Research Article

A pilot study on the potential of photobiomodulation to safely modify symptoms of an overactive bladder

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Abstract

Background: Photobiomodulation (PBM) may stabilize autonomic neural drive from the pontine micturition Center to the urinary bladder in individuals with overactive bladder (OAB) symptoms. **Methods:** A safety profile study preceded a single-case experimental design with repeated measures across subjects to establish the safety and effect direction of PBM to modify symptoms in patients with OAB. **Results:** No adverse events occurred with PBM, specifically blood pressure remained unchanged. Urinary frequency improved significantly during the intervention and at follow-up. PBM therapy was associated with a meaningful impact on OAB-related quality of life and a small to medium-to-high effect size on OAB symptom severity. **Conclusion:** Nasal application of PBM is safe and may impact OAB symptoms. A controlled trial of PBM in patients with lower urinary tract symptoms is warranted.

Keywords: Photobiomodulation, Near-infrared light, Overactive bladder, Incontinence, Urinary urgency

1. INTRODUCTION

Overactive bladder (OAB) clinically refers to urinary urgency/urgency incontinence, usually accompanied by increased frequency to void during the day and night [1]. Increased bladder sensation at an early filling volume is persistent and uncomfortable, profoundly affecting the individual's quality of life. OAB has broad-negative consequences, associated with impaired emotional well-being, personal cost, an increased risk of falls, high health-care utilization, and lower work productivity [2-5]. Patients are bothered by OAB and seek coping strategies and effective treatment [6].

Central sensitization is a well-recognized mechanism of centrally amplified pain perception without acute tissue injury. Low-intensity input triggers persistent peripheral nociceptive signaling in patients with central sensitization. Hypersensitivity develops at the spinal cord, thereby enhancing neuronal responses. Projection of this spinal nociceptive information to the higher central nervous system (CNS) induces a change in the central neurons. Inhibition from descending central processes is reduced, meaning perception is not modulated or moved toward a more normal sensation.

Many hallmarks of central sensitization are evident in patients with OAB [7], such as abnormally increased afferent signals from the bladder and a decreased capacity to modulate signals in the CNS arising from mechanosensation, chemical sensitivity, motor or sensory information that maintains homeostasis during the micturition cycle. The micturition reflex becomes hyper-excitable through activity in Onuf's nucleus, a small group of motor neurons located in the anterior horn of the S2 segment of the spinal cord, and afferent signaling to the pontine micturition center (PMC) that coordinates the mechanical process of micturition, that

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is, the sphincter and detrusor muscle activities of the urinary bladder [8].

Photobiomodulation (PBM) is a therapy that uses non-ionizing red or near-infrared light (NIRL) to modulate biological processes, including reducing immediate neuronal excitability [9]. Light energy is absorbed transcutaneously, with the major photo acceptor molecules being hemoglobin, myoglobin, and the enzyme cytochrome c oxidase that stimulates cell signaling pathways to facilitate membrane stability, increase resistance to depolarization, and ultimately, induce secondary cellular effects in neural tissues [10]. Ongoing CNS responses following the PBM therapy relate to the stimulation of persistent mitochondrial cytochrome oxidase activity stimulation that improves energy metabolism in the brain [11]. Blood oxygen-level-dependent neurocognitive function improvement has been noted in functional magnetic resonance imaging following PBM [12].

Symptoms of neural dysregulation appear to cluster in patients with frequent OAB; hypertension, postural hypotension, insomnia, mood disorders, sleep-disordered breathing, and urge incontinence commonly co-exist [12]. We postulated that PBM may help stabilize the neural drive of the descending pathways from the PMC to the urinary bladder, resulting in reduced OAB symptoms.

The aim of this study was twofold. The first aim was to establish the safety of PBM delivered through the nose in patients with OAB presenting for urodynamic investigation (UDI) and describe any immediate effect on detrusor pressure and volume during filling. The second aim was to evaluate the direction of the effect of repeated PBM as a home-based treatment for reducing the severity of symptoms of OAB.

2. MATERIALS AND METHODS

2.1. Design

The study utilized a two-step methodology: (1) a repeated measures proof-of-concept observational study of the safety profile (primary endpoint) and immediate effect of PBM on UDI measures (secondary endpoint) in 10 participants with the syndrome of OAB proven on UDI (DO) and (2) an exploratory study using a single-case (SC) experimental design with repeated measures during baseline, intervention, and follow-up periods of 1 month each (i.e., non-concurrent) to test the safety and efficacy of NIRL administered repeatedly through a nasal prong in a number of patients with OAB (SC study design requires 3–6 individuals).

2.2. Patients

Individuals of either sex, aged ≥20 years, who were attending a community continence clinic for help in managing urinary tract dysfunction, were eligible for inclusion into the study. Exclusion criteria included pregnancy, bladder outlet obstruction, voiding abnormality on uroflowmetry, hypertension, or cognitive impairment. Potential participants with medical conditions that may have limited response to NIRL or responded adversely to the trial were excluded from the studies. Conditions of concern were heart failure, active cancer, previous pelvic radiotherapy, indwelling catheter, and significant cognitive impairment. Those who were unable to wear the nasal prong or to understand English were also excluded. All inclusion and exclusion criteria were applied to both studies 1 and 2.

2.3. Process

The Institution's Human Research Ethics Committee (HREC/43007/MH-2018-67544) approved this study. The trial was conducted under the Clinical Trial Notification Scheme with data from the study submitted to the Therapeutic Goods Administration after the trial.

2.4. Device

Vielight 810 is a wearable, non-laser NIRL, battery-powered PBM device, with a frequency pre-set at 10 Hz, used to deliver light at very low energy intensity for a fixed duration of 25 min. Treatment was delivered through intranasal diode.

Intervention: The PBM therapy using NIRL was administered through the nasal cavity as it has a high capillary density and thin permeable membrane allowing for irradiation of the blood circulating in the nasal channel and diffusion through soft tissue and bone. In addition, the nasal cavity sits close to cranial nerves V-VII that traverses the pons region of the brainstem. The application of NIRL using Vielight 810 was conducted by a physiotherapist trained in the use of electrotherapeutic devices.

2.5. Study 1

Sequential patients referred for UDI to investigate OAB were informed about the study. When the first cystometric fill confirmed the presence of detrusor overactivity, indicating the presence of OAB, consent was obtained for a second fill with trans-nasal NIRL applied for the duration of the second UDI. The frequency of application was pre-set at 10 Hz, but the duration of PBM was dictated by the time taken to complete the second cystometric fill.

The primary outcome of study 1 was safety, assessed using systolic and diastolic blood pressure (BP) due to the proximity of PBM application in the nasal cavity to respective centers in the brain controlling BP. Any other adverse effects were also recorded. Fitted BP cuffs were used to collect measurements. Secondary outcome measures included detrusor pressure at

the first detrusor contraction, volume at the first involuntary detrusor contraction, volume at a strong desire to void, and the maximum cystometric volume. All measurements were taken at baseline (before PBM treatment) and compared with those at the end of the study. In addition, demographic and clinical information, OAB Symptom Score (OABSS), and Quality of Life measure (OAB-q part A) were also collected.

2.6. Study 2

Informed consent was obtained from another group of individuals presenting with OABSS (urinary urgency and with or without incontinence) which had not resolved upon prior treatments. The participants continued their pre-existing OAB management while awaiting botulinum toxin injection to the detrusor muscle or moved on to a combination drug therapy. The study consisted of three 1-month phases. The initial 4 weeks constituted a baseline period, followed by an intervention month of PBM application. The final month was the follow-up phase, during which no NIRL treatment was given.

At the commencement of the intervention phase, the study therapist administered the initial NIRL dose, and participants learned its application. During the COVID-19 pandemic, when participants could not visit the hospital, NIRL sessions consisted of home-based treatment where 10 Hz was delivered through a single-patient intranasal diode. The session lasted for 25 min and was applied 5 times/week, for a total of 20 sessions over 1 month. Participants documented applications of NIRL and monitored their BP using a home-based digital device. In addition, study staff maintained a weekly telephone contact with participants to monitor any events of concern and troubleshoot issues that arose.

2.7. Outcomes

The primary outcome measure was the patient-reported OABSS [13], a highly sensitive measure of treatment-related changes in OAB symptoms [14]. The minimum clinically significant reduction in total OABSS is considered to be 3.0 out of a possible score of 15 [15]. Secondary measures included frequency of micturition per day, number of urge leak episodes, and nocturia. The variables were recorded by participants and collected electronically using the smartphone "iUflow electronic voiding bladder diary" application that communicated results to study staff through email (https://iuflow.com). In addition, demographic and clinical information and the responses to the ICIQ-OAB-specific health-related quality of life questionnaire (OAB-QoL) [16] were also collected. The OAB-QoL is a validated OAB-specific instrument [17] with a subscale consisting of 27 items, each having six ordinal response levels. Higher scores indicate greater impairment. The minimum clinically significant difference (MCID) for the OAB-QoL symptom subscale has been identified to be ≥10 [18,19]. The Global Impression Improvement Scale rates change from before an intervention relative to the current time. Participants rated their symptoms as follows: 1=very much improved since the initiation of treatment; 2=much improved; 3=minimally improved; 4=no change from baseline (the initiation of treatment); 5=minimally worse; 6= much worse; or 7=very much worse since the initiation of treatment [20].

2.8. Sample size

For the proof-of-concept study for a new indication of NIRL therapy, a sample size of 10 participants was adequate to demonstrate safety and change in bladder storage parameters (Part 1). The pilot study (Study 2) conducted during COVID-19, utilized a repeated measure SC experimental design. This was selected as it had statistical power when the direction of effect had not been established and was appropriate for the small number of subjects available during the pandemic [14]. If no loss to follow-up was to occur, data from four participants would be adequate to meet the standard of at least three demonstrations of effects. This design also measures change over time, a crucial attribute for individuals with OAB.

2.9. Statistical analysis

For both studies 1 and 2, the demographic and clinical characteristics of the participants were tabled following standard procedure. The analysis for study 1 utilized descriptive statistics. Median differences in the four endpoints pre- and post-NIRL were calculated, and inferential statistics were performed using the Wilcoxon signed-rank test. Statistical significance was indicated by a two-sided alpha significance level of 0.05.

For study 2, analysis of SC study repeated measures (baseline, intervention, and follow-up phases) design was employed to explore both safety and direction of effect after repeated application of NIRL. Within-phase level was reported as the mean or median of the phase data points; the trend was determined by assessing whether the data points were monotonically increasing or decreasing; stability of the data was evaluated by calculating the percentage of data points within 15% of the phase mean (or median) with stability satisfied at 80%. Between-phase examination utilized the Tau-U statistic to quantify the proportion of measurements in the intervention phase not overlapping with the baseline measurements. Tau-U score computations were performed using the Tau-U Calculator (SC Research™ USA). Due to variation in OABSS in all participants, all statistics were corrected for the baseline trends.

3. RESULTS

Study 1: PBM was applied for the duration of the 2nd UDI in 10 participants (range 8–20 min). Table 1 reports the safety parameters and urodynamic measures collected. No statistically or clinically significant changes in systolic (z = 0.000, *P* = 1.000) or diastolic BP (z = 0.000, *P* = 1.000) were found during the 2nd UDI with PBM *in situ.* Nil adverse events were reported.

No statistically significant differences were identified for any secondary endpoint during the 2nd UDI fill (detrusor pressure at the first detrusor contraction z = 0.000, *P* = 1.000; volume at the normal desire to void z = −1.636, *P* = 0.102; volume at a strong desire to void z = 0.000, *P* = 1.000; maximum cystometric volume z = −0.535, *P* = 0.593; volume at the first detrusor contraction z = 0.000, *P* = 1.000).

Study 2: Four participants (two males and two females; participants 1–4) with OAB unresponsive to conservative therapy completed the baseline, intervention, and follow-up phases. The participants' ages ranged from 49 to 68 years, all being multi-morbid (participant 1: Obstructive sleep apnea, restless leg syndrome. Participant 2: Cerebrovascular accident, diabetes mellitus. Participant 3: Cerebrovascular accident, multiple sclerosis, restless leg syndrome. Participant 4: Multiple sclerosis). In three of the four participants, the underlying pathophysiology could potentially alter the neural drive to the bladder. However, these individuals had not undergone UDI to establish neurogenic OAB. These participants received treatment for symptoms consistent with the syndrome of OAB.

All participants received conservative therapy for bladder symptoms at the time of the study. Antimuscarinic medication was being used by subject four during study 2 but had been started many months previously with minimal effect. Subjects one and two had also previously tried both anti-muscarinic medication and beta-3 agonists but ceased them well before the study commenced. Systolic BP over 120 mmHg was seen in two participants at baseline; no postural hypotension was observed.

Session cards completed by participants confirmed their adherence to the application schedule. All participants reported baseline urinary frequency (i.e., eight or more voids per day), three of the four cases were OAB-wet (i.e., reported urge leakage) and the same number woke at least twice per night to pass urine. The OABSS at baseline was 5, 10, 10, and 11 out of a possible 15 for each of the participants.

Table 1. Characteristics and outcome measures from safety profile study (*n*=10)

Demographic and clinical variables	**Descriptive statistic**	
Mean age (years)	60.6 (SD 8.3)	
Female: Male	6:4	
Median OABSS	8.5 (IQR 6.8–9.3)	
Median OAB-q part A	28.5 (IQR 22.0–29.3)	
Safety measure		
Participant number	**SBP changes at a normal desire to void during 2nd fill**	**DBP changes at a normal desire to void during 2nd fill**
1	7	1
2	−2	1
3	−1	−5
4	−7	7
5	−8	−5
6	20	7
7	−5	−13
8	−5	−5
9	12	5
10	-	-
Median BP at a normal desire to void	**1st fill**	**2nd fill**
Systolic BP	128 (IQR 119.8–138.0)	136 (IQR 117.0–144.5)
Diatolic BP	82.5 (IQR 76.8–85.8)	83.0 (IQR 71.0–90.5)
UDI parameters	**1st fill**	**2nd fill**
Median detrusor pressure at first detrusor contraction (cmH_2O)	7.00 (IQR 5.0–120.0)	16.0 (IQR 10.0–95.0)
Median volume at a strong desire to void (mL)	210 (IQR 175.0–620.0)	225 (IQR 215.0–510.0)
Median maximum cystometric volume (mL)	255 (IQR 167.5–450.0)	245 (IQR 213.8–480.0)
Volume at first detrusor contraction	190 (IQR 136.3–247.5)	235 (IQR 162.5–240.0)

OABSS: Overactive bladder symptom score; BP: Blood pressure; IQR: Interquartile range.

Visual inspection of individual OABSS scores (Figure 1) showed variation during the baseline across all participants. There was a marked reduction in OABSS in one participant during the intervention relative to baseline that remained during the follow-up phase. Tau-U effect size statistics corresponded to visual observations. A statistically significant reduction in OABSS following the PBM therapy was noted in one participant (Table 2).

A small-to-medium-to-high effect size on OABSS was observed among patients during the intervention phase relative to the baseline phase; Tau-U of −0.81 in participant 3 ($P = 0.001$; Table 2) sustained during the follow-up phase (Tau-U −0.76, $P = 0.007$; Table 2). Over the group, Tau-U score showed a trend toward a small effect size with the intervention reducing OABSS (Tau-U −0.22, $P = 0.125$; Table 2) during both active and follow-up phases (Tau-U −0.23, $P = 0.112$; Table 2).

During the intervention phase, urinary frequency per day showed a significant overall improvement (Tau-U −0.44, $P = 0.003$; Table 2). This change was also noted at follow-up (Tau-U −0.32, $P = 0.003$; Table 2). This indicated that participants with higher OABSS would respond to the therapy (Pearson's correlation coefficient −0.94, $P = 0.056$). This trend was not observed when urinary frequency was higher at baseline (Pearson's correlation coefficient −0.30, $P = 0.694$).

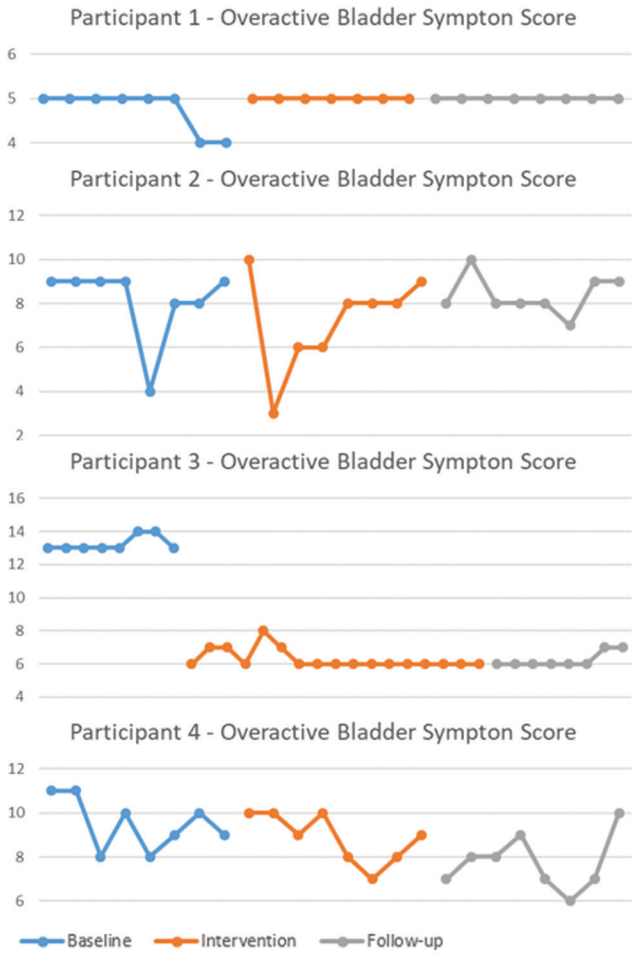

Figure 1. Change in primary outcome measure overactive bladder symptom score

Secondary outcome measures are presented in Table 3. Incontinence episodes were clearly reduced in participant 3 and nocturia was normalized in two of the participants. On visual inspection of repeated intra-participant ICI-OAB-q scores (Figure 1), three of the four participants showed reduced impact on quality of life after the NIRL intervention. The change in score was ≥10 for three of the four participants, suggesting a meaningful impact on the OAB-related quality of life. Change in scores at the end of follow-up, compared to baseline, remained above the cut-off for MCID in three participants. Repeated measures of Global Impression Scores appeared to be in line with OABSS and urinary frequency but not to reflect change in disease-specific quality of life.

Inspection of the individual session cards showed no report of side effects during or after the PBM in three of the four participants. In one female participant previously diagnosed as having a stroke and progressive multiple sclerosis, the initial application of NIRL was uneventful. However, the second treatment triggered a nervous system response. The participant woke from sleep with tinnitus and also experienced visual strobing for 1 min before resolution. The tinnitus lasted for 12 h. The reaction was discussed with the participant's neurologist and with the multidisciplinary clinical team. As per the participant's preference and the clinical team's recommendation, NIRL was re-commenced after 4 days for 5 min per session with a 2–3-day interval between applications. The intervention period was extended to 2 months to allow for equivalent NIRL exposure. Mild tinnitus and vague headache were common for 1 h post-NIRL but the participant was eager to continue with the trial due to marked improvement in bladder function. The BP readings captured during clinic visits are presented in an appendix. It should be noted that COVID-19 restrictions prevented study staff capturing all intended measures, although participants reported BP self-measured at home.

4. DISCUSSION

This study demonstrated that a frequency of 10 Hz, known to modulate detrusor activity [15] and generated by PBM, could be delivered safely through a nasal prong. In a highly selected comorbid cohort, an improvement in OAB-related quality of life was achieved and exceeded the minimally clinically important difference. Although the COVID-19 pandemic restrictions limited study recruitment and necessitated a change to repeated measure design, PBM applied through the nostril had the potential to reduce symptoms in patients with OAB. These early results indicated

Table 2. Effect of photobiomodulation therapy on OABSS and urinary frequency by day

OABSS	Baseline versus intervention			Baseline versus follow-up		
	Tau-U	95% CI	*P*-value	Tau-U	95% CI	*P*-value
Participant 1	0.46	−0.15–1.00	0.133	0.44	−0.15–1.00	0.142
Participant 2	−0.22	−0.81–0.37	0.462	−0.02	−0.61–0.57	0.958
Participant 3	−0.81	−1.00–0.34	0.001	−0.76	−1.00–0.21	0.007
Participant 4	−0.16	−0.77–0.45	0.600	−0.56	−1.00–0.03	0.059
Overall	−0.22	−0.50–0.06	0.125	−0.23	−0.52–0.05	0.112
Frequency						
Participant 1	−0.05	−0.13–0.03	0.862	0.39	−0.22–0.99	0.203
Participant 2	−0.58	−0.69–0.48	0.092	−0.50	−1.00–0.11	0.105
Participant 3	−0.99	−1.00–0.96	<0.001	−1.00	−1.00–0.45	<0.001
Participant 4	0.05	−0.02–0.12	0.875	−0.11	−0.70–0.48	0.713
Overall	−0.44	−0.73–0.16	0.003	−0.32	−0.61–0.03	0.033

Note: Tau-U can be interpreted for significance as small effect (<0.65), medium-to-high effect (0.66– 0.92), or strong effect (0.93–1). Tau-U: Tau-U scores; 95% CI: 95% confidence interval; OABSS: Overactive bladder symptom score.

Table 3. Study 2 secondary outcome measures

Participant	Baseline	After NIRL	1/12 follow-up
Number of UUI episodes/month			
1	1	1	0
2	1	1	3
3	70	18	0
4	3	3	3
Number of nocturia episodes			
1	3	3	3
2	3	1	1
3	2	2	2
4	2	1	1
OAB QoL scores			
1	48	53	57
2	70	51	42
3	93	77	81
4	113	69	81
Global impression scale			
1	N/A	Min improved	Min improved
2	N/A	Min improved	Min improved
3	N/A	Improved	No change
4	N/A	No change	No change

OAB: Overactive bladder; QoL: Quality of life.

that possibly one in four patients with OAB symptoms might benefit from PBM, and others have less associated bother.

Neuromodulation of the bladder has historically been performed percutaneously using a needle or surface electrode, intra-anally using an anal electrode, intravaginally using a vaginal plug, or percutaneously over the tibial nerve [13]. These mechanisms depend, to some extent, on the activation of afferent fibers within the pudendal or peripheral somatic afferent nerves, which in turn inhibit signals from the bladder afferents at the level of the spinal cord and thus disrupt an aberrant micturition reflex [16]. In contrast, the likely mechanism of PBM acting on OAB is supraspinal inhibition of the detrusor reflex through supplementation of descending inhibitory information from the PMC. As with other forms of neuromodulation, PBM may play an adjunctive role in combination therapy for OAB.

The safety profile of PBM in individuals with OAB who wore the device while undergoing cystometric fill was acceptable. Apart from one report of nasal discomfort from the prong clip, participants were free of adverse events. When safety after repeated application was evaluated, only one participant reported post-treatment symptoms. In the reactive participant, symptoms arose from the CNS and mirrored previous responses to new medication. To accommodate a low threshold to sensory information, PBM was subsequently delivered for a shorter duration and at a lower intensity, resulting in less provoked central symptoms. Given that neural hypersensitivity in this individual was coupled with a significant reduction in OAB symptoms, future work should consider whether a lower dose of PBM may be indicated when the nervous system is reactive.

Multiple-dose daily application of PBM through a nasal prong for a 1-month period improved overall urinary frequency and OAB-related quality of life. The post-stimulation effect after neuromodulation of the urinary bladder has been well recognized, with a maximum effect occurring within 1–2 months [15]. In this study, participants with a positive change still showed improvement 1 month after cessation of PBM. Similar findings have been reported in larger studies of patients with OAB from both neurogenic and non-neurogenic causes after implanted sacral neuromodulation [16,21,22]. In those studies, the treatment was applied almost continuously, whereas PBM involved a 25-min daily or a second daily application.

A single application of PBM during cystometry did not change UDI parameters. This is likely to be related to the duration of the second cystometric fill being insufficient to effect a noticeable change. This was consistent with findings from earlier work where 10 Hz was applied through transcutaneous patch electrodes over the sacral outflow to patients with non-neurogenic OAB during second-fill cystometry. In that study, the initial desire to void changed significantly, whereas maximum detrusor pressure at capacity and cystometric capacity did not change [23]. Due to the invasive nature of UDI, post-intervention follow-up cystometric measures are rarely obtained, and as with the present study, the effect of longer-term modulation is measured in terms of clinical outcomes only.

The study design, with its inherent limitations due to the uncertainty about the direction of effect and safety after

repeated application, necessitated a SC approach. In the SC study, outcome measures are recorded repeatedly during different phases, such as pre-intervention, intervention, and post-intervention phases, with the first phase serving as a baseline, allowing each participant to act as their own control [24]. This approach is suitable for 3–6 participants and is used to provide initial insights and to add valuable data to an area with limited existing evidence [25], such as PBM as an intervention for OAB. Despite the small sample size, our findings enhanced the understanding of the possible impact of PBM on the symptoms associated with OAB. Although preliminary, our findings are clinically valuable and underscore the need for larger studies to validate and expand these results.

PBM may offer an adjunctive treatment alternative when pharmacotherapy is of limited benefit or sub-therapeutic due to side effects, or where ongoing botulinum therapy to the lower urinary tract is unsustainable. A clinical trial is warranted to clarify the role of PBM in mitigating the severity of OAB symptoms in both individuals with and without neurogenic disease. Given the heterogeneity of patients with neurogenic bladder dysfunction and the potential we observed for sensitivity within the CNS after the application of PBM, a trial cohort with a single diagnosis may be appropriate, for example, stroke, primary multiple sclerosis, and Parkinson's disease. Given that participants in the current study were highly comorbid and complex, investigation of PBM in newly diagnosed OAB patients who are treatment-naive is suggested.

Future work should consider the impact of PBM on other functions controlled by the brainstem. As we had previously observed clustering of brainstem hypofunction symptoms in patients with OAB, post-PBM measurement of activities involving the reticular activating system would be informative. For example, the brainstem controls the sleep cycle and has also been implicated in sleep disorder breathing through non-dipping BP, both being common presentations in patients with nocturia. Similarly, there exists a significant relationship between anxiety and lower urinary tract symptoms, with OAB carrying a 3–6-fold risk for significant anxiety [26]. Anxiety and depression are influenced by the locus coeruleus, the source of noradrenergic projections to the forebrain, located in the pontine area of the brainstem [27]. We suggest that future work should include measures of insomnia, nocturnal BP, anxiety, depression, and catastrophizing alongside OAB-related quality of life, bladder diary measures, urinary urgency, and urge incontinence episodes.

The present study utilized a SC study design because PBM for urinary bladder symptoms was novel and no previous data were available to indicate the direction of treatment effect. This methodology, while indicated, limited recruitment as participants required multiple measuring points, necessitating a long run-in period before intervention and a similar duration after cessation of PBM before the introduction of another therapy. Overall, patients with imperative and bothersome urgency are unwilling to defer commencing pharmacological or other proven therapies. Other trial designs for new treatments should now be considered.

PBM has not previously been described in the population with OAB, despite the limitations of pharmacological side effects and high personal bother. At present, patients with OAB progress through conservative management comprised behavioral therapies and functional use of pelvic floor muscles, anticholinergic or beta 3-adrenoceptor agonist medication (or a combination of these), botulinum toxin injected into the bladder, or implanted sacral nerve modulation. The latter two interventions have side effects that may necessitate the passing of a catheter to fully empty the bladder or machine malfunction requiring surgical revision. Clearly, a trial of a device that can be worn at home and that potentially offers an effect through a currently unused mechanism would be a welcome addition to the treatment armamentarium for OAB.

5. CONCLUSION

We have confirmed that nasal application of PBM is safe. The study findings indicated a positive direction of effect. The early findings warrant subsequent controlled clinical trials in both treatment-naïve and selected disease group patients with OAB.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Wendy F Bower
Investigation: Wendy F Bower, David Michael Whishaw, Christine Baldrey
Methodology: Wendy F Bower, Erik Biros, Mary P Galea
Writing – original draft: Wendy F Bower, Erik Biros
Writing – review & editing: Erik Biros, Mary P Galea

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA

Data used in this work is available from the corresponding author upon reasonable request.

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