Bulkamid (PAHG) in mixed urinary incontinence: What is the outcome?

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Abstract

Introduction and hypothesis

Mixed urinary incontinence (MUI), defined as mixed symptoms of stress urinary incontinence (SUI) and overactive bladder (OAB), is a difficult entity if conservative treatment has failed. Cure rates are low compared with SUI, particularly the OAB component, may deteriorate after sling insertion. Bulking agents pose an appealing alternative for the treatment of

MUI. They have shown beneficial effect in small case studies, but larger series are lacking. The aim of this prospective study was an analysis of treatment efficacy and safety profile of the bulking agent, Bulkamid, in female patients with MUI.

Methods

One hundred fifty-four women with MUI symptoms (components of SUI/OAB within the limits of 60–40% either way) received bulking therapy with polyacrylamide hydrogel (Bulkamid). Patients were followed-up 3 months postoperatively. Primary outcome was the domain Incontinence impact on the King's Health Questionnaire (KHQ). Secondary outcomes were the other KHQ domains, visual analog scale (VAS), and International Continence Society (ICS) standardized pad weight test as objective measurement of incontinence.

Results

Statistically significant improvements were found for all KHQ domains, pad weight test, and the visual analog scale (VAS) before and after bulking. Overall complication rate was 13%.

Conclusions

This study has shown improvement in MUI after bulking therapy according to both subjective and objective outcomes. We can advocate bulking therapy for treating MUI, as it is simple and safe and shows both objective and subjective improvement and relief. Long-term results (up to 1 year) are awaited.

Keywords

Bulking agent
Bulking therapy
Periurethral bulking
Stress urinary incontinence
Overactive bladder
Mixed urinary incontinence

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Electronic supplementary material

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Introduction

Mixed urinary incontinence (MUI) is defined as involuntary loss of urine associated with urgency and with effort, physical exertion, sneezing, or coughing [1]. It is a combination of stress urinary incontinence (SUI) and overactive bladder (OAB) and is prevalent in 20–36% of women [2]. The pathophysiology of MUI is poorly understood, which impedes choosing appropriate therapies [2, 3]. Treatment is controversial, and an individual strategy is needed, since women with MUI comprise a heterogenous group of patients [4]. Initially, a conservative approach is advocated [4], treating the most bothersome component first [2]. If surgery is needed, urodynamic evaluation is recommended [4], although the role of urodynamics in MUI is also controversial [5].

Retropubic colposuspension is effective for treating SUI, but de novo urge and a higher risk of pelvic organ prolapse (POP) are known side effects [6]. Midurethral slings are safe and efficacious treatment options [7]. Transobturator tape seem to have a good subjective success rate, and frequently, urgency urinary incontinence (UUI) resolves [8]. The main reason for dissatisfaction with a sling in general is overactive bladder [9]. Even if SUI is cured surgically, patients need to be informed that OAB symptoms might persist or even deteriorate [4].

Evidence is available for treating UI with weight loss, SUI with slings and urethropexies, and UUI with anticholinergics. However, there are neither clear diagnostic criteria nor management guidelines for MUI, and evidence for treatment is lacking [2]. Hence, treatment alternatives are required in patients with MUI. Peri- or transurethral bulking is a simple method to treat incontinence in a subset of patients showing objective and subjective symptom improvement [10], and Bulkamid has favorable results in a pooled population of SUI and MUI [11]. The aim of this study was to specify the efficacy of the periurethral bulking agent Bulkamid (polyacrylamide

hydrogel; PAHG) in patients with exclusive MUI.

Materials and methods

Between January 2010 and October 2014, 154 women with MUI were treated by periurethral bulking with polyacrylamid hydrogel (PAHG; Bulkamid) in the University Women's Hospital, Department of Urogynecology, Bern, Switzerland, and the Princess Anne Hospital, Department of Urogynecology, Southhampton, UK. To be included in the study, components of SUI and OAB had to be within the limits of 60–40% either way to avoid predominance of one aspect. This is in contrast to our previous study in which only patients with SUI were included [10]. Primary outcome was the domain of Incontinence impact of the King's Health Questionnaire (KHQ). Secondary outcomes were the remaining domains, visual analogue scale (VAS), and International Continence Society (ICS) standardized pad test as objective measurements of incontinence. Subjective and objective outcomes were measured before and 3 months after intervention. To gather a rather homogenous group of patients with balanced MUI, they rated the stress and OAB components of their bladder problem with the limits of 60:40% to either side. Demographic data of age, body mass index (BMI), parity, and menopausal status were noted. The study was approved by the local ethical committee, and all patients gave informed consent to participate (KEK 127/2009).

The King's Health Questionnaire (KHQ) determines quality of life (QoL) and is widely used in patients with incontinence [12]. The questionnaire is validated in several languages, including German [13], and is used to assess various domains, including general health perception, role limitation (e.g., household, cleaning, shopping), physical and personal limitation (walking, sports, travel, social life, relationship, sex, family life), emotions (depressed, anxious, nervous, feeling bad about oneself), sleep (feeling worn out, tired), and incontinence impact (pad usage, need to change underwear, restrict drinking, fear bad smells). Additionally, bladder problems are specified in the KHQ as questions for frequency symptoms, nocturia, urgency, SUI episodes, coital incontinence, urinary tract infections (UTI), and bladder pain exist. The scores for each domain range from 0 to 5 and 1 to 5, respectively, are totalled, and a change of at least five points is considered significant [13]. Subjective outcome was further assessed with the patients judging their incontinence severity on a visual analogue scale (VAS), a validated tool to assess health and satisfaction, pain, attitudinal attributes, and QoL [14].

Additionally, as objective measurements, a standardized 2-h in-office pad test was performed according to ICS recommendations [15]. Before and after intervention, UTIs were excluded using dipstick screening and infections or bacteriuria was treated. For the injection procedure, women were placed in the lithotomy position, 5–10 ml of 1% lidocaine were injected in the periurethral tissue at 4 and 8 o'clock, and the bulking agent was injected transurethrally into the submucosa under cystoscopic control. Two to three deposits were placed in the midurethra at 6, 2, and 10 o'clock, and quantity was determined by the surgeon's judgement of coaptation. Needle position was corrected if it was suspected to not be in the mucosa or if there was extravasation of the bulking agent. If coaptation was considered appropriate, the bladder was emptied. Patients received a single-shot antibiotic prophylaxis with Co-amoxicillin and were discharged if postmicturition residual volume was <100 ml. Evaluation was performed 3 months postoperatively. All adverse events were monitored and registered. If the procedure was unsuccessful, the woman was offered a further injection after 6 weeks. For statistical analysis, Graph Pad Prism version 5.0 for Windows was used (Graph Pad, La Jolla, CA, USA) to calculate Student's *t* test and Wilcoxon signed rank test.

Results

One hundred and fifty-four patients were injected with Bulkamid periurethrally. Demographic data demonstrated a median age of 68 (range 29–93) years, a median BMI of 24 kg/m^2 (range 17–32), and a median parity of two (range 0–9). Seven patients were pre-, six peri-, and 141 postmenopausal. For 12 patients, menopausal status was lacking. In our collective, 11 patients had previously undergone Burch colposuspension, nine a retropubic sling, and three a transobturator sling. Sixteen patients were lost to follow-up, whereof two died of unrelated causes, 12 moved to other places, and two were lost because of unknown reasons. Analysis with the Wilcoxon signed-rank test for non-normally distributed paired data showed statistically significant improvements for all domains of the KHQ before and after bulking (Fig. 1, all $p < 0.0001$). Likewise, pad-weight test (Fig. 2, $p < 0.0001$), and the VAS as a sujective measure of severity (Fig. 3, $p < 0.0001$) improved significantly after the intervention.

Fig. 1

Results of the King's Health Questionnaire: all domains were significantly improved after bulking therapy ($p < 0.001$, Wilcoxon signed rank test)

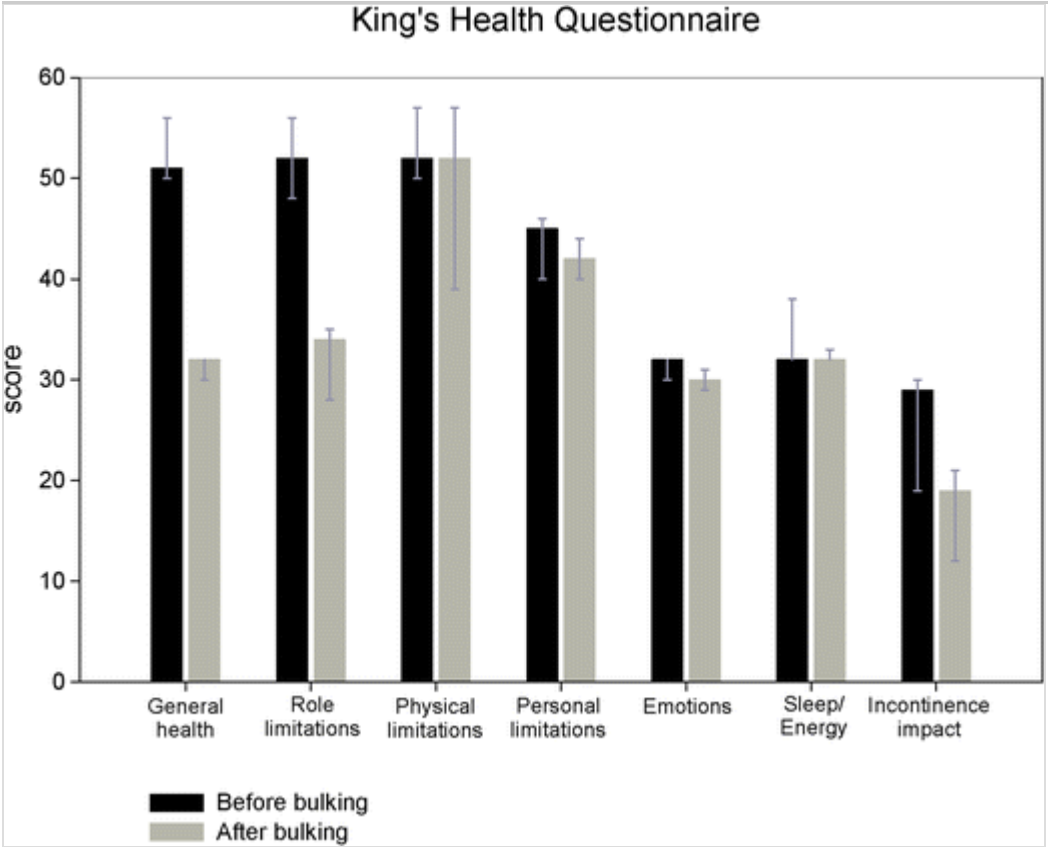


Fig. 2

Pad-weight test results improved significantly after bulking therapy ($p < 0.001$, Wilcoxon signed-rank test)

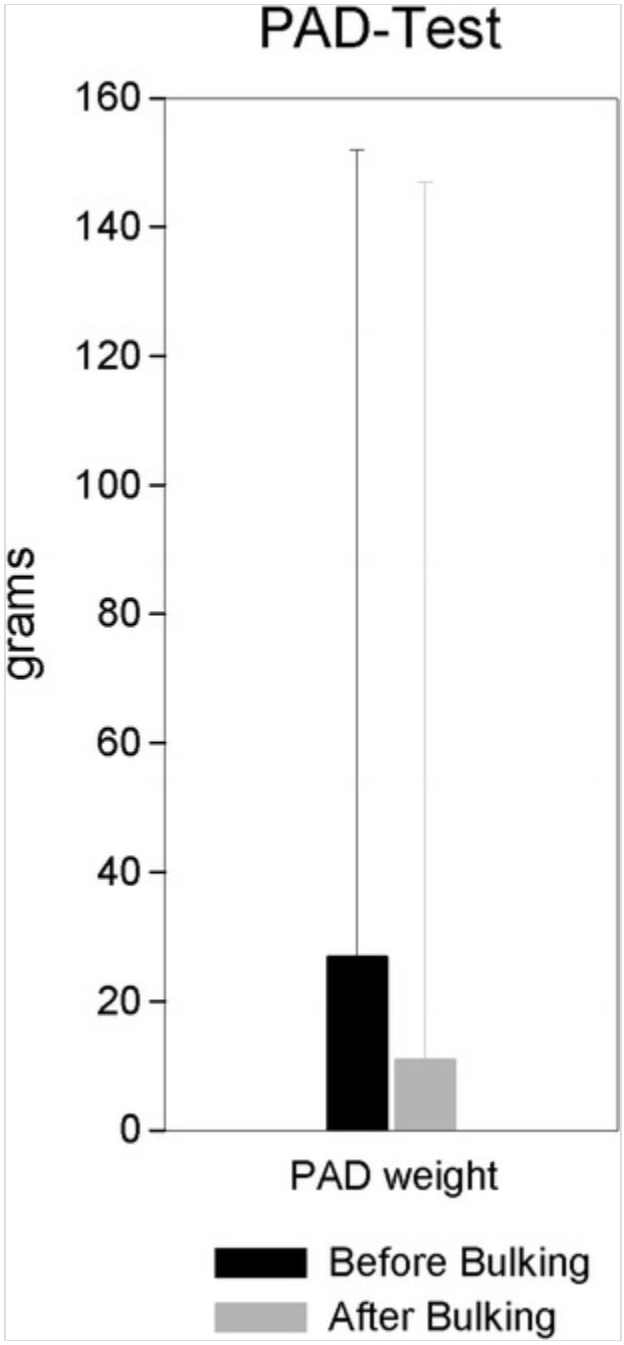
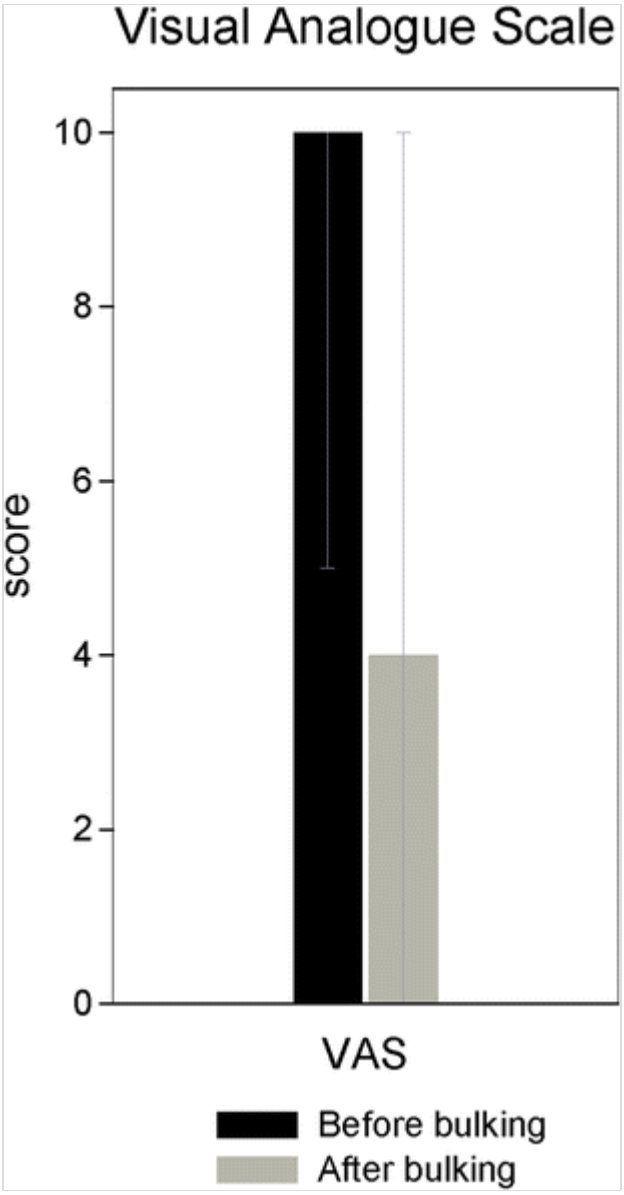


Fig. 3

Visual Analogue Scale results as a subjective measure of incontinence severity with a significant improvement ($p < 0.001$, Wilcoxon Signed Rank Test)



The overall complication rate was 13% due to lower UTIs (n = 12), temporary retention <48 h (n = 3), and pain requiring additional pain medication (n = 4).

Discussion

We show that bulking therapy is a beneficial and valuable alternative to surgical treatment in the rather heterogenous group of patients with MUI. Pad-weight tests showed that patients were not dry after the injections but that leakage was significantly improved, and their satisfaction mirrors QoL improvement on the VAS and KHQ results. Additionally, it also suggests that patient satisfaction is not necessarily dependant on complete dryness.

In MUI, treatment decisions are less obvious than in either SUI or UUI patients, and alternative therapies are needed [2]. Periurethral bulking therapy has been used for for years to treat SUI and shows improvements even over

the long term [16]. Recurrence rates are higher after bulking therapy than after other incontinence surgeries but should be considered as an alternative treatment [17]. Bulking therapy is simple, safe, and shows both objective and subjective improvement and relief in selected SUI patients [10]. Although a Cochrane Review concluded that evidence for urethral injection therapy to treat UI in women remains insufficient to guide practice [18], the minimally invasive nature, efficacy, and safety of periurethral bulking with PAHG favors its use in the correctly selected patient [19, 20, 21].

Moreover, bulking therapy is used to manage failed SUI surgery [22, 23], especially in patients with intrinsic sphincter deficiency [24], and PAHG is used in this respect with good outcome and low complication rates [24, 25]. Repeat midurethral sling after primary sling failure seems to have a lower risk of failure than bulking therapy [26], but the latter is more cost effective than midurethral slings in patients without urethral hypermobility [27]. Furthermore, urethral bulking therapy has been described as a valuable treatment option in SUI after pelvic radiotherapy [28].

In MUI, conservative treatment focusing on the most bothersome component is the first therapeutic step [2, 4]. If conservative treatment fails, surgical alternatives become necessary. Petros suggested that in MUI, uncoupling urge from stress might separate two different symptoms with possibly different etiologies, and these should therefore be treated separately [29]. However, our results suggest that bulking therapy might ameliorate incontinence symptoms holistically. We show significant improvements in both subjective (VAS, KHQ) and objective (pad-weight test) outcomes. Patient-reported outcomes are particularly important, as they better reflect patient satisfaction than do mere objective measurements [30]. Although complications of bulking therapy are not to be neglected [30], side effects were few and mild. Additionally, bulking therapy is minor surgery, with the possibility of using local anaesthetic only, which is usually appreciated by patients.

Strengths of this study are the rather large number of patients, especially as it is the first concentrating on bulking therapy in MUI patients specifically. Advantageous is the inclusion of both objective and subjective outcomes obtained with validated tools, since this might more accurately reflect the patient’s goals [10].

A weakness of this work is the lack of urodynamic data measuring bladder function before and after treatment; however, we felt urodynamic data were

not of great importance in this study. Also, due to the strict inclusion criteria, particularly with the mixture of SUI and OAB being relatively equal, the study was lengthy. By incorporating urodynamics, recruiting patients requiring invasive tests may have lengthened that period. We felt such information—except possibly in patients with detrusor overactivity—was unnecessary for our study. A further weakness is the lack of accurate estimation of the influence of bulking therapy on the urge component. VAS was used to reflect global disturbance for assessing incontinence severity in general. Results of our study do not allow a breakdown of urge and stress components; however, they allow us to make the conclusion that incontinence symptoms generally improve with bulking therapy, even in patients with MUI symptoms.

In conclusion, MUI patients are difficult to treat, since their symptoms are heterogenous and less well understood in general. Randomized trials in women with MUI are needed [2]. Nevertheless, bulking therapy is promising, simple, safe, and provides patient relief. Therefore, we can recommend its use to treat patients with MUI.

Compliance with ethical standards

Conflicts of interest None.

Electronic supplementary material

ESM 1

(JPEG 513 kb)

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