Original article

Experimental Study No. 8: Stress urinary incontinence results from muscle weakness and ligamentous laxity in the pelvic floor

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Abstract: AIM. To assess the roles of muscle damage and of ligamentous laxity in urinary stress incontinence. PATIENTS AND METHODS. Muscle biopsies (n = 47) were taken from the anterior portion of pubococcygeus muscle during the "tension-free" midurethral slingplasty procedure, an operation which corrects laxity in the pubourethral ligament. There were 38 multiparas with stress incontinence, and 9 nulliparas with mainly urge and frequency. The biopsies were examined blindly for evidence of muscle damage. Surgical cure was blindly assessed by means of a cough stress pad test. RESULTS. The results were correlated only after post-operative assessment. In total, 33 of the 39 patients with stress urinary incontinence were cured. In 17 biopsies of multiparas and in one nullipara the sample consisted only of a fibrous connective tissue scar. Fifteen of these 17 multiparas with stress urinary incontinence were cured postoperatively. Of the 21 biopsies of multiparas containing muscle tissue, 20 showed muscle damage; 18 of these patients were surgically cured; the mean urine loss on cough stress test reduced from 11.3 gm to 0.7 gm. Of the 8 nulliparous patients in this group with muscle tissue in the biopsy, only the biopsies of the four oldest patients showed muscle damage; none lost urine on pre or postoperative pad testing. CONCLUSIONS. Muscle and connective tissue damage are linked abnormalities that together lead to pelvic floor dysfunction and incontinence. Correction of ligamentous laxity can cure incontinence, even when there is muscle weakness.

Key words: Incontinence; Muscle damage; Midurethral sling; Tenotomy; Connective tissue; Nullipara.

INTRODUCTION

The cause of "idiopathic" urinary and fecal incontinence is controversial. Based on histological and electrophysiological studies, Swash and colleagues suggested that muscle damage secondary to birth-induced pelvic and perineal nerve damage may cause sphincter and pelvic floor weakness, and so lead to fecal and urinary incontinence.[1-3] Smith et al.[4, 5] confirmed these findings, but it was also noted that many patients with genital prolapse, without impaired fecal or urinary continence, also had electrophysiological evidence of damage to the innervation of pelvic floor sphincter muscles.[4] Sometimes this nerve damage was combined with direct trauma to these muscles.[6-8] Nerve damage was also correlated with increased perineal descent,[13] itself a feature of pelvic floor laxity. More recently, histochemical studies of the superior border of the anterior portion of the pubococcygeus muscle (PCM) indicated no evidence of necessary direct or neurogenic damage to this muscle in patients with stress urinary incontinence.[10] Beginning in 1990, it was reported that creating an artificial pubourethral neoligament [11, 12] achieved a high rate of cure not only in patients with urinary incontinence, but also in fecal incontinence.[9] Since only connective tissue was repaired by that procedure,[9] it was concluded that connective tissue damage may have been the major etiological factor. The aim of this prospective study was to consider the relation between muscle damage, whether due to direct injury, or to neurogenic factors, and connective tissue laxity in the pathogenesis of stress urinary incontinence.

PATIENTS AND METHODS

Forty-seven patients, 38 multiparas and 9 nulliparas were studied. Their mean age was 46.8 years (range 18 to 78), and mean parity 1.7 (range 0 to 5). All the patients were assessed pre-operatively and post-operatively at 8 weeks, symptomatically, using a structured questionnaire, and objectively, using a cough stress pad test, (10 coughs in the upright position with a full bladder).

All 47 patients had muscle biopsies taken from the inner inferior surface of the anterior portion of pubococcygeus muscle during the "tension-free" midurethral slingplasty. [15, 16] This operation creates an artificial pubourethral neoligament, tightening the suburethral vagina by attaching it to underlying ligamentous and muscular structures. As part of this procedure [12, 15] bilateral paraurethral incisions were made in the lateral sulcus of the vagina, for access. The midurethral and muscle reflections of the pubourethral ligaments (PUL) were identified. The lateral reflection of PUL was retracted medially, to reveal the undersurface of the anterior portion of the pubococcygeus muscle (PCM). The muscle biopsies were all taken between the hammock and pubic symphysis insertion points of the PCM by the same surgeon (PP), a distance of approximately 2 cm. The biopsy specimen approximately 0.5 cm x 0.3 cm x 0.2 cm was taken, where possible, from both sides of PCM, and placed in liquid nitrogen.

Histological preparations of these muscle biopsies were examined blindly by MS and BK for evidence of muscle damage. Multiple histological and enzyme histochemical techniques prepared from frozen sections, were used. Standard histological methods included haematoxylin and eosin, ATPase and Gomori stains, and PAS with and without diastase digestion. Enzyme histological methods were used for fibre type distribution studies, including NADH, succinate dehydrogenase, myophosphorylase, phosphofructinase, adenylate deaminase, non-specific esterase, acid and alkaline phosphatase, and cytochrome oxidase.

RESULTS

The 38 multiparas all gave a history of stress incontinence, and this was confirmed by pad testing; mean preoperative loss was 11.3 gm; mean postoperative loss (including failed surgery), was 0.7 gm. Of these 38 multiparas 33 were cured of their stress urinary incontinence following slingplasty. The nulliparous group comprised nine patients with mild symptomatic stress, urgency and frequency, but no stress incontinence demonstrated on cough stress testing. After surgery all nine nulliparas were cured of their stress symptoms, and seven of their urgency and frequency. The clinical results were correlated with the biopsy findings only after the post-operative assessment was available.

Biopsies from 17 patients, 16 multiparas, and one nullipara, revealed connective tissue only, without remaining

muscle fibres. Of the 29 additional biopsies, 21 were from multiparas. Twenty of these biopsies were abnormal, and 18 of these patients were surgically cured. The changes in these 20 abnormal muscle biopsies consisted of partial fibrous tissue replacement of muscle fibres, with increased variation in muscle fibre diameter in the remaining muscle fibres. There were also secondary changes consistent with ongoing muscle damage, such as increased central nucleation, and occasional central cores. A few fibres showed minor subsarcolemmal accumulations of mitochondria. Occasional regenerating fibres were seen. Mild grouped reinnervation of fibre types, involving both Type 1 and Type 2 fibres was seen in some biopsies, but this was not prominent and was difficult to assess because of the marked Type 1 predominance found in all the biopsies of this muscle; a normal feature of pelvic floor muscles.[17] In one biopsy a muscle spindle was found. Four older nulliparous patients, aged 30, 36, 40 and 50 years, had evidence of muscle damage; but the four youngest patients, aged 18 to 28 years, did not. The youngest nullipara had normal histology, but one of these four patients had focal collections of adipose tissue within the endomysial connective tissue. In half the biopsies, thickened. sometimes dense, collagenous tissue was found covering the under surface of the PCM muscle.

DISCUSSION

Our results demonstrate severe damage to the biopsied PCM muscle, yet the patients were cured by a midurethral sling, a procedure which reinforces the pubourethral ligament. This observation implies a role both of muscle weakness and of ligamentous laxity in the pathogenesis of the functional pelvic floor disorder leading to stress urinary incontinence. Improving ligamentous integrity will enable muscle function to be at least partially restored, even when muscles themselves are damaged and weakened.

The changes present in the muscle biopsies ranged from complete absence of muscle fibres, with replacement by fibrous scar tissue, to less marked changes, consisting of increased variation in muscle fibre size, increased central nucleation and increased connective tissue. Classical myopathic changes were infrequent, and frank neurogenic change was difficult to assess because of Type 2 fibre predominance. In many instances, the changes resembled those described following experimental tenotomy.[18, 19] Dimpfl et al.[20] found increased central nucleation and fibrosis in multiparous women that were more marked on the inferior surface of the muscle, and an increasing frequency of similar changes in nulliparous patients with age. Evidence of neurogenic damage was not found in this muscle. They concluded that ageing and vaginal childbirth lead to histomorphological changes of the pelvic floor muscle that are consistent with changes of myogenic origin. Our data support Dimpfl et al's findings and those of Heit.[11] We noted normal findings in one multipara, and in four younger nulliparas, and muscle damage in the four older nullipara. Heit et al.[11] took muscle biopsy specimens from the superior surface of the middle part of the PCM in 13 patients. The decision as to whether or not muscle damage was present was made by comparison of the symptomatic and asymptomatic patients, a method that may have underestimated muscle damage, since it would not take account of pathological changes in the asymptomatic patients. In contrast, our results are based on comparison with normal muscles evaluated in our previously published work.[17]

In limb muscles, biopsies taken near the insertion points of normal striated muscles may exhibit central nucleation and fibre splitting, but this was not an issue in our study since we took biopsies from the body of the pubococcygeus muscle (PCM). The changes we have found were in the anterior portion of the pubocoocygeus muscle, which is innervated by direct branches from the pelvic plexus, rather than from branches of the pudendal nerves. Damage to the latter nerves has been implicated in voluntary sphincter and puborectalis denervation in this functional disorder. The cause of the morphological changes in the PCM muscle in our patients is inevitably a matter of some uncertainty but, at least in part, these changes may result from unloading of the muscle by stretch injury to pelvic floor ligaments, preventing normal force generation in the muscle. The experimental paradigm of muscle unloading is tenotomy, but similar unloading occurs in animals subject to zero gravity, as in space flight. Ohira et al.[21] have described atrophy of both Type 1 and Type 2 fibres after unloading, including after tenotomy, The changes we have noted in PCM, including a few core structures, are similar to those reported after human tenotomy.[18, 19] However, the absence of muscle fibres, with fibrous tissue scarring in so many of our biopsies, indicates primary muscle damage, with or without denervation, rather than any secondary effect of muscle unloading.

These findings show that muscle unloading from ligamentous laxity together with muscle damage, whether due to direct injury or to neurogenic damage, are important and related factors in the aetiology of stress urinary incontinence. The striking results of tension-free urethral slingplasty show that sufficient muscle contractile force can be restored by enhancing ligamentous support, and that there is therefore sufficient functional muscle reserve in these patients. This functional reserve is not utilisable when the ligamentous attachments of the pelvic floor muscles are lax. This finding is consistent with the failure of MRI studies of the pelvic floor to detect abnormal muscle morphometry in patients with urinary incontinence when compared to non-incontinent controls, the major finding being loss of the hammock-like configuration of the vagina.[22]

Using 3D and 4D ultrasound in 781 patients, Dietz et al.[23] demonstrated that even with bilateral avulsion of the pubovisceral muscle (pubococcygeus/puborectalis), there was no greater incidence of urinary or fecal incontinence. Women with levator avulsion defects were, however, twice as likely to show pelvic organ prolapse of stage II or more, compared to those without levator ani injury, mainly due to an increased risk of cystocele and uterine prolapse.

The previously reported finding of delayed pudendal nerve terminal latency in patients with uterovaginal prolapse, without stress incontinence [6] indicates damage to this nerve innervating the external sphincter and puborectalis muscles, but of insufficient degree to lead to major functional disturbance, that is incontinence. Thus, there are many factors leading to incontinence, including neurogenic muscle damage, ligamentous stretch causing muscle unloading and functional weakness, secondary muscle damage to unloaded muscles, and primary damage to pelvic floor muscles and sphincters during vaginal delivery.

Surgical cure following a midurethral sling procedure in 20/21 patients who had muscle damage and stress incontinence reinforces this conclusion. The midurethral slingplasty procedure restores the functional deficit caused by connective tissue damage to the pubourethral ligament, a critical component of the urethral and bladder neck closure mechanisms.[24] We propose that connective tissue laxity prevents the normal action of the pubococcygeus muscle in urethral closure, as a muscle needs firm insertion points to contract efficiently, and should not be stretched and have lost elasticity. With time, this laxity may also cause changes similar to those seen after tenotomy in limb muscles.[12, 13, 21]

These arguments suggest the question "What is the effect of damaged muscle on the urethral closure mechanism?". Clearly a damaged muscle must subtract from the efficiency of a musculoelastic mechanism. However, the force required to close the urethra is only a fraction of the force required to support between 10 and 20 Kg of abdominal viscera. This would appear to give the pelvic muscles considerable reserves of strength, a concept reinforced by MRI findings of no gross morphological changes between GSI and control patients.[22]

Our finding of muscle damage in the four older nulliparas, but not in the younger nulliparous group, can be attributed to age-related connective tissue laxity in the older group, a well-known phenomenon.[25] Symptomatic urinary urge and frequency, usually thought of as neurological in origin, can be initiated following far less connective tissue damage than stress incontinence, which is mechanical in origin.[24]

CONCLUSION

The abnormalities we have described are consistent with our hypothesis that muscle and connective tissue damage are linked, ligamentous laxity increasing muscle insufficiency, and causing secondary muscle damage in muscles that are often already damaged by childbirth injury due to unloading muscle in a similar way to that which occurs in limb muscles after tenotomy. Furthermore, given the close relationship between urinary incontinence and idiopathic fecal incontinence, we believe our findings most likely apply also to patients with idiopathic fecal incontinence.

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