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Transurethral injection of polyacrylamide hydrogel (Bulkamid®) for the treatment of female stress or mixed urinary incontinence

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ABSTRACT

Objective: The aim of this study was to evaluate the cure effect of a transurethral injection (TUI) of Bulkamid® for female urodynamic stress (USI) and stress-predominant mixed urinary incontinence. The hypothesis was that the cure effect of Bulkamid® is positive in patients who have undergone previous unsuccessful anti-incontinence surgery and in patients with ISD (Intrinsic Sphincter Deficiency).
Study design: This retrospective clinical study was performed on 52 patients for whom previous anti-incontinence surgery had failed ($n = 40$) and on patients with ISD. Five patients had a reinjection of Bulkamid®. The efficacy of TUI was evaluated an average of 22 months (minimum – 6 months, maximum – 50 months) after the procedure. Subjective assessment of the leakage of urine was based on the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-UI SF). Objective assessment of leakage of urine was assessed by the cough test. The cure effect of procedures was evaluated by VAS (Visual Analog Scale: VAS score 0–100; 100 – without leakage of urine, dry) and by using the five-point Likert scale. The statistics were calculated using the software STATISTICA 10-StatSoft. Inc software (Tulsa, USA).
Results: A retrospective study was performed on 52 women with urinary incontinence (stress 43, mixed 9), and 51 patients completed the study. One patient with SUI died during the study.

Their mean age was 70 years, mean body mass index (BMI) was 28.65, and mean parity was 1.76. Objective assessment by cough test showed that 19.6% of patients had negative results for this test 22 months after the operation. Subjective assessment by the ICIQ-UI SF questionnaire showed that 15.7% of patients were completely dry, while 45.1% of patients were dry or improved. The mean VAS score was 51.3, and on the Likert scale the cure effect was evaluated as 5 or 4 (“cured” or “improved”) in 54.9% of patients.
Conclusions: The hypothesis that the cure effect of Bulkamid® is positive in patients who have undergone previous unsuccessful anti-incontinence surgery, and in patients with ISD, was confirmed. The procedure is an option for failed anti-incontinence surgery or for patients with ISD.

1. Introduction

The prevalence of stress urinary incontinence (SUI) is reported to range from 12.8% to 46.0% of women [3,31]. Polypropylene mid-urethral slings (MUS) are widely used for the treatment of SUI. This procedure can claim a high success rate, and it is accompanied by only minimum complications, but sometimes this procedure can fail [8,27,34]. Among the options when it is necessary to resolve failed MUS are a repeat of MUS, the use of a pubovaginal sling and the use of a bulking agent [16]. To date there are no guidelines for the recurrent treatment of SUI. Bulking agents were first used for the treatment of stress urinary incontinence by Meyer more than 100 years ago [35]. The success of “bulking agents” is based on a mechanism whereby, according to the hypothesis, the injection of bulking agents into the urethral submucosa creates an artificial urethral mass which improves urethral coaptation and hence restores continence [10,15,25,36]. A second theory explains the efficacy of bulking agents by claiming that the mass in the urethra creates a segment of increased contractility of the rhabdosphincter by prompting increased stretch of the muscle fibers [12,35].

Abbreviations: ISD, Intrinsic Sphincter Deficiency; ICIQ-UI SF, The International Consultation on Incontinence Questionnaire – Short Form; SIS, single incision slings; SUI, stress urinary incontinence; TVT, tension-free vaginal tape; TOT, tension-free obturator tape; TUI, transurethral injection; USI, urodynamic stress incontinence; VAS, Visual Analog Scale.

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Bulkamid® is a biocompatible and homogeneous polymer gel consisting of 2.5% cross-linked polyacrylamide and 97.5% water for injection [2,37]. The gel is inhabited by macrophages and giant cells, later followed by fibroblasts, forming a fine fibrous network. Tissue integration is completed approximately 12 months after surgery [9]. The gel stays in place and does not change in volume or disintegrate. Bulkamid® is integrated into the tissue of the urethra and, as it is hydrophilic, it encourages continuous water exchange between the Bulkamid® and the surrounding tissue, which reduces the risk of later complications.

The aim of this study was to evaluate the cure effect of a transurethral injection (TUI) of Bulkamid® for female stress and stress-predominant mixed urinary incontinence in patients who have undergone previous unsuccessful anti-incontinence surgery and in patients with ISD.

2. Materials and methods

A total of 52 women were recruited to participate in this study between July 2008 and June 2012. This retrospective clinical study was performed on 52 patients with urinary incontinence (stress 43; mixed 9) for whom previous anti-incontinence surgery had failed ($n = 40$) and on patients with ISD (Intrinsic Sphincter Deficiency) – MUCP (Maximal Urethral Closure Pressure $\leq$ 20 cm H_2O) ($n = 12$). Urodynamic stress incontinence (USI) and ISD were assessed urodynamically [18,32]. The multichannel urodynamic studies were performed in the semi-supine position, using a UROMIC 7 recorder (Medkonsult, Czech Republic) and 3-way water perfusion urodynamic catheter, Charr 12 (Medetron, Czech Republic). Total abdominal pressure was determined by a rectal balloon catheter, and detrusor pressure was subtracted (vesical minus abdominal). At the beginning of the study, pressure transducers were set at zero according to atmospheric pressure at the level of the bladder. During filling cystometry normal saline warmed to body temperature (37 °C) was infused until capacity was reached as determined by the patient, or the filling was interrupted when infused volume 500 ml was reached (filling rate 50 ml/s.

Maximum urethral closure pressure (MUCP) was assessed as part of urethral pressure profile measurements. The pressure catheter was withdrawn by an electric catheter puller. Two consecutive urethral pressure profiles were performed at rest and during maximal Valsalva maneuver at bladder volumes of 500 ml (or cystometric capacity). The water perfusion rate was 2 ml/min, and the mechanical withdrawal rate was 1 mm/s.

Three patients had both previous anti-incontinence surgery and ISD. 51 patients completed the study: one patient with USI following MUS died during the study for reasons unconnected to the operation. Five patients had a reinjection of Bulkamid® after a check-up at 3 months after the operation, which established that the procedure had failed; the Bulkamid® was reapplied submucously, and the cure effect of Bulkamid® was evaluated minimally 6 months after the second operation.

The transurethral injection of Bulkamid® was performed under local anesthesia (4 ml, 2% lidocaine in sterile saline – 6 ml, injected into the urethral wall). Bulkamid® was injected under urethroscopic control into the submucosa through the urethra using a 23G needle. Three deposits were positioned 1 cm distal to bladder neck at the 2, 6 and 10 o'clock positions. At each position an average of 0.46, 0.48 and 0.44 ml of Bulkamid was injected, so the total mean mass of Bulkamid® was 1.39 ml (SD 0.28). Before the injections the women received prophylactic antibiotic treatment in the form of an intravenous dose of Sulbactamum 0.5 g + Ampicillinum 1 g (Unasyn 1.5 g). The women were discharged after successful voiding the next day. The efficacy of TUI was evaluated an average of 22 months (minimum – 6 months/172 days; maximum – 50 months/1534 days, mean number of days 660) after the procedure. Subjective assessment of the leakage of urine was based on the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-UI SF) [1,5]. Improvement in urinary incontinence was defined as a drop in the score of more than 50% compared to before the operation. Objective assessment of leakage of urine was assessed by the cough test. A cough test was performed with the patient placed in the supine position and the bladder filled with 300 ml. The cure effect of procedures was evaluated by the five-point Likert scale. The evaluation of the five-point Likert scale was: 5 – cured, very satisfied; 4 – improved, satisfied; 3 – no change to preoperative status; 2 – worsened, not satisfied; 1 – significantly worsened, not satisfied. For the next evaluation of the cure effect the VAS (Visual Analog Scale) was used (VAS score 0–100; 100 – without leakage of urine, dry).

This study was approved by the local Ethics Committee as part of a national grant application, and all subjects gave written consent to their participation in the study. All applicable institutional and governmental regulations were followed during the course of this research.

The statistics were calculated using the software STATISTICA 10-StatSoft. Inc software (Tulsa, USA). All quantitative data were expressed as mean $\pm$ SD. Paired *t*-tests were used to compare patient' scores before and after the operation. Tests were performed at the 5% level of significance.

3. Results

51 patients completed this retrospective study. Their mean age was 70 (SD 13.98; range 18–90), mean body mass index was 28.65 (SD 4.30), and mean parity was 1.76 (SD 0.83).

In the course of the operation procedure we only once experienced a complication in applying Bulkamide® – a rupture of the urethral mucous membrane at the point of the bulking. The material was then applied submucously, at a point other than that of the original injection, into unharmed tissue. We did not observe any major bleeding from the punctures in the urethral wall, nor was there any problem with urine retention after the operation, or with *de novo* urgency. In five patients there was only minimal improvement of USI after the first application of Bulkamide®, or none at all, so a reoperation was carried out after a check-up at 3 months after the operation, when the Bulkamide® was reapplied submucously. There were no significant complications related to the TUI procedure.

Objective assessment by cough test showed that 10/51 (19.6%) of patients had negative results for this test 22 months after the operation. Subjective assessment by the ICIQ-UI SF questionnaire showed that 8/51 (15.7%) of patients were completely dry, while 23/51 (45.1%) of patients were dry or improved. The mean score before the operation was 17.59 (SD 2.67), and after the operation it was 10.55 (SD6.48). There is a statistically significant difference with respect to the ICIQ-UI SF score ($p < 0.001$). The changes in the score in answer to the question "Overall, how much does leaking urine interfere with your everyday life?" before and an average of 22 months after the operation showed a statistically significant difference in the score of improvement from 9.09 (SD 1.28) to 5.37 (SD 3.73) ($p < 0.001$). The mean VAS score was 51.3 (SD 38.3) and on the Likert scale the cure effect was evaluated as 5 or 4 ("cured" or "improved") in 28/51 (54.9%) of patients.

4. Comment

Our study assesses the cure effect of transurethral application of Bulkamid® in patients suffering from stress or mixed-type of

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