

Polynucleotides and terpinenol: an effective aid in preventing mesh exposure in pelvic floor surgery

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Abstract: Objective: Pelvic surgery with mesh has proven to be more effective than conventional reconstructive surgery but cases of complications connected with these prostheses occurred. **Aim of the study:** We aimed to study the effectiveness of Polynucleotides and Terpinenol in preventing these complications. **Patients and methods:** Between January 2010 and December 2011, 166 female patients separated into two series were evaluated: the first treated with vaginal douches with an 0.05% solution of sodium hypochlorite; the second with ovules containing Polynucleotides and Terpinenol (PT). Parameters of success were the absence of signs and symptoms of exposure of the mesh and the trophism and appearance of the mucous membrane of the vagina as assessed by the surgeon, patient satisfaction, discomfort, itching or a burning sensation and signs of a Candida infection. **Results:** Overall, the number of mesh exposures was 6, of which 5 in Group 1 in Group 2 ($p = 0.043$). Trophism improved significantly both at three months and at six months in the PT treated group: even more they complained less of discomfort, itching and/or a burning sensation ($p = 0.001$). No cases of clinical evidence of Candida albicans infection were found in Group 2 at the follow-up examination one month after surgery, compared with 21.5% in Group 1 ($p=0.001$). **Discussion:** This study demonstrated the effectiveness of PT ovules both in preventing complications such as mesh exposure following pelvic floor surgery and in enabling rapid and lasting healing, minimising local symptoms such as discomfort, itching and a burning sensation. Their effectiveness in respect of Candida albicans infection was also demonstrated.

Key words: Pelvic Surgery; Mesh Erosion Prevention; Polynucleotides; Terpinenol; Quality of Life.

INTRODUCTION

Pelvic reconstruction surgery with mesh has proven to be more effective than conventional reconstructive surgery.^{1,2,3}

However, the first cases of complications connected with these prostheses, such as mesh exposure and/or erosion, occurred.⁴

There is still very little international literature on this topic, limited to a few case reports and assessments of their incidence, suggesting possible surgical solutions.⁵ Studies aimed at preventing mesh-related complications are extremely rare.^{6,7}

Similarly, there are only a few studies on the trophism of the pelvic organs and tissues and, specifically, of the mucous membrane of the vagina. The basis for initiating our study was our experience in the use of Polynucleotides as wound-healing adjuvants⁸ in fields other than urogynecology.

An observational and experimental study on the role of Polynucleotides in tissue regeneration and trophism⁸ prompted us to consider a possible role for them in pelvic surgery.

Moreover, an earlier experience regarding their use in the treatment of benign lesions of the vaginal portion of the uterus, the vagina, the vulva and the perineum⁹ confirmed and increased our interest in Polynucleotides, particularly when combined with Terpinenol.

PATIENTS AND METHODS

Between January 2010 and December 2011, a total of 166 female patients, separated into two consecutive series, underwent surgical procedures using polypropylene meshes for treating pelvic perineal disease.

The first series (Group 1) consisted of 68 women, average age 59, who were instructed to use vaginal douches with an 0.05% solution of sodium hypochlorite.

The second series (Group 2) consisted of 98 women, average age 62. Following surgery, they were instructed to use ovules containing a combination of Polynucleotides and Terpinenol (PT) as an adjuvant treatment to improve tissue trophism and wound-healing and also to limit the oc-

currence of post-operative Candida albicans infections.

Vaginal ovules based on Polynucleotides and Terpinenol are a class III medical device (CE0373) (Mastelli S.r.l. - Sanremo).

Both groups followed the same prophylactic pattern calling for one application/day for 30 days after surgery. In accordance with the customary and widely accepted guidelines, all the patients also received perioperative prophylaxis in the form of an antibiotic and an anticoagulant.

All the patients were followed up with examinations 1 week, 1 month, 3 months and 6 months after surgery. The parameters for evaluating success of the treatment were first and foremost the absence of signs and symptoms of exposure of the mesh and, as secondary objectives, the trophism and appearance of the mucous membrane of the vagina as assessed by the surgeon (according to the following scale: 1 = poor trophism of the tissues, 2 = minimum trophism of the tissues, 3 = trophic tissues), patient satisfaction (VAS – Visual Analogue Scale – from 1 to 5 as follows: 1 = patient dissatisfied, 2 = patient not very satisfied, 3 = patient sufficiently satisfied, 4 patient satisfied, 5 = patient highly satisfied), the onset of discomfort, itching or a burning sensation, signs of a Candida infection and, lastly, safety of the product (assessed by monitoring adverse events, if any) an its tolerability.

Patients with complications such as mesh exposure underwent revision surgery, following which they were excluded from the follow-up and monitored as a separate group.

No patients aged under 18, patients with malignant tumours or already being treated with wound-healing substances were included in the study. The written informed consent of each patient was obtained before enrolling them in the study. The study was conducted in accordance with the World Medical Association Declaration of Helsinki.

STATISTICAL ANALYSIS

The continuous variables are shown as mean values \pm SD, while the categorical variables are shown as absolute and percentage occurrences. The comparison between the

normal variables in the two independent samples was made using Student's t-test, while in case of non-normal distribution the Mann-Whitney test was used. The data was collected in a database created in a prospective manner using Microsoft Excel and SPSS 16.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Statistical significance was calculated applying two-tailed tests with a p value of <0.05.

RESULTS

The patients underwent the following surgical procedures: "TVT-O" (Transvaginal Tension-Free Vaginal Tape - Obturator)," TVMA" (Transvaginal Mesh - Anterior), Transvaginal Uterine Sling Suspension (Sling Hysteropexy), "T" plasty (T shaped prosthesis made of biological and polipropylene tissues combination) for treatment of rectocele, either as single procedures or combined and associated with one another in case of defects affecting several organs. All the patients completed the 6-month follow-up and nothing abnormal was reported with regard to the data collection. Comparable in terms of age and distribution of the surgical procedures. Overall, the number of complications (Table 1) such as mesh exposure was 6, of which 5 in Group 1 (that is to say 7.4% of the cases, 1 in Group 2 (that is to say 1 %) (p = 0.043). A total of 6 cases of erosion were recorded, of which 5 in Group 1 (7.4%) and 1 in Group 2 (1%) (p=0.043). In Group 1, one case of dehiscence of the suture and very slight exposure of the sling (TVT-O) (aged 81), one case of exposure of the part made of synthetic material of a "mixed-T prosthesis" on the vaginal side following correction of a rectocele (aged 37), one case of a vaginal abscess following correction of a rectocele with a "mixed T prosthesis" leading to exposure of the portion of the prosthesis made of synthetic material (aged 77) and, lastly, two cases of patients (aged 58 and 72) with exposure in way of the anterior vaginal wall secondary to TVMA occurred. In Group 2, the only case that occurred was that of a patient (aged 68) who complained of exposure in way of the anterior vaginal wall secondary to TVMA. The 6 cases of mesh exposure underwent revision surgery with removal of any excess portions of the prosthesis. They were excluded from the follow-up at the time of corrective surgery and followed up as a separate group. All 6 patients were found to heal effectively and completely within one month in 5 cases out of 6 and within 3 months in the last case, who was also the youngest patient (aged 37). None of the patients had functional complications and none required further surgery. Trophism of the mucous membrane, an aspect considered essential for avoiding complications such as mesh exposure, was found to have improved both at three months (p=0.011) and at six months (p=0.005) in those patients who had been treated with PT. Table 2 shows secondary endpoints evaluation. At all the follow-up examinations the patients treated with PT complained less of discomfort, itching and/or a burning sensation (p=0.001). Patient satisfaction, measured on a VAS scale from 0 to 5, took the overall experience of each patient into consideration. The statistical analysis did not highlight any significant differences between the two groups.

TABLE 1. – Mesh exposure between Group 1 (vaginal douches) and Group 2 (vaginal ovules containing Polynucleotides and Terpinenol).

	GROUP 1 68 patients	GROUP 2 98 patients	P value
Exposure	5 (7.4%)	1 (1%)	0.043

No cases of clinical evidence of *Candida albicans* infection were found in Group 2 at the follow-up examination one month after surgery, compared with 21.5% in Group 1 (p=0.001). This difference was not found to be significant three months after surgery, probably due to the fact the patients who had tested positive at the previous examination had started to receive treatment for the infection. Lastly, six months after surgery the difference between the two groups was again found to be significant (p=0.007). It is essential to stress that the absence of side effects secondary to the administration of PT ovules confirmed the safety of the product study, since its tolerability proved excellent.

DISCUSSION

Nowadays, quality of life is one of the main objectives of medicine, and in particular of surgery for treating functional complaints. Specifically, pelvic-floor surgery involves a vast number of patients requiring prompt and effective action. The continuous quest for excellence includes the investigation of new products able to produce a tangible impact on the quality of life of patients.

It has been shown that PT ovules restore the physiological environment of the vagina thanks to their viscosity and buffering capacity (pH 4/4.5), leading to the formation of a protective film that adheres to the mucous membrane and is able to re-create the best conditions for rapid healing.⁹ The Polynucleotides provide a further stimulus for cell regeneration in the tissues being repaired.^{10,11}

Thus, trophism of the mucous membrane was found to be statistically better in the cases treated with PT ovules. This was also associated with a lower impact of collateral symptoms such as discomfort, itching and a burning sensation. This further supports the effectiveness of PT ovules as a wound-healing adjuvant able to control effects secondary to surgical procedures on the vaginal mucosa. As far as concerns the VAS scale, although no statistically significant differences were highlighted, a small difference one month after surgery should be pointed out. It appeared that this difference could be attributed to the higher incidence of mesh exposure as a complication in Group 1, which was found at about one month after surgery. It led to more severe symptoms in these patients and the need for revision surgery. On the other hand, the absence of significant differences at the time of the various follow-up examinations can be related to the good functional results of the functional surgery on the patients in the study. Terpinenol also enabled effective control of *Candida albicans*, as already demonstrated in other studies.¹² The clinical studies illustrated in the literature confirmed earlier laboratory experience, and were the starting point for our study.

CONCLUSION

This study demonstrated the effectiveness of PT ovules both in preventing complications such as mesh exposure following pelvic floor surgery and in enabling rapid and lasting healing, minimising local symptoms such as discomfort, itching and a burning sensation. Their effectiveness in respect of *Candida albicans* infection was also demonstrated.

PT ovules associated with excellent knowledge of the anatomy of the pelvic floor, a correct surgical technique and careful selection of the patients are effective tools in preventing complications of pelvic perineal prosthetic surgery.

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TABLE 1. – Secondary endpoints evaluation in the 2 groups.

	GROUP 1 68 patients				GROUP 2 98 patients				P value		
TROPHISM OF MUCOSA	T1	T2	T3	T4	T1	T2	T3	T4			
1	38.5%	33.8%	31.3%	28.6%	1	30.8%	22.0%	22.0%	23.0%	T1 p=0.478	
2	38.5%	41.6%	46.8%	49.2%	2	38.4%	29.7%	30.8%	38.5%	T2 p=0.011	
3	23.0%	24.6%	21.9%	22.2%	3	30.8%	48.3%	47.2%	38.5%	T3 p=0.005	
										T4 p=0.104	
DEGREE OF SATISFACTION VAS 1-5	1	0%	3.1%	4.7%	1.6%	1	0%	0%	1.1%	0%	
	2	4.6%	9.2%	6.3%	6.3%	2	0%	2.2%	1.1%	1.1%	
	3	24.6%	21.5%	18.8%	19.0%	3	24.2%	20.9%	19.8%	26.4%	
	4	53.8%	47.7%	50.0%	52.5%	4	58.2%	61.5%	56.0%	50.5%	
	5	17.0%	18.5%	20.2%	20.6%	5	17.6%	15.4%	22.0%	22.0%	
	Average	3.83	3.69	3.75	3.84		3.93	3.90	3.97	3.93	T1 p=0.363
	± sd	±0.76	±0.98	±1.01	±0.88		±0.65	±0.67	±0.75	±0.73	T2 p=0.140
											T3 p=0.147
											T4 p=0.477
DISCOMFORT ITCHING BURNING	Yes	53.8%	60%	31.3%	31.7%	Yes	22%	11%	1.1%	2.2%	T1 p=0.001
	No	46.2%	40%	68.8%	68.3%	No	78%	89%	98.9%	97.8%	T2 p=0.001
											T3 p=0.001
											T4 p=0.001
CANDIDA ALBICANS	Yes	10.8%	21.5%	7.8%	17.5%	Yes	4.4%	0%	1.1%	3.3%	T1 p=0.224
	No	89.2%	78.5%	92.2%	82.5%	No	95.6%	100%	98.9%	96.7%	T2 p=0.001
											T3 p=0.087
											T4 p=0.007

T1 = 1 week, T2 = 1 month, T3 = 3 months, T4 = 6 months

TROPHISM 1 = Tissue not very trophic, 2 = tissue slightly trophic, 3 = tissue trophic

DEGREE OF SATISFACTION: 1 = dissatisfied, 2 = of very satisfied, 3 = fairly satisfied, 4 = satisfied, 5 = Highly satisfied

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