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ABSTRACT

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EFFICACY OF POLYACRYLAMIDE HYDROGEL FOR FEMALE URINARY INCONTINENCE: OUTCOME OF A SINGLE CENTRE

Introduction: Periurethral injection with polyacrylamide hydrogel (PAHG, Bulkamid®) is a minimally invasive treatment option to be considered for women with stress urinary incontinence. The manufacturer recommends injecting between 1.5 ml and 2 ml periurethrally. This study aims to evaluate the long-term efficacy of PAHG, and to determine whether there is a correlation between the volume of PAHG injected and the outcome in terms of symptoms.

Methods: A retrospective study was conducted between 2011 and 2018. Patients were contacted by telephone and the International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) was used to assess their symptoms. A linear regression analysis test was performed to assess the correlation between the outcome and the volume of PAHG injected.

Results: One hundred and fifteen PAHG injections were performed on 101 patients. The volume of PAHG injected ranged from 0.8 ml to 3 ml. Two patients reported procedure-related complications. Of the patients that attended their three-month follow-up, 62 (58.5%) patient-episodes reported an improvement. 62 patients were contacted by telephone and the median length of follow-up was 37.5 months. An improvement in the ICIQ-UI SF score was observed in 45.8% of patients with a mean improvement of 4 points. The volume of PAHG injected did not affect the outcome. 31% also reported a benefit with PAHG five years after their injection following previous incontinence surgery.

Conclusions: PAHG injection is safe and improves symptoms of urinary incontinence at up to 7.5 years in 45.8% of women. PAHG is also useful after previous incontinence surgery. The volume of PAHG injected did not influence the outcome.

Keywords: polyacrylamide hydrogels, urinary incontinence, urinary stress incontinence.

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INTRODUCTION / ВСТУП

Urinary incontinence (UI) is a common condition with an estimated prevalence of 27.6% in women. The commonest type is stress urinary incontinence (SUI), representing half of all UI [1]. Risk factors include age, body mass index (BMI), parity and hysterectomy [2]. SUI is defined as "the involuntary leaking of urine during effort or exertion, or while sneezing or coughing" [3]. Amid the recent controversies on the use of mesh surgery and associated complications, women are considering alternative surgical options for SUI. Periurethral injection with intramural bulking agent is a minimally invasive treatment option. PAHG is a biocompatible polyacrylamide hydrogel (PAHG) which contains 2.5% cross-linked polyacrylamide and 97.5% water. It is non-degradable and produces predictable-sized cushions when injected into the urethral submucosa [4, 5]. Previous studies have shown that PAHG is effective, with 67–77% of patients considering themselves cured or improved at 12 months [6, 7]. It has a strong safety profile with a low risk of procedure related complications [8]. The manufacturer recommends injecting between 1.5–2 mls [9]. However, there are no published studies evaluating the optimal volume of PAHG to inject. This study aims to evaluate the long-term efficacy of PAHG and determine whether there is a correlation between the volume injected and outcome.

Materials and Methods

A retrospective study was conducted between July 2011 and October 2018. Records of 115 PAHG injections in 101 patients were available for analysis. This study was a service evaluation project and was exempt from formal Institutional Review Board and Research Ethics Committee approvals. Periurethral injection of PAHG (Contura Ltd.) was performed using a single use PAHG cystoscope under general anaesthesia. Using a needle through a rotatable sheath, deposits of PAHG were injected into the urethral tissue at 2, 6 and 10 o'clock to achieve coaptation of the urethral lumen [9]. Three experienced surgeons performed the procedure at our centre. The volume of PAHG injected varied and was determined by the surgeon. The volume ranged from 0.8 ml to 3 ml.

Patients were routinely invited for a clinic follow-up at three months and their subjective perception of the effectiveness of their treatment (significant, moderate or mild improvement, no change or worse) was recorded. Long term follow-up was undertaken with a structured telephone consultation by one independent investigator. The median length of follow-up was 37.5 months [interquartile range (IQR) = 12.8 to 66.5]. When patients were telephoned the International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) questionnaire was used [10]. Patients were asked to report both current and pre-procedure symptoms to calculate their scores. Linear regression models were used to evaluate the relationship between volume of PAHG and long-term outcome. Where a patient received more than one PAHG injection, data from their first index procedure was used when performing linear regression. Statistical analysis was performed using SPSS Statistics Version 25 (IBM Corp).

Results

One hundred and one patients had PAHG injected, 11 patients had the procedure twice and one had it four times. The median age, BMI and parity were 53, 26 and two respectively. Of the 101 patients, 91 (90.1%) had pure urodynamic stress incontinence diagnosed prior to the procedure (Table 1). Eighty nine (88.1%) women had physiotherapy prior to the procedure. Sixteen (15.8%) patients had prior incontinence surgery (excluding previous PAHG injection) with colposuspension being the most common procedure (n = 9) (Table 2).

Table 1 – Findings on urodynamic evaluation prior to PAHG injection

Urodynamic study finding	Number
Mild stress incontinence	30
Moderate stress incontinence	32
Severe stress incontinence	26
non-specified stress incontinence	3
Detrusor overactivity	1
Mixed	8
Normal	1

Table 2 – Incontinence surgery prior to PAHG injection

Prior incontinence surgery	Number
Colposuspension	6
Tension-free vaginal tape (TVT)	2
Bladder neck injection with collagen	2
Colposuspension, botulinum toxin injection	1
Colposuspension, TVT, bladder neck injection with collagen	1
Colposuspension, percutaneous posterior tibial nerve stimulation	1
Transobturator tape (TOT)	1
Percutaneous sacral nerve stimulation, TVT, bladder neck injection with collagen	1
Marshall-Marchetti-Krantz (MMK) procedure	1

The volume of PAHG injected is described in Fig. 1 with 100 of the 114 (88%) having between 1.5–2 ml injected in accordance with the manufacturer's guidance. In one patient, the volume of PAHG was not recorded in the operation notes. Procedure related complications were reported by two patients; one (0.87%) urinary tract infection (UTI), and one (0.87%) woman with urinary retention requiring three months of intermittent self catheterisation.

Of the 106 patient-episodes that received a follow-up clinic appointment at three-month post-procedure, 62 (58.5%) reported an overall improvement in their symptoms (Table 3). Twelve patients (11.9%) had repeat PAHG injections. The median time between their initial and repeat procedure was 21.1 months (IQR = 7.3 to 36.6). Nine (8.5%) had further incontinence surgery following PAHG injection with six women opting for a mid-urethral sling (MUS).

Table 3 – Patient outcome at three months

Outcome	Number of patient-episodes (%)
significant improvement	39 (36.8%)
moderate improvement	14 (13.2%)
mild improvement	9 (8.5%)
no change	41 (38.7%)
worse	3 (2.8%)

Telephone follow-up with ICIQ-UI SF questionnaire was undertaken for 61 patients (72 patient-episodes), including eight patients who had PAHG injections twice and one who had it four times. The other patients could not be reached via telephone and were lost to follow-up. The median length of follow-up was 37.5 months (range from 4 to 91 months). An improvement in score was observed in 33 (45.8%) patient-episodes (Table 4).

Table 4 – Long term follow-up at a median of 37.5 months. ICIQ-UI SF: International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form

Change in ICIQ-UI SF score	Number of patient-episodes (%)
no change	37 (51.4%)
improved	33 (45.8%)
worse	2 (2.8%)

The mean ICIQ-UI SF score improved from 15.4 to 11.2 post-procedure (paired t-test, $p < 0.001$ two tailed). Multiple linear regression analysis was used and there was no significant association between the volume of PAHG and the ICIQ-UI SF score after the index procedure (n = 61), after adjusting for age, BMI, parity and length of follow-up (Table 5).

Table 5 – Association between variables and Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) score post index procedure (n = 61)

Variable	B	95% CI for B	P value
Volume	-4.12	-10.07 to 1.83	0.17
Age	-0.02	-0.11 to 0.07	0.67
BMI	-0.02	-0.29 to 0.24	0.86
Parity	0.60	-0.66 to 1.86	0.34
Length of follow-up	0.02	-0.05 to -0.10	0.56
Pre-procedure score	0.52	0.06 to 0.98	0.03

Note: *B is linear regression coefficient. CI is confidence interval*

A further multiple linear regression analysis was performed after excluding women who had prior

incontinence surgery. Similarly, no significant association was observed between the volume of PAHG and the ICIQ-UI SF score after the index procedure (n = 49). Of the sixteen women who had prior incontinence surgery, 64% reported an improvement at three month and this was sustained in 31% at follow-up at a median length of 5 years.

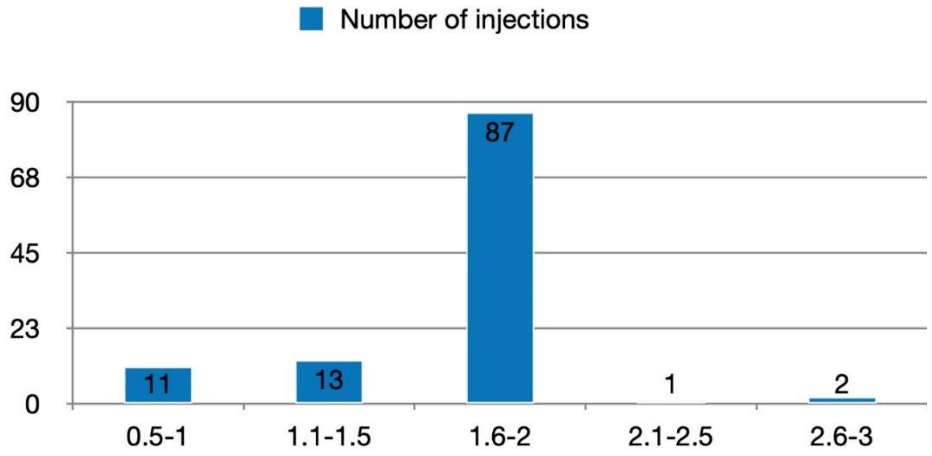

Figure 1 - Volume of PAHG injected (ml)

Discussion

This is the first study to evaluate how the actual volume of PAHG injected influences the outcome. We found that PAHG was safe and 58.5% had an improvement in symptoms after three months and this was sustained in 45.8% of the women after three years. In addition, the volume of PAHG injected did not have an impact on the outcome.

In our study the volume of PAHG injected was determined by the surgeon's subjective assessment of the level of coaptation of the urethra in theatre. Our data suggests that the volume did not have an impact on outcome in terms of symptoms or quality of life. Nearly 90% of women received PAHG at the volume recommended by the manufacturer (1.5-2 mls) with a low complication rate. This study therefore provides evidence for the safety and efficacy of PAHG when used within the manufacturer's guideline. However, given that only three patients had a volume of more than 2 mls injected, it was not possible to determine the safety profile or efficacy of PAHG when injected at a higher volume.

The rate of procedure related complications was 1.7% which is lower than previously reported. Our rate of UTI was 0.87% compared to 2.7–9.8% reported in a recent systematic review. Similarly, we had one woman with urinary retention (0.87%) compared to 1.5% to 14.9% in the published literature [8].

We found that at three months nearly 60% had an improvement in their symptoms. There have been two previous studies investigating subjective outcome at three months which found that between 64% [4] and 82.8% [11] had an improvement. Lose et al. found an improvement in 64% of patients, however, their study only investigated 25 women [4]. In addition Pai et al. assessed outcome at three months differently using question 2 of the ICIQ questionnaire to report cure (completely dry) or significant improvement (leaked once a week or less) [11].

When women had a structured telephone follow-up at a median of 37.5 months, 45.8% reported an overall improvement in symptoms. Pai et al. found that approximately 75% considered themselves to be cured or significantly improved at a median follow-up length of 38 months [11]. However they excluded patients who had previous incontinence surgery. In addition, in our study women were followed up with a telephone consultation which may be different from their methodology which was not specified.

PAHG can be used after previous incontinence surgery. We found that 31% reported a benefit with PAHG five years after injection following various previous incontinence procedures. Similarly Zivanovic et al. reported that 84% improved at a shorter interval of 12 months, their study only evaluating those who had a previous MUS [12].

We acknowledge that recall bias is a potential limitation of this retrospective study as patients were asked to describe their symptoms pre-procedure. A strength of our study however was that a single trained investigator conducted all the structured telephone interviews.

CONCLUSIONS / ВИСНОВКИ

In conclusion PAHG is a safe, minimally-invasive surgical option and improves symptoms of UI at up to 7.5 years post procedure. It is also efficacious for women who have had previous incontinence surgery. Our study demonstrates that when PAHG is injected within the manufacturer's recommendation of 1.5 to 2 mls, it is both efficacious and safe.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Further research could be conducted to evaluate the outcome and safety profile of using larger volumes of PAHG.

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CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The other authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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