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A PRAGMATIC APPROACH TO THE USE OF INTRAVESICAL BOTULINUM TOXIN INJECTION TREATMENT FOR IDIOPATHIC DETRUSOR OVERACTIVITY: A REVIEW OF 5 YEARS' ACTIVITY IN THE REAL WORLD.

Hypothesis / aims of study

Over 16% of the adult population above 40 in Europe suffer from symptoms of overactive bladder (OAB). The first line therapy for OAB includes life style modification, bladder retraining and antimuscarinic pharmacotherapy. Although antimuscarinic treatment is effective and safe, few patients persist with treatment in the long-term: the reported discontinuation rate ranges from 68% to 88% at 6 months (1). Our patients are offered Botulinum toxin A (BTX-A) injection treatment only if maximum dose antimuscarinic treatment with at least two agents have failed and idiopathic detrusor overactivity (IDO) is confirmed on urodynamics. Although the effectiveness of intravesical BTX-A has been proven in several randomised placebo controlled trials (2), the overall number of patients who have undergone the procedure remains relatively low. We summarize our 5 years experience, so prospective patients may be informed of the effects and potential complications of intravesical injections of BTX-A .

Study design, materials and methods

All patients with persistently bothersome OAB symptoms, having tried at least 2 antimuscarinic agents at maximum dose, underwent a urodynamics study with a view to receiving intravesical BTX-A injection treatment. Only patients with confirmed IDO were offered treatment. Women who were pregnant or breast feeding or were planning pregnancy were excluded. All patients had to be able and willing to perform CISC. Preoperatively, all patients completed a patient reported outcomes questionnaire - the Overactive Bladder Symptom Score (OABSS) (3) as well as a Quality of Life assessment.

All treatments were done as day cases under general anaesthetic and with a covering dose of intravenous co-amoxiclav at induction. 250 units of BTX-A (Dysport ®) in 40 mls of saline were injected into the detrusor and suburothelium at 15-25 sites; the trigone was not injected. Patients were advised to stop antimuscarinic medication following treatment, but to resume it (up to maximum dose) when symptoms recurred. If, despite being on maximum dose medication, symptoms remained bothersome, patients were direct-listed for further BTX injection treatment.

All patients were followed up at 6 weeks. As well as completing an OABSS and QoL questionnaire, a urine dipstick test and post-void residual (PVR) measurement were performed. Patients with a PVR of over 150 mls in the presence of persistent symptoms were taught CISC. Primary outcome was measured by Patient Reported Outcomes (PRO) using the Overactive Bladder Symptoms score (OABSS) and a Quality of Life score (QoL). The scores for OABSS and QoL increase directly with symptom severity; maximum scores are 15 and 6 respectively. Symptomatic improvement was considered to be represented by a decrease of 2 or more points in OABSS (at least a 10% improvement).

The data was collected prospectively and recorded on Microsoft Excel and transferred to SPSS 17.0 for analysis. Descriptive statistics were performed for continuous data. A paired t-test was used to compare pre- and post- treatment outcomes.

Results

Seventy patients (12 men, 58 women) with a mean age ± SD of 53 ± 13.1 years received 112 treatments between 2005 and 2010. The mean duration of OAB symptoms was 7.3 ± 5.8 years. Forty-five patients received one treatment, 13 received two, 7 received three and 5 received four treatments over this period. Three patients were lost to follow up. Table 1 shows the results of individual treatments.

	Pre-BTX	**Post-BTX**	**Change**
OABSS	10.58 ± 2.57	6.82 ± 4.03	3.8 ± 4.0 (p<0.001)
QoL	5.28 ± 0.71	3.27 ± 2.06	2.0 ± 2.2 (p<0.001)
PVR	41.13 ± 71.9mls	80.03 ± 125.7mls	38.9 ± 136.2mls (p=0.028)
CISC	3 (2.7%)	21 (19.2%)	18 (16.5%)

Table 1.

An improvement in OABSS of 2 or more points was observed following 82 (75.2%) procedures. Thirty eight patients (34.8%) were referred back at a later stage for further treatment. In this group, the mean duration of effect of the previous treatment was 7.6 ± 5.5 months; the mean interval between injection treatments was 414 ± 254 days, and this interval increased with successive treatments.

De-novo CISC was required following 18 treatments, but only for periods of 4-6 weeks. Non-parametric Mann-Whitney testing suggest that those who required post-treatment CISC had a shorter duration of symptoms and a higher functional bladder capacity preoperatively (Table 2).

Number of procedures	Group of patients	Mean functional capacity (mls)	Mean Duration of symptoms (years)
88	No CISC after BTX	30.89 ± 43.42	7.78 ± 6.01
21	CISC Post BTX	92.82 ± 135.34	5.83 ± 5.41

Table 2.

Interpretation of results

The reported success rate for BTX injection treatment for OAB ranges from 50% to 80%. This variation may be attributed to differences in the type of botulinum toxin used, injection technique and in the measured outcomes criteria. Our regime insists on failure of maximum dose antimuscarinic medication as being the trigger for initial and all subsequent intravesical BTX-A injection treatments. In terms of efficacy, our results show that a dose of 250 units is as effective as the standard 500 unit dose of Dysport, with 75% of treatments providing symptomatic relief for periods of over 7 months.

There is no consensus as to what PVR should demand CISC; the literature varies from 100ml to 150-200ml. Higher doses of BTX-A are associated with increased higher PVRs; the reported CISC rate ranges from 2% to 43%. We offered CISC only to symptomatic patients with a PVR of over 150 ml.

Concluding message

Our regime, whereby patients resume antimuscarinic therapy at maximum dose as soon as OAB symptoms recur following BTX treatment, enables Botulinum toxin A injection treatment to be rationed more cost-effectively. It is a pragmatic approach that is understood and liked by family doctors and patients alike and which provides a mean efficacy of 7.6 months with a de novo CISC rate of 16.5%.

References

1. Alhasso, A. A., McKinlay, J., Patrick, K. et al.: Anticholinergic drugs versus non-drug active therapies for overactive bladder syndrome in adults. Cochrane Database Syst Rev: CD003193, 2006
2. Anger, J. T., Weinberg, A., Suttorp, M. J. et al.: Outcomes of intravesical botulinum toxin for idiopathic overactive bladder symptoms: a systematic review of the literature. J Urol, 183: 2258, 2010
3. Homma, U., Yoshida, M., et al.: Symptom assessment tool for overactive bladder syndrome – overactive bladder symptom score.Urol.68: 318, 2006

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require ethics committee approval because	**It is recognized treatment of detrusor overactivity.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**