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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology

ESPS manuscript NO: 22809

Title: How botulinum toxin in neurogenic detrusor overactivity can reduce upper urinary tract damage ?

Reviewer's code: 03433656

Reviewer's country: United States

Science editor: Jin-Xin Kong

Date sent for review: 2015-10-06 00:34

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> [Y] Grade B: Very good	<input type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> [Y] No	<input type="checkbox"/> [] Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

A very nice review on a clinically relevant topic that is increasingly being incorporated in our practices. It is critical to understand the pathophysiologic mechanism of botox to easily identify potential complications of the treatment and to maximize its clinical potential as we are still very much exploring how to maximize the utility of this drug in our clinical practice. A few comments on the paper a. in the section covering the urodynamic changes seen with injection, there is a lot of data mentioned. As this is a review tailored for a non-urologic population, the data should be simplified to include only data relevant to the upper tract deterioration and decrease in detrusor pressure, which is the focus of the paper. Rather than incontinence data etc. which are important to mention but not critical for the goal of preserving the upper tract. b. In the section of the pathophysiology. Please elucidate on the Hoffman reflex c. in the section on VUR and botox, it is important to note that in pediatric populations it indicated the utility of urodynamics prior to VUR repair. As primary VUR may reflect a dysfunctional voider or unrecognized neurologically induced high pressure voiding rather than an anatomical defect. d. lastly although it is mentioned in the



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introduction, it should be mentioned that when DO is associated with DSD, botox can be used in some cases at the sphincter as opposed to intravesical injections. Perhaps a comment can be made indicating that when DSD is present with neurogenic DO, upper tract preservation may be better preserved by reducing outlet obstruction rather than detrusor hypereflexia



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Title: How botulinum toxin in neurogenic detrusor overactivity can reduce upper urinary tract damage ?

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Reviewer's country: Greece

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors are invited to address the following points: 1. In the proof of concept study Schurch et al had injected 300 U of Botox, not 200 IU. Please correct 2. Also, Schurch et al did not compare 200 to 300U Botox, as their study was not designed to detect differences between the 2 doses. This needs to be clarified. 3. The authors spend a good size text in the Bladder effect section pinpointing some studies from the earlier literature on Botox and NDO, but there are already several systematic reviews discussing this comprehensively and producing accumulative data which the authors could have used instead. Please include collective data from systematic reviews 4. Discussion of UTI pathophysiology is confusing. The authors have not taken a robust route on whether Botox actually decreases or increases UTIs. As a result they produce hypotheses on both induction of UTIs by Botox and decrease of UTIs by Botox in the same paragraph! Please revise appropriately. Further, they have not discussed the apparent discrepancies between level of evidence 3 studies which show a decrease of UTIs and the level of evidence 1 studies which show no change in SCI patients and a definitive increase in MS patients. Please discuss 5. Despite improvements seen in VUR after BTX-A injections,



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results also suggest a surprising decrease in GFR. The discussion proposed by the authors is not satisfactory, particularly since Botox has been found to reduce all risk factors for renal impairment in SCI patients. Could other factors, such as retrograde transport of the toxin to the kidney have such a contradictory effect? Please discuss if appropriate 6. Conclusions are not justified by the evidence the authors have produced in the manuscript! Please revise accurately 7. Extensive editing is needed as a lot of typos can be identified throughout the manuscript 8. The title of the manuscript could be revised to something less ambitious. For example, CAN BOTULINUM TOXIN IN NEUROGENIC DETRUSOR OVERACTIVITY REDUCE UPPER URINARY TRACT DAMAGE?