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REPEATED ONABOTULINUMTOXINA INJECTIONS FOR THE MANAGEMENT OF REFRACTORY IDIOPATHIC DETRUSOR OVERACTIVITY: MEDIUM TERM OUTCOMES, SAFETY PROFILE AND DISCONTINUATION RATES.

Hypothesis / aims of study

Over the last decade onabotulinumtoxinA injections have become an increasingly popular treatment option for patients with refractory idiopathic detrusor overactivity (IDO). Improvements in bladder symptoms and quality of life (QoL) scores are supported by level 1 evidence. However, longer term data with repeated injections is sparse in the IDO population. Our aims are to report our clinical experience over the last 7 years, with particular emphasis on clinical outcomes, number of patients continuing / discontinuing therapy and adverse events.

Study design, materials and methods

Since 2004 bladder onabotulinumtoxinA injections have been available at our institution, initially administered as part of clinical trials but later as "off licence" treatment on a named patient basis for patients with symptomatic IDO refractory to anticholinergics. The majority of patients received 200 U onabotulinumtoxinA (Botox®) via a flexible cystoscopic, trigone sparing technique. Data was recorded in a prospective database including, dates of injection, 3 day voiding diary data, QoL as assessed by the UDI-6 and IIQ-7, reasons for discontinuing treatment and adverse events. Patients were re-injected when they reported a return of symptoms. Clean intermittent self catheterisation (CISC) was commenced in symptomatic patients with a post void residual of greater than 150 mL.

Results

A total of 205 injections were performed. One hundred patients underwent 1 injection, 53 had 2, 20 had 3, 13 had 4, 10 had 5, 5 had 6, 3 had 7 and 1 had 8. Data regarding which patients had decided not to undergo further injections, inter-injection interval and a record of adverse events was available for all patients. Complete data regarding bladder symptoms and quality of life was available for 60% of patients. Statistical analysis performed for patients with up to 5 injections. A statistically significant reduction in urinary frequency, urgency and urge urinary incontinence as well as UDI-6 and IIQ-7 scores were seen following the first onabotulinumtoxinA injection compared with baseline values. This improvement was maintained for up to 5 injections and was not statistically different when comparing differences between injections. The number of patients who decided not to undergo further injections and their reasons why are described in table 1. Injection interval data is presented in table 2. The incidence of CISC after the 1st injection was 35% overall. All patients requiring CISC after the 1st injection required it after subsequent injections. Twenty one percent of patients suffered a UTI after their first injection, although 6% suffered from recurrent UTIs before therapy.

Table 1 – Drop out rates and reasons why following botn-A injections

Injection number	1	2	3	4	5	6	7	8
Total dropouts (N° of injections)	25 (100)	12 (53)	0 (20)	0 (13)	3 (10)	0 (5)	0 (3)	0 (1)
Poor response	9	3			1			
Disliked CISC	5	4						
Unable to perform CISC	2	0						
Too invasive	2	0						
Moved out of area	4							
Lost to follow-up	3	3						
Other	0	2			2			

Table 2 - Interval between injections of botn-A

	1 to 2	2 to 3	3 to 4	4 to 5	5 to 6	6 to7	7 to8
Mean(day)	466.2	372.7	272.8	311.7	351.2	298.3	379.0
n	49.0	20.0	13.0	10.0	5.0	3.0	1.0

Interpretation of results

Repeated injection of onabotulinumtoxinA significantly improve bladder symptoms and QoL of patients with no evidence of a deterioration in effect in up to 5 injections analysed. The main adverse events appear to be CISC and UTI and these can be expected in approximately 1 in 3 and 1 in 7 patients, respectively. In this cohort the number of patients who drop out after the first and second injection is approximately 24%. The main reasons for discontinuation are lack of efficacy (< 10 %) and CISC (7%). However, many patients tolerated CISC if this translated into good symptom control in our series. Subsequent to this, drop outs are low, suggesting that if patients are happy with the first two injections they are likely to continue. The inter-injection interval appears to decrease but this may simply reflect our practice outside clinical trials. Typically the inter-injection interval is 10-11 months.

Concluding message

Outcomes from our dedicated onabotulinumtoxinA service demonstrate repeated injections are efficacious for the majority of patients, providing a significant improvement in symptoms and QoL measures, with as yet no evidence of diminishing effect. It should be noted however that there is a significant “drop out” rate after injections 1 and 2. A requirement for CISC and UTIs are the most common adverse effects.

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Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Guy's and St Thomas' Research Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**