ORIGINAL ARTICLE

Vol. 40 (1): 37-43 January - February, 2014
doi: 10.1590/S1677-5538.IBJU.2014.01.06

Polyacrylamide Hydrogel (Bulkamid®) in Female Patients of 80 or More Years with Urinary Incontinence

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ABSTRACT

Introduction: To assess the effectiveness of polyacrylamide hydrogel (Bulkamid ®) in injection therapy for urinary incontinence in women of 80 or more years.
Materials and Methods: Twenty consecutive women mean age 84.5 (range 80-87) with stress or mixed urinary incontinence were enrolled in this prospective study. All subjects were evaluated at baseline and re-evaluated 7 days, 6,12,18 and 24 months after treatment. A detailed clinical evaluation, physical examination, daily pad count, urodynamic investigation and evaluation of urethral mobility by trans-labial ultrasound were performed.
Results: A statistically significant decrease in the number of pads was observed in the follow-up (p = 0.0002 after 24 months). Physical examination showed a statistically significant lack or reduced lost of urine with stress test (p = 0.0163 after 24 months). Urodynamic findings showed an increase of Valsalva leak point pressure, maximum urethral closure pressure and functional length. Maximum flow and post void residual were respectively observed to be significantly reduced and increased only after 7 days from injection therapy. Quality of life (QoL) assessed with the Incontinence Impact questionnaire short form (IIQ-7) showed a statistically significant improvement (p = 0.0001 after 24 months). Patient satisfaction assessed with the Visual Analogue Scale and Patient Global Impression of Improvement questionnaire respectively produced evaluation of "satisfied" and "much improved" even after 24 months.
Conclusions: Polyacrylamide hydrogel (Bulkamid®) is an effective treatment with low morbility in patients of 80 or more years.

ARTICLE INFO

Key words:
Injections; Neuromuscular Blocking Agents; Urinary Incontinence; Female; Quality of Life

Int Braz J Urol. 2014; 40: 37-43

Submitted for publication:
February 13, 2013

Accepted after revision:
January 16, 2014

INTRODUCTION

The first report on the use of urethral injection therapy was in 1904 (1). Since then many substances have been used in the treatment of stress urinary incontinence in women looking for "agents" that were durable, non-migratory, hypoallergenic, biocompatible and which does not evoke granuloma formation (2): polytetrafluorethylene, bovine collagen, autologous fat, silicone, carbon spheres, calcium hydroxylapatite, porcine dermal implant, ethylene vinyl alcohol copolymer, hyaluronic acid and polyacrylamide hydrogel.

Polyacrylamide hydrogel (Bulkamid®) was introduced in Europe as a bulking agent in 2006 (3): it is a polymer gel consisting of 2.5% cross-linked polyacrylamide and 97.3% water for injection (4). It seems to have the necessary characteristics required of a bulking agent and appears to be effective and safe in women with stress or mixed incontinence (5).

Minimal invasiveness, low complication rate, use of local anaesthesia and non-hospitalization of patient make this a particularly recommended therapy for older women.

Therefore we decided to evaluate the efficacy of Bulkamid® on women of 80 or more years in a follow-up of 24 months.

MATERIALS AND METHODS

From January 2010 to September 2010, 20 consecutive women of 80 or more years (mean age 84.5, range 80-87) with stress or mixed urinary incontinence were enrolled in this prospective study.

A detailed clinical evaluation including a complete history, physical examination , daily pad count, urodynamic investigation and evaluation of urethral mobility by trans-labial ultrasound were performed.

Urodynamic investigation was performed including spontaneous uroflowmetry with post void residual (PVR) measurement, urethral pressure profile at rest, water cystometry (filling rate 30mL/min.; catheter used: 6 Fr double lumen; patients' position: sitting) with pressure/flow study and abdominal Valsalva leak point pressure (AVLPP).

All patients underwent transurethral injection in lithotomic position after local anesthesia (EMLA cream and after 10 minutes, lidocaine 5%: 8mL). Bulkamid® (2mL) was injected into the submucosa of the mid urethra using a 23 G needle and a special cystoscope (Bulkamid Urethral Bulking System®). The drug was injected at 6,3 and 9 o'clock. All subjects were evaluated at baseline and re-evaluated 7 days, 6,12,18 and 24 months after treatment.

Patients with urge incontinence, urinary tract infection, neurological disease, bladder lithiasis, prolapse of anterior vaginal wall and/or prolapse of the apical segment of vagina ≥ stage II on POP-Q system or pelvic tumours were excluded.

End points: reduction in number of pad per 24 hours was considered the primary efficacy endpoint in this study. Secondary end-points included changes in urodynamic findings evaluated (maximum flow (Qmax), PVR, AVLPP, functional length (FL) and maximum urethral closure pressure (MUCP).

Stress test assessment was performed with patients coughing in lithotomy position and bladder filled with 300mL of saline solution.

Patients were divided into four groups according to the extent of leakage: (-) no leakage; (+) low leakage (a few drops from the urethral meatus); (++) a discrete urine leakage (weak stream from the urethral meatus); (+++) a considerable urine leakage (strong jet from the urethral meatus).

Quality of life (QoL) was assessed with the Incontinence Impact Questionnaire short form (IIQ-7). The questionnaire consists of 7 items relating to the impact of UI on the woman's life with 5 possible options ranging from "not at all" (score = 0) to "almost always (score = 4) with a total score ranging from 0 (no impact of UI on the life of the subject) to 28 (maximum disturbance of UI on the life of the subject). Patient satisfaction was assessed with: a) Visual Analogue Scale (VAS) with the least satisfaction expressed as 0 and most satisfaction expressed as 10. Results between 0-3 were considered as not satisfied, 4-7 moderately satisfied and 8-10 as satisfied. b) Patient Global Impression of Improvement Questionnaire (PGI-I). The PGI-I is a validated generic tool for assessment of the overall improvement or deterioration that patients experience following the treatment. It is a 7-point scale from "very much improved" (score = 1) to very much worse (score = 7).

Number of pads, urodynamic findings, stress test and quality of life were performed before and at every periodic control. VAS and PGI-I were performed only after treatment at every periodic control.

All patients signed an informed consent before starting treatment.

Statistical analyses: Statistical analysis was performed using the MedCalc® software package (version 9.4.2.0.). Data are expressed as means ± SD and median. Comparisons were carried out using Wilcoxon test.

For stress test, statistical analysis was performed by Chi square test.

A p value of < 0.05 was considered significant.

RESULTS

Patients' characteristics are described in Table-1.

Average execution time of injection was 7 minutes (range 5-10).

Two patients required a further treatment. 18 women completed 24 months of follow-up. Urinary retention was present in two patients but only immediately after urethral injection.

Table 1 - Patients' characteristics.

Nº of patients at baseline	20
Nº of patients at 24 months	18
Mean age	84.5 (80-87)
Stress urinary incontinence	12
Mixed urinary incontinence	8
Previous anti-incontinence surgery	6
Body Mass Index	27 (20-34)
Hypermobility	7
Detrusor overactivity	7
Prolapse	4

In one patient mild urethral bleeding was observed. *De novo* urge incontinence was present in two patients only for a short period.

The number of pads showed a statistically significant reduction from the first control after 7 days, to the end of follow-up (Table-2).

Stress test showed both a statistically significant reduction of incontinent patients and a reduction in the amount of urine lost in all the controls carried out (Table-3).

Table-4 describes urodynamic results.

After 7 days Qmax showed a reduction with a subsequent moderate increase. PVR increased only after 7 days without a statistical significance and then decreased.

AVLPP showed a statistically significant increase in the controls performed after 7 days and after 6 months, whilst in successive controls values were still higher than pre-operative results, but there was no statistical significance. FL showed a statistically significant increase after 7 days and after 6 months.

MUCP showed a statistically significant increase for all 24 months considered.

Responses to items in the IIQ-7 showed a considerable improvement in the women's quality of life with a statistical significance that remained until the end of the follow-up (Table-5).

Table 2 - Number of pads used by the patients before and after treatment with Bulkamid®.

	Number of Pads					
	Before Treatment	After 7 days	After 6 months	After 12 months	After 18 months	After 24 months
mean ± st. dev.	5.5 ± 2.5	0.7 ± 1.6	1.1 ± 2.0	1.5 ± 2.6	1.6 ± 2.7	1.9 ± 2.8
median	5	0	0	0	0.5	1
*p-value		< 0.0001	< 0.0001	0.0001	0.0001	0.0002

*Wilcoxon test (paired samples).

Table 3 - Degree of urinary incontinence assessed by stress test before and after treatment with Bulkamid®.

	Stress Test					
	Before treatment	After 7 days	After 6 months	After 12 months	After 18 months	After 24 months
Degree	Patients	Patients	Patients	Patients	Patients	Patients
-	3	8	7	5	4	4
+	1	9	8	8	8	8
++	10	2	3	3	4	3
+++	6	1	1	3	2	3
*p-value		0.0005	0.0024	0.0135	0.0179	0.0163

*Chi Square test

Table 4 - Urodynamic findings before and after treatment with Bulkamid®.

	Before treatment	After 7 days	After 6 months	After 12 months	After 18 months	After 24 months
QMAX						
mean ± st. dev.	24 ± 11.7	19.6 ± 12.4	22.2 ± 13.7	22 ± 11.6	21.6 ± 12.1	22 ± 12.3
median	20	16	17	18	16.5	18
*p-value		0.0141	0.1089	0.0348	0.0448	0.1594
PVR						
mean ± st. dev.	15.7 ± 14.4	17 ± 20	6.6 ± 9.4	7.4 ± 9.6	7.2 ± 13	5 ± 8.8
median	15	10	0	0	0	0
*p-value		0.7197	0.0266	0.0353	0.0398	0.0034
AVLPP						
mean ± st. dev.	48.6 ± 17.3	75.5 ± 17.7	68.2 ± 23	58.3 ± 19	59.4 ± 17	59 ± 17.6
median	49	72.5	70	65	57.5	55.5
*p-value		0.0002	0.0591	0.1870	0.4954	0.6436
LF						
mean ± st. dev.	29.2 ± 5	36 ± 4.8	33.4 ± 3.5	31.6 ± 4.2	31.2 ± 4.7	30.7 ± 4.4
median	29	35.5	34	31	30.5	30
*p-value		0.0012	< 0.0001	0.5376	1	1
MUCP						
mean ± st. dev.	42.4 ± 18	59.7 ± 18.8	52 ± 17.3	50 ± 18.7	51 ± 16	50 ± 16.6
median	40	54.5	50	48	46.5	45
*p-value		< 0.0001	0.0066	0.0204	0.0056	0.0305

*Wilcoxon test (paired samples).

Table-6 presents patient evaluations of the results by VAS and PGI-I. After 7 days VAS showed very satisfactory results which remained even after 24 months, albeit with slightly lower values. Similar results were also obtained with PGI-I with most patients reporting a great improvement after 24 months.

The eight patients with mixed urinary incontinence in seven cases had a detrusor overactivity in the urodynamic examination. Three of these seven

Table 5 - Quality of life (QoL) assessed by Incontinence Impact Questionnaire short form (IIQ-7).

	IIQ-7					
	Before treatment	After 7 days	After 6 months	After 12 months	After 18 months	After 24 months
mean ± st. dev.	19.5 ± 7	3.1 ± 5.7	3.4 ± 5.5	5.3 ± 8.7	5.5 ± 5.7	6 ± 9.3
median	22	0	0	0	0	0
*p-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0001

*Wilcoxon test (paired samples).

Table 6 - Patients' satisfaction after treatment with Bulkamid®, assessed by Visual Analogue Scale (VAS) and Patient Global Impression of Improvement questionnaire (PGI-I).

	After 7 days	After 6 months	After 12 months	After 18 months	After 24 months
VAS (mean)	9.0	8.5	8.2	8.2	8.1
PGI-I					
Degree of improvement	1.7	1.7	2.1	2.2	2.2

patients (45%) continued to have urgency after injection therapy with worse clinical results (an average of 5.2 pads a day after 24 months). The six patients who previously underwent suburethral slings showed no clinical and urodynamic differences in the results compared to other patients. Furthermore no difference was found in the results between patients with or without urethral hypermobility as well as in relation to the body mass index.

DISCUSSION

The results of this study seem to confirm the validity of Bulkamid® in the treatment of stress urinary incontinence, even in women of 80 or more years who often suffer from a more severe level of urinary incontinence and who have a higher percentage of mix incontinence compared to younger women.

The reduced number of pads used by patients that stays low even 24 months after treatment is most probably the most important result of this study and which leads to a positive evaluation in the responses to items in the questionnaire about QoL and in the results of VAS and PGI-I. Regarding the stress test and urodynamic findings, the good results obtained with the former and the improvement in the urodynamic parameters used in the evaluation of urinary incontinence (AVLPP, LF, MUCP) should be underlined. These results appear to be in agreement with finding of other authors (6-8).

Results of Qmax and PVR highlight the low obstructing capacity of Bulkamid® with Qmax values significantly reduced only at the 7th day control with values then returning approximately to normal. PVR shows a slight increase only at the 7 day control, then reduces. These results can explain the low incidence of post-treatment urine retention, reported also in other studies (3,5,9).

The presence of urgency and/or detrusor overactivity is very important in elderly women. In our experience 45 percent of patients with detrusor overactivity in the urodynamic study remain with urgency, with clinical results lower than patients without DO.

In previous articles some authors underlined that injection therapy was contraindicated in patients with DO (10-12). More recently, Chappel et al. (9) claimed that the success of injection therapy was reduced in patients with DO, but that its use should not be excluded because surgical procedures such as colposuspension and urethral slings more significantly cause *de novo* DO. Furthermore, positive results were achieved both in patients with stress incontinence and mixed incontinence (5).

In this study, the presence of previous anti-incontinence surgery (suburethral slings) did not influenced the success of injection therapy. These data are in agreement with those reported by others authors (9,13-15).

Body mass index did not affect the results probably because few patients were overweight.

Moreover, Bulkamid® was effective regardless of the presence or absence of urethral hypermobility confirming results described by other authors (16).

The study was partially conditioned by the fact that the patients we evaluated were aged 80 or more years. Almost from the start of the study we observed that the patients found it difficult to compile the micturition diary, normally used in this type of study, in particular those patients with severe incontinence who were not able correctly to quantify their loss of urine. For this reason we decided not to make use of this tool.

Compilation of the quality of life questionnaire was performed under supervision of a physi-

cian not involved in the study to facilitate the interpretation of the questions without influencing patients' assessments.

Indeed, the difficulties encountered in understanding the QoL questions represented a possible bias (9).

We also observed how these women were often resigned to their condition and in some cases they only came to request pads. It was rare for them to ask to be cured of incontinence, whilst more often they simply wanted to improve their condition, to be able to lead a better life.

They accepted injection therapy for its characteristics of low invasiveness, rapidity of execution, use of local anesthesia, lack of hospitalization and low complication rate. They would not have accepted more invasive surgical procedures preferring to remain incontinent.

In addition, the elderly woman is often affected by chronic diseases therefore more invasive surgical procedures are contraindicated.

Robinson et al. (17) suggested that women would choose to undergo less invasive procedures with a lower risk of complications, even though the chance of cure may be lower than with a major operation.

Although intervention for SUI is generally focused on minimizing urine leakage, the overall impact of treatment on patient QoL is arguably more important than the treatment outcome regarding leakage (2). This consideration is even truer for an aging patient. It is thus of great importance to inform elderly women of this treatment opportunity.

Another interesting question is if in elderly patients urodynamic assessment should be performed before injection therapy. Whilst there is no doubt regarding the need to perform urodynamic assessment before more invasive surgical procedures (colposuspension, suburethral slings), the evidence base to date supports the view that simple evaluation is adequate before injection therapy (14).

Studies published about injection therapy are numerous and often difficult to evaluate because of their heterogeneity: the various materials used, the technique (transurethral or periurethral), the injection site (bladder neck, mid-urethral), the heterogeneity of patients, the length of follow-up and the different urodynamic findings (presence of absence of DO). The results are also heterogeneous with percentages of improvement or cure between 40 and 100% (18), 15 and 94% (16). In literature, we found only one study on very old women (older than 75 years) with a percentage of 77% of patients cured or improved (19).

In a recent analysis of 500 cases, Mohr et al., in a review of literature, underlined in an elderly population a subjective and objective improvement in incontinence after bulking therapy (8).

In spite of the complexity of the theme and the lack of consistency in results, injection therapy should be seen as an important surgical therapy, in particular in patients who cannot or do not accept to undergo other forms of therapy.

The moderate reduction of the positive effects after 2 years also detected in other surgical procedures performed in patients with urinary incontinence and the occasional necessity to repeat the treatment do not reduce the validity of the therapy and allows a further period of good health. We must also emphasize that these patients have a low life expectancy and every year spent in a satisfactory manner is a good result.

CONCLUSIONS

The results of this study showed the effectiveness and low morbidity of Bulkamid® in women of 80 or more years with stress and mixed urinary incontinence. In these patients, often affected by chronic diseases and other health problems, this treatment should be considered as first line therapy.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Meyer L: To tilfælde af incontinentia urinæ helbredede ved parafininjektioner. Ugeskr Læger 1904;104:5.
2. Kotb AF, Campeau L, Corcos J: Urethral bulking agents: techniques and outcomes. Curr Urol Rep. 2009; 10: 396-400.
3. Lose G, Mouritsen L, Nielsen JB: A new bulking agent (polyacrylamide hydrogel) for treating stress urinary incontinence in women. BJU Int. 2006; 98: 100-4.

4. Bello G, Jackson IT, Keskin M, Kelly C, Dajani K, Studinger R, et al.: The use of polyacrylamide gel in soft-tissue augmentation: an experimental assessment. Plast Reconstr Surg. 2007; 119: 1326-36.
5. 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: 1471-7.
6. Kuhn A, Stadlmayr W, Lengsfeld D, Mueller MD: Where should bulking agents for female urodynamic stress incontinence be injected? Int Urogynecol J Pelvic Floor Dysfunct. 2008; 19: 817-21.
7. Faerber GJ: Endoscopic collagen injection therapy in elderly women with type I stress urinary incontinence.J Urol. 1996; 155: 512-4.
8. Mohr S, Siegenthaler M, Mueller MD, Kuhn A: Bulking agents: an analysis of 500 cases and review of the literature. Int Urogynecol J. 2013; 24: 241-7.
9. Chapple CR, Wein AJ, Brubaker L, Dmochowski R, Pons ME, Haab F, et al.: Stress incontinence injection therapy: what is best for our patients? Eur Urol. 2005; 48: 552-65.
10. Su TH, Hsu CY, Chen JC: Injection therapy for stress incontinence in women. Int Urogynecol J Pelvic Floor Dysfunct. 1999; 10: 200-6.
11. Bartholomew B, Grimaldi T: Collagen injection therapy for type III stress urinary incontinence. AORN J. 1996; 64: 75-83, 85-6.
12. Appell RA: Collagen injection therapy for urinary incontinence. Urol Clin North Am. 1994; 21: 177-8.
13. Monga AK, Robinson D, Stanton SL: Periurethral collagen injections for genuine stress incontinence: a 2-year follow-up. Br J Urol. 1995; 76: 156-60.
14. Peeker R, Edlund C, Wennberg AL, Fall M: The treatment of sphincter incontinence with periurethral silicone implants (macroplastique). Scand J Urol Nephrol. 2002; 36: 194-8.
15. Haab F, Zimmern PE, Leach GE: Urinary stress incontinence due to intrinsic sphincteric deficiency: experience with fat and collagen periurethral injections. J Urol. 1997; 157: 1283-6. Erratum in: J Urol 1997; 158: 188.
16. Lightner DJ, Itano NB, Sweat SD, Chrouser KL, Fick F: Injectable agents: present and future. Curr Urol Rep. 2002; 3: 408-13.
17. Robinson D, Anders K, Cardozo L, et al.: What do women want? Interpretation of the concept of cure. J Pelvic Med Surg. 2003;9:273-7.
18. Chapple CR, Wein AJ, Artibani W, Brubaker L, Haab F, Heesakkers JP, et al.: A critical review of diagnostic criteria for evaluating patients with symptomatic stress urinary incontinence. BJU Int. 2005; 95: 327-34.
19. Zullo MA, Ruggiero A, Montera R, Plotti F, Muzii L, Angioli R, et al.: An ultra-miniinvasive treatment for stress urinary incontinence in complicated older patients. Maturitas. 2010; 65: 292-5.

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