithelial integrity. The resulting pain may produce contraction of pelvic smooth and skeletal muscles, finally leading to lower urinary tract symptoms, ejaculatory pain and pain in other regions such as back and abdomen. Prolonged pain may sensitize central and peripheral nervous systems and finally cause hyperalgesia and allodynia. Chronic pain may have damaging psychological effects and cause a depressive state[18,19].

METHODS

We performed a selective literature search for chronic prostatitis/chronic pelvic pain syndrome.

RESULTS

As there are no biomarkers of CP/CPPS to guide therapy the validated outcome index is the National Institute of Health Chronic Prostatitis Index (NIH-CPSI)[20]. A clinical phenotyping was proposed to classify patients with CP/CPPS to offer therapy according to the individual complains. The UPOINT system was validated in several clinical trials[21,22]. A strong correlation between the number of positive UPOINT domains and the total score of the NIH-Chronic Prostatitis Symptom Index (CPSI) measured in patients was shown. Shoskes et al.[21] first demonstrated that a majority (84%) of patients treated based on the UPOINT phenotype had a clinical improvement of CP/CPPS symptoms measured by an at least 6-point improvement in the total score of the NIH-CPSI symptom questionnaire. This strategy was followed in other studies[22].

In a large German-Italian study, a total of 1,227 patients with CP/CPPS were evaluated. The correlation between the UPOINT and CP/CPPS was confirmed for the total and for the Italian subgroup whereas, in the German subgroup the correlation was achieved only after sexual dysfunction (ED) was added as a domain to create UPOINTS[23]. The authors suggested that adding sexual dysfunction to the domain system may be helpful, as sexual dysfunction is a frequent complaint of patients suffering from CP/CPPS. Two additional studies from China and Canada supported this observation[24,25]. The prevalence of sexual dysfunction is 65%[26]. CP/CPSS has been clearly shown as a risk factor of ED[27].

Several therapy options are available for each UPOINT domain. In a prospective randomised placebo-controlled study Pollen extract (Cernilton) was shown to significantly improve the total score of the NIH-CPSI as well as the pain and the quality of life domains in patients with inflammatory CP/CPPS (NIH IIIa)[28]. The treatment with Pollen extracts can be more helpful when supplements are added[29]. Alpha-receptor blockers alone and with Pollen extract improve urinary flow parameters in patients with prostatitis[30,31]. The probability of the beneficial effects of alpha-receptor blockers is higher in the presence of storage and voiding symptoms in CP/CPPS patients (U in UPOINT)[31]. Even though 5-alpha-reductase

inhibitors are not recommended in general (EAU Guidelines 2017) some studies showed a tendency to improve symptoms. Phosphodiesterase-5 inhibitors may help to improve sexual function. Antidepressants may be effective to treat the psychological domain of the UPOINT system. Xia et al., reported that an antidepressive therapie with Fluoxetin not only had a positive effect on the depression score but also significantly improved the quality of life and urinary domains of CPSI[32]. Special physiotherapy treatment options such as myofascial physical therapy may be helpful as it releases tightness of soft tissue and helps to release pain[33]. Acupuncture has been shown to be an effective therapy especially in decreasing pain[34,35]. According to the EAU guidelines NSAIRs have a moderate treatment effect. Celecoxib was shown to be significantly beneficial and improved the pain subscore, the QoL subscore and the total NIH-CPSI score in placebo controlled clinical studies[36].

In placebo-controlled studies antibiotics were proven not to significantly improve the symptoms of CP/CPPS if no infection in prostate is present[37]. In contrast with these findings a network meta-analysis showed a significant benefit of antibiotic treatment in total symptom, pain, voiding and QoL scores in CP/CPPS patients[38]. In the EAU guidelines the use of quinolones or tetracyclin for a treatment period of at least six weeks is recommended if an antibiotic treatment is applied (EAU Guidelines 2017). It has been assumed that an antibiotic treatment helps in cases of an infectious cause of CP/CPPS when microbiological cultures failed to detect uropathogens that are present in the prostatic fluid. In 8% of patients with suggested CP/CPPS positive prostatitis cultures can be found[36].

Investigations show that treatment of some UPOINT(S) domains may be beneficial for other domains. In a large Italian study patients with CP/CPPS NIH-III were treated with alpha-receptor blocker alfuzosin and S repens extract alone or in combination with supplements lycopene and selenium[22]. Only after a positive microbiological culture of prostate-specific specimen an antibiotic ciprofloxacin or azithromycin was added to the therapy. Although no therapy for the erectile dysfunction was given 54% of patients had an improvement of sexual function. The authors suggested a two-step algorithm for CP/CPPS patients. As a first treatment option a combination of an alfa-blocker, phytotherapy (pollen extract) optional with supplements (lycopene and selenium) and in the case of proven or highly suspected infection an antibacterial agent. In case of persistent complains antidepressant, anxiolytics, myorelaxants and other agents can be added as a second step to the treatment.

CONCLUSION

The recent treatment strategies of CP/CPPS take into account the multimodal origin of this disease as well as its heterogenous phenotype. There are diverse options available for patients and treating doctors to achieve significant symptom relief. Clinical results are promising so far. Based on the modern understanding of the etiology, future investigations may provide further therapeutic options in a multimodal setting[39]. However, treatment of CP/CPPS remains challenging and requires from the treating doctor fundamental knowledge in different fields of modern medicine.

REFERENCES

1. Nickel JC, Alexander RB, Anderson R, Berger R, Comiter CV, Datta NS, Fowler JE, Krieger JN, Landis JR, Litwin MS, McNaughton-Collins M, O'Leary MP, Pontari MA, Schaeffer AJ, Shoskes DA, White P, Kusek J, Nyberg L; Chronic Prostatitis Collaborative Research Network Study Groups. Category III chronic prostatitis/chronic pelvic pain syndrome: insights from the National Institutes of Health Chronic Prostatitis Collaborative Research Network studies. Curr Urol Rep. 2008 Jul, 9 (4), 320-7.
2. Schaeffer AJ. Epidemiology and demographics of prostatitis. Andrologia. 2003 Oct; 35 (5), 252-7.
3. Krieger JN, Ross SO, Riley DE. Chronic prostatitis: epidemiology and role of infection Urology. 2002 Dec; 60 (6 Suppl), 8-12.
4. Marszalek M, Wehrberger C, Hochreiter W, Temml C, Madersbacher S. Symptoms suggestive of chronic pelvic pain syndrome in an urban population: prevalence and associations with lower urinary tract symptoms and erectile function. J Urol. 2007 May, 177 (5), 1815-9.
5. Baranowski AP. Chronic pelvic pain. Best Pract Res Clin Gastroenterol. 2009, 23 (4), 593-610.
6. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain. 2006 May, 10 (4), 287-333.
7. Nickel JC, Shoskes DA. Phenotypic approach to the management of the chronic prostatitis/chronic pelvic pain syndrome. BJU Int. 2010 Nov; 106 (9), 1252-63.
8. Chuang YC, Weng SF, Hsu YW, Huang CL, Wu MP. Increased risks of healthcare-seeking behaviors of anxiety, depression and insomnia among patients with bladder pain syndrome/interstitial cystitis: a nationwide population-based study. Int Urol Nephrol. 2015 Feb, 47 (2), 275-81.
9. Vehof J, Zavos HM, Lachance G, Hammond CJ, Williams FM. Shared genetic factors underlie chronic pain syndromes. Pain. 2014 Aug; 155 (8), 1562-8.
10. Tunitsky E, Barber MD, Jeppson PC, Nutter B, Jelovsek JE, Ridgeway B. Bladder pain syndrome/interstitial cystitis in twin sisters. J Urol. 2012 Jan; 187 (1), 148-52.
11. Poletti F, Medici MC, Alinovi A, Menozzi MG, Sacchini P, Stagni G, Toni M, Benoldi D. Isolation of Chlamydia trachomatis from the prostatic cells in patients affected by nonacute abacterial prostatitis. J Urol. 1985 Oct; 134 (4), 691-3.
12. Weidner W, Brunner H, Krause W. Quantitative culture of ureaplasma urealyticum in patients with chronic prostatitis or prostatosis. J Urol. 1980 Nov; 124 (5), 622-5.
13. Brunner H, Weidner W, Schiefer HG. Studies on the role of Ureaplasma urealyticum and Mycoplasma hominis in prostatitis. J Infect Dis. 1983 May; 147 (5), 807-13.
14. Skerk V, Schönwald S, Granić J, Krhen I, Barsić B, Mareković I, Roglić S, Desnica B, Zeljko Z. Chronic prostatitis caused by Trichomonas vaginalis-diagnosis and treatment. J Chemother. 2002 Oct; 14 (5), 537-8.
15. Benson PJ, Smith CS. Cytomegalovirus prostatitis. Urology. 1992 Aug; 40 (2), 165-7.
16. Golz R, Mendling W. Candidosis of the prostate: a rare form of endomycosis. Mycoses. 1991 Sep-Oct; 34 (9-10), 381-4.
17. Nickel JC, Downey J, Ardern D, Clark J, Nickel K. Failure of a monotherapy strategy for difficult chronic prostatitis/chronic pelvic pain syndrome. J Urol. 2004 Aug; 172 (2), 551-4.
18. Nickel JC, Baranowski AP, Pontari M, Berger RE, Tripp DA. Management of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome who have failed traditional management. Rev Urol. 2007 Spring; 9 (2), 63-72.
19. Stones RW, Selfe SA, Fransman S, Horn SA. Psychosocial and economic impact of chronic pelvic pain. Baillieres Best Pract Res Clin Obstet Gynaecol. 2000 Jun; 14 (3), 415-31.
20. Litwin MS, McNaughton-Collins M, Fowler FJ Jr, Nickel JC, Calhoun EA, Pontari MA, Alexander RB, Farrar JT, O'Leary MP. The National Institutes of Health chronic prostatitis symptom index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. J Urol. 1999 Aug; 162 (2), 369-75.
21. Shoskes DA, Hakim L, Ghoniem G, Jackson CL. Long-term results of multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome. J Urol. 2003 Apr; 169 (4), 1406-10.
22. Magri V, Marras E, Restelli A, Wagenlehner FM, Perletti G. Multimodal therapy for category III chronic prostatitis/chronic pelvic pain syndrome in UPOINTS phenotyped patients. Exp Ther Med. 2015 Mar; 9 (3), 658-666.
23. Magri V, Wagenlehner F, Perletti G, Schneider S, Marras E, Naber KG, Weidner W. Use of the UPOINT chronic prostatitis/chronic pelvic pain syndrome classification in European patient cohorts: sexual function domain improves correlations. J Urol. 2010 Dec; 184 (6), 2339-45.
24. Davis SN, Binik YM, Amsel R, Carrier S. Is a sexual dysfunction domain important for quality of life in men with urological chronic pelvic pain syndrome? Signs "UPOINT" to yes. J Urol. 2013 Jan; 189 (1), 146-51.
25. Zhao WP, Zhang ZG, Li XD, Yu D, Rui XF, Li GH, Ding GQ. Celecoxib reduces symptoms in men with difficult chronic pelvic pain syndrome (Category IIIA). Braz J Med Biol Res. 2009 Oct; 42 (10), 963-7.
26. Li HJ, Kang DY. Prevalence of sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome: a meta-analysis. World J Urol. 2016 Jul; 34 (7), 1009-17.
27. Chen X, Zhou Z, Qiu X, Wang B, Dai J. The Effect of Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) on Erectile Function: A Systematic Review and Meta-Analysis. PLoS One. 2015 Oct 28; 10 (10), e0141447.
28. Wagenlehner FM, Schneider H, Ludwig M, Schnitker J, Brähler E, Weidner W. A pollen extract (Cernilton) in patients with inflammatory

chronic prostatitis-chronic pelvic pain syndrome: a multicentre, randomised, prospective, double-blind, placebo-controlled phase 3 study. Eur Urol. 2009 Sep; 56 (3), 544-51.
29. Morgia G, Mucciardi G, Galì A, Madonia M, Marchese F, Di Benedetto A, Romano G, Bonvissuto G, Castelli T, Macchione L, Magno C. Treatment of chronic prostatitis/chronic pelvic pain syndrome category IIIA with Serenoa repens plus selenium and lycopene (Profluss) versus S. repens alone: an Italian randomized multicenter-controlled study. Urol Int. 2010; 84 (4), 400-6.
30. de la Rosette JJ, Karthaus HF, van Kerrebroeck PE, de Boo T, Debruyne FM. Research in 'prostatitis syndromes': the use of alfuzosin (a new alpha 1-receptor-blocking agent) in patients mainly presenting with micturition complaints of an irritative nature and confirmed urodynamic abnormalities. Eur Urol. 1992; 22 (3), 222-7.
31. Nickel JC, Touma N. α-Blockers for the Treatment of Chronic Prostatitis/Chronic Pelvic Pain Syndrome: An Update on Current Clinical Evidence. Rev Urol. 2012; 14 (3-4), 56-64.
32. Xia D, Wang P, Chen J, Wang S, Jiang H. Fluoxetine ameliorates symptoms of refractory chronic prostatitis/chronic pelvic pain syndrome. Chin Med J (Engl). 2011 Jul; 124 (14), 2158-61.
33. Fitzgerald MP, Anderson RU, Potts J, Payne CK, Peters KM, Clemens JQ, Kotarinos R, Fraser L, Cosby A, Fortman C, Neville C, Badillo S, Odabachian L, Sanfield A, O'Dougherty B, Halle-Podell R, Cen L, Chuai S, Landis JR, Mickelberg K, Barrell T, Kusek JW, Nyberg LM; Urological Pelvic Pain Collaborative Research Network. Randomized multicenter feasibility trial of myofascial physical therapy for the treatment of urological chronic pelvic pain syndromes. J Urol. 2013 Jan; 189 (1 Suppl), S75-85.
34. Chang SC, Hsu CH, Hsu CK, Yang SS, Chang SJ. The efficacy of acupuncture in managing patients with chronic prostatitis/chronic pelvic pain syndrome: A systemic review and meta-analysis. Neurourol Urodyn. 2017 Feb, 36 (2), 474-481.
35. Qin Z, Wu J, Zhou J, Liu Z. Medicine (Baltimore). Systematic Review of Acupuncture for Chronic Prostatitis/Chronic Pelvic Pain Syndrome. 2016 Mar; 95 (11): e3095.
36. Nickel JC, Pontari M, Moon T, Gittelman M, Malek G, Farrington J, Pearson J, Krupa D, Bach M, Drisko J; Rofecoxib Prostatitis Investigator Team. A randomized, placebo controlled, multicenter study to evaluate the safety and efficacy of rofecoxib in the treatment of chronic nonbacterial prostatitis. J Urol. 2003 Apr; 169 (4), 1401-5.
37. Alexander RB, Propert KJ, Schaeffer AJ, Landis JR, Nickel JC, O'Leary MP, Pontari MA, McNaughton-Collins M, Shoskes DA, Comiter CV, Datta NS, Fowler JE Jr, Nadler RB, Zeitlin SI, Knauss JS, Wang Y, Kusek JW, Nyberg LM Jr, Litwin MS; Chronic Prostatitis Collaborative Research Network. Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. Ann Intern Med. 2004 Oct 19; 141 (8), 581-9.
38. Thakkinstian A, Attia J, Anothaisintawee T, Nickel JC. α-blockers, antibiotics and anti-inflammatories have a role in the management of chronic prostatitis/chronic pelvic pain syndrome. BJU Int. 2012 Oct; 110 (7), 1014-22.
39. Magistro G, Wagenlehner FM, Grabe M, Weidner W, Stief CG, Nickel JC. Contemporary Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome. Eur Urol. 2016 Feb; 69 (2), 286-97.

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Multidisciplinary comment

We have read the review by Hoffmann et al. regarding the treatment of chronic prostatitis/Chronic pelvic pain syndrome with interest. According to the National Institute of Health classification for prostatitis, there are 4 different types of prostatitis syndromes[1,2]. Syndromes I&II have a proven bacterial infection (acute and recurrent respectively), allowing a fairly straightforward approach. Syndrome IV is asymptomatic and so rarely requires treatment. Hoffmann et al. in their review have focused on category III, in which no source of infection is found. These patients may or may not have inflammatory findings in the semen (IIIA and IIIB respectively), in either case they are symptomatic.

Patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) typically present primarily with chronic pain and as such have a strong negative impact on their quality of life. The UPOINT classification system, initially described in 2009, uses a clinical phenotype-based system that helps to profile specific patients and assists in choosing individual treatment targets[3,4]. Treatment results are usually assessed using the NIH-CPSI score[5,6].

Without a clear cause, management of CPPS is challenging and frustrating to both the patient and physician, also involving a significant economic burden[7]. Patients with CP/CPPS typically have a history of repeated physician visitations, involving multiple doctors. These patients typically undergo multiple diagnostic investigations and treatment trials. Sadly, as described by the authors, although several therapeutic agents exist, they are moderately effective at best, and these patients frequently require multimodality strategies. Considering this, patients suffering from CP/CPPS can benefit from referral to centers of excellence experienced in treating them. Centers of excellence can reduce unnecessary diagnostic tests, reassure patients regarding their diagnosis and prognosis, and implement an early individualized multimodal therapeutic regimen achieving the best long-term results.

REFERENCES

1. Krieger JN, Nyberg L, Jr., Nickel JC. NIH consensus definition and classification of prostatitis. Jama. 1999; 282: 236-7.
2. Nickel JC. Prostatitis: diagnosis and classification. Current urology reports. 2003; 4: 259-60.
3. Nickel JC, Shoskes D. Phenotypic approach to the management of chronic prostatitis/chronic pelvic pain syndrome. Current urology reports. 2009; 10: 307-12.
4. Shoskes DA, Nickel JC, Dolinga R, Prots D. Clinical phenotyping of patients with chronic prostatitis/chronic pelvic pain syndrome and correlation with symptom severity. Urology. 2009; 73: 538-42; discussion 42-3.
5. Wagenlehner FM, van Till JW, Magri V, Perletti G, Houbiers JG, Weidner W et al. National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) symptom evaluation in multinational cohorts of patients with chronic prostatitis/chronic pelvic pain syndrome. European urology. 2013; 63: 953-9.
6. Litwin MS, McNaughton-Collins M, Fowler FJ, Jr., Nickel JC, Calhoun EA, Pontari MA et al. The National Institutes of Health chronic prostatitis symptom index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. The Journal of urology. 1999; 162: 369-75.
7. Duloy AM, Calhoun EA, Clemens JQ. Economic impact of chronic prostatitis. Current urology reports. 2007; 8: 336-9.

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A challenging case

A series of difficult cases in pelvic floor diseases are presented with an educational purpose following the teaching module of the Integral Theory. The proposer describes symptoms, clinical findings and management plan. Opinions and suggestions of a number of Colleagues are reported. In the next two issues of Pelviperineology, together with new "challenging cases", results and further comments on this case will be published at three and six months follow up.

The case. A 67 year old female with a history of urinary retention and prolapse was complaining hesitancy in micturition and severe dysuria. Appendectomy at 36yrs, and 4 month before hysteroscopic removal of endometrial polyps. Difficulty in voiding urine since one year. *Urogynaecological examination*: 4th degree cystocele (HWS), 2th degree hysterocele and rectocele; POP-Q: Aa:+3; Ba:+6; C:+1; Gh:4; pb: 1.5; Tvl: 8; Ap:0;Bp:+1; D: -1. PC test:1. Q tip test:2. Stress test and Bonney test: negative. At bimanual examination uterus was of regular size, behind and on the left of the womb a 10 cm mass was observed, regular the right ovary, the left was impalpable. *Ultrasounds* confirmed a 10 cm solid mass between left ovary and lateral margin of uterus compatible as first hypothesis with fibroid belonging either to the uterus or to the left ovary (Fig. 1). Bilateral mild hydronephrosis, decreased after emptying by catheter, was detected. A *CT scan* confirmed the diagnosis without giving the certainty of belonging. *Urodynamic* testing showed: large bladder capacity (700 ml), normal bladder compliance, no urodynamic SUI, no detrusor overactivity. Uroflowmetry revealed a urinary strongly remitting curve with kinking effect, and 300 ml post-void residual urine was detected. At cystoscopy the bladder mucosa was regular except for moderate trabeculation. The patient was planned for surgery.

Main issues to face: 1 vaginal, laparoscopic or abdominal route? **2** prophylactic incontinence procedure: yes or no? **3** any specific procedures for each compartment? **4** intraoperative histological examination should be performed?

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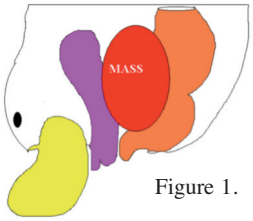

Figure 1.

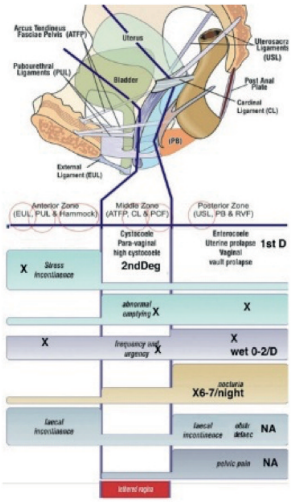

Figure 2.

Comment. I thank Professor Leanza for a most interesting case. I commend the use of the Pictorial Diagnostic Algorithm (Fig. 2). It ensures that all relevant pelvic symptoms are searched for, it vastly simplifies diagnosis and it acts as an excellent guide for surgery. His figure summarizing the prolapse is also excellent.

Diagnosis. A history of urinary stress incontinence (USI), but no evidence of USI on testing suggests that this woman has latent stress incontinence. The urinary retention and hesitancy indicate cardinal (CL)/uterosacral (USL) laxity. The mass is a concern.

The first task is to assess what the mass is all about. A diagnostic laparoscopy with or without biopsy is the first task to ensure it is not malignant. If, as appears, it is obstructing the ureter, it needs to be removed.

Management. Most likely she will need a midurethral sling at some stage, but this should be delayed until after the other surgery so a more adequate assessment can be made of her USI. The uterus is normal in size, so there is no need to remove it. This is an important consideration as a hysterectomy would most likely worsen the posterior zone symptoms which are summarized in the algorithm. CL and USL repair would cure most of the prolapse problems. Dislocation of CL and anterior vaginal wall from their attachments to the anterior cervical ring in my experience account for 80% of all cystoceles (Fig. 3). Surgical cure for POP is best performed vaginally, ideally using a Tissue Fixation System (TFS) CL and USL tape (Fig. 4)[1]. CL/USL reconstruction will also improve the urinary hesitancy residual urine. The anatomical basis for this was detailed in a 2015 publication[2]. This publication details the anatomical and physiological factors behind the hesitancy and residual urine reported by Professor Leanza. Alternative to TFS, the PIVS technique as detailed by Shkapura[3] or Wagenlehner[4] would give equivalent results. The laparoscopic route in my opinion is far too imprecise and it would not address the ligament defects causing the prolapse problems.

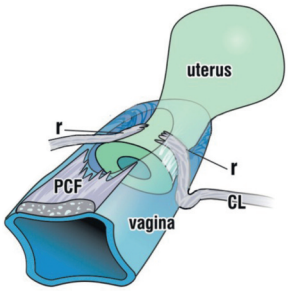

Figure 3. – Pathogenesis of "high cystocele" (transverse defect). Dislocation of cardinal ligament (CL) and the pubocervical fascial layer of the anterior vaginal wall (PCF) from their attachments to the anterior cervical ring allow PCF to rotate down as a cystocele.

REFERENCES

1. Sekiguchi Y et al. Reinforcement of suspensory ligaments under local anesthesia cures pelvic organ prolapse: 12-month results (n=60) IUJ 2014; 25: 783-789
2. Petros P, Lynch W, Bush M. Surgical repair of uterosacral/cardinal ligaments in the older female using the tissue Fixation system improves symptoms of obstructed micturition and residual urine Pelviperineology 2015; 34: 112-116
3. Shkarupa D et al. The hybrid technique of pelvic organ prolapse treatment: apical sling and subfascial colporrhaphy, IUJ DOI 10.1007/s00192-017-3286-7 (n=148)
4. Wagenlehner F et al. Vaginal apical prolapse repair using two different sling techniques improves chronic pelvic pain, urgency and nocturia– a multicentre study of 1420 patients Pelviperineology 2016; 35: 99-104 (n=1420)

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Comment. **Patient symptoms**. Urge incontinence, nocturia x6-7 per night, bladder emptying problems, stress incontinence.

Examination. 4th degree cystocele (HWS), 2th degree hysterocele and rectocele

The first concern is to deal with the mass and the bilateral mild hydronephrosis. I suggest:

1. Put in ureteral stents on both sides to protect kidneys and ureters

2. Take out unclear mass on left side by open incision. Once this is dealt with, I would address her prolapses (cystocele and rectocele) taking care not to excise vagina, as this will only decrease the collagen and elastin needed for proper function. With regard to her symptoms, based on the al-

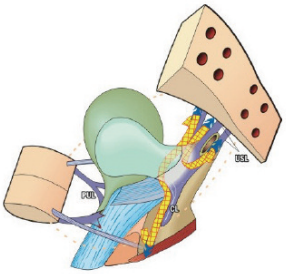

Figure 4. – Cardinal (CL) and uterosacral (USL) ligaments are shortened and reinforced by a 7mm TFS tape placed along their length.

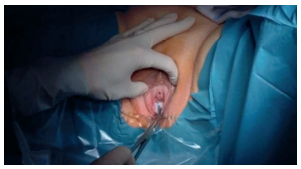

Figure 5. – See video on-line https://youtu.be/uBJOB_FiKbY

gorithm (which I have found to be very accurate) she would need a midurethral sling for her stress urinary incontinence and reinforcement of the cardinal and uterosacral ligaments for all the other symptoms.

3. The prolapse should be preferably corrected via the vaginal route. Alternatively, simultaneously perform open sacrocolpopexy by taking out the mass, though sacrocolpopexy by itself is unlikely to be sufficient to cure the cystocele and rectocele.

4. As a general rule, those of us who follow the Integral Theory try and preserve the uterus. So don't remove it if it can be avoided.

5. It seems that the stress urinary incontinence is latent. Don't correct it - wait for the results of prolapse surgery and do possible USI surgery at the earliest 3 months later (residuals!)

Diagnosis of latent stress incontinence. I attach a video (www.pelviperineology.org - https://youtu.be/uBJOB_FiKbY) (Fig. 5) which shows a test for latent stress incontinence. Reduction of the cystocele can induce stress incontinence on coughing.

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Letter to the Editor

Dear Editor,

I congratulate Pelviperineology on its initiative in seeking new directions for diagnosis and management of chronic pelvic pain as published in the September 2017 issue[1-4].

I present below a recent experience where these concepts were directly tested for truth or falsity.

Today Jan. 25th 2018, I reviewed a patient with Ehlers Danlos disease who had been complaining of strong pelvic pain since many years. The speculum test[5] reduced the pain significantly but the tampon in the posterior fornix suppressed pain and the need to urinate. It was an amazing experience for both doctor and patient as it indicated the problem was potentially curable. After lidocaine injection into the utero-sacral ligament, the pain significantly reduced but only for 30 minutes, exactly as described by Zarfati[4].

This case raised further questions: Would hysterectomy, a common treatment for this condition, relieve the problem or not? What is the data for pain cure in patients who have had hysterectomy? Would promontofixation with mesh reduce or suppress the problem?

Sincerely

1. Weintraub A, Petros P, Editorial "Dedicated to Professor Heinrich Martius, pioneer in the ligamentous origin of chronic pelvic pain in the female" Pelviperineology 2017; 36: 66 http://www.pelviperineology.org.
2. Petros PE, Pelviperineology 2017; 36: 71-73Pelviperineology 2017; 36: 66.
3. Sekiguchi Y, Inoue H, Liedl B et al. Is Chronic Pelvic Pain in the female surgically curable by uterosacral/cardinal ligament repair? Pelviperineology 2017; 36: 74-78.
4. Zarfati D, Petros P, The Bornstein Test- a local anaesthetic technique for testing uterosacral nerve plexus origins of chronic pelvic pain Pelviperineology 2017; 36: 89-91.
5. Wu Q, Luo L. Petros PEP Case report: Mechanical support of the posterior fornix relieved urgency and suburethral tenderness, Pelviperineology 2013; 32: 55-56.

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Authors' reply

Curiosity, the engine of discovery

We thank Dr Beco for his observations which confirm key aspects of the Pelviperineology September 2017 issue on chronic pelvic pain (CPP). We commend this open-minded approach. Those who read the March 2018 issue on CPP will realize that Dr Beco, a significant authority on CPP caused by pudendal nerve injury, was sufficiently curious to test and evaluate a different, competing paradigm that CPP may be caused by pain derived from lax uterosacral ligaments. Dr Beco's investigations of the USL pain paradigm are the very essence of scientific enquiry. Scientific enquiry underlies the mission of Pelviperineology journal, its focus on discovery and the evidence which flows from discovery. Curiosity is the engine which drives the motivation, recruits the energy and the dedication needed for discovery, to test the discovery with scientific trials and ultimately, to test its clinical effectiveness with all the tools of the Cochrane Database of Systematic Reviews. However, Cochrane Reviews do not provide the whole picture which we call science. Without discovery, there is no Cochrane and without curiosity there is no discovery. Pelviperineology journal encourages all readers to challenge the concepts presented in the pages of the two pelvic pain issues for truth or falsity, using the classic deductive method recommended by Karl Popper[1], exactly as tested by Dr Beco.

With regard to Dr Beco's three final questions, we present our view en linea

Q1. *Would hysterectomy, a common treatment for this condition relieve the (pain) problem?*

Given the stated etiology of USL laxity, if during hysterectomy the surgeon tightened the USLs sufficiently to support the ligaments, the pain should improve. However, the same tightening of USLs without hysterectomy would be expected give equivalent cure.

Q2. *What is the data for pain cure in patients who have had hysterectomy?*

Hysterectomy involves severing the descending branch of the uterine artery, the main blood supply of the proximal USLs as they attach to the cervical ring. This explains the high incidence of pelvic floor dysfunction reported in hysterectomized older women, especially after the menopause.

Q3. *Would promontofixation with mesh reduce or suppress the problem (of pain)?*

The data from Claerhout et al.[2], showed no significant decrease in overall CPP at 3 months after surgery.

REFERENCES

1. Popper K R, Theories, Falsifiability, The Logic of Scientific Discovery (1980), Unwin, Hyman, London, 27-146.
2. Clairhout F et al, Medium-Term Anatomic and Functional Results of Laparoscopic Sacrocolpopexy Beyond the Learning Curve, European Urology 2009; 55: 1459-1468.

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Editors Pelviperineology Pain Issues I&II


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