Prospective Randomised Controlled Trial Comparing Trigone-Sparing versus Trigone-Including Intradetrusor Injection of AbobotulinumtoxinA for Refractory Idiopathic Detrusor Overactivity

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Abstract

Background: Botulinum toxin A is effective for treatment of idiopathic detrusor overactivity (IDO). The trigone is generally spared because of the theoretical risk of vesicoureteric reflux (VUR), although studies assessing injection sites are lacking.

Objective: Evaluate efficacy and safety of trigone-including versus trigone-sparing intradetrusor injections of abobotulinumtoxinA in patients with IDO.

Design, setting, and participants: Twenty-two patients from one centre were randomised to trigone-including or trigone-sparing injections.

Intervention: Injection of 500 U abobotulinumtoxinA diluted to 20 ml into 20 trigone-including or trigone-sparing sites.

Measurements: The primary outcome measure was total overactive bladder symptom score (OABSS) at 6 wk. The OABSS questionnaire was completed at 0, 6, 12, and 26 wk. Baseline and postinjection urodynamic studies and micturating cystourethrograms were performed. Baseline values and subsequent time points were compared by t test. A mixed-effect model was used for repeated measures in time.

Results and limitations: For symptom scores at baseline compared with scores at 6 wk postinjection, the mean total OABSS improved from 22.4 to 8.7 (p < 0.001) in the trigone-including group compared with 22.7 to 13.4 (p < 0.03) in the trigone-sparing group. The difference in mean change from baseline was 4.4 points in favour of the trigone-including group (p = 0.03). The total OABSS at 12 and 26 wk and the urgency subscale scores at 6, 12, and 26 wk showed significant improvement in favour of the trigone-including group. Mean postvoid residual volumes and clean intermittent self-catheterisation rates between the two groups were similar. No patients developed VUR. Performing injections under general anaesthetic was a limitation, as tolerability under local anaesthetic was not assessed. A further limitation is the lack of a trigone-only arm.

Conclusions: Trigone-including injections are superior to trigone-sparing injections for the treatment of refractory IDO and did not cause VUR in this study.

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1. Introduction

Intradetrusor injection of botulinum toxin A (BoNT-A) is effective for patients with pharmacologically refractory idiopathic detrusor overactivity (IDO) [1–4]. BoNT-A is a potent neurotoxin produced by Clostridium botulinum. BoNT-A cleaves the synaptosomal-associated protein 25 (SNAP-25) protein, preventing the formation of the soluble N-ethylmaleimide sensitive factor attachment receptor (SNARE) complex. This prevents fusion of the synaptic vesicles containing acetylcholine to the neuronal membrane and prevents the consequential release of neurotransmitter [5]. In urology, the two most widely used brands of BoNT-A are Botox (Allergan Pharmaceuticals, Irvine, CA, USA), now referred to as onabotulinumtoxinA, and Dysport (Ipsen Biopharm Ltd., Wrexham, UK), referred to as abobotulinumtoxinA, as enforced by the US Food and Drug Administration. The trigone is generally spared because of the theoretical risk of inducing vesicoureteric reflux (VUR). However, sensory nerve endings are particularly dense within the trigone and bladder base [6]; therefore, including this area may improve efficacy. In a nonrandomised study, Mascarenhas et al. showed trigone-including injections of onabotulinumtoxinA did not cause VUR in neurogenic patients and Karsenty et al. demonstrated similar safety in patients with IDO [7,8]. The first randomised controlled trial of onabotulinumtoxinA in neurogenic overactive bladders showed superiority of including, rather than excluding, the trigone [9]. Lucioni et al. conducted a nonrandomised study using onabotulinumtoxinA comparing trigone inclusion versus trigone-sparing and showed no difference [10]. Two further studies, also using onabotulinumtoxinA, showed that bladder base/trigone injections were as effective as bladder body/trigone [11,12]. A European consensus report recommends that BoNT-A be injected within the detrusor muscle outside the trigone (grade C recommendation), as the data assessing injections sites were considered inadequate [13]. A recent review revealed most data for studies on IDO in adults involved onabotulinumtoxinA with very little data on abobotulinumtoxinA [14].

2. Materials and methods

2.1. Objectives

The purpose of our study was to evaluate the efficacy and safety of trigone-including versus trigone-sparing intradetrusor injections of BoNT-A in patients with IDO. To our knowledge, this is the first study to evaluate injection sites using abobotulinumtoxinA (Dysport).

2.2. Study design

From September 2010 to November 2010, patients with urodynamic-proven IDO refractory to anticholinergic therapy were recruited. This study received approval from the Hospital Research/Ethics Committee (REC reference 2008/08/12) and was registered with Current Controlled Trials (ISRCTN12589059).

Male and female patients ≥17 yr with urodynamic-confirmed detrusor overactivity, who had failed ≥6 wk anticholinergic therapy or discontinued therapy due to intolerability were eligible. All patients gave written consent and were given an information leaflet. At recruitment and prior to surgery, urine was tested for infection, and for pregnancy in women of childbearing age; infection and pregnancy excluded participation. Patients previously injected with BoNT-A were excluded. Patients with any neurologic condition or coagulopathies were excluded, as were men with clinical or urodynamic evidence of bladder outflow obstruction. All patients discontinued anticholinergic medication at least 2 wk prior to injection and remained off anticholinergic medication for the study duration.

Patients were randomised using a random digit table to receive trigone-including or trigone-sparing BoNT-A injections and were blinded throughout the study.

2.3. Assessment

All patients were assessed at baseline, 6, 12, and 26 wk after injection. Baseline and 6-wk assessment comprised history, physical examination, the overactive bladder symptom score (OABSS) questionnaire [15], uroflowmetry, postvoid residual (PVR) volume, cystometrography (CMG), and micturating cystourethrogram (MCUG). Twelve and 26-wk assessment comprised history, physical examination, PVR volume measurement, and the OABSS questionnaire. PVR volume measurement was performed using an ultrasound bladder scanner (Verathon BVI 3000, Verathon Medical, UK, Ltd., Aylesbury, Buckinghamshire, UK). Patients who had not already discontinued anticholinergic medication were instructed to do so 2 wk prior to baseline assessment. CMG was performed according the International Continence Society recommendations [16]. Symptoms were evaluated using the validated seven-question OABSS questionnaire (Appendix A) (score range: 0–28). The urgency subscale (questions 3–6) was used to assess severity of urgency (score range: 0–16) [15].

2.4. Injection technique

AbobotulinumtoxinA (500 U) was reconstituted with 20 ml 0.9% saline. Patients received general anaesthesia and 400 mg intravenous ciprofloxacin at induction. Intradetrusor injections were performed with a rigid 21F ACMi cystoscope, a flexible injector sheath, and disposable inner sheath/needle with a 27G tip (Olympus, reference numbers NM-101C-0427, MAJ-656; Olympus KeyMed, Southend, UK) with bladder volume at about 150 ml. Patients randomised to trigone-sparing injections had 1-ml injections at 20 sites into the bladder wall, sparing the trigone. Patients randomised to trigone-including injections had 5-ml injections into the trigone and 15-ml injections into the bladder wall, for a total of 20 injections (Fig. 1). The depth of injection was approximately 2 mm (half the length of the 4-mm injection needle), without raising a bleb, as described by Kuo [11]. All procedures were performed as day cases, with no inpatient stay required.

2.5. Follow-up, data collection, primary and secondary outcomes

Patients had follow-up at 6, 12, and 26 wk. All patients had MCUG and urodynamic studies 6 wk after injection, and clinical review including PVR measurement and the OABSS questionnaire at weeks 6, 12, and 26. The primary outcome was change in total OABSS at 6 wk. Secondary outcomes were changes in total OABSS at weeks 12 and 26, OABSS urgency subscale at 6, 12, and 26 wk, changes at 6 wk of maximum cystometric capacity (MCC), maximum detrusor pressure in filling phase (MDP), volume at first desire to void (VFDV), volume at urgent desire to void (VUDV), PVR, and incidence of VUR. MDP during the filling phase (including phasic or terminal detrusor overactivity) was reported as a measure of the amplitude of involuntary detrusor contractions.
2.6. Statistical analysis

The study was designed to have 80% power to detect a mean difference in total OABSS of four points between trigone-including and trigone-sparing groups, assuming the standard deviation is four points using a two-sided type-I error of 5%. A sample size of 18 patients (9 patients in each group) was required. Statistical analysis consisted of the t-test to compare differences in baseline values and at subsequent time points, and Fisher’s exact test to compare baseline proportions for female-to-male ratio. Repeated measures in time were analysed using a mixed-effects model with observations clustered within patients. Analysis was performed using R v.11.0 (http://www.r-project.org/) [17].

3. Results

A total of 22 patients were randomised to either trigone-including ($n=11$) or trigone-sparing ($n=11$) groups (Fig. 2). Baseline characteristics were comparable for both groups...
There was a difference of 9 yr in mean age between groups, but this was not statistically significant (p = 0.2).

### 3.1. Primary outcome

#### 3.1.1. Total overactive bladder symptom score at 6 wk

Within-group analysis demonstrated a statistically highly significant improvement when baseline total OABSS were compared with scores at 6 wk after injection. The trigone-including group had a mean reduction in total OABSS of 13.7 points compared to baseline (p < 0.001) and the trigone-sparing group had a mean reduction in total OABSS of 9.3 points compared with baseline (p < 0.03). Between-group analysis showed the difference in the mean change from baseline was 4.4 points in favour of the trigone-including group (p = 0.03) (Table 2).

### 3.2. Secondary outcome

#### 3.2.1. Total overactive bladder symptom score at 12 and 26 wk

For both groups, there was a strong and significant time effect when baseline total OABSS were compared with scores at 12 and 26 wk after injection. In addition, there was a significant time-by-group interaction effect, with trigone-including injections producing a greater reduction in total OABSS compared with trigone-sparing injections. This effect favouring trigone-including injections was sustained through all time periods. Within-group analysis demonstrated a statistically highly significant improvement when baseline total OABSSs were compared with scores 12 and 26 wk after injection (trigone-including group at 12 wk: p < 0.001, and 26 wk: p < 0.001; trigone-sparing group at 12 wk: p < 0.03, and 26 wk: p < 0.03). Between-group analysis showed a greater reduction in mean total OABSS in the trigone-including group compared with the trigone-sparing group at 12 wk (p = 0.002) and at 26 wk (p = 0.03) (Table 2).

#### 3.2.2. Overactive bladder symptom score urgency subscale score

The OABSS urgency subscale score for both groups similarly showed a strong and significant time effect when baseline scores were compared with 6, 12, and 26 wk after injection. In addition, there was a significant time-by-group interaction effect, with trigone-including injections producing a greater reduction in OABSS urgency subscale score compared with trigone-sparing injections, which was sustained through all time periods.

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### Table 1 – Baseline parameters

<table>
<thead>
<tr>
<th>Demographics</th>
<th>TRIG+</th>
<th>95% CI</th>
<th>TRIG-SP</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, no.</td>
<td>11</td>
<td></td>
<td>11</td>
<td></td>
<td>0.2</td>
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<tr>
<td>Mean patient age, yr</td>
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<td>43.9–63.8</td>
<td>45</td>
<td>34.0–56.9</td>
<td>0.2</td>
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<tr>
<td>Patient age range, yr</td>
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<td>17–76</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male:female</td>
<td>1:10</td>
<td></td>
<td>2:9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean CMG parameters</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MCC, ml</td>
<td>330</td>
<td>248.7–421.5</td>
<td>286.1</td>
<td>212.2–362.3</td>
<td>0.4</td>
</tr>
<tr>
<td>MDP, cm H2O</td>
<td>49.1</td>
<td>38.0–61.9</td>
<td>62</td>
<td>28.2–82.4</td>
<td>0.3</td>
</tr>
<tr>
<td>PVR, ml</td>
<td>36.7</td>
<td>–4.05–69.5</td>
<td>27.8</td>
<td>–23.2–78.1</td>
<td>0.8</td>
</tr>
<tr>
<td>VFDV, ml</td>
<td>103.1</td>
<td>55.6–145.2</td>
<td>96</td>
<td>45.8–169.7</td>
<td>0.8</td>
</tr>
<tr>
<td>VUDV, ml</td>
<td>281.2</td>
<td>213.2–358.8</td>
<td>228.3</td>
<td>173.5–300.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean symptom scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OABSS</td>
<td>22.4</td>
<td>20.2–24.5</td>
<td>22.7</td>
<td>20.0–25.4</td>
<td>0.86</td>
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<tr>
<td>OABSS urgency subscale score</td>
<td>14.2</td>
<td>13.1–15.3</td>
<td>13.9</td>
<td>12.5–16.1</td>
<td>0.95</td>
</tr>
</tbody>
</table>

TRIG+ = trigone-including; TRIG-SP = trigone-sparing; CI = confidence interval; CMG = cystometry; MCC = maximum cystometric capacity; MDP = maximum detrusor pressure (in filling phase); PVR = postvoid residual; VFDV = volume at first desire to void; VUDV = volume at urgent desire to void; OABSS = overactive bladder symptom score.

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### Table 2 – Overactive bladder symptom scores (OABSS) at 6, 12, and 26 wk compared with baseline

<table>
<thead>
<tr>
<th></th>
<th>TRIG+</th>
<th>95% CI</th>
<th>TRIG-SP</th>
<th>95% CI</th>
<th>Difference in change from baseline</th>
<th>p value §</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total OABSS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>22.4</td>
<td>20.2–24.5</td>
<td>22.7</td>
<td>20.0–25.4</td>
<td>–</td>
<td>0.86</td>
</tr>
<tr>
<td>6 wk</td>
<td>8.7</td>
<td>5.6–11.8</td>
<td>13.4</td>
<td>9.0–17.8</td>
<td>–9.3 (&lt;0.001)</td>
<td>4.4</td>
</tr>
<tr>
<td>Difference (p value)</td>
<td>–13.7 (&lt;0.001)</td>
<td>–9.3 (&lt;0.03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 wk</td>
<td>8.2</td>
<td>5.5–11.8</td>
<td>14.5</td>
<td>10.2–18.7</td>
<td>–8.2 (&lt;0.03)</td>
<td>6</td>
</tr>
<tr>
<td>Difference (p value)</td>
<td>–14.2 (&lt;0.001)</td>
<td>–8.2 (&lt;0.03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 wk</td>
<td>9.5</td>
<td>7.3–11.8</td>
<td>14.1</td>
<td>9.5–18.7</td>
<td>–4.6 (&lt;0.03)</td>
<td>4.3</td>
</tr>
<tr>
<td>Difference (p value)</td>
<td>–12.9 (&lt;0.001)</td>
<td>–8.6 (&lt;0.03)</td>
<td></td>
<td></td>
<td></td>
<td>0.03 §</td>
</tr>
</tbody>
</table>

TRIG+ = trigone-including; TRIG-SP = trigone-sparing; CI = confidence interval.

Primary outcome: total OABSS at 6 wk compared with baseline; secondary outcome: total OABSS at 12 and 26 wk compared with baseline.

Mean change from baseline.

Statistically significant.
Within-group analyses demonstrated a statistically highly significant improvement when baseline OABSS urgency subscale scores were compared with scores 6, 12, and 26 wk after injection (trigone-including group at 6 wk: $p < 0.001$, 12 wk: $p < 0.001$, and 26 wk: $p < 0.001$; trigone-sparing group at 6 wk: $p < 0.05$, 12 wk: $p < 0.05$, and 26 wk: $p < 0.05$). Between-group analysis showed a greater reduction in mean OABSS urgency subscale score in the trigone-including group compared with the trigone-sparing group at 12 wk ($p = 0.004$). This reduction did not quite reach statistical significance at 6 wk ($p = 0.06$) and 26 wk ($p = 0.06$) (Table 3).

### 3.2.3. Cystometrography parameters

Within-group analysis show significant improvements in all urodynamic parameters after treatment when compared with baseline (Table 4). However, between-group analysis for all CMG parameters did not show statistically significant differences (Table 4).

#### 3.2.4. Vesicoureteric reflux

No patients in either group had preexisting VUR on preoperative MCUG study and no patients in either group developed VUR following BoNT-A injection.

#### 3.2.5. Postvoid residual volumes and adverse events

PVR at 6 wk increased in both groups following injection when compared with baseline. This was significant in the trigone-sparing group, but not in the trigone-including group (Table 4). Between-group analysis showed no significant difference in the mean PVR at 6 wk (trigone-including group: 192 ml; trigone-sparing group: 186 ml; 34 ml; 0.03).

### Table 3 – Secondary outcome: Overactive bladder symptom score (OABSS) urgency subscale at 6, 12, and 26 wk compared with baseline

<table>
<thead>
<tr>
<th></th>
<th>TRIG+</th>
<th>TRIG-SP</th>
<th>Difference in change from baseline</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OABSS urgency subscale:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>14.2 (13.1–15.3)</td>
<td>13.9 (12.5–16.1)</td>
<td>–</td>
<td>0.95</td>
</tr>
<tr>
<td>6 wk</td>
<td>6.2 (4.02–8.3)</td>
<td>8.9 (5.9–11.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference ($p$ value)</td>
<td>$-8.0$ (&lt;0.001)</td>
<td>$-5.0$ (&lt;0.005)</td>
<td>3.0</td>
<td>0.06</td>
</tr>
<tr>
<td>12 wk</td>
<td>5.5 (3.5–7.4)</td>
<td>9.4 (6.1–12.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference ($p$ value)</td>
<td>$-8.7$ (&lt;0.001)</td>
<td>$-4.5$ (&lt;0.005)</td>
<td>4.2</td>
<td>0.004</td>
</tr>
<tr>
<td>26 wk</td>
<td>6.3 (4.9–7.8)</td>
<td>9.0 (5.9–12.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference ($p$ value)</td>
<td>$-7.9$ (&lt;0.001)</td>
<td>$-4.9$ (&lt;0.005)</td>
<td>3.0</td>
<td>0.06</td>
</tr>
</tbody>
</table>

TRIG+ = trigone-including; TRIG-SP = trigone-sparing; CI = confidence interval.

### Table 4 – Cystometrography parameters at 6 wk postinjection compared with baseline

<table>
<thead>
<tr>
<th></th>
<th>TRIG+</th>
<th>TRIG-SP</th>
<th>Difference between means</th>
<th>$p$ value</th>
</tr>
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<tbody>
<tr>
<td>MCC, ml:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>330 (248.7–421.5)</td>
<td>286.1 (212.2–362.3)</td>
<td>–</td>
<td>0.4</td>
</tr>
<tr>
<td>6 wk</td>
<td>498.5 (387.1–614.5)</td>
<td>535.9 (309.0–606.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference ($p$ value)</td>
<td>168.5 (0.004)</td>
<td>249.8 (0.01)</td>
<td>–37.4</td>
<td>0.61</td>
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<tr>
<td>MDP, cmH$_2$O:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>49.1 (38.0–61.9)</td>
<td>62 (28.2–82.4)</td>
<td>–</td>
<td>0.3</td>
</tr>
<tr>
<td>6 wk</td>
<td>13.5 (9.45–20.7)</td>
<td>16.4 (12.1–21.4)</td>
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<tr>
<td>Difference ($p$ value)</td>
<td>$-35.6$ (&lt;0.0001)</td>
<td>$-45.6$ (&lt;0.02)</td>
<td>–2.9</td>
<td>0.29</td>
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<tr>
<td>PVR, ml:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>36.7 (4.05–69.5)</td>
<td>27.8 (23.2–78.1)</td>
<td>–</td>
<td>0.8</td>
</tr>
<tr>
<td>6 wk</td>
<td>192 (19.25–364.2)</td>
<td>186 (38.1–334.6)</td>
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<td></td>
</tr>
<tr>
<td>Difference ($p$ value)</td>
<td>155.3 (0.06)</td>
<td>158.2 (0.03)</td>
<td>18.1</td>
<td>0.73</td>
</tr>
<tr>
<td>VFDV, ml:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>103.1 (55.6–145.2)</td>
<td>96 (45.8–189.7)</td>
<td>–</td>
<td>0.8</td>
</tr>
<tr>
<td>6 wk</td>
<td>346.1 (129.4–478.5)</td>
<td>312.1 (123.9–448.3)</td>
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<tr>
<td>Difference ($p$ value)</td>
<td>243 (&lt;0.02)</td>
<td>216.1 (&lt;0.03)</td>
<td>34</td>
<td>0.99</td>
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<td>VUDV, ml:</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>281.2 (213.2–358.8)</td>
<td>228.3 (173.5–300.9)</td>
<td>–</td>
<td>0.2</td>
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<tr>
<td>6 wk</td>
<td>471.6 (351.1–607.1)</td>
<td>498.3 (296.7–577.6)</td>
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<tr>
<td>Difference ($p$ value)</td>
<td>190.4 (&lt;0.003)</td>
<td>270 (&lt;0.02)</td>
<td>–26.7</td>
<td>0.85</td>
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TRIG+ = trigone-including; TRIG-SP = trigone-sparing; CI = confidence interval; CMG = cystometrography; MCC = maximum cystometric capacity; MDP = maximum detrusor pressure (in filling phase); PVR = postvoid residual; VFDV = volume at first desire to void; VUDV = volume at urgent desire to void.

$^a$ Mean change from baseline.

* Statistically significant.
p = 0.73), at 12 wk (p = 0.52), or at 26 wk (p = 0.54). In both groups, 2 of 11 patients (18%) each had PVR volumes >150 ml, requiring clean intermittent self-catheterisation (CISC). By week 12, only one patient (9%) in each group required CISC, which persisted at 26 wk. Adverse events are summarised in Table 5. The most frequently reported adverse event was mild haematuria; in all cases this resolved within 48 h, requiring no intervention (Table 5).

### 4. Discussion

There is high-quality evidence confirming efficacy of BoNT-A compared with placebo in patients with IDO [1,3,4]. Dmochowski et al, in a dose-ranging trial comparing 50, 100, 150, 200, and 300 U onabotulinumtoxinA in patients with IDO, showed that 100 U may be the optimum dose that appropriately balances the benefits with adverse events [18]. There are no dosing studies for abobotulinumtoxinA.

In this study, we used the abobotulinumtoxinA brand stocked in our hospital formulary (Dysport). Most studies involving BoNT-A in the bladder, including efficacy studies and dosing studies, have used onabotulinumtoxinA. Conversion ratios ranging from 1:1 to 1:6 (onabotulinumtoxinA: abobotulinumtoxinA) have been reported in the published literature [19–21]. More contemporary data would suggest a conversion ratio of 1:3 as being clinically equivalent [21]. We elected to use 500 U abobotulinumtoxinA based on our earlier experience [2]; with a 1:3 conversion ratio, this approximates 160 U onabotulinumtoxinA.

This study reports greater improvement in symptom score when the injection sites include the trigone at the primary end point of 6 wk, but this improvement is sustained through weeks 12 and 26. In previously reported studies using onabotulinumtoxinA, Lucioni et al, however, found no difference in the trigone-including group; each patient received only two injections into the trigone [10]. Kuo, using 100 U onabotulinumtoxinA, reported comparable outcomes with bladder body and bladder base injections; however, the bladder body group received injections at 40 sites compared with just 10 sites in the bladder base group [11]. Kuo subsequently reported a further study, again using 100 U onabotulinumtoxinA, and compared body (20 injections), body/trigone (20 injections in total), and base (10 injections). All three groups had comparable safety and efficacy [12]. There were differences in injection sites, number of injections per site, and the conversion dose equivalence between abobotulinumtoxinA and onabotulinumtoxinA that may explain the differences in outcome observed in this study using abobotulinumtoxinA compared with the previously reported studies using onabotulinumtoxinA.

In this study, there was a large increase in mean PVR compared to baseline in both groups, although there was no statistical difference in mean PVR and CISC rates between the groups. The CISC rate in this study was 18%. Other studies quote CISC rates of 0–48%, although there was considerable variation in the definitions of large PVR (>150 ml to >350 ml) and PVR thresholds for instituting CISC [1–3,8,11,12]. No patients developed VUR when assessed at 6 wk. Although it is not known if VUR is a short-term consequence, previous studies have also demonstrated similar safety at 6–12 wk [7–12].

During clinical assessment at baseline, no female patients had symptoms of pelvic organ prolapse or hypocontractility, and none had obvious pelvic organ prolapse on vaginal examination intraoperatively.

A limitation of this study is that all patients received general anaesthesia. There is a trend toward administering BoNT-A under local anaesthesia, using flexible cystoscopy in men and either flexible or rigid cystoscopy in women. The tolerability of injecting the trigone under local anaesthetic has not been ascertained and, given the increased density of sensory fibres in the trigone, this potentially may be more painful. Further studies are required to examine this. A further limitation is that we did not examine the effect of trigone-only injections; a further study is being designed to address this question. There may be a difference in the duration of treatment effect between the two groups, but the follow-up period of 26 wk was too short for the authors to assess this.

### 5. Conclusions

Trigone-including injections result in greater reduction in OABSS total and OABSS urgency subscale scores. CMG parameters for both techniques were comparable. Trigone-including injections did not induce VUR at 6 wk postinjection. We recommend that the trigone be included in all patients with refractory IDO receiving intradetrusor injections of abobotulinumtoxinA.

### Author contributions

Rustom P. Manecksha had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Manecksha, McNeill.

**Acquisition of data:** Manecksha, Cullen.

**Analysis and interpretation of data:** Manecksha, Ahmad.

**Drafting of the manuscript:** Manecksha.

**Critical revision of the manuscript for important intellectual content:** Flynn, Thornhill.

**Statistical analysis:** Manecksha.

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**Supervision:** Grainger, McDermott.

**Other (specify):** None.
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Appendix A. Overactive bladder symptom score questionnaire

NAME: ________________________________ DATE: ___________

1. **How often do you usually urinate during the day?**
   - No more often than once in 4 hours
   - About every 3–4 hours
   - About every 2–3 hours
   - About every 1–2 hours
   - At least once an hour

2. **How many times do you usually urinate at night (from the time you go to bed until the time you wake up for the day)?**
   - 0–1 times
   - 2 times
   - 3 times
   - 4 times
   - or more times

3. **What is the reason that you usually urinate?**
   - Out of convenience (no urge or desire)
   - Because I have mild urge or desire (but can delay urination for an hour if I have to)
   - Because I have moderate urge (but can delay urination for more than 10 but less than 60 minutes if I have to)
   - Because I have severe urge (but can delay urination for less than 10 minutes if I have to)
   - Because I have desperate urge (must stop what I am doing and go immediately)

4. **Once you get the urge or desire to urinate, how long can you usually postpone it comfortably?**
   - More than 60 minutes
   - About 30–60 minutes
   - About 10–30 minutes
   - A few minutes (less than 10 minutes)
   - Must go immediately

5. **How often do you get a sudden urge or desire to urinate that makes you want to stop what you are doing and rush to the bathroom?**
   - Never
   - Rarely
   - A few times a month
   - A few times a week
   - At least once a day

6. **How often do you get a sudden urge or desire to urinate that makes you want to stop what you are doing and rush to the bathroom, but you do not get there in time (ie, you leak urine or wet pads)?**
   - Never
   - Rarely
   - A few times a month
   - A few times a week
   - At least once a day

7. **In your opinion how good is your bladder control?**
   - Perfect control
   - Very good
   - Good
   - Poor
   - No control at all
References


