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Minimally Invasive Treatment of Female Stress Urinary Incontinence with Polyacrylamide Hydrogel (Bulkamid®): Outcomes of a Contemporary Turkish Cohort Including Cases with Mixed Urinary Incontinence and Previously Failed Prior Surgery

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What's known on the subject? and What does the study add?

Heightened concerns about the safety of mesh-based surgery for treating female stress urinary incontinence following reports from various organizations worldwide have boosted the interest in alternative management options. Urethral bulking agents have regained popularity within this context owing to their minimally invasive nature and favorable safety profile. Our study showed that polyacrylamide hydrogel injection appears to be a safe and effective minimally invasive surgical treatment option for women with pure stress urinary incontinence and stress-predominant mixed urinary incontinence in both primary and secondary settings in a Turkish cohort.

Abstract

Objective: We aimed to describe the outcomes and patient satisfaction (PS) rates of transurethral polyacrylamide hydrogel (PAHG) (Bulkamid®) injection for the treatment of female stress urinary incontinence (SUI) in a Turkish cohort.

Materials and Methods: Twenty-two patients who underwent injection primarily or secondarily between December 2019 and March 2023 due to SUI or stress-predominant mixed urinary incontinence (MUI) were retrospectively evaluated. All patients underwent an invasive urodynamic study (UDS) before the procedure. The primary outcome was treatment success (TS), defined as no pad use, negative International Continence Society (ICS) uniform cough stress test (CST), and no SUI on International Consultation on Incontinence Questionnaire-Short Form question 6. The secondary outcome was PS.

Results: The median age was 61.5 (41-84) years. Six patients had stress-predominant MUI and 15 had SUI. PAHG injection was the primary and secondary treatment in 17 and 4 patients, respectively. ICS uniform CST was positive in all patients. In 8 patients, intrinsic sphincter deficiency (ISD) was detected during UDS. One patient developed transient urinary retention after surgery. At a median follow-up of 17 (1-38) months, the overall TS rate was 85.7%. Success rates in primary vs. secondary setting and pure SUI vs. MUI were 88.2% vs. 75% and 80% vs. 100%, respectively. The overall PS rate was 90%. Satisfaction rates in the primary vs. secondary setting and pure SUI vs. MUI were 93.6% vs. 75% and 85.7% vs. 100%, respectively. TS and PS rates were 100% in all patients with ISD.

Conclusion: PAHG injection proved to be a safe and effective minimally invasive treatment for pure stress and stress-predominant MUI in both primary and secondary settings.

Keywords: Bulkamid, injection, polyacrylamide hydrogel, stress, urinary incontinence

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Introduction

Heightened concerns about the safety of mesh-based surgery for treating female stress urinary incontinence (SUI) following reports from various organizations worldwide have boosted the interest in alternative management options (1). Urethral bulking agents have regained popularity within this context owing to their minimally invasive nature and favorable safety profile.

Bulking agents are divided into two groups: particulate agents (composed of solid microparticles in an absorbable liquid or gel carrier) and non-particulate agents (comprising a homogenous gel resistant to absorption). Carbon-coated zirconium oxide (Durasphere®), calcium hydroxylapatite (Coaptite®), and polydimethylsiloxane are particulate products in the market. Polyacrylamide hydrogel (PAHG) (Bulkamid®) is the only non-particulate product that gained FDA approval in 2006 for female SUI treatment. PAHG is a polymer gel consisting of 2.5% cross-linked polyacrylamide and 97.5% water for injection. It is resistant to degradation. PAHG has been used in aesthetic, plastic, and reconstructive surgery in Europe for many years, and long-term as well as experimental studies have shown that the gel is gradually integrated into host tissue through a fine network of vessel-bearing connective tissue, without capsular fibrosis or calcification (2-4). PAHG entered the market in Turkiye by the end of 2019. Our cohort also included the first patient who underwent PAHG injection on December 9th, 2019 in Turkiye.

The primary aim of this study was to describe the treatment outcomes and patient satisfaction rates of PAHG injection for the treatment of female SUI in a Turkish cohort.

Materials and Methods

After ethical approval obtained from the Institutional Review Board of Koc University (2023.068.IRB1.020) on 27.02.2023, the data of all female patients who underwent transurethral PAHG injection as a primary or secondary treatment between December 2019 and March 2023 due to SUI or stress-predominant mixed urinary incontinence (MUI) were retrospectively evaluated. A total of 22 PAHG injection procedures were performed. One patient who underwent oncological pelvic surgery (due to endometrium cancer) complicated by bladder perforation and who received adjuvant pelvic radiotherapy, brachytherapy, and chemotherapy was excluded (Figures 1 and 2). The indications for PAHG injection were detection of intrinsic sphincter deficiency (ISD) on invasive urodynamic study (UDS), failure of previous SUI surgery, and patient preference toward minimally invasive treatment. ISD was defined as a Valsalva leak point pressure below 60 cmH_2O (5). All injections were performed by the same surgeon, who had more than 30 years of experience in functional, female, and reconstructive urology and in injection treatment for various urological indications such as vesicoureteral reflux and post-prostatectomy UI as well as female SUI. Age, duration of complaints, pelvic examination findings, frequency of micturition, postvoid residual urine volume, and invasive UDS results were recorded.

Pelvic examination included the International Continence Society (ICS) uniform cough stress test (CST) (6). As defined by the Q-tip test, the degree of displacement of the intraurethral cotton swab on the horizontal plane upon increased intraabdominal pressure was used to assess urethral mobility (7). 0° immobile urethra, 0-30° decreased urethral mobility, >30° hypermobile urethra (8).

All patients underwent invasive UDS preoperatively according to the ICS standards (9).

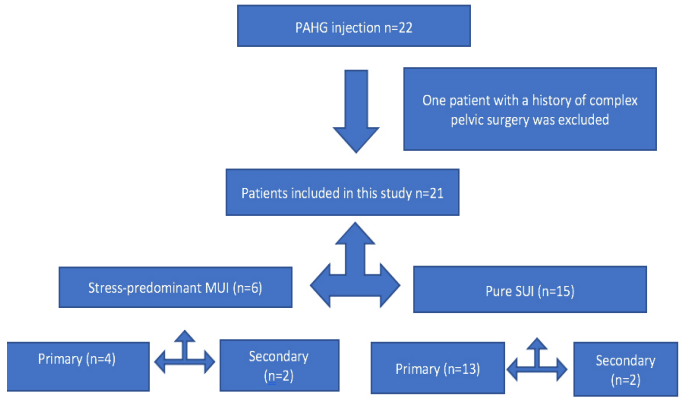

Figure 1. Flowchart showing the methodology and patient distribution with regards to type of urinary incontinence

PAHG: Polyacrylamide hydrogel, MUI: Mixed urinary incontinence, SUI: Stress urinary incontinence

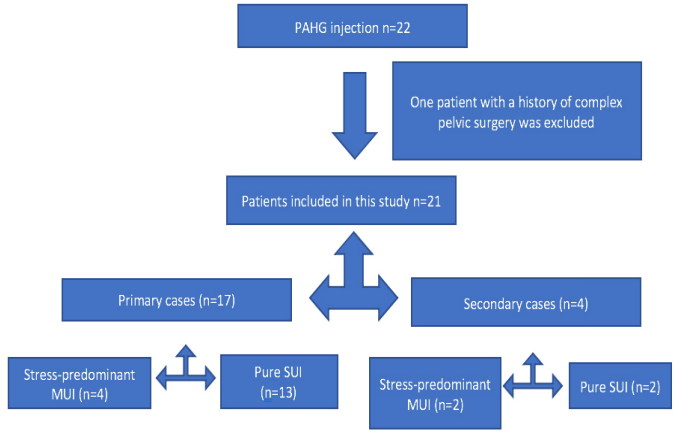

Figure 2. Flowchart showing the methodology and patient distribution with regards to history of previous SUI surgery

PAHG: Polyacrylamide hydrogel, MUI: Mixed urinary incontinence, SUI: Stress urinary incontinence

All procedures were performed on an outpatient basis under general anesthesia in the lithotomy position with a proprietary delivery system and a 23-G injection needle. After completing the cystoscopic evaluation, 2 cc PAHG was injected at 4 different sites on the bladder neck-urethral junction (Figure 3) (10). The bladder was emptied with an 8-Fr feeding tube at the completion of the procedure.

ICS uniform CST was repeated at follow-up visits. The number of pads per day and International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) scores related to SUI (item #6) were questioned during a phone interview (11). Additionally, patients were asked to weigh the change in their continence status as "cured", "improved", "not changed" or "worsened". Patients were asked whether they would recommend PAHG injection to a friend. Additional treatment for SUI following PAHG injection was also questioned.

The primary outcome measure was treatment success, which was defined as no pad use, negative ICS uniform CST, and declaration of no SUI on ICIQ-SF question 6.

The secondary outcome measure was satisfaction with treatment outcome. Defining post-injection continence status as "cured" and recommending PAHG injection to a friend were accepted as satisfaction criteria.

Patients with a history of complex pelvic surgery were excluded. Patients who received invasive SUI treatments after PAHG injection were excluded from the satisfaction evaluation.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0. Continuous variables are reported as medians with ranges.

Results

The median age of the patients was 61.5 (41-84) years. Six patients had stress-predominant MUI, whereas 15 had pure SUI. PAHG injection was the primary treatment in 17 patients, whereas 4 had previous SUI surgeries. The median duration of symptoms was 24 (6-100) months. The median urinary incontinence frequency was 3/day (2-8).

None had grade 3 or higher pelvic organ prolapse. ICS uniform CST was positive in all patients. Eight (38%) of 21 patients had increased urethral mobility. Three patients had decreased urethral mobility and 10 had immobile urethra.

The median pre-injection maximum urine flow rate, average urine flow rate, voided volume (VV), and postvoid residual urine volume (PVR) were 20.8 (10-39) mL/s, 9 (2-19) mL/s, 407.5 (120-840) mL, and 10 (10-30) mL, respectively. Invasive UDS revealed urodynamic SUI in all patients and ISD in 8 patients. In 5 patients, pressure-flow studies could not be completed because of catheter dislodgement or inability to void with a urethral catheter. Table 1 summarizes the invasive UDS results.

Seventeen patients (80.9%) had no previous SUI surgery. Two patients previously underwent transurethral injection with another bulking agent (dextranomer/hyaluronic acid copolymer, Deflux®) and 4 had mid-urethral sling (MUS) surgery at other institutions [3 transobturator tape (TOT), 1 transvaginal tape (TVT)]. Another patient had a history of deflux injection and TOT insertion. Among those with a history of MUS surgery, 2 underwent tape cutting due to mesh erosion before PAHG injection.

The median operative duration was 15 (10-30) minutes. The mean cystoscopic bladder capacity was 700 (100-1000) mL. One patient developed urinary retention early after surgery, which subsided spontaneously following drainage of the bladder with a feeding tube.

At a median follow-up of 17 (1-38) months, the median post-injection maximum urine flow rate, average urine flow rate, VV, and PVR were 32 (12-48) mL/sec, 13 (6-19) mL/sec, 400 (210-840) mL and 10 (0-40) mL, respectively.

The success rate was 85.7% (18/21). In 1 patient, TOT was performed 3 months after PAHG injection because of persistent SUI. In another patient who previously underwent TOT, duloxetine treatment was initiated (Table 1).

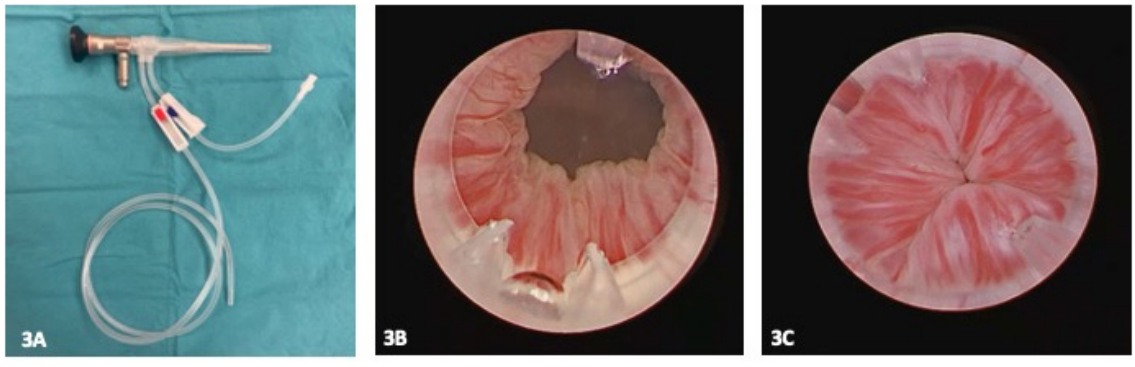

Figure 3. Proprietary system, bladder neck before and after hydrogel injection. 3A. Proprietary system, 3B. Pre-injection, 3C. Post-injection

Table 1. Demographical, clinical, operative and follow-up data including all patients

Patient	Age	Follow-up (months)	Type of UI	Primary/ Secondary	Previous SUI treatment	Urethral mobility	ALPP	DOA	Bladder compliance	Maximum cytometric capacity	Pdet @Q_{max}	Pads/ day (preop)	Pads /day (postop)	ICS uniform CST (postop)	ICIQ-SF SUI Score (postop)	Patient reported satisfaction	Additional Treatment	Suggest this procedure to a friend?	Treatment success	Patient satisfaction
1	63	38	S	P	-	IM	51	None	>40	560	3	3	0	Negative	0	Cured	No	Yes	Yes	Yes
2	79	38	M	P	-	IM	56	Yes	15	362	13	3	0	Negative	8	Cured	OAM	Yes	Yes	Yes
3	56	35	S	S	TOT Deflux Tape cut	DM	11	None	>40	170	13	NA	0	Negative	0	Cured	No	Yes	Yes	Yes
4	57	32	M	P	-	IM	90	None	>40	510	41	1	0	Negative	0	Cured	No	Yes	Yes	Yes
5	51	32	S	P	-	HM	100	None	>40	547	10	NA	0	Negative	0	Cured	No	Yes	Yes	Yes
6	76	21	S	P	-	DM	155	None	>40	312	-	3	3	Negative	21	Not changed	No	No	No	No
7	46	21	S	S	TOT	IM	80	None	>40	340	27	2	1	Negative	10	Improved	Duloxetine	No	No	No
8	60	38	M	P	-	IM	97	None	>40	350	25	NA	0	Negative	0	Cured	No	Yes	Yes	Yes
9*	72	15	M	S	Deflux	HM	94	None	26	400	-	NA*	NA*	Negative	NA*	NA*	Botulinum toxin injection	NA*	NA*	NA*
10	72	17	S	P	-	IM	45	None	>40	409	-	3	0	Negative	0	Cured	No	Yes	Yes	Yes
11	46	17	S	P	-	HM	34	None	>40	509	10	2	0	Negative	0	Cured	No	Yes	Yes	Yes
12	84	10	S	P	-	IM	40	None	>40	314	-	4	0	Negative	0	Cured	No	Yes	Yes	Yes
13	46	10	S	P	-	HM	130	None	>40	582	-	1	0	Negative	0	Cured	No	Yes	Yes	Yes
14	43	10	S	P	-	HM	120	None	>40	520	33	2	0	Negative	0	Cured	No	Yes	Yes	Yes
15	76	10	S	P	-	IM	80	None	>40	360	32	NA	0	Negative	0	Cured	No	Yes	Yes	Yes
16	58	7	M	P	-	HM	133	None	>40	563	7	3	0	Negative	0	Cured	No	Yes	Yes	Yes
17	72	6	M	S	TVT Tape cut	IM	115	Yes	9	110	19	4	0	Negative	0	Cured	No	Yes	Yes	Yes
18	71	4	M	S	TOT	IM	25	None	>40	428	8	NA	0	Negative	0	Cured	OAM	Yes	Yes	Yes
19	60	35	S	P	-	HM	98	None	>40	506	30	NA	0	Negative	0	NA**	TOT	NA**	No	NA**
20	70	2	S	P	-	HM	182	None	>40	350	0	2	0	Negative	0	Cured	No	Yes	Yes	Yes
21	62	1	S	P	-	DM	56	None	>40	536	0	1	0	Negative	0	Cured	No	Yes	Yes	Yes
22	41	1	S	P	-	HM	100	None	>40	646	3	1	0	Negative	0	Cured	No	Yes	Yes	Yes

* The patient who underwent oncological pelvic surgery (endometrium cancer) and had adjuvant pelvic radiotherapy, brachytherapy and chemotherapy complicated by bladder perforation was excluded.
**Patient excluded from satisfaction evaluation due to undergoing TOT 3 months after PAHG injection, UI: Urinary incontinence, SUI: Stress urinary incontinence, ALPP: Abdominal leak point pressure, DOA: Detrusor overactivity, Pdet@Q_{max}: Detrusor pressure recorded at the maximum urine flow rate during pressure-flow study, CST: Cough stress test, IM: Immobile urethra, DM: Decreased mobility, HM: Hypermobile urethra, TOT: Transobturator tape, TVT: Transvaginal tape, NA: Not available, OAM: Oral antimuscarinic treatment, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form

Table 2. Treatment success and patient satisfaction rates for primary, secondary, pure stress urinary incontinence and stress-predominant mixed urinary incontinence

Total	Treatment success* (n, %)	Patient satisfaction** (n, %)
	18/21, 85.7	**18/20, 90**
Urethral mobility		
Hypermobile	7/8, 87.5	7/7, 100%
Decreased mobility	2/3, 66	2/3, 66%
Immobile	9/10, 90	9/10, 90
ALPP <60 cmH_20	8/8, 100	8/8, 100%
Immobile urethra + ALPP <60 cmH_20	5/5, 100	5/5, 100
Primary	15/17, 88.2	15/16, 93.6
Secondary	3/4, 75	3/4, 75
Pure SUI	12/15, 80	12/14, 85.7
Stress-predominant MUI	6/6, 100	6/6, 100
Primary	15/17, 88.2	15/16, 93.6
Pure SUI	11/13, 84.6	11/12, 91.6
Urethral mobility		
Hypermobile	6/7, 85.7	6/6, 100
Decreased mobility	1/2, 50	1/2, 50
Immobile	4/4, 100	4/4, 100
ALPP <60 cmH_20	5/5, 100%	5/5, 100%
Stress-predominant MUI	4/4, 100	4/4, 100
Urethral Mobility		
Hypermobile	1/1, 100	1/1, 100
Decreased mobility	-	-
Immobile	3/3, 100	3/3, 100
ALPP <60 cmH_20	1/1, 100	1/1, 100
Secondary	3/4, 75	3/4, 75
Pure SUI	1/2, 50	1/2, 50
Urethral mobility		
Hypermobile	-	-
Decreased mobility	1/1, 100	1/1, 100
Immobile	0/1, 0	0/1, 0
ALPP <60 cmH_20	1/1, 100	1/1, 100
Stress-predominant MUI	2/2, 100	2/2, 100
Urethral mobility		
Hypermobile	-	-
Decreased mobility	-	-
Immobile	2/2, 100	2/2, 100
ALPP <60 cmH_20	1/1, 100	1/1, 100

*Defined as: Negative ICS uniform CST, no pad use after injection, ICIQ-SF Q6 score of 0
**Defined as: Self-defined as "cured" after PAHG injection and recommending the procedure to a friend. One patient excluded from satisfaction evaluation due to undergoing TOT 3 months after PAHG injection, PAHG: Polyacrylamide hydrogel, MUI: Mixed urinary incontinence, SUI: Stress urinary incontinence, ALPP: Abdominal leak point pressure, ICS: International Continence Society, CST: Cough stress test, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form

The patient satisfaction rate was 90% (18/20). None of the patients defined post-injection continence status as "worsened". Eighteen patients defined their new status as "cured" and all declared that they would recommend PAHG injection to a friend. One patient defined post-injection continence status as "not changed" and another as "improved". The patient who underwent TOT procedure following PAHG injection was excluded from this assessment, despite achieving "improved" status.

Among 6 patients who had stress-predominant MUI preoperatively, 2 (33.3%) continued anticholinergic oral pharmacotherapy.

Treatment success and patient satisfaction rates for primary and secondary SUI as well as pure SUI and stress-predominant mixed UI are summarized in Table 2.

Discussion

With increasing awareness of complications related to mesh use in sling surgery, injection of urethral bulking agents has started to occupy a larger space in our armamentarium as a minimally invasive surgical treatment option for female SUI not only in the primary setting but also for cases with persistent leakage despite previous surgery (12,13). According to the American Urological Association and the National Institute for Health and Clinical Excellence guidelines, the indications of urethral bulking agents could be listed as being surgically unfit for a procedure under general anesthesia, patient's desire to undergo a minimally invasive intervention, decreased urethral mobility, and history of failed SUI surgery (12,14). In our study, 61.9% (13/21) of the patients had decreased urethral mobility, 4 of 21 (19%) reported persistent SUI despite previous surgeries, and the majority expressed their willingness to undergo a minimally invasive procedure to treat their incontinence.

An ideal bulking agent should be non-immunogenic, biocompatible, and trigger minimal inflammatory and fibrotic responses (15). Polyacrylamide hydrogel (Bulkamid®) is the only FDA-approved non-particulate bulking agent in the market. PAHG's bulking effect occurs as a result of host cells' entrance into the hydrogel and building a long-lasting network that stabilizes the gel *in situ* (4). In addition, the endoscope used for PAHG injection has a rotatable sheath with inflow/outflow apertures, and its working channel can accommodate a needle of 23-G caliber and 12 cm length. These instrumental nuances served well for the standardization and replicability of PAHG injection (16). Owing to these structural and technical advantages, PAHG was introduced as a potentially safer and more effective option than other bulking agents.

The reported success rates of PAHG injection show significant variation due to non-standardized outcome assessment. Studies have shown treatment success rates ranging between 42 % and 70% (17-21). The most commonly used success criteria were improvement in the ICIQ-SF and visual analog scale scores, the number of incontinence episodes, pad weight tests, and negative ICS uniform CST (21). Our overall treatment success rate, which was defined as no pad use, negative ICS uniform CST, and declaration of no SUI on ICIQ-SF question 6, was 85.7%. The follow-up duration and re-injection ("top-up") rates of the studies involving patients who underwent PAHG injection ranged between 3 to 96 months and 7-70%, respectively (21). None of the patients in our study underwent repeat injection at a mean follow-up duration of 19.8 months.

Our subjective success rate was 90% as determined by post-injection continence status being defined as "cured" and feeling confident enough to recommend PAHG injection to a friend. This is at the upper end of the success range (61-95%) reported in relevant studies (16,22-24). This might be a result of the heterogeneity of the outcome assessment tools, such as the visual analog scale, Likert scale, ICIQ-SF, Patient Global Improvement Questionnaire, Incontinence Impact Questionnaire, and patients' definitions of their new conditions on a scale from worsened to improved (25).

In a recent review, Braga et al. (20) reported subjective and objective cure rates of PAHG injection in recurrent SUI ranging between 11.8% to 83%. Our results demonstrated 75% cure rate in patients with SUI despite previous surgery, which is compatible with the literature.

Only a few studies have compared the outcomes of PAHG injection in patients with pure SUI vs. stress-predominant MUI and reported better outcomes in pure SUI (16,23). In contrast, we detected higher objective and subjective cure rates in stress-predominant MUI. This might be a reflection of the small sample size (13 pure SUI vs 8 MUI). Eight patients had ALPPs below 60 cmH_2O on pre-operative invasive UDS. Regardless of being in the primary or secondary setting or having pure SUI or stress-predominant MUI, treatment success was 100% in these women with ISD. Supporting this data with a larger sample size might better reveal the value of ISD in predicting the outcome of urethral bulking treatment.

Various studies comparing the safety profile of bulking agents revealed that PAHG had the lowest rate of adverse events (26). The most common adverse events related to PAHG injection were urinary retention (0-73.1%), dysuria (0-46.2%), urgency (0-24.7%), and urinary tract infection (0-23.8%). Hematuria (0-7.7%), pain (0-2.5%), and complications related to the injection site are relatively rare (21,27). In our series, transient urinary retention was the only recorded complication (n=1, 4.7%). The low complication rates in our study might be related to the expertise level of the operating surgeon (over 500 injections during his career), small sample size, and limited follow-up duration. Hansen et al. (28) showed that performing >75 injections/surgical career and more than 15 injections/year increased the chance of cure and decreased the readmission rates after treatment.

To the best of our knowledge, this is the first study to present the outcomes of PAHG injection for the treatment of female SUI in Turkiye. Reflecting the experience of a single surgeon who is highly experienced in the field of female and functional urology adds uniformity to patient evaluation, surgical technique, and outcome assessment. Another study strength was the use of standardized diagnostic methods such as ICS uniform CST, Q-tip test, and invasive UDS in all patients. In addition, the results of this study add to the growing body of evidence that supports the use of PAHG injection for female SUI and provide a local snapshot regarding its safety and efficacy.

Study Limitations

This study is not without drawbacks. A retrospective design with inherent selection biases, small population size, and relatively short follow-up duration are the main limitations. Future studies, including larger populations and comparison groups, will improve the data that our study provided.

Conclusion

With its high success and patient-reported satisfaction rates together with low likelihood of injection-related adverse events, as demonstrated in this Turkish cohort, PAHG injection appears to be a safe and effective minimally invasive surgical treatment option for women with pure SUI and stress-predominant mixed UI in both primary and secondary settings.

Ethics

Ethics Committee Approval: Ethical approval obtained from Koç University Institutional Review Board on 27.02.2023. Approval number is 2023.068.IRB1.020

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.K., M.K., T.T., Concept: Ö.A., Design: E.K., T.T., Data Collection or Processing: E.K., M.K., Analysis or Interpretation: Ö.A., T.T., Literature Search: M.K., Writing: E.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

References

1. Giammò A, Geretto P, Ammirati E, Manassero A, Squintone L, Falcone M, Costantini E, Del Popolo G, Finazzi Agrò E, Giannantoni A, Li Marzi V, Mancini V, Musco S, Pastorello M, Pistolesi D, Risi O, Gontero P. Urethral Bulking in the Treatment of Stress and Mixed Female Urinary Incontinence: Results from a Multicenter Cohort and Predictors of Clinical Outcomes. J Clin Med 2022;11:1569.
2. Toozs-Hobson P, Al-Singary W, Fynes M, Tegerstedt G, Lose G. Two-year follow-up of an open-label multicenter study of polyacrylamide hydrogel (Bulkamid®) for female stress and stress-predominant mixed incontinence. Int Urogynecol J 2012;23:1373-1378.
3. Christensen LH, Breiting VB, Aasted A, Jørgensen A, Kebuladze I. Long-term effects of polyacrylamide hydrogel on human breast tissue. Plast Reconstr Surg 2003;111:1883-1890.
4. Christensen LH, Nielsen JB, Mouritsen L, Sørensen M, Lose G. Tissue integration of polyacrylamide hydrogel: an experimental study of periurethral, perivesical, and mammary gland tissue in the pig. Dermatol Surg 2008;34(Suppl 1):S68-77; discussion S77.
5. McGuire EJ, Fitzpatrick CC, Wan J, Bloom D, Sanvordenker J, Ritchey M, Gormley EA. Clinical assessment of urethral sphincter function. J Urol 1993;150:1452-1454.
6. Guralnick ML, Fritel X, Tarcan T, Espuna-Pons M, Rosier PFWM. ICS Educational Module: Cough stress test in the evaluation of female urinary incontinence: Introducing the ICS-Uniform Cough Stress Test. Neurourol Urodyn 2018;37:1849-1855.
7. Chen Y, Wen JG, Shen H, Lv YT, Wang Y, Wang QW, Konttinen YT. Valsalva leak point pressure-associated Q-tip angle and simple female stress urinary incontinence symptoms. Int Urol Nephrol 2014;46:2103-2108.
8. Kim SO, Jung HS, Jang WS, Hwang IS, Yu HS, Kwon D. Measurement of the Q-tip angle before and after tension-free vaginal tape-obturator (TVT-O): preoperative urethral mobility may predict surgical outcome. Int Urogynecol J 2013;24:1005-1009.
9. Rosier PFWM, Schaefer W, Lose G, Goldman HB, Guralnick M, Eustice S, Dickinson T, Hashim H. International Continence Society Good Urodynamic Practices and Terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study. Neurourol Urodyn 2017;36:1243-1260.
10. Itkonen Freitas AM, Mikkola TS, Rahkola-Soisalo P, Tulokas S, Mentula M. Quality of life and sexual function after TVT surgery versus Bulkamid injection for primary stress urinary incontinence: 1 year results from a randomized clinical trial. Int Urogynecol J 2021;32:595-601.
11. Abrams P, Andersson KE, Apostolidis A, Birder L, Bliss D, Brubaker L, Cardozo L, Castro-Diaz D, O'Connell PR, Cottenden A, Cotterill N, de Ridder D, Dmochowski R, Dumoulin C, Fader M, Fry C, Goldman H, Hanno P, Homma Y, Khullar V, Maher C, Milsom I, Newman D, Nijman RJM, Rademakers K, Robinson D, Rosier P, Rovner E, Salvatore S, Takeda M, Wagg A, Wagner T, Wein A; members of the committees. 6th International Consultation on Incontinence. Recommendations of the International Scientific Committee: Evaluation and Treatment of Urinary Incontinence, Pelvic Organ Prolapse and Faecal Incontinence. Neurourol Urodyn 2018;37:2271-2272.
12. Urinary incontinence in women: management. National Institute for Health and Care Excellence Clinical Guideline on Urinary Incontinence in Women: management, guideline CG171 November 2015.
13. The US Food & Drug Administration Information for Health Care Providers for SUI. March 2018.
14. American Urology Association, Incontinence. 2016.
15. Kirchin V, Page T, Keegan PE, Atiemo K, Cody JD, McClinton S. Urethral injection therapy for urinary incontinence in women. Cochrane Database Syst Rev 2012:CD003881.
16. Lose G, Sørensen HC, Axelsen SM, Falconer C, Lobodasch K, Safwat T. An open multicenter study of polyacrylamide hydrogel (Bulkamid®) for female stress and mixed urinary incontinence. Int Urogynecol J 2010;21:1471-1477.
17. Tincello DG, Armstrong N, Hilton P, Buckley B, Mayne C. Surgery for recurrent stress urinary incontinence: the views of surgeons and women. Int Urogynecol J 2018;29:45-54.
18. Rodríguez D, Carroll T, Alhalabi F, Carmel M, Zimmern PE. Outcomes of Macroplastique injections for stress urinary incontinence after suburethral sling removal. Neurourol Urodyn 2020;39:994-1001.
19. Myhr SS, Rakovan M, Schiøtz HA. Periurethral injection with polyacrylamide after previous TVT surgery. Int Urogynecol J 2022;33:1017-1022.
20. Braga A, Caccia G, Papadia A, Treglia G, Castronovo F, Salvatore S, Torella M, Ghezzi F, Serati M. Urethral bulking agents for the treatment of recurrent stress urinary incontinence: A systematic review and meta-analysis. Maturitas 2022;163:28-37.
21. Hoe V, Haller B, Yao HH, O'Connell HE. Urethral bulking agents for the treatment of stress urinary incontinence in women: A systematic review. Neurourol Urodyn 2021;40:1349-1388.
22. Mouritsen L, Lose G, Møller-Bek K. Long-term follow-up after urethral injection with polyacrylamide hydrogel for female stress incontinence. Acta Obstet Gynecol Scand 2014;93:209-212.
23. Trutnovsky G, Tamussino K, Greimel E, Bjelic-Radisic V. Quality of life after periurethral injection with polyacrylamide hydrogel for stress urinary incontinence. Int Urogynecol J 2011;22:353-356.
24. Zajda J, Farag F. Urolastic-a new bulking agent for the treatment of women with stress urinary incontinence: outcome of 12 months follow up. Adv Urol 2013;2013:724082.
25. Siddiqui ZA, Abboudi H, Crawford R, Shah S. Intraurethral bulking agents for the management of female stress urinary incontinence: a systematic review. Int Urogynecol J 2017;28:1275-1284.
26. de Vries AM, Wadhwa H, Huang J, Farag F, Heesakkers JPFA, Kocjancic E. Complications of Urethral Bulking Agents for Stress Urinary Incontinence: An Extensive Review Including Case Reports. Female Pelvic Med Reconstr Surg 2018;24:392-398.
27. Chapple C, Dmochowski R. Particulate Versus Non-Particulate Bulking Agents In The Treatment Of Stress Urinary Incontinence. Res Rep Urol 2019;11:299-310.
28. Hansen MF, Lose G, Kesmodel US, Gradel KO. A national population-based cohort study of urethral injection therapy for female stress and mixed urinary incontinence: the Danish Urogynaecological Database, 2007-2011. Int Urogynecol J 2017;28:1309-1317.