

DOES PRIOR TREATMENT WITH INTRAVESICAL BOTULINUM TOXIN A AFFECT THE OUTCOME OF SACRAL NEUROMODULATION EVALUATION IN PATIENTS WITH REFRACTORY DETRUSOR OVERACTIVITY?

Hypothesis / aims of study

Patients with overactive bladder syndrome refractory to behavioural interventions and pharmacotherapy remain a difficult-to-treat population. Second-line treatment options include either intravesical injection of botulinum toxin A or sacral neuromodulation (SNM). Whilst neuromodulation requires surgical intervention for both test evaluations and permanent implantation, the use of intravesical botulinum toxin requires repeated treatments, with the potential for development of urinary tract infections, incomplete emptying and need for intermittent self-catheterisation.

In the UK, the National Institute for Health and Care Excellence (NICE) guideline for incontinence recommends both botulinum toxin A injections and sacral neuromodulation to treat refractory detrusor overactivity⁽¹⁾. Currently NICE suggest botulinum toxin should be tried before SNM. Despite this, the guideline highlights the lack of consensus on which treatment option is the most effective, and there is scant data available on whether administration of botulinum toxin affects the efficacy of subsequent neuromodulation. The American Urological Association (AUA) guideline on overactive bladder recommends both botulinum toxin A injections and sacral neuromodulation as treatments for refractory detrusor overactivity⁽²⁾, but without any recommendation as to sequencing. There is therefore an evidence gap with regards to the correct sequencing of treatments for this patient group, the only current identifiable data coming from a low volume observational study⁽³⁾.

We aimed to determine whether there is an observed difference in the objective success rates of SNM evaluations in patients with overactive bladder who received prior treatment with botulinum toxin A, when compared to those who proceeded straight to sacral neuromodulation following failure of medical therapy.

Study design, materials and methods

Trials of sacral neuromodulation were performed by a single surgeon using either a unipolar wire electrode (PNE) or a quadripolar electrode (first stage tined lead, FSTLP), between September 2011 and June 2014.

Data was prospectively collected from consecutive patients undergoing SNM between the above dates using voiding diaries. Review of medical records collected both objective and subjective outcomes. Objective parameters included: daytime frequency, nocturia, incontinent episodes and voided volumes. Primary outcome measures were objective success rate; defined as $\geq 50\%$ improvement in ≥ 2 of the above parameters, and subjective success (patient reported). Those with incomplete records were excluded.

All patients underwent urodynamics confirming a diagnosis of detrusor overactivity +/- incontinence.

Results

73 patients were identified and 62 procedures were included (84.9%). The 11 patients who were excluded from analysis were those who had failed to adequately complete voiding diaries or did not attend for follow up. 36 patients had previously received botulinum injections (58%). The majority of patients underwent test SNM by PNE (94%), with only 4 patients receiving FSTLP.

In the prior botulinum group the median number of intravesical treatments was 1 (range 1-5). The majority (86.4%) received a 200 unit dose, which is the standard in our centre. Mean interval between last botulinum toxin A injection and first SNM evaluation was 665.6 days (range 190-1896 days). 2/3 of patients had discontinued botulinum toxin injections due to lack of efficacy, and the other 1/3 because of incomplete emptying with or without the need for intermittent self-catheterisation.

The objective success rate for the botulinum group was 62.86% compared to 61.54% in the primary neuromodulation group. Concordance between objective and subjective success (patient reported) was 69.4% and 76.9% respectively.

For further analysis we stratified the 14 patients undergoing their first SNM evaluation by the interval between the last botulinum treatment and the procedure date. This identified a trend towards better outcome of SNM evaluation if the patients had a shorter interval time. The 7 patients with shorter intervals (190-420 days) had an objective success rate of 85.7%, compared with 42.9% in the 7 patients with a longer interval between treatments (526-1896 days). This is statistically significant using a Z-test ($p < 0.05$).

Interpretation of results

We have not demonstrated any significant difference in the success rates of SNM evaluation when comparing patients who have or have not received prior botulinum toxin A treatment, suggesting that this sequence does not have a negative effect.

We demonstrated a trend towards better objective success rate with a shorter interval time between last botulinum treatment and 1st neuromodulation evaluation, however this analysis was within a small group of patients. It is unclear from our data what the potential cause of this trend is, and if it would be reproducible across a larger population of patients undergoing their 1st SNM after botulinum toxin A injections.

Concluding message

Patients who have failed to respond to botulinum toxin treatment or who develop side effects such as incomplete emptying should be considered for further treatment of their refractory detrusor overactivity with sacral neuromodulation. The aim of treating these patients should be to avoid unnecessary delays in progressing onto further treatments once a lack of or inadequate response is identified to achieve the best outcomes. Current sequencing of treatments as per UK and US guidelines does not appear to be to the detriment of treatment outcome. It is likely that further guidelines with regards to sequencing will be based mainly on cost-effectiveness data, which can only be accurately demonstrated within the confines of a randomised control trial with an adequate follow up period.

References

1. National Institute for Health and Care Excellence. Urinary incontinence: The management of urinary incontinence in women (CG 171). Available at: <https://www.nice.org.uk/guidance/cg171>. Accessed 31/03/2015
2. American Urological Association. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. Available at: <http://www.auanet.org/common/pdf/education/clinical-guidance/Overactive-Bladder.pdf> Accessed 31/03/2015
3. Smits MA et al. Sacral neuromodulation in patients with idiopathic overactive bladder after initial botulinum toxin therapy. J Urol. 2013 Dec;190(6):2148-52. Available from: doi: 10.1016/j.juro.2013.07.017. Accessed 31/03/2015

Disclosures

Funding: Nil to disclose **Clinical Trial:** No **Subjects:** HUMAN **Ethics not Req'd:** Clinical audit without any identifiable data.
Helsinki: Yes **Informed Consent:** Yes