A retrospective analysis of 47 procedures using a bioresorbable polycaprolactone based injectable for the treatment of mild to moderate stress urinary incontinence in adult females

Andelo Mojsović,[1] Evert Koldewijn[2]

[1]Department of Urology, Šibenik General Hospital, Croatia; [2]Department of Urology, Catharina Hospital, Eindhoven, The Netherlands

Abstract

Over the recent years, potential long-term complications of permanent implants for urinary incontinence has become a topic of debate. As a result there is an increasing interest in less invasive and bioresorbable procedures from both healthcare professional as well as patients that ideally can be performed in an out-patient setting. This brief report describes our initial results using a novel bioresorbable injectable product for the treatment of female mild to moderate stress urinary incontinence. The results show that the majority of patients respond well to treatment and remain continent for the initial 12 months following injection. Complication rate is low and consisted of mild and transient events. These initial results are promising and merit further investigation into using this procedure as first-choice after unsuccessful conservative treatments such as pelvic floor muscle therapy.

Introduction

The treatment armamentarium for female Stress Urinary Incontinence (SUI) consists of a variety of options ranging from conservative treatment (*e.g.*, pelvic floor muscle therapy, pessary or electric stimulation) to invasive surgical intervention (*e.g.,* Burch colposuspension).[1] In many cases, a conservative approach often results in unsatisfactory results, leaving women untreated and gradually worsening as they are unfit or unwilling to undergo surgery. Also, there sometimes still is a false belief that SUI is a normal part of postpartum life. Hence, many females suffering from mild-to-moderate SUI are left untreated for too long.

The most used surgical intervention for female SUI is the Mid-Urethral Sling (MUS).[2] With the recent safety concerns and suggested underestimation of complications associated with MUS procedures,[3-5] there is a growing demand from both patients and physicians for less invasive treatment options with lower risk of complications. Moreover, when asking patients what they expect or prefer from a SUI treatment, this often differs from the physician's perception of success. Whereas physicians often look for a long-term solution or cure, patients are often looking for minimally invasive procedures providing relief and reduced impact on their quality of life.[4-6]

In this retrospective study we analyzed the effectiveness and safety of a new procedure for the treatment of mild-to-moderate SUI using a bioresorbable and collagen-stimulating injectable based on polycaprolactone. Moreover, we describe a small adjustment to the standard 3-point injection technique commonly used, which in our experience that enhances effectiveness. If successful, this procedure has the potential to bridge the gap between conservative treatment and more invasive surgical intervention with permanent materials, while leaving the latter option open for future treatment if needed.

Materials and Methods

In 2017 the General Hospital in Šibenik (Croatia) started with the out-patient treatment of SUI using Urethral Bulking Agents (UBA) based on periurethral dextranomer-microparticles/cross-linked hyaluronic acid (Urodex®) and non-resorbable (permanent) 2-component silicon elastomer (Urolastic®). Due to product characteristics such as non-bioresorbability, an alternative procedure was sought for female patients suffering from mild-to-moderate SUI. We therefore started to evaluate a new injectable product based on the medical polymer polycaprolactone (Urolon®, AQLANE Medical BV, The Netherlands) because of its bioresorbability and neocollagenesis characteristics. Between April 2019 and July 2020, we treated 47 female patients suffering from stress urinary in different age groups and incontinence severity with this injectable (see Table 1).

The product consists of 30% polycaprolactone microspheres (25-50µm) suspended in a carboxymethyl cellulose-based carrier-gel (70%). Here we present the initial results of our treatments and 12-month follow-up. Primary parameter was the return of continence, the duration of the continence period using the Stamey incontinence grading scale (SGS),[7] as well as complication rate.

As the procedure was new to our department, the initial 6 patients were treated in the operating theatre using propofol sedation. However, as the procedure is relatively easy and can be performed within 15 minutes, we soon changed to the out-patient setting using a periurethral block using 2%

Correspondence: Andelo Mojsović, Department of Urology, Šibenik General Hospital, Ul. Stjepana Radića 83, 22000, Šibenik, Croatia.
Tel.: +385.91.444.4979.
E-mail: anmojs@net.hr

Key words: Incontinence; injectable; UBA; polycaprolactone; bioresorbable.

Contributions: Both authors contributed to the treatment of patients, data analysis and preparation of the manuscript. The contribution in patient treatments of AM's exceeded that of EK. Both authors contributed equally to data analysis and manuscript preparation.

Conflict of interest: AM provides training services on the procedure on behalf of the manufacturer since 2020. EK was involved as principal investigator in the product's clinical trial for regulatory purposes and performs training activities for the manufacturer.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate: The Ethics approval was not necessary at the instutution where this study was carried out.

Informed consent: Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Received for publication: 1 March 2022.
Revision received: 18 May 2022.
Accepted for publication: 23 May 2022.

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

©Copyright: the Author(s), 2022
Licensee PAGEPress, Italy
Urogynaecologia 2022; 34:283
doi:10.4081/uij.2022.283

Publisher's note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guar-

lidocaine and dexketoprofen (1%; 2mL intramuscular) eliminating the need for the presence of an anesthesiologist. Moreover, there is no need for an operating theatre and therefore cheaper for the hospital and patient or healthcare insurer. Prophylactic gentamycin was administered to prevent urinary tract infection.

Procedures are performed as a transurethral cystoscopy-guided treatment, providing visual confirmation of correct product placement. Procedures are performed with standard cystoscopes (Olympus, Wolf and Storz as available in our urology department) with a ≥5 Fr working channel and standard cystoscopic injection needle (Williams Cystoscopic Needle 90001, 23G, 35cm, Cook Medical, Ireland).

Approximately 1.5 cm distal to bladder neck (mid-urethral) the needle was introduced into the submucosal tissue at a depth of approximately 3-5mm. In general, three (3) injections are done at the 2, 6 and 10 o'clock position using an average of 1.5 - 2.0 mL of product for SGS-1 (mild SUI), 2.0 - 2.5 mL for SGS-2 (moderate SUI) and up to 3.0 mL for SGS-3 (severe SUI). Contrary to the standard recommendation, we use our initial injection site as the main bulking area by injecting the largest volume of the three sites. This leads to the maximum coaptation possible from the initial injection site, using the other 2 sites for support and optimization. Moreover, in our experience it is preferred to maximize bulking to the point of urinary retention, followed by insertion of a 12Fr catheter for several minutes to allow the product to settle. Maximal bulking, in our experience, improves efficacy and prevents the need for re-treatments as described in literature for bulking agents in general. After treatment patients are discharged from the hospital on the same day after they have shown spontaneous voiding.

Results

Of the 47 females treated, all patients were dry immediately following treatment. In the follow-up period, 46 remained dry or had significant improvement of their incontinence 6 to 12 months post-treatment (see Table 2). In one patient with severe SUI incontinence we have no successes.

Although incontinence returned in 4 patients at 6 months post treatment (8.5%) and 6 patients at 12 months post treatment (12.8%), these patients were still improved versus baseline on the Stamey scale. Moreover, these patients also described their condition as improved and indicated to be satisfied with the results. In 1 patient with severe SUI a re-treatment was performed after 3 months due to insufficient results. However, this did not result in an improved result. We hypothesize that this was caused by an anatomically very short urethra of the patient (less than 3 cm). It is noteworthy, however, that none of the other patients received a re-treatment regardless of the SUI severity or initial result.

After 6 months, 43 patients (91,5%) are still continent. Per severity group this result was achieved in 93.9% (mild; 31/33), 91.7% (moderate; 11/12) and 33.3% (severe; 1/3), respectively. After 12 months the results showed an over effectiveness to continence of 87.2%. Per severity group showed as 93.9% (mild; 31/33), 75.0% (moderate; 9/12) and 33.3% (severe; 1/3), respectively (see Table 2).

Until today, December 2021, only 2 patients requested retreatment to improve their continence, which was performed after 14 months.

The treatment was generally well tolerated, both in the operating theatre as well as in the out-patient setting. Of course, patient management, distraction and some level of handholding is helpful, as patients may still feel some discomfort despite the local analgesia. No serious complications occurred and few mild and transient complications were observed (Table 3).

Discussion and Conclusions

In our hospital there was a need for an innovative injectable procedure for the

Table 1. Baseline demographic data; 43 of 47 patients were not treated for the SUI before. Age all patients (n=47): 56.2 (37 – 85).

	Age Average Yrs (range Yrs)	Previous treatments for SUI
SUI mild (n=32)	57.5 (37 – 74)	Dextranomer-microparticles/cross-linked hyaluronic acid (Urodex®); n=2 TVT; n=2
SUI moderate (n=12)	56.8 (39 – 85)	2-component silicon elastomer (Urolastic®); n=1 TVT; n=1
SUI severe (n=3)	44.3 (38 – 52)	N/A

Table 2. Effectiveness results 6 and 12 months post treatment shown per baseline severity group. Percentage of total patient group between brackets.

	Mild SUI (SGS1)			Moderate SUI (SGS2)			Severe SUI (SGS3)		
	Baseline	6 Mo (%)	12 Mo (%)	Baseline	6 Mo (%)	12 Mo (%)	Baseline	6 Mo (%)	12 Mo (%)
Continent	0	31 (93.9)	31 (93.9)	0	11 (91.7)	9 (75)	0	1 (33.3)	1 (33.3)
Mild	33	2 (6.1)	2 (6.1)	0	1 (8.3)	3 (25)	0	1 (33.3)	1 (33.3)
Moderate	0	0	0	12	0	0	0	0	0
Severe	0	0	0	0	0	0	3	1 (33.3)	1 (33.3)

Table 3. Overview of observed complication.

Cases	Observed complications	Intervention	Prolonged hospitalization	Resolved
1	Urinary retention	12Fr catheter	No	Yes, within 48h
5	UTI	Antibiotics	No	Yes
7	Urge incontinence	Solfenacin (5mg)	No	Yes, within 24h

OPEN ACCESS

treatment of SUI that could be used as a first-choice treatment option in different patient types and SUI severities. Although the results described here with the novel polycaprolactone-based injectable are still limited, it is suggested this complies with most to all of our needs in such first-option treatment. The procedure is shown to be safe, effective and well tolerated in both naïve patients as in patients who already had other interventions.

In line with the international recommendation for bulking agents,[8,9] this procedure is suited for women suffering from SUI but i) are planning pregnancy, ii) unwilling or unable to undergo surgery, iii) are looking for a procedure with a low complication rate rather than a high efficacy rate, and iv) had unsatisfactory results from surgical intervention. In addition, we feel the bioresorption and neocollagenesis characteristics of this specific product gives it the potential to become the first-choice interventional treatment after Pelvic Floor Muscle Training (PFMT) was tried with insufficient results. As such the product may bridge the treatment-gap between conservative and surgical intervention. In addition, if the treatment does not provide satisfactory results, it leaves the option for surgical intervention as it is bioresorbed, reducing the risk of interaction-induced complications.

Results from our study show a higher rate of complete continence as previously reported for this product.[10] This may be explained by the slightly different method of injection. However, as the published data concern a first-in-man study, it is like that a suboptimal initial injection was given. This is supported when comparing the injection volumes, which are higher in this report. Moreover, re-treatments were more frequently needed, also supporting our hypothesis. Nevertheless, in both studies satisfying results were found suggesting the product to be advantages and suitable as a first-choice treatment after insufficient results with PFMT.

More data is needed to further determine the position of this product within the range of treatment options. We are further building our experience in treating female SUI and simultaneously exploring other conditions that may benefit from the combination of non-permanent tissue bulking and connective tissue stimulation.

References

1. Lukacz ES, Santiago-Lastra Y, Albo ME, et al. Urinary incontinence in women: A review. JAMA 2017;318:1592-604.
2. Rovner ES, and Wein AJ. Treatment options for stress urinary incontinence. Rev Urol 2004;6:S29-47.
3. Blaivas JG, Purohit RS, Benedon MS, et al. Safety considerations for synthetic sling surgery. Nat Rev Urol 2015;12: 481-509.
4. Dwyer L, Weaver E, Rajai A, et al. "Voice your choice": a study of women's choice of surgery for primary stress urinary incontinence. Int Urygynecol J 2020;31:769-77.
5. Ong HL, Sokolova I, Bekarma H, et al. Development, validation and initial evaluation of patient-decision aid (SUI-PDA©) for women considering stress urinary incontinence surgery. Int Urogyn J 2019;30:2013-2022.
6. Robinson D, Anders K, Cardozo L, et al. What women want – their interpretation of the concept of cure. J Pelvic Med Surg 2003;9:273-77.
7. Stamey TA. Endoscopic suspension of the vesical neck for urinary incontinence in females. Ann Surg 1980;192:465–71.
8. Ghoniem G, Stanford E, Kenton K, et al. Evaluation and outcome measures in the treatment of female urinary stress incontinence: International Urogynecological Association (IUGA) guidelines for research and clinical practice. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:5-33.
9. Kastelein AW, Dicker MFA, Opmeer BC, et al. Innovative treatment modalities for urinary incontinence: a European survey identifying experience and attitude of healthcare providers. Int Urogynecol J 2017;28:1725-31.
10. Koldewijn EL, Oerlemans DJAJ, Beulens A, et al. Treatment of Mild to Moderate Stress Urinary Incontinence with a Novel Polycaprolactone-Based Bioresorbable Urethral Bulking Agent. Urogynaecologia Int J 2022;34:287.

Non-commercial use only