Lidocaine solution vs. lidocaine gel instillation for pain management during intravesical botulinum injections

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ABSTRACT

Introduction: Most Canadian urologists use lidocaine solution prior to botulinium toxin (BoNT) administration; however, this requires additional time. The aim was to compare pain scores in patients undergoing office-based BoNT using lidocaine instillation and lidocaine gel vs lidocaine gel alone.
Methods: All patients undergoing office based intradetrusor BoNT between March 1 and September 1, 2022, were included. Group 1 received intravesical lidocaine solution (20 ml 2% lidocaine solution + 30 ml 0.9% normal saline) instillation for 30 minutes and lidocaine gel. Group 2 received lidocaine gel only. The Verbal Numeric Rating Scale (VNRS) was used to measure pain. Patient demographics were compared with t-test for continuous and Chi-squared for categorical variables. The Mann-Whitney U test was used to compare pain scores.
Results: A total of 79 patients were included (mean age 61 years, 74.7% female, 58.2% with overactive bladder, and 30.4% received first treatment). Group 1 had 39 patients and group 2 had 40. There was no significant difference in pain scores between groups: group 1 median VNRS

KEY MESSAGES

- Lidocaine gel offers an acceptable analgesia for intravesical botulinum toxin injections during office cystoscopy.
- Lidocaine gel offers a similar pain control compared to traditional lidocaine solution for intravesical botulinum toxin injections.
- Compared to lidocaine solution, lidocaine gel improves administration efficacy of intravesical botulinum toxin injections during office cystoscopy.

3.0 (interquartile range [IQR] 2.5) vs. group 2 median VNRS 4.0 (IQR 2.0) (p=0.11). No significant differences in pain scores were noted between groups based on sex, indication for treatment, or number of previous BoNT treatments (p>0.05). Post-procedural complications were low. Treatment failure did not occur.

Conclusions: Lidocaine gel alone may be an acceptable analgesic alternative while improving availability and efficiency of treatment delivery. Our findings are limited by the retrospective nature of the study and the small sample size.

INTRODUCTION

Intravesical botulinum (BoNT) toxin is a safe and effective third line treatment option for patients with refractory overactive bladder and neurogenic lower urinary tract dysfunction (NLUTD).[1–4] Despite its widespread usage, no specific guidelines exist on its administration and preprocedural pain management in the office-based setting.[1,2,5] Multiple pain management options have been described, including instillation of various forms of lidocaine solution for 30 min before the procedure, lidocaine gel injection, and even no local anesthesia.[6,7]

A previous survey identified that most Canadian urologists use intravesical instillation of lidocaine solution prior to BoNT for pain control.[8] However, this requires additional time, catheterization, and nursing resources, increasing potential barriers to treatment delivery for some providers.[8] This cohort study was designed to compare pain scores in patients undergoing office-based BoNT using intravesical lidocaine instillation and lidocaine gel vs lidocaine gel alone. We hypothesized that there would be no significant difference in pain scores between groups. Secondary objectives were to compare post-procedural complications, treatment failures and pain scores between patient subgroups (sex, indication, first versus subsequent treatment).

METHODS

This is a pragmatic cohort study using retrospective chart review for data extraction. All patients over 18 years of age with normal sensory function undergoing office-based BoNT between March 1st and September 1st, 2022, were included. Patients who had the procedure performed in the operating room were excluded. Patients undergoing BoNT before June 1st, 2022 received intravesical lidocaine solution (20 ml 2% lidocaine solution + 30 ml 0.9% normal saline) instillation for 30 minutes and lidocaine gel (Instillagel™) prior to BoNT for pain control (Group 1). Patients undergoing treatment on or after June 1st, 2022 received lidocaine gel (Instillagel™) alone immediately before BoNT (Group 2). In Group 1, a rigid cystoscope was used for female patients and a flexible scope for male patients. Whereas in Group 2, a flexible scope was used for both female and male patients. BoNT was diluted in 10 mL of sterile saline and delivered in 1 mL aliquots followed by a 1 mL saline flush for a total of 11 intradetrusor injections in the bladder sparing the trigone. Injections were administered using a 22 gauge, 4mm Coloplast

BoNee® needle for all patients. Intravesical BoNT was administered by three separate urologists with subspecialty training in reconstructive and neuro-urology.

The Verbal Numeric Rating Scale (VNRS) from 0 to 10 was used to measure patient reported pain immediately following each BoNT administration (0 being no pain and 10 being the worst pain in their life). To reduce reporting bias, pain scores were collected by nurses and supporting staff at the end of the procedure rather than the urologists performing the procedure. VNRS was chosen for immediacy, ease of use and compliance.[9,10] Additionally, compared to the visual analogue scale, the VNRS has been reported to help overcome physical and cognitive barriers for some patients.[9] Baseline demographics, indication for treatment (overactive bladder vs. NLUTD vs. other), post-procedural complications, and treatment failure were routinely collected from patients' electronic medical charts using pre-established collection forms. Clinically significant change in VNRS was established as 1.5 based on previous work by Holdgate et al.[9] Any post-procedural complication reported by the patient or documented by a nurse/physician were collected from the chart and classified according to Clavien-Dindo classification. Treatment failure was defined as a patient who did not tolerate treatment or requested that future treatments be performed under sedation.

Patient demographics and clinical variables were compared using basic descriptive statistics with t-test for continuous and chi-square for categorical variables. The Mann-Whitney U Test, a non-parametric test, was used to compare difference in pain scores based on the fact that pain scores were not normally distributed, and that the two groups of patients were independent. Secondary analysis was performed on following subgroups: sex, indication for treatment and history of previous intradetrusor botulinum treatment. The sample size was calculated to 34 in each group to detect a minimum clinically significant difference of 1.5 in VNRS with a standard deviation of 2, alpha of 0.05 and beta of 0.80. All statistical analyses were performed with SAS version 9.4.

RESULTS

A total of 79 patients were included. Thirty-nine patients (49.4%) were included in Group 1 compared to 40 (50.6%) in Group 2. Baseline characteristics were well balanced between groups (Table 1, $p>0.05$). The mean age of patients was 61 years, and approximately 75% of the population were female. There was no statistically significant difference in indication for BoNT between the groups. The most common indication for BoNT was overactive bladder in both groups (59% in group 1 and 57.5% in group 2, $p=0.88$). NLUTD was the second most common indication with 38.5% of patients receiving the treatment in group 1 and 40.0% in group 2 ($p=0.88$). Multiple sclerosis was the most frequent etiology for NLUTD in both groups. 69.2% and 70.0% of patients in group 1 and 2, respectively, had previous BoNT injections ($p=0.88$).

There was no significant difference in overall pain scores between groups: Group 1 median VNRS 3.0 (IQR: 2.5) vs Group 2 median VNRS 4.0 (IQR: 2.0); $p = 0.11$ (Table 2). Furthermore, there were no significant differences in pain scores between groups based on sex or indication for BoNT. Lastly, patients who had previous intravesical treatment had similar pain

scores between treatment groups (group 1: 4 vs. group 2: 5, p=0.14). Similar findings were seen in patients who were treatment naïve in both groups (group 1: 3 vs. group 2: 4, p=0.81).

Post-procedural complications were all classified as Clavien-Dindo grade 1. Three urinary tract infections (UTI) and one episode of gross hematuria occurred in Group 1 compared to two UTI in Group 2 (p>0.05). Treatment failure did not occur in either group.

DISCUSSION

During office-based BoNT administration, the application of lidocaine gel alone resulted in similar levels of pain control compared to the traditional combination of lidocaine solution instillation and lidocaine gel administration. Moreover, there were no statistically or clinically significant differences in perceived pain scores based on sex, treatment indication, and history of previous intravesical BoNT. There were no treatment failures and rates of post-procedural complications were low in both groups. As a result of our findings, we have changed our protocol for BoNT injections under local cystoscopy and lidocaine gel alone is now routinely used for pain management.

The findings of our study are comparable with previously reported data. Alkalinized lidocaine solution instillation plus Aquagel showed similar pain control as compared lidocaine gel alone in patients undergoing BoNT.[7] In this study Aquagel was used with lidocaine solution instead of lidocaine gel which may have introduced bias due to variability in contained ingredients. We addressed this limitation by administering lidocaine gel in both arms and still found no differences in VNRS scores. It is important to highlight that patients in the Aquagel arm received their instillation via a urethral catheter with a dwelling time of 20 minutes; whereas in our study, patients received the lidocaine gel via urethral injection which minimizes administrative burden on patients and improves efficiency. The omission of bladder catheterization prior to the procedure further saves associated financial costs.

There were no patients who requested to stop the procedure or to have future BoNT injections performed under sedation. This indicates that overall pain scores were acceptable for patients. Additionally, the minimal clinically important difference in VNRS between the groups of 1.5 was not reached in our study. Taken together, our findings may motivate urologists to offer BoNT injections more frequently in their practice.

To the best of our knowledge, no studies have examined differences in pain scores during intradetrusor BoNT injections based on sex and indication for treatment. In this study, no differences were noted in pain scores between groups based on sex and indication for treatment. Furthermore, no statistically significant difference in pain scores was noted in patients with prior experience of intravesical BoNT compared to those without.

Our findings are limited by a relatively small sample size, although the study was adequately powered to detect a minimum clinically important difference of 1.5 in VNRS. Nevertheless, the small sample size could have led to issues with precision and inadequate power for a subgroup analysis. Due to retrospective nature of the study and absence of random assignment, selection bias and unmeasured confounders could have biased the results. Pain

scores were collected verbally which could have led to reporting bias. To address this shortcoming, VNRS have been collected by nurses and supporting staff instead of treating physicians to minimize potential pain underrating by the patients. Additionally, VNRS is a validated tool with high compliance and patient preference.[10] Another potential limitation is the use of rigid cystoscope in females from Group 1 prior to June 2022. While this could be a cofounder, there is randomized data to suggest that both flexible and rigid cystoscopy have comparable minimal associated discomfort in females (visual analogue score 0.5 (0-2.4) for flexible cystoscopy and 0.9 (0.1-2.72) for rigid cystoscopy, p=0.505).[11] Therefore, we believe rigid cystoscopy had minimal impact on our results.

CONCLUSIONS

The use of lidocaine gel alone may be an acceptable analgesia alternative to traditional intravesical lidocaine solution instillation while improving efficiency of administration and availability of treatment. Further randomized studies are required to identify optimal analgesia regimens for this procedure and their effect on BoNT efficacy and safety.

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FIGURES AND TABLES

Table 1. Descriptive characteristics of patients undergoing intravesical botulinum toxin under local cystoscopy stratified by groups

Variable			**Group 1 (n=39)**	**Group 2 (n=40)**	**p**
Age (years) mean (SD)			62.2 (16.0)	59.9 (17.2)	0.47
Sex, n (%)					
	Female		30 (76.9)	29 (72.5)	0.70
	Male		9 (23.1)	11 (27.5)	
Indication, n (%)					
	OAB		23 (59.0)	23 (57.5)	0.88
	NLUTD		15 (38.4)	16 (40.0)	
		Multiple sclerosis	10 (25.6)	6 (15.0)	
		Spinal cord injury	2 (5.1)	4 (10.0)	
		Transverse myelitis	2 (5.1)	–	
		Cerebral palsy	1 (2.6)	2 (5.0)	
		Spina bifida	–	1 (2.5)	
		Spinal muscular atrophy	–	1 (2.5)	
		Meningitis	–	1 (2.5)	
		Spastic ataxia syndrome	–	1 (2.5)	
	Other*		1 (2.6)	1 (2.5)	
Previous treatment n (%)					
	Yes		27 (69.2)	28 (70.0)	0.88
	No		12 (30.8)	12 (30.0)	

Group 1: intravesical lidocaine solution and lidocaine gel; group 2: lidocaine gel alone. *Other indications included spontaneous bladder perforation in the context of previous radiation and tuberculosis. NLUTD: neurogenic lower urinary tract dysfunction; OAB: overactive bladder; SD: standard deviation.

Table 2. A comparison of pain scores for patients undergoing intravesical botulinum toxin under local cystoscopy stratified by groups				
Pain variables		**Group 1: Solution & gel (n=39)**	**Group 2: Gel (n=40)**	**p**
Overall		3.0 (2.0, 5.0)	4.0 (3.0, 5.0)	0.11
Sex				
	Female	4.0 (2.0, 5.0)	4.5 (3.0, 5.0)	0.14
	Male	3.0 (3.0, 4.0)	3.0 (2.0, 5.0)	0.81
Indication				
	OAB	4.0 (3.0, 6.0)	4.5 (3.0, 5.0)	0.54
	NLUTS	3.0 (1.0, 4.0)	4.0 (2.0, 5.0)	0.21
	Other	NA	NA	NA
Previous treatment				
	Yes	4.0 (2.0, 5.0)	5.0 (3.0, 5.0)	0.14
	No	3.0 (2.0, 5.0)	4.0 (2.0, 4.5)	0.81

Group 1: intravesical lidocaine solution and lidocaine gel and Group 2: lidocaine gel alone. Data is presented using medians (Q1, Q3). NLUTS: neurogenic lower urinary tract symptoms; OAB: overactive bladder.