Reviewer's report

Title: Unilateral versus bilateral thyroarytenoid Botulinum toxin injections of in adductor spasmodic dysphonia

Version: 1 Date: 8 December 2008

Reviewer: Youri Maryn

Reviewer's report:

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MAJOR COMPULSORY REVISIONS
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ABSTRACT - Objectives
"We also developed a Neurophysiological Scoring (NPS) system which has utility in the treatment administration".

> The reviewer certainly can support any method to improve communication between disciplines (in this case neurophysiology and ENT). However, NPS is not under research in this article and has not been under research in earlier studies (as far as the reviewer can tell), and thus its utility has not been proven. The reviewer suggests to mention only that the Dysport infiltrations were done under EMG-guidance, without elaboration on NPS, throughout the whole manuscript. Furthermore, the authors can mention that they used this scale on a non-inferential basis. Another suggestion would be to add elaboration and discussion on NPS, especially in the results section.

INTRODUCTION - page 4
"ADSD, a disabling disorder of voice, is characterised by involuntary disruption of phonation with functional, social and emotional consequences."

> The author can agree with this sentence but would like to ask the authors to validate this sentence with references.

INTRODUCTION - page 5
"The toxin has seven serotypes (A-G)."

> Which serotype(s) is (are) typically used in SD-patients?

INTRODUCTION - page 5
"... Both unilateral and bilateral thyroarytenoid muscle injections have been reported to be successful. To date, published literature has been inconclusive in comparing their effectiveness [2-5]."

> What about the references 10, 14 and 16? These references seem to be especially interesting in the discussion of this specific item and therefore the reviewer wonders if the outcomes of these studies were considered in the
introduction of this manuscript.

INTRODUCTION - page 6

"... and had completed 5 concomitant self-rated efficacy and complication scores questionnaires related to the previous injections."

> Everywhere in the text is mentioned that the subjects filled in questionnaires etc. on 5 moments. However, in Figures 3 and 5 there are only 4 moments of data gathering related to voice score and interval between injections, respectively. This is not clear for the reviewer and necessitates further explanation.

MATERIALS AND METHOD - general remarks

> A lot of important information on the subjects is provided in Table 4. However, this table is introduced in the results section. Shouldn't this table (or parts of this table) be introduced in the methods section?

> How was ADSD initially diagnosed? Was there a specific clinical assessment protocol (perception, laryngoscopy, ...) followed or was the diagnosis of ADSD based on therapeutic trial? Was there differential diagnosis with for example MTD considered?

> Table 1: shouldn't a table have at least two columns? The reviewer suggests to omit Table 1 and to integrate its 4 items in the text.

RESULTS – general remarks

> The manuscript should also state when the data were gathered. Except for the fact that data related to the previous injections were gathered, the reviewer can't find any information on when the data were gathered. However, given the time-related variance in the effect of the toxin, this is an important issue. Where the questionnaires answered immediately before a new injection?

> The description of the results on page 11 would be helped with the referral to their respective Figures (for example Figure 3 where the voice score results are described).

RESULTS – page 10

“... was 136 days as compared to 122 in the bilateral group (Figures 3, 4 and 6).”

> This information is given in Table 4 and in Figures 5 and 6, and not in Figures 3 and 4 (?).

> Table 4 says that in the unilateral group there was a mean interval of 132.05 days in stead of 136 days as mentioned in the text. Is this a misinterpretation by the reviewer?

RESULTS – page 10

“The averaged voice score of 94% is consistent with other published results reported.”

> What are the references of the published results/studies?
RESULTS – page 10
“Our study revealed greater mean dysphagia duration and a shorter breathiness with the bilateral injections … were not statistically significant.”

> “Greater mean dysphagia duration” seems to indicate a more negative result when comparing bilateral and unilateral injections. “Shorter breathiness” on the other hand seems to indicate a more positive result. Is this a correct interpretation? If so, it is strange that both results, the one negative and the other positive, are mention in one and the same sentence. Is it possible to mention both results separately?

DISCUSSION – page 13
“The efficacy and complications profile were not significantly different.”

> What is meant with “efficacy profile”? Is it the voice score, or is it something else?

DISCUSSION – page 13
“Reduced afferent feedback may cause … to the contra-lateral larynx.”

> Are there references or rationale to validate this statement? If yes, please elaborate more profoundly. If no, address other explanations or state that the findings remain unexplained.

DISCUSSION – page 13
“We used a lower equivalent … than in many published studies …”

> The authors should at least give one or more references of such studies.

DISCUSSION – page 13
“We used a lower equivalent dose of Botox® preparation (Dysport®) than in many published studies but with similar effectiveness. It is possible that this is due to more exact needle placement guided by the electrophysiological waveform of the laryngeal adductors.”

> Do the authors mean that the injections in other voice clinics (from the other studies) are not EMG guided? Do the authors have objective arguments to state that their injections are better done than the injections in other clinics? If there is no objective control of this feature, the authors should omit this suggestion.

DISCUSSION – page 14
“This supports the cumulative dose theory …”

> Much further an explanation is given for this theory (page 16). However, it would be more appropriate (and reader-friendly) to mention this theory already in the introduction and to offer there an explanation.

DISCUSSION – page 15
“… there may be a patient reporting bias.”
If this bias truly is the case, how reliable are the results of this study? What is measured than: the thoughness of the case (bilateral because earlier therapy was insufficient) or the effect of bilateral versus unilateral injection? This is an important methodological issue. Are the statistically not significant worse results, for example for voice score, due to the therapeutic choice (bi vs. uni), or just due to the fact that the cases with bilateral injections were harder to treat or had more severe ADSD already before the study started? This question is hard to answer considering the experimental setup.

DISCUSSION – page 18

“Some studies including … varied and remain controversial.”

This short paragraph comes out of nowhere and is rather solitary in the surrounding texts. Can’t this discussion be integrated in another paragraph where the comparison of Botox® and Dysport® is discussed.

DISCUSSION – page 18

“The neurophysiological score (NPS) … and specificity of the EMG response.”

The term “specificity” really needs further classification in this context, especially because it is a methodologically important term (in the context of diagnostic precision etc.). It is unclear to the reviewer what is exactly meant with this term in the context of EMG response: is it that EMG indicates a ‘healthy’ person correctly as being ‘healthy’?

FIGURE 3 – Figure’s caption

“… Showing a trend for the unilateral group …”

In the results section, we find the following text: “There was a significant difference in the mean voice score between unilateral and bilateral groups with the unilateral groups doing better (Student t test p<0.05).” However, it is the intuition of the reviewer that there is at least a semantic difference between a trend and a statistically significant item. A trend can or can’t be statistically significant. The reviewer suggests that this caption is edited, maybe with something like “a statistically significant trend” or …. 

MINOR ESSENTIAL REVISIONS

ABSTRACT - Method and materials

"... Dose and unilateral/ bilateral injections ..."

Remove space between "unilateral/" and "bilateral".

ABSTRACT - Conclusion

"... in the treatment of Adductor Spasmodic Dysphonia."

Use lower case in stead of Title Case.
INTRODUCTION - page 4
"ADSD, a disabling disorder of voice, is characterised by involuntary disruption of phonation with functional, social and emotional consequences."
> Shouldn't it be "characterized"?

INTRODUCTION - page 5
"in a reversible but long standing manner. The toxin ...
> Shouldn't it be "manner"?

INTRODUCTION - page 5
"... the dosing requirements ... has varied significantly ...
> Shouldn't it be "have"?

RESULTS – page 10
“... its 1st injection ...
> Shouldn't it be "first"?

DISCUSSION – page 13
“Reduced afferent feedback may cause … to the contra-lateral larynx.”
> Shouldn't it be “contralateral”?

DISCUSSION – page 17
“Moreno-Lopez et al. indicated that …”
> The reviewer can’t find this reference in the reference list.

CONCLUSION – page 20
“... the use of voice related quality of life V-RQOL.”
> Replace: “... the use of voice-related quality of life questionnaires (i.e. V-RQOL, VHI, etc.).

TABLE 4
In several cells of this table the sign “+/-” is used between two numbers. The reviewer believes that before this sign a mean of some variable is standing and that after this sign a standard deviation of the same variable is standing. However, the reviewer is not sure that that is correct and suggests to add some kind of legend (for example “mean (SD)” in the top cell of the columns).

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Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.