Research Article

Urethral bulking agents and pelvic floor muscle training for the treatment of stress urinary incontinence in female patients with multiple sclerosis

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Abstract

Background: Stress urinary incontinence (SUI), characterized by involuntary urine leakage during increased abdominal pressure, is prevalent among women with multiple sclerosis (MS), significantly impacting their quality of life (QoL). Traditional treatments are less suitable for MS patients due to potential complications, highlighting the need for less invasive alternatives, *that is*, urethral bulking agents (UBAs) and pelvic floor muscle training (PFMT). UBAs increase urethral tissue volume, while PFMT strengthens pelvic muscles. Despite promising outcomes, their efficacy in MS-related SUI is under-researched. **Objective:** This study assessed the effectiveness of UBAs and PFMT in managing SUI among female patients with MS. **Methods:** This nine-month study involved 14 female MS patients with moderate SUI, who were equally divided into two groups to evaluate the effectiveness of UBAs and PFMT. UBAs were administered through injections to enhance urethral resistance, while PFMT used guided exercises to improve pelvic control. Outcomes were assessed in terms of urinary pad usage, scores of International Consultation on Incontinence Questionnaire-Short Form, and QoL metrics to evaluate reductions in incontinence and symptom severity. **Results:** Both treatment groups showed significant improvement with SUI management. Daily pad usage decreased to 0–1 in both groups, with reductions in symptom severity and improvements in QoL scores. UBAs provided quicker symptomatic relief, while PFMT supported long-term management. However, two participants in the PFMT group discontinued follow-up due to MS-related complications, highlighting the challenges of maintaining adherence in progressive conditions. **Conclusion:** UBAs and PFMT are effective management options for SUI in MS patients, improving symptom control and QoL. This study underscored the importance of individualized, multimodal approaches to optimize outcomes for women with MS-related SUI. Nevertheless, further research is needed for long-term validation.

Keywords: Stress urinary incontinence, Multiple sclerosis, Urethral bulking agents, Pelvic floor Muscle training, Quality of life

1. INTRODUCTION

Stress urinary incontinence (SUI) is defined as the involuntary leakage of urine during activities that increase intra-abdominal pressure, such as coughing, sneezing, laughing, or physical exertion [1,2]. It is a common and distressing condition, particularly in women, affecting both their physical and psychological well-being. Although SUI is common in the general female population, its incidence is notably higher among women with multiple sclerosis (MS), a chronic neurological disease characterized by demyelination and neuroinflammation within the central nervous system [3]. MS can impair bladder function by disrupting signals between the brain, spinal cord, and lower urinary tract, contributing

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to several lower urinary tract symptoms, including urinary urgency, frequency, and incontinence [4-6]. When SUI presents alongside MS, it can significantly reduce a patient's quality of life (QoL), increase emotional distress, and lead to social withdrawal [7].

Managing SUI in women with MS presents significant challenges due to the complex interplay between neurological damage and muscle function. Unlike non-neurogenic SUI, treatment for MS-related SUI must consider the progressive nature of MS, mobility limitations, and the potential impact of MS therapies [8,9]. Standard approaches for SUI, such as surgical procedures, may not be feasible or desirable in these patients due to surgical risks, recovery concerns, and the need for long-term maintenance of function [10]. Therefore, less invasive treatment options, such as urethral bulking agents (UBAs) and pelvic floor muscle training (PFMT), are gaining attention for their safety, reduced complications, and benefits for this population.

UBAs are injectable substances that increase tissue volume around the urethra, improving its coaptation and closing pressure during physical activities. Common agents include polyacrylamide hydrogel, silicone particles, and dextranomer/hyaluronic acid copolymers [11]. UBAs offer a minimally invasive solution with a relatively low risk, making them an attractive option for patients with complex medical histories and multiple comorbidities [12]. However, the long-term effectiveness of UBAs in MS patients remains uncertain, as neurological factors may complicate the maintenance of continence.

PFMT is a non-invasive intervention that focuses on strengthening the pelvic floor muscles, which support the bladder and urethra. Through repetitive muscle contractions and biofeedback techniques, PFMT aims to restore pelvic stability and enhance voluntary control over urinary continence [13]. While it has shown promising outcomes in the general population, the presence of neurological impairments in MS raises questions about the effectiveness and sustainability of PFMT for these patients [14].

This paper explored the efficay, safety, and limitations of combined UBAs and PFMT in managing SUI among female MS patients. By evaluating these treatment options, this study aimed to offer insights that can assist clinicians in developing individualized management plans, ultimately improving the QoL for women with MS.

2. MATERIALS AND METHODS

This study included female patients diagnosed with MS and moderate SUI. The diagnosis of SUI was confirmed using a clinical stress test, bladder diary (3 days), and urodynamic studies [15]. All participants had low disability levels, with an Expanded Disability Status Scale (EDSS) score between 1 and 2, indicating mild MS-related impairment.

Patients were offered two treatment options based on their needs and preferences: UBAs or PFMT. Both interventions were selected for their minimally invasive nature and suitability for MS patients. Patients were randomized into the UBAs or PFMT groups using a network randomizer (https://www.randomizer.org).

UBAs involve the injection of biocompatible materials into the urethral walls to increase tissue volume and improve urethral coaptation, thereby alleviating SUI symptoms. In this study, Urolon®, a non-pyrogenic bulking agent supplied in single-use 1 mL syringes, was used. Each procedure required 1.5 mL of the agent, administered according to the manufacturer's instructions.

PFMT consists of exercises designed to strengthen the pelvic floor muscles, enhancing bladder control. Patients were guided on correctly contracting these muscles through supervised sessions and were advised to continue the exercises at home regularly. Both treatment modalities were performed by a urologist and physiotherapist, respectively, following the same protocol for each intervention.

The participants were followed for a total duration of 9 months to assess the effectiveness of the interventions. Comparative measuring tools included urinary pad usage, International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) scores, and QoL scores [16] (Figure 1).

During the 9-month follow-up period, patients were regularly monitored to track changes in incontinence severity, pad usage, symptom scores, and QoL scores. Outcome measures at the study endpoint included reductions in urinary pad use and improvements in ICIQ-SF and QoL scores. The effectiveness of the interventions was assessed by comparing baseline and endpoint values.

This methodology ensured a structured evaluation of both treatment approaches, offering insights into the feasibility, safety, and benefits of UBAs and PFMT for treating SUI in female MS patients.

3. RESULTS

The study included 14 female patients with MS and moderate stress SUI, with a mean age of 40.5 years. Among these participants, 12 had isolated SUI, while two were diagnosed with mixed urinary incontinence (MUI). The two patients with MUI had been taking 50 mg of mirabegron for the past 6 months, which resulted in a complete resolution of urgency urinary incontinence symptoms and an 80% overall reduction in urinary incontinence episodes. All participants

had low disability scores, with EDSS scores between 1 and 2, reflecting mild MS-related impairments.

Participants were offered either UBAs or PFMT as treatment options, with seven patients assigned to each intervention. Both groups were followed for 9 months to assess changes in symptom severity, pad usage, and QoL scores. At baseline, patients in both groups reported using 2–3 pads per day. The initial mean ICIQ-SF score for the UBAs group was 15.3, with a mean QoL score of 7.4. In the PFMT group, the initial ICIQ-SF score was 15.1, and the mean QoL score was 6.9 (Table 1).

After 9 months, both treatment groups demonstrated substantial improvements across all evaluated parameters. Patients in the UBAs group reduced their pad usage to 0–1 pad per day. The mean ICIQ-SF score decreased from 15.3 to 2.9, while the mean QoL score improved from 7.4 to 0.7, indicating marked symptomatic relief and a significant enhancement in QoL. Similarly, the PFMT group also experienced significant improvements, with pad usage decreasing to 0–1 pad per day, and the mean ICIQ-SF score dropping from 15.1 to 2.4. In addition, the mean QoL score improved from 6.9 to 0.4, reflecting enhanced well-being and a reduction in the impact of incontinence on daily life. However, two participants in the PFMT group discontinued follow-up due to MS-related factors, which may have influenced the group's overall outcomes (Table 1).

Both patients with MUI achieved complete resolution of their incontinence symptoms by the end of the study, further underscoring the effectiveness of these interventions.

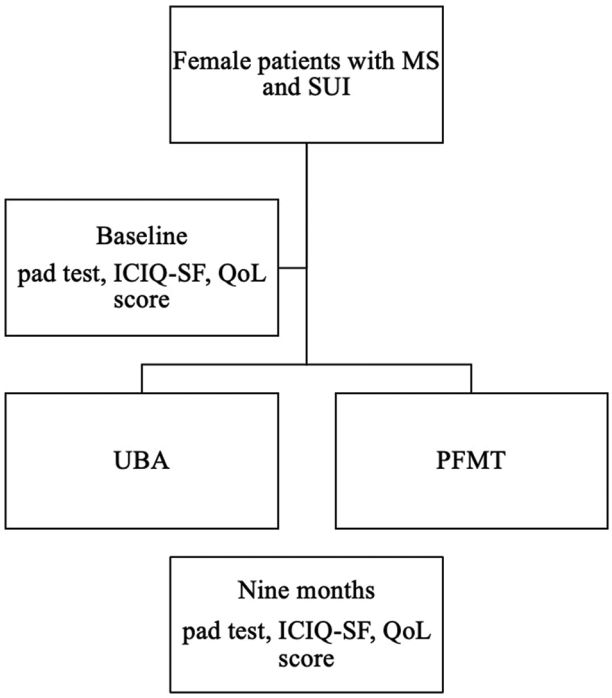

Figure 1. Flowchart of study design.
ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form; MS: Multiple sclerosis; PFMT: Pelvic floor muscle training; QoL: Quality of life; SUI: Stress urinary incontinence; UBA: Urethral bulking agents.

4. DISCUSSION

This study evaluated the effectiveness of UBAs and PFMT in treating SUI in female patients with MS. The findings demonstrated that both interventions led to significant improvements in urinary incontinence symptoms, with reductions in pad usage, improvements in ICIQ-SF scores, and enhancements in QoL scores. These results highlight the potential of using both minimally invasive approaches in managing SUI among women with MS, who face unique challenges due to neurological impairments and disease progression.

The observed reduction in pad usage and improvement in symptom scores across both groups suggest that UBAs and PFMT can effectively restore continence in MS patients with mild disability (EDSS 1–2). UBAs provided immediate structural support to the urethra through injection of biocompatible material, as reflected by the decrease in ICIQ-SF scores from 15.3 to 2.9 and improved QoL from 7.4 to 0.7. Similarly, PFMT improved bladder control by strengthening the pelvic floor muscles, achieving comparable outcomes with a reduction in ICIQ-SF scores from 15.1 to 2.4 and a QoL improvement from 6.9 to 0.4. These findings align with existing research, demonstrating the benefits of these therapies in non-neurogenic SUI populations [17-19], while offering new insights on their applicability to MS patients with more complex clinical profiles.

Table 1. Results on urinary pad usage, International Consultation on Incontinence Questionnaire-Short Form scores, and quality of life metrics at baseline and 9-month follow-up

Treatment group	Baseline parameters				Nine-month follow-up parameters			
	Number of patients	Pads used	ICIQ-SF score (mean)	QoL score (mean)	Number of patients	Pads used	ICIQ-SF score (mean)	QoL score (mean)
UBA	7	2–3	15.3	7.4	7	0–1	2.9	0.7
PFMT	7	2–3	15.1	6.9	5	0–1	2.4	0.4

ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form, PFMT: Pelvic floor muscle training, QoL: Quality of life, UBA: Urethral bulking agents.

Notably, both patients with MUI achieved complete resolution of symptoms by the end of the study, suggesting that the combination of pharmacological therapy (mirabegron) for urgency and targeted interventions for SUI can yield optimal outcomes. This finding underscores the importance of tailored, multimodal treatment strategies for MS-related incontinence, as a single therapeutic modality may not adequately address the full range of symptoms [5]. The complete remission of MUI further highlights the value of individualizing treatment based on symptom type and severity, leading to improved outcomes [6].

Despite the overall positive results, two participants in the PFMT group discontinued follow-up due to MS-related factors, emphasizing the impact of disease progression on treatment adherence. This discontinuation suggests that MS-related fatigue, physical limitations, or cognitive decline might influence the long-term feasibility of exercise-based interventions such as PFMT. Clinicians should consider these challenges when recommending PFMT, possibly integrating support strategies such as telemonitoring or supervised sessions to boost adherence [20].

While the improvements observed in both groups are encouraging, some differences between UBAs and PFMT warrant consideration. The UBAs group exhibited slightly better QoL outcomes than the PFMT group, which may reflect the more immediate effect of bulking agents compared to the gradual improvements achieved through muscle training. This difference suggests that UBAs might be preferable for patients seeking faster symptomatic relief, particularly those with limited capacity to engage in exercise-based therapies [21]. Conversely, PFMT offers a non-invasive, low-risk option that does not require repeated procedures, making it an attractive alternative for patients concerned about injections or those aiming for long-term self-management [22].

The study's limitations include the small sample size, which restricts the generalization of the results, and the relatively short follow-up period that may not capture long-term outcomes, particularly for PFMT, which relies on sustained practice. The small sample size may also explain the low number of patients with urge incontinence compared to existing literature. Nevertheless, the study focused on a targeted group of women with MS and SUI.

Future studies with larger cohorts and extended follow-up are needed to confirm the durability of these interventions. In addition, exploring the role of combined therapies, such as integrating UBAs with PFMT or pharmacological treatments, may provide further insights into optimization of care for MS-related SUI. For example, PFMT could be combined with UBAs and β3-agonists to attain the best outcomes for women with MUI. In the context of PFMT, more detailed strategies, such as tele-monitoring or motivational interventions, could be implemented to address adherence challenges. Moreover, recruiting patients with varying or higher EDSS scores could provide more data to support personalized and tailored treatment approaches.

5. CONCLUSION

Both UBAs and PFMT are effective treatment options for managing SUI among female patients with MS, accomplishing significant improvements in symptom severity and QoL. While UBAs may provide quicker symptom relief, PFMT offers a sustainable and non-invasive alternative. Clinicians should consider patient preferences, disease progression, and functional capacity when selecting a treatment approach. These findings underscore the importance of individualized, multimodal strategies to improve outcomes for women with MS suffering from urinary incontinence.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

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Writing – review & editing: Michael Samarinas

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Local Hospital's Ethical Committee, Scientific Council of General Hospital of Larissa (approval code: 112/15-02-2022). Patients recruited signed an informed consent form.

CONSENT FOR PUBLICATION

Patients signed a consent form to publish their data.

AVAILABILITY OF DATA

Data are available from the authors on reasonable request.

REFERENCES

1. Abrams P, Cardozo L, Fall M, *et al*. The standardization of terminology in lower urinary tract function: Report from the Standardization Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2010;19(3):321-327.
2. Haylen BT, Ridder DD, Freeman RM, *et al*. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J*. 2010;21(1):5-26. doi: 10.1007/s00192-009-0976-9
3. Ghasemi V, Kiani Z, Alizadeh S, *et al*. Prevalence of stress urinary incontinence and urge urinary incontinence in multiples sclerosis patients: A systematic review and meta-analysis. *Neurol Sci*. 2024;45(9):4197-4210. doi: 10.1007/s10072-024-07570-0
4. Beckel JM, Holstege G. Neurophysiology of the lower urinary tract: Central control, peripheral control, and therapeutic strategies. *Physiol Rev*. 2011;91(2):393-481.
5. Fowler CJ, Panicker JN, Drake M, *et al*. A UK consensus on the management of the bladder in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2009;80(5):470-477. doi: 10.1136/jnnp.2008.159178
6. Panicker JN, Fowler CJ, Kessler TM. Lower urinary tract dysfunction in the neurological patient: Clinical assessment and management. *Lancet Neurol*. 2015;14(7):720-732. doi: 10.1016/S1474-4422(15)00070-8
7. Chow PM, Chuang YC, Hsu KCP, Shen YC, Liu SP. Impact of female stress urinary incontinence on quality of life, mental health, work limitation, and healthcare seeking in China, Taiwan, and South Korea (LUTS Asia): Results from a cross-sectional, population-based study. *Int J Womens Health*. 2022;14:1871-1880. doi: 10.2147/IJWH.S383651
8. Vecchio M, Chiaramonte R, Di Benedetto P. Management of bladder dysfunction in multiple sclerosis: A systematic review and meta-analysis of studies regarding bladder rehabilitation. *Eur J Phys Rehabil Med*. 2022;58(3):387-396. doi: 10.23736/S1973-9087.22.07217-3
9. Al Dandan HB, Galvin R, McClurg D, Coote S. Management strategies for Lower Urinary Tract Symptoms (LUTS) among people with Multiple Sclerosis (MS): A qualitative study of the perspectives of people with MS and healthcare professionals. *HRB Open Res*. 2019;2:31. doi: 10.12688/hrbopenres.12960.1
10. Norton P, Brubaker L. Urinary incontinence in women. *Lancet*. 2006;367(9504):57-67. doi: 10.1016/S0140-6736(06)67925-7
11. Hussain SM, Bray R. Urethral bulking agents for female stress urinary incontinence. *Neurourol Urodyn*. 2019;38(3):887-892. doi: 10.1002/nau.23924
12. Capobianco G, Saderi L, Dessole F, *et al*. Efficacy and effectiveness of bulking agents in the treatment of stress and mixed urinary incontinence: A systematic review and meta-analysis. *Maturitas*. 2020;133:13-31. doi: 10.1016/j.maturitas.2019.12.007
13. Bø K, Sherburn M. Evaluation of pelvic-floor muscle function and strength. *Int Urogynecol J*. 2005;16(5):1-14.
14. Kajbafvala M, Ashnagar Z, Lucio A, *et al*. Pelvic floor muscle training in multiple sclerosis patients with lower urinary tract dysfunction: A systematic review and meta-analysis. *Mult Scler Relat Disord*. 2022;59:103559. doi: 10.1016/j.msard.2022.103559
15. Avery K, Donovan J, Peters T, Shaw C, Gotoh M, Abrams P. ICIQ: A brief and robust measure for evaluating the symptoms and impact of urinary incontinence. *Neurourol Urodyn*. 2004;23(4):322-330. doi: 10.1002/nau.20041
16. Rosier PFW, Schaefer W, Lose G, *et al*. International continence society good urodynamic practices and terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study. *Neurourol Urodyn*. 2017;36(5):1243-1260. doi: 10.1002/nau.23124
17. Dumoulin C, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev*. 2018;10(10):CD005654. doi: 10.1002/14651858.CD005654.pub4.
18. Tsikopoulos I, Lazarou L, Tzelves L, Sakalis V, Papathanasiou C, Samarinas M. The effect of pelvic floor muscle training on urodynamic parameters in women with stress urinary incontinence. *Cent European J Urol*. 2023;76(4):315-321. doi: 10.5173/ceju.2023.148
19. Leone Roberti Maggiore U, Bogani G, Meschia M, *et al*. Urethral bulking agents versus other surgical procedures for the treatment of female stress urinary incontinence: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2015;189:48-54. doi: 10.1016/j.ejogrb.2015.03.025
20. Cho ST, Kim KH. Pelvic floor muscle exercise and training for coping with urinary incontinence. *J Exerc Rehabil*. 2021;17(6):379-387. doi: 10.12965/jer.2142666.333
21. Braga A, Caccia G, Papadia A, *et al*. Urethral bulking agents for the treatment of recurrent stress urinary incontinence: A systematic review and meta-analysis. *Maturitas*. 2022;163:28-37. doi: 10.1016/j.maturitas.2022.05.007
22. Mantilla Toloza SC, Villareal Cogollo AF, Peña García KM. Pelvic floor training to prevent stress urinary incontinence: A systematic review. *Actas Urol Esp* (*Engl Ed*). 2024;48(4):319-327. doi: 10.1016/j.acuroe.2024.01.007