Treatment of Stress Urinary Incontinence in Neurogenic Patients by an Injectable Elastomer Prosthesi: Preliminary Results


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Introduction:

Stress urinary incontinence is a common burden in neurological patients where lesion is located at a sub-sacral level (spinal cord lesion, spina bifida, myelomeningocele). The classic combination in these patients consists in underactive bladder and stress incontinence due to sphincter insufficiency. Unfortunately, in comparison urge incontinence which finds many solutions (antimuscarinic drugs, detrusor botulinum toxin injection), stress incontinence has always been of more tedious management (1). Furthermore, various treatment options such as artificial sphincters, hydraulic prosthesis, which are considered the most effective, are of difficult management mostly due to the higher risk of erosions and to the frequent need for self catheterization in this category of patients. (2) As far as classic injectable agents are concerned, many have already been described. Unfortunately either they do not ensure enough bulking, or migrate in time from their infiltration position (3) Furthermore all injectable products they can determine allergic inflammatory reactions but mostly none of them can be removed.

In spite of these considerations new products have been designed with a prime indication in women mild stress urinary incontinence or in male after prostate surgery. Urolastic (Urogyn BV, Nijmegen, The Netherlands) is a new bulking agent that consists of vinyl dimethyl terminated polydimethylsiloxane (PDMS) polymer, tetrapropoxysilane cross-linking agent, platinum vinyltetramethyl siloxane complex catalyst, and titanium dioxide radiopacifying agent. Its efficacy has already been described in the setting of female stress urinary incontinence (4) management and was considered an effective and long-standing urethral bulking agent with good and lasting efficacy for one year. However up to now, there are no descriptions of its use in the setting of neurological patients. The aim of this study is to present preliminary data with this device.
Material and methods.

This study is a pilot study. It aims at demonstrating the possible use of a novel bulking agent which is defined as an « injectable prothesis » in the setting of urinary stress incontinence in neurological patients and evaluate its efficacy. The secondary endpoint of the study is to evaluate pertinence of a future randomized control trial.

Five patients with urinary incontinence due to intrinsic sphincter insufficiency were identified. All were offered the possibility to participate in this study and were informed on the novel character of the device and signed informed consent for procedure. Inclusion criteria was the presence of symptomatic urinary stress incontinence due to intrinsic sphincter insufficiency and linked exclusively to lower chord lesion. Exclusion criteria consisted in the presence of an overactive bladder, organ prolapse, previous radiotherapy or procedure in the perineum or urethral region.

Patients grade of incontinence was based preoperatively on the need of auxiliary devices (condom, diaper) and their eventual number (daily requirements). Post operative continence was defined as perfect when dryness occurred between regular micturation or self catheterization. Persistence of incontinence was declared when patient did not observe any improvement or changes in device use whereas treatment of incontinence was considered successful when patient observed a significant improvement and reduced its use or type of devices.

Surgical technique:

Urolastic ® (Urogyn BV, Nijmegen, The Netherlands) is composed a Vinyl dimethyl polydimethylsiloxane PDMS, titanium coated, non bioabsorbable elastomer. It is presented in a prefilled, sterile, dual container of 5 mL (2 syringes x 2.5 mL), supplied with a static mixer that allows for adequate premixing of the syringe content. From a practical point of view it can be defined as an hybrid between bulking agent as it is injected at mid urethra but creates a soft cuff effect as it solidifies around it and therefore remains in the instillation site. Procedure can be performed under local.
anesthesia or no anesthesia depending on the lesion and therefore sensibility level. Patient is placed in a dorsal gynecological position. Antibiotic prophylaxis is performed by a tertiary cephalosporin (or other based on patients urinary infectious history). In woman, procedure is performed without cystoscope. Bladder is filled by 200 ml of sodium chloride and using a simple foley catheter which is put in tension, the length of urethra is measured and marked on catheter (fig 1-3). Before injection patient is asked to cough in order to evaluate the loss of urine before and after injection. This length is the reported on the applicator in order to perform injection with an 18 gauge needle (connected to dispenser) at mid urethra (fig 4-6). Injection of product is performed in 4 sites (12, 3, 6, 10 o'clock). In male patients, precise injection sites (at 5 and 9 o'clock) are identified thanks to a dedicated device placed on cystoscope (fig 7-8) and injection is performed under direct view at the level of the membranous urethra (fig 9 and 10); it is important to bear in mind that neurological patients suffer from stress incontinence with an indwelling prostatic gland). At the end of procedure, the bladder is filled up to 200 ml of saline solution and a cough test is performed. In these first procedures, radioscopic control of injection was performed as the product is radiolucent and therefore enables control but mostly follow up of the injected material (eventual migration even if not declared by manufacturer)

Assessment of outcome was performed through controls performed at regular intervals:

Results:

Results and preoperative characteristics are summarized in table 1. Of the five patients 2 were males and 3 females. Mean age was 48 (40-65) years old. Neurological disorder was medullary ischemia in two cases, one myelomeningocele, one infectious myelitis and one lower chord partial section (L1 ASIA C). All patients presented urinary incontinence due to intrinsic sphincter insufficiency confirmed by preoperative urodynamic evaluation showing full incontinence in 2 cases and loss of 50% of bladder capacity for the remaining patients. All patients needed preoperatively either urinary condom or diaper (mean 3/day). Peri-operative results

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showed a mean operative time of 45 minutes. No complications were recorded peri- or postoperatively.

With a mean follow up of 7.8 (5-12) months from surgery, 4 out of 5 patients referred subjective improvement of urine loss. Objective results through assessed bladder diary showed in men complete resolution of incontinence by passing from condom use to dry patients. In one case, of male patient, underactive bladder was associated with sphincter insufficiency. In the post operative control patient referred self-catheterization for volumes up to 500 ml with complete dryness in between catheterization. The other male patients referred to be completely dry not even using pads. As far as females patients are concerned, two present an improvement of incontinence passing from full diapers (mean use of 2-3 devices/day) to one small pad. The only treatment failure was observed in a patient with a low compliance bladder at preoperative urodynamic evaluation. This patient subsequently required detrusor botulinum toxine injection.

Discussion:

Treatment of stress urinary incontinence remains a major issue in non neurogenic patients. The addition of a neurogenic condition over it makes management even more difficult. In this study we demonstrate the efficacy of a novel agents which acts as an injectable prosthesis in the very particular setting of neurological patients. We believe it appears as a valid alternative to available techniques. In fact, although the gold standard remains artificial sphincter placement, no one neglects the possible complications of its use in a neurogenic patient: the frequent need for intermittent self-catheterization that increases the incidence of cuff erosion if the cuff is bulbous; pressure applied to bulbous urethra in wheelchair-bound patients; open bladder neck with sacral cord lesions with urine-filled prostatic urethra which is a potential source of infection with a bulbous cuff; and future endoscopic treatment risks erosion of a bulbous cuff (5). In fact one of the main advantages that we observed in these cases was first the soft cuff effect created by this device which we believe lowers the risk of erosion compared to artificial sphincters, ACT® or pro-ACT® which are of rigid composition. In fact Urolastic® hardens in situ into a flexible rubber-like plug which adapt itself to the shape of the local environment (4) therefore reducing the risk of
erosions. We acknowledge that grade of evidence is low as both our study or data available in literature for non neurogenic patients are very few. Nevertheless we believe that this singular characteristic for a prosthesis should be confirmed by larger randomized studies.

The composition of this device is also responsible for other advantages in confront to other injectable agents. Migration is considered to be one of the pitfalls of injectable agents and the reason of their dislike (6,7).

Indeed many promising agents have been in a first step approved by FDA and subsequently withdrawn from market for this reason (autologous fat; teflon) (8). In our experience and with a maximum follow-up of one year, patient did not complain from loss of effect when treatment had been effective. This confirms the observation made by Zadda (4) who did not encounter migration in 19 patients over a 12 month follow up period. He describes that Urolastic is effective and durable this being explained by the flexibility of the implant which enables it to adapt itself to the shape of the local environment during injection, thus reducing the chances for migration. He also states in the same article that Urolastic is a biocompatible and not biodegradable agent, giving him therefore long-term efficacy in the non neurological patient. With our case series description, we are able to confirm these findings in the case of neurological patients.

Another attractive aspect of Urolastic lies in its minimal invasiveness and its reversibility. Injection is fast, easy and requires at most introduction of a cystoscope as the procedure is percutaneous in confront to classical prosthesis procedures which now span from open to robotic surgery (5) adding a problem of costs to invasiveness. Furthermore, the radiolucence, the non migration of agent make it removable. In fact some bulking agents have been the cause of abscess formation, bladder hyperactivity, dispereumia. Although we did not observe any, authors authors have emphasized the importance of a possible removal thanks to easier localisation (Xray and fairly hard texture) and absence of migration.

Urolastic appears therefore as a feasible safe and durable treatment option for stress urinary incontinence in neurological patients. It is important to state that this case series is very small and as for all bulking agents, confirmation of these characteristics
should be confirmed by a randomized control trial in an homogeneous neurological patient population with a long follow-up.

Conclusions:

These preliminary results show that this procedure is feasible, safe and effective in neurological patients. The main advantages in confront to other options are:
1) Creation of a "soft cuff effect" easily and completely removable
2) No risk of migration
3) Minimal invasivity

However, a larger number of patients is required to fully confirm its indication in this setting.

8. Dani Zoorob, Mickey Karram. Bulking Agents A Urogynecology Perspective
Table 1: pre and postoperative results

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>Neurogenic disorder</th>
<th>Incontinence grade</th>
<th>Pre-treatment</th>
<th>Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>65</td>
<td>Medullary ischemia</td>
<td>Complete</td>
<td>Diaper</td>
<td>Small pad (1/day)</td>
</tr>
<tr>
<td>Female</td>
<td>42</td>
<td>Spina-Bifida</td>
<td>50% of urine loss</td>
<td>Diaper</td>
<td>Small pad (1/day)</td>
</tr>
<tr>
<td>Female</td>
<td>50</td>
<td>Myelitis</td>
<td>Complete</td>
<td>Diaper</td>
<td>No progress</td>
</tr>
<tr>
<td>Male</td>
<td>41</td>
<td>Spine lesion L1 ASIA C</td>
<td>50% of urine loss</td>
<td>Condom</td>
<td>Dry</td>
</tr>
<tr>
<td>Male</td>
<td>51</td>
<td>Medullary ischemia</td>
<td>50% of urine loss</td>
<td>Condom</td>
<td>Dry (self cath up to 500 ml)</td>
</tr>
</tbody>
</table>
Measurement of urethra length in female

101x57mm (150 x 150 DPI)
Measurement of applicator
101x57mm (150 x 150 DPI)
Dispenser with 18 gauge needle
196x56mm (150 x 150 DPI)
device placed on cystoscope and injection at level of perineum
111x61mm (150 x 150 DPI)
device placed on cystoscope and injection at level of penile
111 x 62mm (150 x 150 DPI)
endoscopic view before injection
102x98mm (150 x 150 DPI)
endoscopic view after injection
102 x 102 mm (150 x 150 DPI)