URETHRAL MINI-SLING FOR THE TREATMENT OF NEUROGENIC SPHINCTERIC INCOMPETENCE IN PEDIATRIC AND YOUNG ADULT PATIENTS

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Summary.- OBJECTIVES: A first experience was carried out in three research centers using a new urethral sling for the treatment of male and female pediatric and young adult population with urinary incontinence caused by neurogenic sphincteric incompetence.

METHODS: This was a prospective pilot study of patients with neurogenic sphincteric incompetence needing clean intermittent catheterization. All patients were treated by the implantation of Nephis® mini-sling (Promedon, Argentina) over the proximal urethra. Twenty-eight patients were included, 19 females and 9 males. Mean age was 13.4 (SD 7.8 years). The median follow-up was 16.5 (12-24) months. Urodynamic studies were carried out pre and postoperatively to assess the nature of the incontinence and to quantify the outcomes after implantation. A voiding diary was also used to evaluate the Daytime Dryness Intervals between catheterization.

RESULTS: Leak Point Pressure increased from a preoperative mean value of 24.3 cmH2O (SD 6.5) to 51.0 cmH2O (SD 14.3) (p<0.0005). The initial mean for Daytime Dryness Interval was 60.4min (SD 9.1) and postoperatively rose to 195.6 (SD 59.4) (p<0.0005). Only one major complication was registered: a sling had to be removed due to erosion in a patient who underwent a concomitant bladder neck reconstruction due to an ectopic ureter repair.

CONCLUSIONS: The mini-sling was easy to implant and urodynamic results suggest it is effective in the treatment of neurogenic sphincteric incompetence. This statement is also supported by voiding diary records.

Keywords: Neurogenic sphincteric incompetence. Mini-sling. Polypropylene. Cervicourethral resistance.

Resumen.- OBJETIVO: Se ha realizado una primera experiencia en tres centros de investigación usando un nuevo mini-sling uretral para el tratamiento de pacientes pediátricos y jóvenes adultos masculinos y femeninos con incontinencia de orina causada por incompetencia esfínteriana neurogénica.
INTRODUCTION

In the pediatric population, Neurogenic Lower Urinary Tract Dysfunction is the most common reason for sphincteric mechanism incompetence. Many surgical alternatives exist for the management of incontinence due to this pathology: injection of bulking agents, insertion of grafts (autologous [1,2], xenografts [3-5] and synthetic sling materials [6]), bladder neck reconstructions, artificial sphincter implantation and, in the most severe cases, bladder neck closure. At best, the final success rates of these interventions do not exceed 70% - 80% (7-10). In the adult population, synthetic tension-free slings have been widely used for stress incontinence (11) as well as neurogenic incontinence (12). Easier methods of implantation have been developed and today it is possible to be accomplished as an outpatient surgery (13). Previous publications have reported the use of a variety of different materials including resorbable collagen slings, many of them having limited efficacy and poor long term outcomes (3-5). Other previously attempted slings using Gore-Tex® material have been placed circumferentially around the urethra and resulted in a very high erosion rate (6). The hypothesis which was set for this study stated that a non tension free sling which exerts an acceptable compression stress at the urethral wall should increase bladder outlet resistance and, as a result, should improve urinary incontinence in the targeted population. Additionally, the reduced contact area compared to slings implanted circumferentially around the urethra should help in avoiding erosion. The results presented in this work correspond to the initial experience of three investigational centers with Nephis® mini-sling (Promedon, Argentina) in a group of young male and female patients with urinary incontinence caused by neurogenic sphincteric incompetence.

MATERIALS AND METHODS

From June 2009 to January 2011 twenty-eight patients (19 females and 9 males) were included in this prospective international multicentre pilot study. The study was carried out in two investigational sites in Argentina (Buenos Aires and Córdoba) and one in Quito, Ecuador.

To be enrolled in this study, patients must have a previous history of clean intermittent catheterization (CIC). A voiding diary was used to record the Daytime Dryness Interval (DDI) which is the mean value of time between catheterization when the subject remains completely dry. Other authors have reported the use of the DDI in previous works to assess surgery outcomes from a clinical approach (1,10,13,14). The inclusion criteria included pediatric and young adults subjects with a bladder capacity at least 60% (at 40 cm H2O) of the expected bladder capacity according to patient age, Leak Point Pressure (LPP) less than 50 cmH2O of detrusor pressure (measured with a 6 Fr catheter) and baseline DDI of less than 180 minutes. Overactive bladder symptoms must be discharged prior to implantation.

Normal bladder volume by age was calculated based on standard equations adapted from published data (15-17), presented in Table I. Postoperative DDI and LPP were utilized as success measurements in the follow-up visits. A postoperative DDI of at least 180 minutes was necessary to consider...
the procedure successful. For comparative purposes, subjects were stratified by gender to assess differential DDI and LPP outcomes. The standard deviation will be shown here as mean±SD.

The mean age at the time of surgery was 13.4±7.8 years. Twenty-five (89.3%) patients had myelomeningocele and 3 lipo meningocele. Fifteen patients (54%) had a history of previous surgery before mini-sling implantation. Eight (28.6%) patients presented a previous bladder augmentation because of bad compliance. Five (17.9%) patients had been implanted with an Artificial Urinary Sphincter all removed secondary to infections. Other procedures which had been previously carried out were: five (17.9%) Mitrofanoff stoma, four cases (14.3%) of bulking agents in the bladder neck and one (3.6%) patient had undergone a vesicostomy procedure. In five cases, concomitant procedures were also performed in the same surgical act: a vesicostomy closure, a bladder augmentation, a laparoscopic Mitrofanoff procedure, a laparoscopic Malone stoma and one ectopic ureter was resected from the bladder neck.

Nephis (Figure 1) is a mini-sling which consists of a central polypropylene type I mesh, with two lateral fixation arms. Thanks to these arms, the mini-sling is a self-anchoring device, designed to be placed under tension in the proximal urethra. Two retractable insertion guides are used to facilitate the implantation procedure.

In males, the mini-sling is inserted through a perineal incision. The inferior face of the bulbar urethra is dissected, with minimal lateral dissection, just enough to place the middle segment of the mini-sling. In females, a small section of the anterior wall of the vagina is incised to expose the posterior urethral wall. Then, in both cases, the fixation arms are placed through each obturator muscle with the retractable insertion guides.

The mini-sling placement aims to increase the bladder outlet resistance. To quantify this effect during surgery, the urethral retro-resistance pressure (URP) (18) is measured with an empty bladder and an acclussive catheter (Figure 2A). The higher this pressure is, the higher the resistance. First, the initial URP is measured. Then, the mini-sling is inserted leaving the retractable insertion guides in place and the URP is measured again (Figure 2B). If there is an increase of less than 10 cmH_2O, the sling is tightened to reach at least this level. A polypropylene thread that is attached to the mini-sling could be used to loosen the sling by pulling it out, if it necessary.

Results were analyzed by means of descriptive statistics performed in SPSS® 17 (IBM®). The same software was used to perform paired and independent T-Student tests for longitudinal analysis and comparison among different groups within the sample, respectively. For all comparison made in this work an alfa level of 0.05 was considered significant.

RESULTS

The median time of postoperative follow-up was 16.5 (12-24) months. Three patients failed in completing the postoperative voiding diary and thus, their results were considered out of the analysis of DDI. The operative time presented a mean value of 40.0±13.4 min, and the investigators did not report any difficulty related to the surgical procedure. The mean values of URP were 28.4±12.5 and 44.9±10.7 cmH_2O prior and posterior to mini-sling placement, respectively.
Baseline information is presented in Table II and overall results are summarized in Table III. In the initial urodynamic study the mean LPP was 24.3±6.5 cmH₂O and increased up to 51.0±14.3 cmH₂O (95% CI of the difference 18.6-37.6; p<0.0005) showing an average improvement of 123.7% from basal condition. The mean preoperative DDI was 60.4±59.1 min while the postoperative values were 195.6±59.4 (95% CI of the difference 106.5-173.5; p<0.0005) representing a 198.6% of improvement. According to these figures, the mean DDI after surgery triplicated the initial record. More precisely 21/25 (84.0%) of them achieved a DDI ≥ 180 min and 13/25 (52.0%) a DDI = 240 min. Eighteen (72.0%) patients remained dry during the night postoperatively.

The p-value for the gender comparison of DDI was low (0.058) but it did not reach the significance level imposed before the test was done. The mean values of LPP were 57.3 and 44.7 cmH₂O for females and males respectively. There was not a statistically significance in this difference.

A female patient had an early complication of postoperative bleeding that stopped with a simple compression. One patient with history of an ectopic ureter at the bladder neck needed sling removal due to erosion. The mini-sling was place right after bladder neck reconstruction was made. Subsequent to a first period of continence the sling eroded the urethral wall and was removed by a cystoscopic approach six months after the first procedure. At this time, a second mini-sling was implanted trough a vaginal incision in the same patient, getting complete dryness since then. There were no infections. In one patient with previous history of two AUS who catheterize trough an urinary ostoma, with an important fibrosis, was very difficult to achieve the proposed increase of 10 cmH₂O in the URP. Finally, the target pressure was reached because the surgeon decided to place 3 slings over the urethra in the same surgical act. None male patient had difficulties with catheterization.

DISCUSSION

One incision slings also known as mini-slings have been used since the last decade for stress urinary incontinence (SUI) in women with reports of high success rates, comparable to those with standard midurethral retropubic or transobturator slings, claiming less invasiveness and morbidity (19-21). Initial results using the one incision sling Ophira® (Promedon, Argentina) showed 88% dryness (1-h pad test) 12 months after surgery in 18 women19. These outcomes were confirmed by the 90.2% of dryness (according to Stamey Urinary Incontinence Scale) in a larger study with one year follow-up20. Many studies have reported the safety of such implants made of polypropylene type I mesh (19-21).

The initial data regarding the performance of Ophira supported the idea that a mini-sling of similar characteristics would help in managing neurogenic incontinence. However, it is not possible to directly extrapolate these good results to the neurogenic
population because they need an important compression stress over the urethra (instead of the free-tension approach used in women with SUI) and no evidence was made before for male patients with this mini-sling.

The fixation of the implant needed to support the compression forces over time must be extremely reliable. A biomechanical study which used in-vivo implantation of different fixation systems in Wistar rats demonstrated that the multipoint fixation system used in Nephis presented the highest values of primary fixation at 7, 14 and 30 days after implantation (22). This means that this multipoint fixation system needed the highest mechanical strength to be pulled out from the implant sites. This fact do not guarantee efficacy in long-term compression support but provides evidence of high mechanical resistance in the fixation interface which is responsible for keeping the device in the right place to exert the compression forces.

The overall results got in this study with 12 to 24 months of follow-up are promising since not only the postoperative improvement was statistically significant but the clinical outcomes lead to a sensible difference compared to its basal condition. The mean DDI was three times greater after the mini-sling placement allowing patients to remain dry for longer periods while they were waiting for CIC. In addition, after analyzing case by case, 21/25 (84.0%) subjects resulted continent for at least 3 hours. Moreover, 13/25 (52.0%) achieved a dryness interval of at least 4 hours. This 84.0% of patients who were able to wait at least 3 hours for the CIC without urine leakage represent the group for which the procedure was considered successful.

The mean postoperative LPP reached a 51.0±14.3 cmH2O which doubles the initial value of 24.3±6.5 cmH2O and could be seen as a reliable indicator of the magnitude of the increase in urethral resistance. The Nephis mini-sling increased the proximal urethral resistance by compressing only the anterior wall of the urethra. This approach seems to decrease the risk of erosion compared to those devices which compress the urethra circumferentially since the authors only faced one case of erosion in a patient who had undergone a surgery to correct an ectopic ureter at the bladder neck just before the mini-sling implantation. This study deals with mid-term safety reports but longer follow-up periods must be considered to evaluate the evolution of the urinary tract function under this increased compression forces.

A stratification of the results by gender was made to assess differential outcomes. The DDI shows a greater increase in male patients because they had started with a lower value but the final result is very similar in both groups. Independently of the p-value associated with the comparison, the difference found in the postoperative results lacks clinical significance.

### Table II. Baseline information.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13.4 (7.8)</td>
<td>4-30</td>
</tr>
<tr>
<td>LPP (cmH2O)</td>
<td>24.3 (6.5)</td>
<td>20.0-40.0</td>
</tr>
<tr>
<td>Bladder capacity (mL)</td>
<td>220.0 (99.2)</td>
<td>70.0-440.0</td>
</tr>
<tr>
<td>DDI (minutes)</td>
<td>60.4 (59.1)</td>
<td>0.0-180.0</td>
</tr>
</tbody>
</table>

### Table III. Postoperative overall results.

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>p-value*</th>
<th>Range</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPP (cmH2O)</td>
<td>51.0 (14.3)</td>
<td>&lt;0.0005</td>
<td>18.0-80.0</td>
<td>NA</td>
</tr>
<tr>
<td>Diary – DDI (minutes)</td>
<td>195.6 (59.4)</td>
<td>&lt;0.0005</td>
<td>30.0-240.0</td>
<td>NA</td>
</tr>
<tr>
<td>DDI &lt; 180 min</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>4 (16.0)</td>
</tr>
<tr>
<td>DDI ≥ 180 min</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>21 (84.0)</td>
</tr>
<tr>
<td>DDI = 240 min</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>13 (52.0)</td>
</tr>
</tbody>
</table>

*The p-value corresponds to a two-tailed T-test for related samples (compared to baseline).
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(195.0 min in females and 196.7 min in males). The LPP difference was considerable, but again it did not show statistical significance. This has been possible because of the presence of outliers in both groups. The mean is sensible to extreme values, and this is the reason why the difference between means is broad. However, these isolated outliers are not enough to make this difference statistically significant.

It is believe that valuable information has been introduced regarding this new device. DDI revealed a clinical improvement and urodynamics observations represented an objective evidence of the increase of the urethral resistance. Safety related to this device and the procedure performed to implant it has been proved for this group of subjects since only one major complication was reported and this patient remains dry after the complication was overcome. Nevertheless, some limitations related to this study have to be recognized. The sample is small, represents a non homogenous group and there was unbalanced enrollment per centre. In addition, the follow-up is still being short to properly evaluate the long term response of the urinary tract, especially the urethra which is under compression stresses.

CONCLUSION

This mini-sling is easy to implant and does not negate additional procedures to be done at the bladder neck. In our limited experience, it has been shown to be a useful alternative for the treatment of incontinence due to neurogenic sphincteric incompetence using clean intermittent catheterization. Postoperatively, the mini-sling effectively increased DDI as well as LPP. Results must be confirmed by future larger studies.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

Promedon Argentina provided the mini-Sling Nephis used in this study.

REFERENCES AND RECOMMENDED READINGS

(*of special interest, **of outstanding interest)