Editorial

Third-line treatment options for refractory urgency urinary incontinence in women—a commentary to ROSETTA trial

Pawel Miotla, Tomasz Rechberger

2nd Department of Gynaecology, Medical University of Lublin, Lublin, Poland

Correspondence to: Dr Pawel Miotla. 2nd Department of Gynaecology, Medical University of Lublin, ul. Jaczewskiego 8, 20-954 Lublin, Poland. Email: pmiotla@wp.pl.

Comment on: Amundsen CL, Richter HE, Menefee SA, *et al.* OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women: A Randomized Clinical Trial. JAMA 2016;316:1366-74.

Received: 14 January 2017; Accepted: 20 February 2017; Published: 21 March 2017.

doi: 10.21037/jxym.2017.03.09

View this article at: http://dx.doi.org/10.21037/jxym.2017.03.09

According to the American Urological Association (AUA) and Society of Urodynamics and Female Urology (SUFU) guidelines third-line treatment options for refractory overactive bladder (OAB) include: intradetrusor onabotulinumtoxinA injections (100 units, Botox, Allergan) or sacral neuromodulation (SNS), or peripheral tibial nerve stimulation (PTNS). Intravesical onabotulinumtoxinA injections are ranked as standard treatment (evidence strength: grade B), which is equally to the strongest statement. AUA/SUFU guidelines rank SNS and PTNS as recommended option (evidence strength: grade C). Patients qualified for intravesical onabotulinumtoxinA injections should be warned about the potential risk of urine retention and must be willing to perform clean intermittent self-catheterization (CISC). Sacral neuromodulation may be offered to selected patients, who are willing to undergo two-step surgical procedure (1). SNS is also benefit for patients with idiopathic urinary retention and with urgency symptoms. However, there is still a lack of evidence, which third-line treatment option is superior in patients with refractory overactive bladder (OAB). Interestingly, in the recent study published by Hashim *et al.* (2) 34% patients with refractory OAB were willing to try sacral neuromodulation and only 9% of patients preferred intravesical Botox injections as a third-line treatment option. On the other hand it is much easier for physicians to inject the detrusor with onabotulinumtoxinA than implant the neurostimulator (the learning curve for Botox is very short and interestingly enough treatment effectiveness does not depend on the experience of performing physician). We should also remember about the cost of procedures. In many countries there is still no health reimbursement either for onabotulinumtoxinA nor SNS.

Amundsen *et al.* (3) in the prospective, open-label study have assessed the efficacy, quality of life outcomes and adverse events in women with refractory urgency incontinence (UI) treated with onabotulinumtoxinA injections or sacral neuromodulation. Female patients with at least 6 urgency urinary incontinence episodes reported in 3-day bladder diary were included into this study. Women with UI in ROSETTA study (The Refractory Overactive Bladder: Sacral Neuromodulation *vs.* Botulinum Toxin Assessment) trial were randomly assigned for onabotulinumtoxinA injections (200 units, Botox, Allergan) or to undergo sacral neuromodulation (Interstim, Medtronic). This study was conducted since 2012 and in this period of time there was still no consensus, which dose of onabotulinumtoxinA was most preferable to OAB treatment. Included patients were instructed to avoid additional treatment for OAB during participation in ROSETTA trial. According to the United States Food and Drug Administration (FDA) guidelines concerning SNS treatment only patients with at least 50% improvement in urgency incontinence episodes in testing phase received permanent sacral neurostimulation implant. Women who did not respond to neurostimulation in testing phase were excluded from participation in trial. However, there is impossible to predict which patients will not respond to onabotulinumtoxinA. Therefore, response to treatment in onabotulinumtoxinA group was defined as ≥50% reduction in urgency incontinence episodes at week 4.

After 6 months, 26 (20.4 %) patients in onabotulinumtoxinA group and 2 (2 %) in SNS group were completely dry and the rate of dryness was significantly higher in the first group (P<0.001). Moreover, the percentage of ≥75% reduction in urgency incontinence episodes was also significantly higher in patients treated with onabotulinumtoxinA in comparison to SNS, 50% *vs.* 27%, respectively (P=0.004). At 6 months follow-up the greater reduction of the mean number of urgency incontinence episodes in 3-day bladder diary was observed in onabotulinumtoxinA group in comparison to sacral neuromodulation (–3.89 *vs.* –3.25, respectively, P=0.01). Greater improvements in the Overactive Bladder Satisfaction questionnaires were observed in Botox group for treatment and endorsement domains. Interestingly, there was no difference between SNS and onabotulinumtoxinA groups in other domains, including treatment preference, convenience and adverse effects. However, the need for performing CISC was observed in 38 (20%) patients injected with onabotulinumtoxinA and none of the women in SNS group required CISC. Moreover, the risk or urinary tract infection (UTI) was three times higher in onabotulinumtoxinA group (35% *vs.* 11% in SNS group, P<0.001). Only 3% of patients in SNS group required surgical wound revision or removal of neurostimulator. Dmochowski *et al.* (4) have observed a dose dependent, transient increase in post-void residual after Botox treatment with the greatest increase at the 200 units dose. Twenty percent of the patients injected with 200 units onabotulinumtoxinA required CISC, whilst in 100 units group this number decreased to 11%. They have also noticed that over 40% of patients in 200 units group reported UTI symptoms. The optimal balance between efficacy and adverse events was observed in 100 units dose. In January 2013 the United States Food and Drug Administration has approved use of Botox (100 units) to treat adult OAB patients with urgency urinary incontinence.

Based on results of this study and previous randomized clinical trials we can conclude that all patients should be warned before receiving onabotulinumtoxinA injections about the potential risk of urine retention. In our department patients who perform CISC are checked with abdominal ultrasound in out-patient clinic every 7-10 days. Moreover, the kidneys' scans are performed in all patients with urine retention due to the risk of upper urinary tract dilation and renal insufficiency. Patients on CISC are advised to take oral antibiotic prophylaxis as prevention of urinary tract infection. CISC is stopped when the patient have no clinical symptoms and post-void residual as measured by ultrasonography was smaller than 300 ml. Patients may have great concerns about the technical aspects of CISC performing, because it depends on patients' dexterity. Therefore, for this reason SNS might be superior than intravesical onabotulinumtoxinA in patients with impaired mobility.

The ROSETTA trial is the first study, which directly compares the effectiveness of onabotulinumtoxinA *vs.* sacral neuromodulation in the treatment of refractory urgency urinary incontinence. The results showed slightly greater reduction of urgency urinary incontinence episodes in onabotulinumtoxinA group. The major limitations of the study published by Amundsen *et al.* were: the lack of placebo control group and the lack of male patients with urgency urinary incontinence. Women in this study were treated with 200 units dose, which can be consider as suboptimal. Finally, there is still a need to find out whose OAB patients will be more satisfied with onabotulinumtoxinA injections or SNS.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned and reviewed by the Section Editor Longfei Liu, MD, PhD and Assistant Editor Zhao Wang, MD (Department of Urology, Xiangya Hospital, Central South University, Changsha, China).

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jxym.2017.03.09). Miotla P. serves as speaker, paid investigator for Allergan, Astellas, Bayer. Rechberger T serves as speaker, paid investigator for Allergan, Astellas, Bayer.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Gormley EA, Lightner DJ, Faraday M, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. J Urol 2015;193:1572-80.
2. Hashim H, Beusterien K, Bridges JF, et al. Patient preferences for treating refractory overactive bladder in the UK. Int Urol Nephrol 2015;47:1619-27.
3. Amundsen CL, Richter HE, Menefee SA, et al. OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women: A Randomized Clinical Trial. JAMA 2016;316:1366-74.
4. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol 2010;184:2416-22.

doi: 10.21037/jxym.2017.03.09
Cite this article as: Miotla P, Rechberger T. Third-line treatment options for refractory urgency urinary incontinence in women—a commentary to ROSETTA trial. J Xiangya Med 2017;2:27.