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Is Cystoscopic Intravesical Injection of OnabotulinumtoxinA Acceptable in an Outpatient Clinic?

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Purpose: Cystoscopic intravesical onabotulinumtoxinA injection is a safe and effective minimally invasive treatment for refractory overactive bladder. While the procedure can be performed in outpatient clinics under local anesthetic, some clinicians still use sedation or general anesthesia in an operating theatre. Our study aimed to assess acceptability of intravesical onabotulinumtoxinA injection versus widely accepted diagnostic cystoscopy in the outpatient setting via the medium of patient experience.

Methods: A 16-item patient experience survey was administered following diagnostic cystoscopy or intravesical onabotulinumtoxinA injection in an outpatient clinic. Both procedures were performed using a flexible cystoscope with local anesthetic gel. A visual analogue scale (VAS) assessed intraprocedure pain. Dichotomous questions assessed whether significant pain or postprocedure symptoms were experienced and if these required medical attention. A free-text question assessed which symptoms had occurred.

Results: One hundred responses from 188 patients were received (53.2% response rate). Sixty-eight patients underwent cystoscopic intravesical onabotulinumtoxinA injection and 32 diagnostic cystoscopy. Mean VAS scores were higher for onabotulinumtoxinA injection (24 of 100) than diagnostic cystoscopy (11 of 100) (P=0.002). VAS scores were higher among patients reporting preprocedure anxiety (31 of 100 vs. 14 of 100, P=0.0013). Twenty-four percent of onabotulinumtoxinA injection patients experienced symptoms postprocedure versus 41% for cystoscopy. Medical attention was sought more frequently in the diagnostic cystoscopy group (9.4% vs. 1.5%). Common symptoms following both procedures were dysuria, urinary frequency, urgency, abdominal pain and urine discoloration.

Conclusions: Cystoscopic intravesical injection of onabotulinumtoxinA appears more painful than diagnostic cystoscopy. However, as VAS scores were relatively low, this is unlikely to represent clinically significant discomfort burdensome to the patient. There were no significant complications postprocedure. Cystoscopic intravesical onabotulinumtoxinA injection is acceptable in an outpatient setting.

Keywords: Acceptability of health care; Intravesical administration; Overactive bladder; Type A botulinum toxins; Visual analogue scales

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- **Research Ethics:** This study was conducted according to the principles of the Declaration of Helsinki. This study was a retrospective analysis of a service evaluation comprising patients receiving usual care. As such, formal research ethics committee approval was not necessary as per the advice of the National Health Service Health Research Authority. The service evaluation was registered and approved internally (GYN_DC_23-24_A04). Written informed consent was obtained from each participant as part of their survey response.
- **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

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INTRODUCTION

Intravesical onabotulinumtoxinA injection is a safe and effective minimally invasive treatment for refractory overactive bladder [1, 2], and is recommended in American, European and United Kingdom guidance following pharmaceutical treatments [3]. While the procedure can be performed under local anesthetic in an outpatient clinic, some clinicians still perform it under sedation or general anesthesia in an operating theatre.

Our study aimed to assess the acceptability of intravesical onabotulinumtoxinA injection in the outpatient setting against a control procedure of diagnostic cystoscopy. Our primary outcome of interest was the difference in reported discomfort using a 100-mm visual analogue scale (VAS) pain score. Secondary outcomes were reported anxiety, embarrassment and postprocedure complications, with these felt to represent measurable components of acceptability (particularly the patient's affective attitude and burden to them), in addition to procedure-related discomfort [4].

MATERIALS AND METHODS

Consecutive, nonselected patients were approached to provide responses to a bespoke, nonvalidated patient experience survey following their appointment in the designated urogynaecology procedure clinic of a tertiary urogynaecology referral unit. This clinic offers both diagnostic cystoscopy and intravesical onabotulinumtoxinA injection. The clinic is provided across 2 sites within the hospital trust by 2 consultant urogynaecologists.

Both procedures were performed using a CST-5000 flexible video cystoscope (Laborie Medical Technologies, Portsmouth, NH, USA) with 6-mL Instillagel local anesthetic gel (CliniMed Limited, High Wycombe, Buckinghamshire, UK). No further local anesthetic instillation or infiltration was performed for either procedure. A 27G, 4-mm needle (NM-221C-0427, Olympus Corporation, Shinjuku City, Tokyo, Japan) was used for the cystoscopic injections of onabotulinumtoxinA. All women undergoing intravesical onabotulinumtoxinA injection received postoperative antibiotics. In line with local guidance, patients undergoing diagnostic cystoscopy did not routinely receive postoperative antibiotics unless the indication for cystoscopy was recurrent urinary tract infection.

The survey itself was primarily designed to assess patient experience of the urogynaecology procedure clinic in the form of a 16-item paper-based questionnaire. Participants were asked to complete the VAS immediately after the procedure and the rest of the survey a minimum of 7 days after their appointment and return their responses via a prepaid envelope provided. Participants were informed in writing that "the findings of the survey… may be used for sharing learning more widely in the medical community via conference presentations or medical publications" and were reassured that non-participation would not adversely affect their treatment. The project was approved as service evaluation by the local audit department.

The questions featured in the survey are shown in Table 1. Those with particular relevance to the acceptability of outpatient provision of intravesical onabotulinumtoxinA injection are numbered 5 to 8 and 10–12. These address patient anxiety, embarrassment, pain and postprocedure complications. The VAS described in question 8 asked participants to mark on a single horizontal line the amount of pain that was experienced during their procedure. In the print version, this was a 100-mm VAS with "no pain" marked at the left end and "extreme pain" at the right. This facilitated physical measurement to the nearest millimeter when analyzing the responses to generate a score out of 100.

Data were input into a spreadsheet in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA), which was used to facilitate analysis of free-text responses. More detailed statistical analysis and production of descriptive statistics was performed in GraphPad Prism ver. 10.2.2 (GraphPad Software, La Jolla, CA, USA). Participants were divided into 2 groups by which procedure they had undergone (diagnostic cystoscopy versus intravesical onabotulinumtoxinA injection). As our data could not be assumed to be parametric, statistical comparison between the 2 groups was completed using a Mann-Whitney test for the VAS and a Fisher exact test for the dichotomous questions. Additional analysis of the effect of anxiety on perception of pain via the VAS was conducted using a Kruskal-Wallis test.

RESULTS

One hundred responses were received from 188 patients and included in the analysis (53.2% response rate). Thirty-two participants had undergone diagnostic cystoscopy and 68 intravesical onabotulinumtoxinA injection.

Mean VAS pain scores were higher with intravesical onabotulinumtoxinA injection (24 of 100) than diagnostic cystoscopy (11 of 100) (exact $P = 0.002$). Graphical representation of the VAS pain scores is shown in Fig. 1, with error bars repre-

Table 1. Questions included in this patient experience survey

Question	Question type	Free-text follow-up question
1. Did you feel you were given enough information about your procedure before your visit?	Dichotomous – "yes" or "no"	If "no," please tell us why.
2. Did you receive written information about your procedure?	Dichotomous – "yes" or "no"	
3. Did you understand the reason for carrying out your procedure?	Dichotomous – "yes" or "no"	If "no," please tell us why.
4. Please tell us here if you have any further comments about the information provided to you.	Free text	
5. Did you feel any anxiety at the time of the procedure?*	Dichotomous – "yes" or "no"	If "yes," please tell us why.
6. Did you feel any embarrassment during the procedure?*	Dichotomous – "yes" or "no"	If "yes," please tell us why.
7. Did you feel significant pain during the procedure?*	Dichotomous – "yes" or "no"	If "yes," please tell us at which stage during the procedure.
8. Please mark this line to indicate the amount of pain that you experienced.*	100-mm visual analogue scale	
9. Please tell us here if you have any further comments you have about the procedure.	Free text	
10. Did you experience any discomfort after your procedure?*	Single selection – "none," "slight," "moderate," or "severe"	
11. Did you experience any after-effects following the procedure?*	Dichotomous – "yes" or "no"	If "yes," please tell us what these were.
12. Did any of the after-effects result in you consulting your general practitioner?*	Trichotomous – "yes," "no," or "not applicable"	If "yes," please provide details of any treatment provided.
13. Please tell us here if you have any further comments about after the procedure.	Free text	
14. Was the experience of your procedure in line with your expectations?	Dichotomous – "yes" or "no"	
15. Do you feel more informed about your condition following your procedure?	Dichotomous – "yes" or "no"	
16. Please provide any further comments about your procedure or experience.	Free text	

*Questions (#5-8, 10-12) particularly relevant to acceptability.

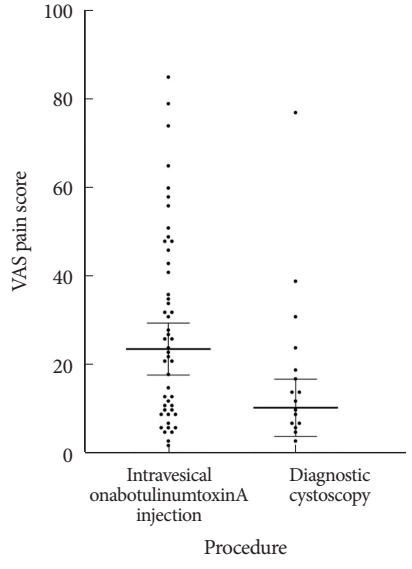

Fig. 1. Visual analogue scale (VAS) pain scores by procedure; error bars represent mean values and 95% confidence intervals.

senting the 95% confidence interval around each mean. In the preceding question in the survey, which asked if significant pain had been experienced, those undergoing diagnostic cystoscopy were more likely to answer "yes" (odds ratio [OR], 1.45; 95% confidence interval [CI], 0.55–3.89): the reverse of what might be expected given the VAS pain scores, though this was not statistically significant (P = 0.579).

Participants reported anxiety prior to the procedure in 27% of cases. One third of these participants (9 respondents) commented that this was in relation to either having an anxiety disorder or "being an anxious person." A further 8 respondents were anxious that the procedure may be painful, 4 were anxious because it was their first time having the procedure, 3 were concerned about postprocedure complications, including urinary tract infection, and the final 3 were anxious either about treatment success or diagnostic results. There was no statistically significant difference in the proportion of patients who reported anxiety between diagnostic cystoscopy (31%) or intravesical

onabotulinumtoxinA injection (25%). Participants were not specifically asked if they had undergone either procedure before, but 4 commented in free-text questions that their prior experience had affected their attitude towards the procedure: 2 were more anxious, whilst 2 were more comfortable.

To assess the effect of preprocedure anxiety on VAS pain scores, participants were grouped by their answer to the dichotomous question as to whether they had been anxious prior to the procedure. Higher mean VAS pain scores were seen in the group reporting preprocedure anxiety (31 of 100) than the group that denied this (14 of 100) (exact P = 0.0013). When subdivided again by procedure to create 4 groups (with or without anxiety; diagnostic cystoscopy or intravesical onabotulinumtoxinA injection), a significant variance was seen (P = 0.0002), suggesting both preprocedure anxiety and the procedure undertaken have an impact on pain experienced.

Embarrassment was experienced by 13% of patients across the cohort. All of the follow-up responses noted that this was because of the intimate nature of the procedure, and several commented that the staff had made them feel more comfortable. There was again no difference between the 2 procedures. 95% of patients in the study answered affirmatively that their experience of the procedure they underwent matched their expectations beforehand.

Forty-one percent of participants who underwent diagnostic cystoscopy reported experiencing symptoms postprocedure, compared to 24% who had intravesical onabotulinumtoxinA injection (OR, 2.22; 95% CI, 0.94–5.20), though this again did not reach statistical significance (P = 0.100). Medical attention was sought more often in the diagnostic cystoscopy group (9% vs. 1%), reflecting the greater presence of symptomatology. Reported symptoms did not vary between the 2 groups and included dysuria, urinary frequency, urgency, abdominal pain and urine discolouration.

DISCUSSION

To our knowledge, this is the first study to use patients' experience to assess the acceptability of intravesical onabotulinumtoxinA injection in the outpatient setting. The main finding of our study is that, whilst intravesical onabotulinumtoxinA injection is more painful than widely accepted diagnostic cystoscopy, it nonetheless satisfies criteria for acceptability.

In our study, VAS pain scores were significantly higher for intravesical onabotulinumtoxinA injection (24 of 100) versus diagnostic cystoscopy (11 of 100) (exact P = 0.002). This is similar to the mean VAS pain scores (3.3 on an 11-point scale) described by Popat et al. [5]. Whether this level of pain represents a significant burden is where this concept meets acceptability. Myles et al. [6] described that VAS pain scores of 33 points or fewer likely indicated an acceptable level of pain but that a difference of more than 10 points was clinically important. This would imply that onabotulinumtoxinA injection is indeed noticeably more painful than diagnostic cystoscopy, but a mean VAS pain score of 24 also represents an acceptable level of pain, without significant patient burden.

Across the entire cohort, VAS pain scores were higher among patients that reported preprocedure anxiety (31 of 100) than did not (14 of 100) (exact P = 0013). There was also significant variation when participants were divided both by anxiety state and by procedure, suggesting that both components impacted on the resulting VAS pain scores. Anxiety, particularly where this is related to the pain-inducing stimulus itself, is well described as exacerbating the perception of procedural pain [7-9]. There is a strong relationship between anxiety and pain well described in dentistry, which carries the additional relevance of pertaining to injections [10]. It is important to note that there was no significant difference in the proportion of patients reporting anxiety prior to intravesical onabotulinumtoxinA injection than diagnostic cystoscopy, suggesting no significant impact from affective attitude against the acceptability of the procedure.

There was no significant difference in the frequency of symptoms reported postprocedure, although this tended towards patients undergoing diagnostic cystoscopy reporting symptoms and seeking medical attention more frequently. This perhaps reflects the universal use of prophylactic antibiotics for intravesical onabotulinumtoxinA injection where these are not used for diagnostic cystoscopy. Reflecting the objective of the study, this finding indicates that, as a minimum, patients undergoing intravesical onabotulinumtoxinA injection are no more likely to experience symptoms postprocedure. Therefore, burden from postoperative symptoms has no relative negative impact on the acceptability of intravesical onabotulinumtoxinA injection.

Sekhon et al. [4] summarized 43 reviews and outlined a theoretical framework defining acceptability of healthcare interventions. This framework contained 7 component constructs: affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness and self-efficacy.

Through the use of diagnostic cystoscopy as a control intervention, we were able to control for several of the component constructs of acceptability: the ethicality, self-efficacy and opportunity cost to the patient could be expected to be very similar. Through the provision of quality preprocedure literature, we could also ensure that participants were aware of what the procedure would entail and its proven effectiveness, satisfying the components of intervention coherence and perceived effectiveness. This therefore left 2 component constructs which could be assessed as variables in this study: burden, which consisted of pain and physical symptoms experienced postprocedure, and affective attitude, related to embarrassment and anxiety.

Despite several studies claiming the tolerability of intravesical onabotulinumtoxinA injection [11, 12], there have been multiple studies investigating interventions to improve the tolerability of the procedure. These were summarized in a systematic review by Faure Walker et al. [13], with intravesical alkalinized lidocaine (with or without electromotive administration) and a reduction in the number of injection sites associated with improvements in tolerability, though a more recent randomized controlled trial showed no difference in pain when the number or injection sites were halved [14].

Our study method for intravesical onabotulinumtoxinA injection used a standard approach of 20 injections sites using flexible cystoscopy, which has been shown to be less painful than rigid in a female population [15]. It is possible that the VAS pain scores seen in our study might be reduced by making adaptations to the analgesia used: intravesical alkalinized lidocaine may be more effective than local anesthetic gel.

One other study investigated patient experience with intravesical onabotulinumtoxinA [16]. This study used a validated patient reported experience measure, demonstrating a high level of patient satisfaction with the service. However, it did not assess acceptability of the intervention.

Our study does have some limitations. As the project was a service evaluation, we did not conduct a power calculation, and we opted for a convenience sample of 100 patients. When examining postprocedure symptoms, it would have been useful to control for the provision of postoperative antibiotics, but this would require deviation from usual care: inappropriate for service evaluation. The response rate of 53.2% means that outcomes for the entire cohort were not reported, which might introduce a risk of bias. As this was a patient experience survey, demographic information was not collected, and the procedure duration was not measured. However, in our hospital the usual durations are 15 minutes for intravesical onabotulinumtoxinA injection and 10 minutes for diagnostic cystoscopy. Finally, the questionnaire used was bespoke for the purpose of this service evaluation; whilst the 100-mm VAS for pain is well-validated [6, 17], the remainder of the questionnaire is not.

In order to further confirm the acceptability of intravesical onabotulinumtoxinA injection being performed in the outpatient setting, further research could utilise patient experience to compare the acceptability of the procedure across inpatient (under general anesthetic or sedation) and outpatient settings.

Our study has shown that despite intravesical onabotulinumtoxinA injection being considered more painful than diagnostic cystoscopy, pain during the procedure does not represent a significant burden as to affect the acceptability of the procedure. Anxiety may mean that patients perceive the procedure to be more painful, but there is no greater degree of anxiety with intravesical onabotulinumtoxinA injection than diagnostic cystoscopy. Postprocedure symptoms do not represent an additional burden for intravesical onabotulinumtoxinA injection than diagnostic cystoscopy. Intravesical onabotulinumtoxinA injection can therefore be considered acceptable in an outpatient setting under local anesthetic gel.

AUTHOR CONTRIBUTION STATEMENT

· Conceptualization: *TJC, MD, TGG, IG*
· Data curation: *TJC, MD*
· Formal analysis: *TC*
· Methodology: *TJC, MD, IG*
· Visualization: *TC*
· Writing - original draft: *TC*
· Writing - review & editing: *MD, TGG, IG*

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