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FUNCTIONAL UROLOGY

# 300 IU vs. 200 IU of OnabotulinumtoxinA for detrusor overactivity

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Botulinum toxin is probably the newest addition in the treatment armamentarium for overactive bladder, but, despite its late FDA approval, a significant experience exists in several centers around the world with this type of treatment. Because of its experimental status, the treatment with botulinum toxin is still lacking the much needed standardization, allowing for a great variety when it comes to dosing, frequency and injection sites.

Although the efficacy of this treatment is well proven, the correct dose for each particular condition is still a matter of debate, despite a vast number of dose finding clinical trials. The authors of this paper report data from a retrospective analysis done in a single center with significant experience [1]. The idea behind their work is to assess the efficacy of treatment with botulinum toxin, using a significantly lower dose, in patients with neurogenic or idiopathic detrusor overactivity. The rationale behind the plan to decrease the toxin dose is based on strong evidence from literature, which led to a change in the standard of care offered in their institution about five years ago.

The study population included patients with proven detrusor overactivity who started treatment with the standard dose of 300 IU and were then shifted to the lower dose of 200 IU. The results were then compared, with the main focus set on efficacy. The tools for this assessment were limited to interview and bladder diary, both being subject to interpretation and potential subjectivity. This raises the discussion of the objectivity of the conclusions that are not supported by urodynamic measurements. This could reveal increased storage pressures and other potentially dangerous conditions that don't have a clinical expression for the moment but may lead to serious complications, especially in the neurogenic bladder group. It is a known saying that the bladder is an unreliable witness, and such investigation protocol leaves a great amount of matters unaddressed. There are many aspects which raise questions, such as injecting or avoiding the trigone, the underlying condition behind the neurogenic bladder and the concomitant medication of each patient. Another aspect which is not clear is the previous treatment each patient had for detrusor overactivity, which could further bias the response and tolerability to botulinum toxin. A classical talk related to the treatment for detrusor overactivity is about adherence and persistence. These aspects are not discussed by the authors, although it seems that only one patient was lost to follow up. The overall conclusion of this study is that if one has reasons to start botulinum toxin treatment with the 300 IU dose, might want to try lowering the dose to 200 IU.

The results of the study show that down titration is both safe and effective, while most patients are satisfied with the results of their treatment. Because the patients were informed about the decrease of the dose, the continued improvement can't be attributed to the placebo effect.

In the neurogenic bladder group, the majority of patients reported similar outcomes after treatment with botulinum toxin of the lower dose, compared to the initial dose of 300 IU. Only one patient reported a significantly reduced effect after 200 IU of toxin, but we can speculate that shifting back to 300 IU would bring back the better effect.

The idiopathic detrusor overactivity group showed an overall similar response to 200 IU compared to the initial 300 IU dose, although the results are slightly less optimistic if compared to the neurogenic bladder group. One interesting aspect is that 7% of these patients had to start intermittent catheterization after receiving the lower dose of toxin, and the authors do not offer any explanation of this de novo retention.

The authors report about 25% incidence of UTI in their study group, but we speculate that this is not related to the dose used, but more to the procedure itself, so it is less relevant for the final results.



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There are some similar studies in literature, showing similar results concerning both safety and efficacy. One study even offers urodynamic data to support the results. Another aspect in discussion is the price of the treatment using the lower dose. Depending on each medical system, the price of 200 IU might be equal or significantly lower compared to 300 IU. A decrease of the total price of the treatment could mean more patients treated, better availability of the drug or could even make the difference between the substances being reimbursed or not for the patient.

The study concludes that down–titration is effective and feasible, although some patients may require returning to their initial dose. This is a pioneering work, which will need further support from larger scale trials in order to establish a recommendation concerning the doses that are to be used for each patient.
The authors did a great job putting together a study which is based on their current practice, and in giving the medical community good evidence on down–titration of botulinum toxin for detrusor overactivity.

## References

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