ORIGINAL RESEARCH ARTICLE

The Safety and Efficacy of Periurethral Injections of Bulking Agent in Women with Urinary Incontinence

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ABSTRACT

Background: At present, among the most widely used procedures carried out in the treatment of stress urinary incontinence (SUI), urethral bulking agent (UBA) injection comes second. It is a second-choice treatment procedure after urethral sling placement. Urinary incontinence attributable to intrinsic sphincter deficiency (ISD) is treated with UBA injection. Although several bulking agents have been suggested and tried while some have been removed from the market because of safety reasons, the hunt for a perfect bulking agent is still on.

Aim of Study: To evaluate the efficacy of the treatment of stress and mixed urinary incontinence (UI) in women using a peri-urethral injection of the bulking agent hyaluronic acid dextranomer gel (NASH.DX)-Urodex.

Patients and method: A prospective cohort study that included 24 women with SUI was was carried out in Ghazi Al-hariri hospital for Surgical Specialties between November 2016 and December 2017.

Results: Mean patients' age is 44 years (range13–75 years) with a mean parity of 5.5 (range from 2–9 child). The mean operating time is 14 minutes (ranging from 13-15 minutes). Postoperative complications occur in four patients (16.6%), two patients have urgency 8.3% and 1-patient dysuria 4.16% and one patient failed. No patient has developed an infection at site of injection or hematoma or retention

Conclusion: The UBA procedure can be employed for the management of patients with SUI and MUI as an effective and safe technique.

Keywords: Bulking agents, MUI, SUI.

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INTRODUCTION

Urinary incontinence (UI) has been defined as "the complaint of an involuntary leakage of urine." UI occurs if the bladder does not receive proper brain signals, the contraction of the sphincters are not strong enough, or both. There may be too much or not enough contraction of the bladder muscles as a result of muscular problems or a problem with the nerves that control it. The sphincter may perform poorly due to damage to its muscles or the nerves that control these muscles. These problems may be simple or complex. UI is a long-lasting, irking problem that increases with age. In long-term care facilities, it affects 50-84% of the elderly and is more than twice as common in females than in males at any age.[1]

UI is Classified as:

Stress urinary incontinence (SUI); Urgency urinary incontinence (UUI), and Mixed urinary incontinence (MUI)[2]

Stress urinary incontinence (SUI) has been defined by the International Continence Society (ICS) as an involuntary leakage of urine that results from inherited or acquired defects of the pelvic organs with the absence of vesicourethral anatomic support.[3,4]

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Non-surgical Treatment Method

A. Behavior changes B. Exercises (Pelvic floor muscle training (PFMT), also called Kegel exercises) C. Bladder training.[5,6]

Medical Devices: A. Electric stimulation B. Magnetic stimulation and C. Percutaneous Tibial Nerve Stimulation (PTNS).[7,8]

Medical Treatment

Depending on the type of UI that a patient has, several different kinds of medicines can be used to help improve UI by doctors.

Medicines for Stress Incontinence

A. Estrogen: As a female hormone, estrogen production in the body decreases as one ages. Topical estrogen comes in the form of skin patches, tablet or ring that is placed in the vagina, and is sold under various brand names.

B. Duloxetine: This medicine is used in treating patients with depression, anxiety, and chronic muscle pain and tiredness. However, it is used for treating stress incontinence by some doctors as well.[9]

Medicines for Urgency Incontinence

All the medicines that are used for the treatment of urgency incontinence were made for that purpose. Urgency incontinence was improved by all the medicines studied; for example, they either reduced the number of times leakage occurred or reduced the leakage amount. With the help of some medicines, women have been able to prevent leakage totally. These medicines can be used for treating mixed incontinence (where a woman has both stress and urgency incontinence).

Surgical Procedures

- Retropubic suspension
- Transvaginal suspension
- Sling procedure
  - » Autologous rectus fascia, fascia lata (from the thigh), vaginal wall slings.
  - » Non-autologous allograft fascia lata from donated cadaveric tissue.
  - » Synthetic monofilament polypropylene tape [tension-free vaginal tape (TVT)]
- Artificial urinary sphincter[10]

Injection Therapy with Urethral Bulking Agents (UBAs)

The use of injection of urethral bulking agents (UBAs) is a good illustration of less invasive treatment of SUI. In clinical trials, a diverse array of urethral bulking materials have been employed. A perfect bulking agent should be nonantigenic, acellular, bio-compactible, non-immunogenic and after infiltrating the urethral tissue, should not cause fibrosis.[11,12] UBIs that can be injected fall along this spectrum and provide an option for selected women with SUI less invasive. The use of bulking agents dates as far back as 1900, when Gersuny was reported to have described an injection therapy with periurethral paraffin wax for SUI.[13]

After this report, the use of UBAs has developed greatly and now includes new materials, injection techniques, and an increasing body of clinical data. However, the role played by UBAs in the management of SUI, is currently still a matter of debate. The restoration of normal mucosal coaptation (augmentation) remains the mechanism of action of UBAs. An elevation of the urethral mucosa is obtained by injecting the bulking agent into the submucosal space. As a result, coaptation and urethral resistance is increased.[14] Easy injectability, cost-effectiveness, biocompatibility, etc., should be characteristics of the ideal bulking agent.[15]

Available Bulking Agents for UI

- *Polytetrafluoroethylene (Teflon):* has been investigated as an implant material no longer used little evidence of efficacy.[16]
- *Autologous fat:* no longer used. Local discomfort associated with harvesting procedures.[17]
- *Macroplastique:* silicone elastomer polydimethylsiloxane suspended in polyvinylpyrrolidone PVP Carrier. It is a permanent implant applied by transurethral technique – injection beneath the lining of the urethra can cause urethral erosion with irreversible damage in case of failure of the procedure must be done in the operation room.[18]
- *Contigen:* Glutar aldehyde cross-linked bovine collagen: it begins degradation within 12 weeks with complete degradation within 19 months, and the patient must undergo a skin test to exclude hyper insensitivity due to collagen (animal origin) before one month of the procedure.[11]
- *Bulkamid:* 25% polyacrylamide hydrogel, 97% pyrogenic water, is a permanent implant (non-biodegradable).[19]
- *Durasphere:* Carbon-coated zirconium oxide particles suspended in a water-soluble B-glucan vehicle is a permanent implant; upon clinical trials. Durasphere migrates from implantation site, which might cause permanent urinary retention.[20]
- *Coaptite:* calcium hydroxyapatite particles suspended in sodium carboxymethylcellulose, water, glycerin gel form carrier, upon clinical trials the particles becomes deformed, irregular along with migration from injection site resulting in periurethral fibrosis, obstruction, prolapse.[21]
- *Tegress:* formerly known as URYX: ethylene-vinyl alcohol copolymer suspended in dimethyl sulfoxide: have discontinued sales due to reports of 37% erosion rates.[22]

Hyaluronic Acid/Dextranomer Gel (NASHA/dx)

Why use (NASHA/dx)? What are the added benefits of (NASHA/dx)? The benefits of it are summarized as follows:

A. Biocompatible: as the used materials is a natural component of human body tissues, it is non-immunogenic (non-animal origin), and biocompatibility is optimal due to formation of fibroblast and collagen fibers that surrounds the microparticles.

B. Biodegradable: the used materials are completely degradable with a safe clinical profile.

C. Long action duration: due to cross-linking process that extends up to 5 years.

D. No Migration from implant site: due to positively charged microparticles, the positive charge plays a role in (anchoring) the implant through inter-cellular interactions

leading to fibroblasts and collagen fibers surrounding the implant material as well that microparticles size used ensures no migration. (Safe particle size–80 micron)

E. *Stimulation of collagen formation:* due to positive charges.[23]

PATIENTS AND METHODS

A prospective cohort study included (24) women with SUI (19) and mixed UI (5) in Ghazi al-Hariri Surgical Specialities Hospital between November 2016-December 2017

Inclusion criteria: Women from 13 to 75 years of age, diagnosed with SUI during urodynamics (urodynamic SUI) and with a Stamey grade of 1-2-3 were considered. A bladder capacity of 300 mL or above and a postvoid residual urine volume that exceeds 100 mL was required for all patients. Before any anti-incontinence behavior therapy, persistent SUI requires UBA (NASHA/dx) because it is more suitable. Patients who were at high risk to anesthesia and with advanced age. Other indications include Young patients who may want to get pregnant in the future was among other indications

Exclusion criteria: Women were excluded who had pure urgency incontinence as the principal component, a detrusor overactivity (DO) that had been proven urodynamically, pelvic organ prolapse (POP), women who had a neurogenic (flaccid) bladder or were using an indwelling urinary catheter on a chronic basis. Women with urinary tract infection that is active and a history of hypersensitivity to the bulking agent.

Procedure

Patients were placed in the lithotomy position. 6–10 mL lidocaine 1% was used for local anesthesia; wait 8–10 minutes for anesthesia to take full effect before measuring the length of the urethra.

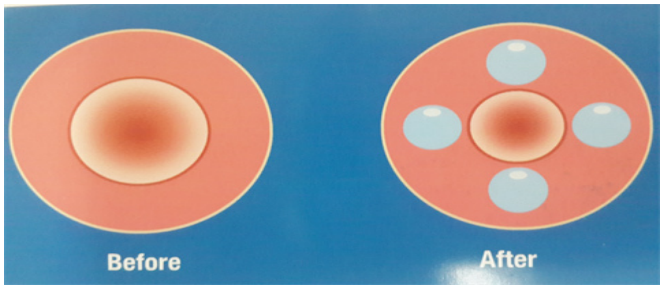

Figure 1: After injection.

A. insert balloon catheter to the bladder
B. inflated catheter
C. pull catheter till it stops
D. mark catheter by marker clamp, or hold with our hand while deflating balloon
E. pull catheter all the way out and measure length between balloon and mark on the applicator, mark the length of the urethra with elastic rubber band, or use the marking on the applicator.

Application

- Insert applicator in urethra to the marking, and hold it secure remember the first injection direction
- Insert 20 gauge needle in applicator until it clicks. The click means the needle is all the way in. make sure the bevel of needle is facing toward the applicator
- Inject one syringe of UBA with gentle continuous flow.
- Hold applicator, and withdraw the syringe and needle

All patients were treated with UBA Applicator, a special design for minimal invasive and safe implantation. Controlled implantation in a 4 position (3, 6, 9, 12) symmetrical placement with an injection volume of 1 mL per position and symmetrical depth of implantation in 4 positions (Figure 1). Periurethral Injection technique in Mid-Urethra. They were designed with measurements for implantation in the precise site (Mid-Urethra). The patient was asked to drink water so that the urinary bladder became filled up to 200 mL, and a cough test was performed after an ultrasound check. After the procedure, a prescription of 1 g AB was issued for 5 days.

RESULTS

24 patients were enrolled in this study, mean patient age was 44 years (range 13–75 years) (Figure 2). One of them single 4.16% the other 23 were married 95.8% and 7 pt post menopause 29.16% the other 16 premenopausal 66.6% and parity range (2–9 child) mean 5.5 the mean operating time 14 minutes (13–15 minutes). 4 patients had surgical intervention 16.6% (3-hysterectomy + 1anterier repair)

5 patients had mixed urinary incontinence 20.8%, and 19 patients had SUI 79.1% (Figure 4); all patients underwent local anesthesia. The total incidence of postoperative complications was 16.6% (4/24).

2 patients have urgency 8.3% treated with the anti-cholinergic drug for 2 weeks and 1 patient dysuria 4.16%

Table 1: Summary of main study outcomes at the 12-month

	1-month follow-up	*3 months follow-up*	*6 months follow-up*	*12 months follow-up*
Number of patients (24)	12/24	22/24	20/22	14/16
Dryness	12 (50%)	22 (91.6%)	20 (90.9%)	14 (87.5%)
Urinary retention	-	-	-	-
Urgency	2	8.3%	0%	0%
Dysuria	1 patient	4.16%	0%	0%
Hematoma	0%	0%	0%	0%
Allergy	0%	0%	0%	0%
Failed	1 patient	4.16%	4.16%	

Figure 2: Age distribution.

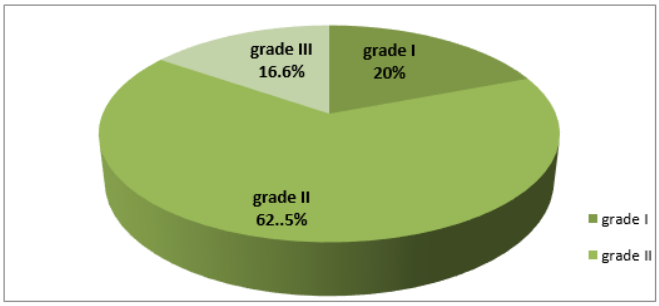

Figure 3: Stamy scale grade

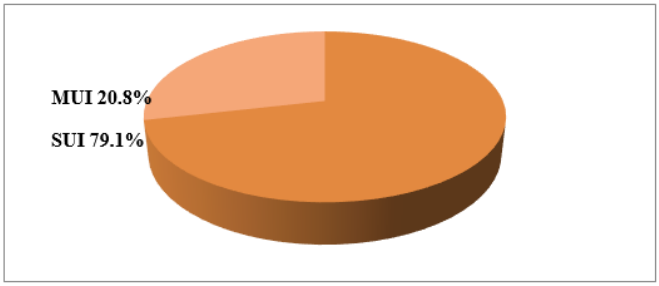

Figure 4: Type of UI in this study

disappeared after 1 week of treatment with simple analgesic and one patient failed no patient developed infection at the site of injection or hematoma or retention, hospitalization 5 hours post-operation depended on subsequent satisfactory urinary flow then patients followed up before discharge and 1month, 3, 6, and 12 months (Table 1). 22 patients were followed up at 3 months and at 6 months; 2 patients did not have a complete follow-up visit at 6 months as a result of loss of contact. There was a significant decrease in the mean Stamey incontinence grade from (visit I) at 4 weeks (visit II) at 3 months (visit III) at 6 months and 12 months (visit IV). The percentage of patients who were dry 50%. At the visit I (12/24). Stamey G,2,1, change to G0(dry) percentage increased to be 91.6 % at visit II(22/24), 90.9% at visit III (20/22), and 87.5% (14/16) at visit IV. 4 patients G3 16.6%, 15 patients G2 62.5%, 5 patients G1 20% (Figure 3).

DISCUSSION

The SUI may be of extrinsic or intrinsic origin in women. Extrinsic origin, on the one hand, is caused by a lack of support to the urethra and bladder neck by the pelvic floor, causing hypermobility of the urethra. On the other hand, the intrinsic origin is due to a dysfunction of the sphincter mechanism of the urethra (i.e., intrinsic sphincter deficiency). A finite cure to most of these conditions is by surgical correction, for example, mid-urethral slings. These procedures, however, are associated with morbidities, risk of failure and redo because they are invasive. As a result, many women seek for therapies with reduced complication rates and that are less invasive.[24]

After 3, 6, and 12 months of follow-up, there was an improvement in the Stamey scale of 95.8% of the women that were included in the study, and by this, we successfully achieved the primary efficacy of our study. This is similar to, or even better than, the 12-month outcome of other studies, in which the application treated SUI of Macroplastique silicone material bulking agent. 10 out of 18 (55%) patients were reported by Ter Meulen *et al*.[25] to have become dry with a Stamey grade of 0 after 12 months of initial therapy. 57% of patients were reported to be dry after 12 months of initial therapy by Ghoniem *et al*.,[26] After 12 months of initial therapy, 73% of patients with Stamey grade 0 were reported by Tamanini *et al*.[27] When other complications such as, urine retention, hematoma, abscess at the site of injection, and embolism are compared, our study is better than other studies. An indwelling catheter was used to resolve this for 3 days in 2 patients; After using clean intermittent catheters for 3 weeks, 1 patient could void spontaneously.[28]

CONCLUSION

Stress and mixed incontinence can be treated with a periurethral injection of NASHA/dx because it is both minimally invasive and convenient. Patients' quality of life and satisfaction can be improved significantly by injection of this agent. With a careful selection of patients, better results with high efficiency can be obtained using modern periurethral methods. However, on the average, duration of effect may take up to a year, and retreatment is required for maintenance.

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