



## Letter to the Editor

**Reply to Giuseppe Brisinda, Serafino Vanella and Giorgio Maria's Letter to the Editor re: Athanassios Oeconomou, Helmut Madersbacher, Gustav Kiss, Thomas J. Berger, Michael Melekos and Peter Rehder. Is Botulinum Neurotoxin Type A (BoNT-A) a Novel Therapy for Lower Urinary Tract Symptoms Due to Benign Prostatic Enlargement? A Review of the Literature. Eur Urol 2008;54:765–77**

During the last decade, use of botulinum neurotoxin type A (BoNT-A) became popular for a number of indications in the urologic field [1–5], although it was not yet licensed for them. This widespread use of BoNT-A underlines the pressing need for studies with a high level of evidence and a high grade of recommendation.

We concluded our review of the literature [5] with the following statement: “What we need are large scale, clinical, placebo-controlled, randomized studies, including long-term surveillance.” Additionally, according to the recently published European Consensus Report on recommendations on the use of botulinum toxin in the treatment of lower urinary tract disorders and pelvic floor dysfunctions [6], the grade of recommendation for the need of further placebo controlled studies on BoNT-A in benign prostatic enlargement associated with lower urinary tract symptoms (LUTS) is A.

We read, with interest, the study by Brisinda et al [7], which partly fulfils these demands. Although their study provides long-term results up to 30 mo after single or repeated injection of 200 U of BoNT-A, the study remains open label with a low level of evidence. The authors demonstrated sustained efficacy (in terms of American Urological Association symptom score, prostate-specific antigen, prostatic volume reduction, and increase of peak urinary flow rate) during follow-up and similar safety of intraprostatic injection of BoNT-A in comparison with the previously published studies [5]; however, almost half of the patients (36 of 77) required BoNT-A reinjection during the follow-up period. Why was reinjection needed? This subgroup of patients should be further analyzed to identify reasons for treatment failure.

Some of the data are not clear to us. Brisinda et al [7] state: “At the 18-month evaluation, all 77 patients reported good voiding condition without worsening of LUTS or urinary retention development. At the 24-month evaluation, 63 patients continued to have satisfactory voiding.”

The authors then state, “We proposed a rescue treatment to the 7 patients without symptomatic improvement,” but the authors do not report the time frame during which these 7 patients are without symptomatic improvement. Later in the paper, the authors state, “At the 30-month evaluation all 77 patients continued to have good voiding without worsening of LUTS or development of urinary retention.” It is unclear to us how seven patients who did not get a rescue treatment at 24-month evaluation and who, at that time, did not belong to that group with satisfactory voiding were able to achieve good voiding without treatment and without worsening of LUTS or development of urinary retention at 30 mo. How was good voiding “continued” for these patients?

This lack of clarity further stresses the need for a placebo-controlled study, with a larger number of patients, to document the evidence of this therapy and, eventually, to register BoNT-A for this indication. The only placebo-controlled study to date is from Maria et al [8]; however, that study only included 30 patients.

Finally, it is hasty to claim an anticancer effect of BoNT-A based on the limited experience from an open-label study with 30 mo of follow-up without a biopsy protocol. Further studies are required to reach to such an important conclusion.

We should recognize that, at present, this therapy is still experimental. Although the results of the clinical studies are encouraging, the level of evidence is low. Clearly, we need large-scale, clinical, placebo-controlled, randomized studies, including long-term surveillance, to determine the best route, the best sites within the prostate for BoNT-A injections, suitable dosing and dilution, long-term effects, and safety. Moreover, comparative studies with  $\alpha$ 1-blockers, 5 $\alpha$ -reductase inhibitors, and transurethral resection of the prostate are required. The potential effects of BoNT-A on erectile function, on risk of retrograde ejaculation, and on sperm abnormalities and the potential role of BoNT-A in the treatment of chronic pelvic pain syndrome and prostate cancer should be considered as areas for future investigation.

*Conflicts of interest:* The authors have nothing to disclose.

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