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COMPARISON OF BOTOX® WITH A CHINESE BOTULINUM TOXIN TYPE A (PROSIGNE®) FOR THE TREATMENT OF REFRACTORY NEUROGENIC DETRUSOR OVERACTIVITY.

Hypothesis / aims of study
The injection of botulinum toxin type A (BTX-A) into the bladder has recently emerged as an atractive alternative for the treatment of refractory neurogenic detrusor overactivity. While the overwhelming majority of investigators have used the BTX-A formulation BOTOX® (Allergan, Irvine, California) other BTX-A formulations are being marketed. There is a lack of evidence on the clinical efficacy and safety of the recently released Chinese BTX-A (Prosigne®, Lanzhou Biological Products Institute, China) for the treatment of detrusor overactivity. The aim of our study was to evaluate the short-term clinical and urodynamic effect of Prosigne in the treatment of detrusor overactivity and compare it to Botox.

Study design, materials and methods
Between April 2003 and August 2006, 40 consecutive patients with refractory neurogenic detrusor overactivity received a single dose of BTX-A into the detrusor at one institution. BOTOX® was used for the first 22 patients (Group 1), while the following 18 patients received Prosigne® (Group 2). The different BTX-A formulations were used because the hospital changed the BTX-A formulation due to cost restrictions, since Prosigne is marketed at 60% of the Botox price in Brazil. All patients complained of urinary incontinence which was caused by detrusor overactivity as demonstrated by urodynamics and all were in a program of clean intermittent catheterization. Baseline and postoperative evaluation after 12 weeks of BTX-A injection included a clinical assessement of continence and a standard urodynamic study. The evaluated parameters were maximum cystometric capacity, reflex detrusor volume, maximum detrusor pressure during bladder contraction and compliance. All patients underwent detrusor injection of 300 units of BTX-A. The primary outcomes were the continence status and urodynamic parameters.

Results
The study included 28 men and 12 women, with a mean age of 35.2 $\pm$ 14.7 years (range 19 to 73 years). The condition resulted from spinal cord injury in 31 (77.5%) patients, viral myelitis in 6 (15.0%) and multiple sclerosis in 3 (7.5%) patients. There were no statistically significant differences between the two groups for any demographic or baseline characteristics. Of the 40 recruited patients, 3 were excluded for not returning for the postoperative followup evaluation, including one from Group 1 and 2 from Group 2. In the two groups, significant improvements in the continent status were observed at week 12. In Group one, 18 (85.7%) were totally continent or had less than one episode of urinary incontinence/day while In Group 2, 10 (62.5%) had achieved the same level of continence.
Urodynamic findings: Within group comparisons: In both groups, a significant number of patients became arreflexic at the 12 week evaluation, including 11 (52.4%) patients in Group 1 and 6 (37.5%) in Group 2. Cystometric capacity was significantly improved in both groups. It increased from 184 $\pm$ 61 to 374 $\pm$ 109 ml ($p<0.001$) in Group 1 and from 229 $\pm$ 100 to 312 $\pm$ 120 ml ($p=0.004$) in Group 2. Reflex volume varied from 180 $\pm$ 78 to 225 $\pm$ 78 ml ($p=0.145$) in Group 1 and from 182 $\pm$ 83 to 197 $\pm$ 101 ml ($p=0.160$) in Group 2. Maximum detrusor pressure reduced from 68 $\pm$ 32 to 27 $\pm$ 17 cmH2O ($p<0.001$) in Group 1 and from 73 $\pm$ 26 to 42 $\pm$ 26 cmH2O ($p=0.005$) in Group 2. Compliance increased from 19 $\pm$ 12 to 43 $\pm$ 29 ml/cmH2O ($p<0.001$) in Group 1 and from 21 $\pm$ 11 to 42 $\pm$ 40 ml/cmH2O ($p=0.046$) in Group 2. Between group comparisons revealed a significantly higher change in Group 1 in terms of cystometric capacity in comparison with Group 2 ($p= 0.019$). No significant adverse event wa noted in any patient. Mild events included 2 cases of transient hematuria in the first postoperative day (not requiring specific treatment) and 3 cases of urinary tract infection.

Interpretation of results
Determining a more precise role of the different formulations of BTX-A in the treatment of detrusor iveractivity is of paramount importance, because botulinum toxin type A treatments have a huge economic implication in health services, especially in developing countries. While our study was not designed to compare the two different BTX-A formulations, an umpredictable change of the hospital supplier of BTX-A gave us the opportunity to evaluate the new formulation (Prosigne) and compare its effects in the detrusor with those of Botox. Given the significantly lower costs of Prosigne, it is expected that this drug may gain a significant share of the BTX-A market if it proves to be as effective and safe as the other formulations. In the present study. we used the same BTX-A dose for both drugs, since Prosigne manufacturers claim that the two formulations are comparable in potency. Patients from each group did not differ significantly in any of the baseline parameters. Botox promoted a significantly greater increase in bladder capacity and showed a tendency for better results in other clinical and urodynamic parameters in this short-term follow-up. Both drugs were well tolerated by patients and no significant adverse event occurred in any group. Whether Botox and Prosigne have different effects on the detrusor of patients with neurogenic detrusor overactivity or other causes of voiding dysfunction will need further studies, with a randomized design and longer follow-up.

Concluding message
Despite the limitations of this study, our results suggest that Prosigne and Botox are not comparable with respect to efficacy for the short-term treatment of neurogenic detrusor overactivity. Future studies should explore further the comparability of different BTX-A formulations based on cost-effectiveness.

References

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