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A DOUBLE BLIND, PLACEBO CONTROLLED, RANDOMISED, CROSS OVER STUDY OF TRIGONE SPECIFIC INJECTIONS OF BOTULINUM TOXIN B FOR TREATING PATIENTS WITH IDIOPATHIC DETRUSOR OVERACTIVITY REFRACTORY TO OTHER CONSERVATIVE TREATMENTS.

Hypothesis / aims of study

The known increased density of sensory receptors in the trigone offers it as an attractive site for the injection of botulinum toxin in the treatment of idiopathic detrusor overactivity (IDO). Injecting the trigone however, is traditionally avoided as it may be painful, and cause ureteric reflux or stress incontinence. The aim of this double blind, placebo controlled, randomised, cross over study was to assess the feasibility, efficacy and morbidity of TRIGONE SPECIFIC injections of botulinum toxin type B compared to placebo as a treatment for IDO refractory to conservative therapies.

Study design, materials and methods

Patients with IDO, refractory to at least 2 anticholinergic therapies, were randomised and given trigone specific injections with either Botulinum Toxin Type B (BTX B) 5000units (chosen deliberately for its known short duration of action) or placebo (normal saline). After 10 weeks they were crossed over to receive the other treatment. All injections were administered using the same anaesthetic method for each patient. 1ml of either placebo or BTX B was injected, using a rigid cystoscope, into 3 sites on the trigone only. Randomisation was computer generated, and patients, practitioners and assessors were blinded to the treatment given.

3 day diaries measured urinary frequency, incontinence episodes, mean functional capacity, nocturia and pad usage at baseline and 2 and 10 weeks post each injection. Quality of life (as assessed by the King's Health Questionnaire and UDI-6) was also assessed at baseline and 2 and 10 weeks post each injection.

Assuming an 80% improvement with BTX B and a 30% improvement with placebo, 20 patients would be required in each group to detect this difference with 80% power (alpha = 0.05). As this is a crossover study 20 patients were required in total.

Results

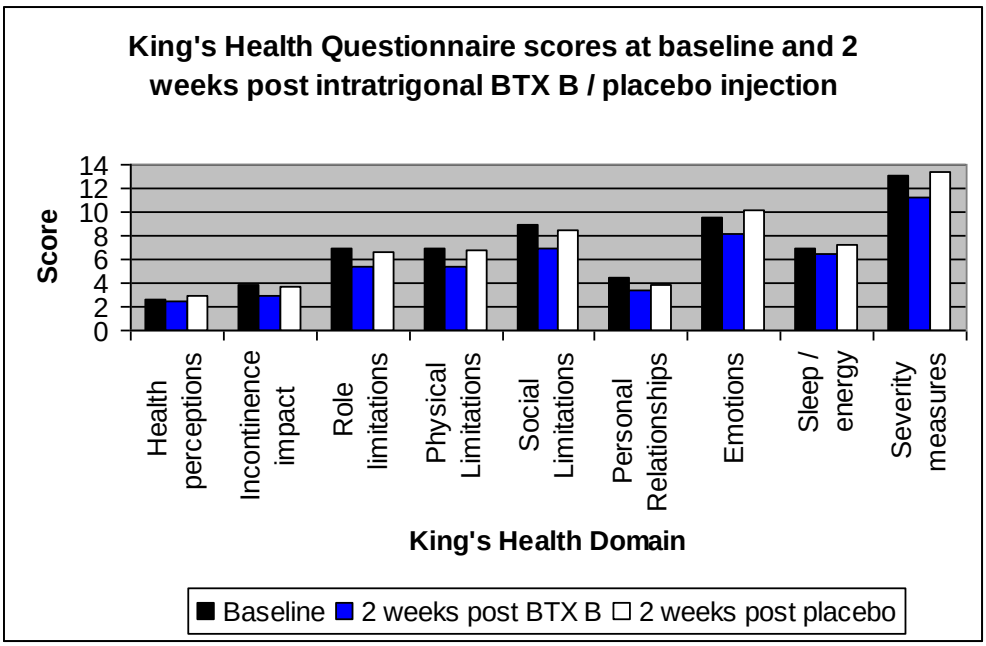
20 patients were recruited into the study. The following table summarises the results from the voiding diaries.

Results of voiding diaries at baseline, 2 and 10 weeks post BTX B and placebo trigone specific injection. p value is determined by 1 tailed student t-test.

Parameter	**Botulinum toxin B (p value Vs baseline)**	**Placebo (p value Vs baseline)**	**p value BTX B Vs placebo**
Mean Voids / 24 hrs:			
Baseline	11.5	11.5	
2 weeks	9.65 (0.009)	10.2 (0.17)	0.008
10 weeks	9.46 (0.013)	9.76 (0.02)	0.35
Incontinence episodes /24 hrs: Baseline	5.5	5.5	
2 weeks	3.12 (0.0001)	4.17 (0.006)	0.03
10 weeks	4.19 (0.02)	4.25 (0.02)	0.28
Mean functional capacity:			
Baseline	350	350	
2 weeks	386 (0.03)	359 (0.10)	0.35
10 weeks	357 (0.46)	364 (0.13)	0.40
Nocturia:			
Baseline	1.9	1.9	
2 weeks	1.62 (0.08)	1.98 (0.41)	0.14
10 weeks	1.49 (0.04)	1.89 (0.23)	0.45
Pads used:			
Baseline	3.75	3.75	
2 weeks	2.33 (0.0004)	3.52 (0.29)	0.03
10 weeks	2.88 (0.001)	3.82 (1)	0.27

Mean UDI-6 score improved from 1.87 at baseline to 1.39 two weeks after trigonal BTX B injection (p=0.02) but this significant improvement was lost by week 10. Mean UDI-6 score was 1.65 two weeks after injection of placebo into the trigone (p=0.06).

The following graph illustrates the results of the King's Health Questionnaires at baseline and 2 weeks post trigonal injection of BTX B or placebo. There was significant improvement in 6 domains following trigone specific BTX B injection



Following 40 injections, 22 patients complained of pain on day one post injection, with a mean pain score of 1.95/10. There was no difference in adverse events between the 2 groups.

Interpretation of results

Trigone specific injection of BTX B gives significant improvements in most measured outcomes at 2 weeks when compared to placebo, without significant adverse events. These effects have worn off by week 10, reflecting the known short duration of action of BTX B. There was minimal change in the measured parameters following trigone specific placebo injection. This finding justifies further investigation of the clinical utility of BTX A in trigone specific or trigone inclusive, compared to trigone sparing injections.

Concluding message

Whilst being short acting, TRIGONE SPECIFIC injection of botulinum toxin B improves the symptoms of idiopathic detrusor overactivity without apparent serious risk.

Specify source of funding or grant	**None**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Dyfed Powys Research Ethics Committee.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**