

SAFETY AND EFFICACY OF ONABOTULINUMTOXINA FOR THE TREATMENT OF NEUROGENIC AND IDIOPATHIC OVERACTIVE BLADDER: A META-ANALYSIS OF TEN RANDOMIZED CONTROLLED TRIALS

Hypothesis / aims of study

Overactive bladder (OAB) affects 10.4% of worldwide population and adversely impacts the quality of life. Antimuscurinic agents are a widely used treatment for OAB but they are often ineffective or not tolerated. OnabotulinumtoxinA (Botox) has been evaluated as an alternative therapy for OAB patients who do not respond optimally to first line treatment.

The aim of this study is to synthesize evidence from published Randomized Controlled Trials (RCTs) about the safety and efficacy of Botox compared to placebo for the treatment of patients with OAB.

Study design, materials and methods

A computer literature search for PubMed was carried out using the following key words: "OnabotulinumtoxinA; overactive bladder". We included RCTs comparing Botox and placebo for patients with idiopathic and neurogenic overactive bladder. Data were extracted and analysed using RevMan version 5.3 for windows.

Changes in frequency of micturition/24 hours, maximum cystometric capacity (MCC), mean detrusor pressure (MDP), urgency episodes, urinary incontinence, and volume void per micturition were pooled as standardized mean difference (SMD between Botox group and placebo group) in a meta-analysis model using inverse variance (IV) method. Heterogeneity was assessed by visual inspection of the forest plots and measured by I-square and Chi-square tests. In case of significant heterogeneity (Chi-square $P < 0.1$), a random effect model was used. Otherwise, a fixed effect model was used. Complications were pooled as relative risk (RR) in a fixed effect model using Mantel Haenzel (M-H) method. To investigate effects of different Botox doses, we performed subgroup analysis. Heterogeneity was resolved by sensitivity analysis. P value below 0.05 was considered significant.

Results

Ten RCTs were included in this study with a total of 2648 patients (OnabotulinumtoxinA group $n = 1591$ and placebo group $n = 1057$). Botox doses ranged from 50 units to 300 units mg and were expressed as five subgroups: 50 units, 100 units, 150 units, 200 units, and 300 units. The overall effect estimate favoured Botox than placebo in terms of: frequency of micturition/24 hours (MD -1.31, 95% CI [-1.58, -1.05], $P < 0.00001$), MCC (MD 137.17, 95% CI [118.79, 155.55], $P < 0.00001$), MDP (MD -31.61, 95% CI [-37.02, -26.20], $P < 0.00001$), urgency episodes (MD -2.17, 95% CI [-2.59, -1.74], $P < 0.00001$), urinary incontinence (MD 1.57, 95% CI [-1.80, -1.35], $P < 0.00001$), and volume void per micturition (MD 45.51, 95% CI [25.67, 65.35], $P < 0.00001$).

Botox in a dose of 50 units did not achieve significant improvement in terms of frequency of micturition, MCC, urinary incontinence, or volume voiding per micturition. However, higher doses 200 units and 300 units achieved significant improvement in frequency of micturition, MCC, urinary incontinence, and volume voiding per micturition.

For complications, the pooled effects were: (1) urinary tract infection (RR 1.62, 95% CI [1.19, 2.20], $P = 0.002$); (2) urine retention (RR 12.80, 95% CI [5.94, 27.55], $P < 0.00001$); (3) dysuria (RR 1.50, 95% CI [1.07, 2.11], $P = 0.02$); (4) haematuria (RR 1.85, 95% CI [1.03, 3.31], $P = 0.04$); and (5) pyrexia (RR 1.06, 95% CI [0.54, 2.09], $P = 0.86$).

Interpretation of results

Botox is effective for the treatment of neurogenic and idiopathic overactive bladder. This improvement was significant in the subgroups of 200 units and 300 units of Botox. Urinary tract infection was higher in Botox group. However, the risk of pyrexia did not differ significantly between either of the two groups. The risk of urine retention was 12 folds higher in patients treated with botox compared to those assigned to placebo.

Concluding message

Intradetrusor injections of Botox is effective for the treatment of neurogenic and idiopathic overactive bladder in doses of 200 units and 300 units. However, possible complications particularly urine retention should be taken into consideration.

Disclosures

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