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THE USE OF INTRAVESICAL BOTULINUM TOXIN IN OVERACTIVE BLADDER SYNDROME: A SYSTEMATIC REVIEW.

Hypothesis / aims of study

Overactive bladder (OAB) is a common condition with a significant negative impact on quality of life. Intravesical injection of botulinum toxin (BTX) is becoming increasingly popular as an intervention for refractory OAB, with a considerable body of case reports and series in the literature describing its beneficial effects. As yet no systematic review of randomised controlled trials involving BTX has been published assessing the safety and effectiveness of this treatment for the overactive bladder.

The objective was to compare intravesical BTX injection with other treatments for neurogenic and idiopathic OAB in adults.

Seven specific hypotheses were addressed:

1 Intravesical injection of botulinum toxin is better than placebo or no treatment.
2 Intravesical injection of botulinum toxin is better than pharmacological interventions.
3 Intravesical injection of botulinum toxin is better than other non-pharmacological interventions.
4 Higher doses of intravesical botulinum toxin are better than lower doses.
5 Intravesical injection of botulinum toxin combined with other treatments is better than other treatments alone.
6 One formulation of botulinum toxin is better than another.
7 One intravesical injection technique is better than another.

Study design, materials and methods

The search strategy developed for the Cochrane Incontinence Group was used to identify relevant articles. Randomised and "quasi randomised" trials of treatment of OAB in adults in which at least one arm involved intravesical injection of BTX, were identified from the Cochrane Incontinence Review Groups Specialist Register of Controlled Trials. The most recent search was November 2005.

Participants had either neurogenic or idiopathic OAB, with or without stress incontinence, and comparison interventions could include no intervention, placebo, lifestyle modification, bladder retraining, pharmacological treatments, surgery, bladder instillation techniques, neuromodulation, and different types, doses, and injection techniques of BTX.

Evaluation for methological quality and appropriateness for inclusion was performed using the Incontinence Groups assessment criteria [1]. All trials were evaluated independently by at least two reviewers and data extracted separately. Binary outcomes were presented as relative risk, and continuous outcomes by mean differences. No data comparisons between studies could be made due to differing designs, and outcome measures. For data representation purposes, data were combined where appropriate. Where possible, data were represented on forest plots.

Results

Initially 19 studies were identified, but 11 of these did not meet inclusion criteria. The included studies were three full articles and five abstracts.

Results varied, and no data could be quantitatively compared between studies due to differences in study design, and different outcome measures. Numbers of participants in the studies was uniformly small. Some studies did not measure quality of life, and urodynamic measures were variable. Apart from one study that used BTX-B, BTX-A was the formulation of botulinum toxin used for treatment. The great majority of patients had neurogenic OAB, and had refractory disease.

For the most part BTX-A showed superiority to placebo in such outcomes as incontinence episodes, bladder capacity, maximum detrusor pressure, and quality of life.

Low doses of BTX (100U-150units) appeared to have beneficial effects, but higher doses (300units) may be more effective.

Botulinum toxin appeared to have beneficial effects in OAB that exceed the effects of intravesical resiniferatoxin, which also did not have the effect of reducing maximum detrusor pressure found with BTX-A.

Using ten injection sites appeared as effective as using the more common 30 sites, and caused less post-procedural pain.

There were few adverse events, the most common being the need to start intermittent self-catheterisation.

No studies were identified that compared different formulations of BTX, BTX with non-pharmacological interventions, or that combined BTX with other treatments.

Interpretation of results

Although the number of participants studied was small, there seems to be a positive effect of intravesical BTX over placebo and resiniferatoxin in the studies reviewed. For the most part this was demonstrated on patients with refractory neurogenic OAB. The benefits of intravesical BTX over most other existing pharmacological and non-pharmacological interventions has not been investigated. The optimal dose of BTX for OAB remains inconclusive, as does its duration of action, and limited safety data have been gathered. There appears to be a risk of requiring intermittent self-catheterisation following BTX therapy.

Concluding message

Intravesical BTX shows promise as a therapy for OAB, but as yet too little experimental data exist on safety and efficacy compared with other interventions, or with placebo. Practitioners should be aware that at present there is little more than anecdotal evidence in the form of case reports to support the efficacy of intravesical BTX, and not much in the way of substantial, robust safety data. Furthermore, the optimal dose of BTX for efficacy and safety has not yet been proven. As most data are based on patients with neurogenic OAB, the generalisability of results to those with idiopathic OAB is uncertain.

More robust and powerful studies need to be conducted in order to establish exactly how effective and safe intravesical injection of BTX is for treatment of OAB. Long term follow up data would be valuable in assessing safety and duration of effect.

Reference

1. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5; Oxford, May 2005.