

Peer Review File

Article Information: <http://dx.doi.org/10.21037/ajo-21-1>

Reviewer A

Comment 1:

Unfortunately, the Introduction is too long, it should be shortened by summarizing evidences with less detail, focusing more on the topic of the article: neurogenic cough and botulinum toxin.

Reply 1:

Changes as below

Changes in the text:

- Introduction shortened from 658 to 462 words
- Focus on neurogenic cough and botulinum toxin in paragraphs 2, 3, 4

Comment 2:

Please add the diagnostic tests used on the "Adelaide protocol" to rule out the other causes of chronic cough

Reply 2:

- Paragraph 2 of the methods section of the manuscript notes that chest xray, pulmonary function tests were performed on all participants, and that CT sinuses and modified barium swallow were considered.
- Added that a sleep study was performed where OSA is suspected
- Additional information added regarding the diagnosis of allergic rhinitis

Changes in the text:

- Regarding allergic rhinitis, paragraph 2 in the methods now reads: *When a history consistent with allergic rhinitis was elicited, antihistamines and nasal corticosteroids were prescribed empirically. If there was an insufficient response, referral was made to an Immunologist with specific expertise in nasal allergy.*
- Regarding OSA, paragraph 2 in the methods now reads: *If screening questions for obstructive sleep apnoea (OSA) were positive, polysomnography was performed and appropriate treatment implemented if a diagnosis of OSA was made.*

Comment 3:

"Stroboscopic examination of the vocal cords was performed", please add why you performed this exam.

Reply 3:

Stroboscopy was used to assess the impact Botox injection had on the supraglottic tissues, specifically looking for subtle paresis not obvious on white light laryngoscopy.

Changes in the text:

Paragraph 7 of the methods section now reads: *Stroboscopic examination of the vocal cords was performed to assess for any subtle paresis not obvious on white light laryngoscopy.*

Comment 4:

line 193: "to assess for objective change" this is not an objective evaluation! Please change

Reply 4:

This has been changed

Changes in the text:

Paragraph 7 of the methods section now reads: *Pre- and post-procedure VAS, LCQ and NLHQ scores were compared to assess for change in the participants cough symptoms as a result of the Botox injection.*

Reviewer B

Comment 1:

My only comment would be enumerate the percentage of post-op dysphonia related to botox, including if any bilateral paresis was noted given synchronous bilateral injections.

Reply 1:

Regarding enumeration of post op complications, 1 patient had moderately weak voice, 2 had mildly weak voice, these lasted for the duration of Botox effect. Most patients anecdotally felt their voice was better post Botox injection. 5 patients had mild dysphagia, lasting 1-2 weeks. These were not measured in a formal way, but were recorded as mild, moderate or severe.

Regarding whether any bilateral paresis was noted, there were no signs of bilateral vocal cord paresis clinically. Stroboscopy was done to assess for subtle paresis not detectable on white light laryngoscopy, and there was no evidence of bilateral paresis in any of the cases of dysphonia.

Changes in the text:

Final paragraph of results now reads: Complications of the procedure included dysphonia and dysphagia. Dysphonia was reported in 3/20 (15%) of participants, one with a moderately weak voice and two with mild weakness. Minor dysphagia was common in the first two weeks after Botox injection, seen in 5 participants (25%), and anecdotally correlated with improvement in cough.

Comment 2:

Can the authors also comment on relapse rates beyond 6-9 months?

Reply 2:

The follow up duration of this study was a minimum of 6 months and a maximum of 12 months. 12 of the 20 patients were followed up to 12 months with no relapse in this time frame. An additional 2 patients were followed to 6 months with no relapse.

Relapse when the botox wore off occurred in 6 of the 20 patients, requiring multiple injections of botox to alleviate symptoms.

Anecdotally, long term follow up of these patients beyond 12 months suggests that recurrence rate is higher, however this was not part of the present study duration. A larger multicentre study with longer follow up periods is planned to further characterise this.

Changes in the text:

Discussion paragraph 7 now reads: *Studies with larger patient cohorts as well as a longer duration of follow up are needed to better characterise the efficacy and long-term effects and relapse rates of laryngeal Botox therapy.*

Comment 3:

Is reinjection offered?

Reply 3:

Yes, where relapse of symptoms occurs when the botox wears off around 3 months post treatment, reinjection with botox is offered. In our experience, patients are willing to have further injections given the symptom relief provided by botox therapy.

Changes in the text:

Paragraph 8 in the methods section now reads: *If symptoms recurred after Botox wore off, reinjection was offered.*

批注 [11]: New change