Clinical and electrophysiological correlates of Retrograde Cricopharyngeal Dysfunction (R-CPD) treated by EMG-guided Botulinum Toxin injection

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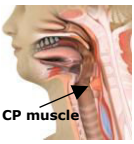
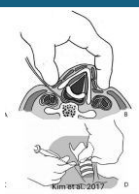
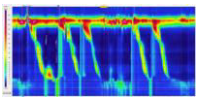
BACKGROUND

Retrograde cricopharyngeus dysfunction (R-CPD) is a disorder characterized by an inability to belch due to impaired cricopharyngeus muscle relaxation. The pathophysiology of R-CPD is unknown, and an altered esophageal motility is hypothesized to play a role in some patients. Standard treatment involves high-dose (50-100 U) bilateral endoscopic Botulinum Toxin (BoNT) injections under general anesthesia. This study evaluates the clinical effects of increasing doses (10 to 30 U) of EMG-guided unilateral BoNT injection in male and female patients and the electromyographic (EMG) parameters of the cricopharyngeus muscle.

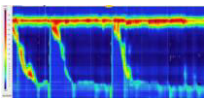




Injection technique: the needle is inserted laterally to the lateral edge of the cricoid cartilage at an angle of approximately 45°



Swallowing

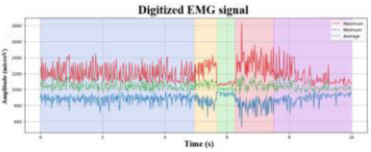


Provocative test with 200 mL of sparkling water

High-resolution manometry in a patient with R-CPD

METHODS

A total of 67 patients were screened and treated (40 females and 27 males). Of these, 22 received a low-dose (10-20 U) and 45 a medium-dose (25-30 U) BoNT injection. Symptom severity and quality of life were assessed at baseline, and at 1 and 4 months post-treatment. Patients were classified as responders with a satisfaction score ≥6/10 at 1-month post-treatment. We also investigated treatment response comparing the improvement across the two dosage groups and between sexes. EMG parameters of the cricopharyngeus were recorded to explore their association with symptom burden and treatment response.



Electromyographic analysis of cricopharyngeus muscle activity during dry swallowing in a RCPD patient

First domain	Second domain
Ability to burp: complete inability to burp: 56/67 patients (83.6%); incomplete burping, achievable only through specific strategies: 11/67 (16.4%)	**Anxiety symptoms:** 26/67 (39%)
Burp frequency: never: 53/67 (79%); rarely: 14/67 (21%)	**Retrosternal heartburn or acid reflux episodes:** 44/67 (66%)
Gurgling noises: 64/67 (95.5%)	**Improvement of symptoms in lying-down position:** improvement: 30/67 (45%); no difference: 21/67 (31%); worsening: 16/67 (24%)
Abdominal bloating: 62/67 (92.5%)	**Symptom progression throughout the day (from morning to evening):** worsening: 60/67 (90%); no difference: 5/67 (7%); improvement: 2/67 (3%)
Discomfort or pain in the chest after meals: 62/67 (92.5%)	**Smoke:** non-smokers: 53/67 (79%)
Flatulence: 67/67 (100%)	**Alcohol:** abstainers: 24/67 (36%); occasional/social drinkers: 42/67 (63%); daily consumption: 1/67 (1.5%)
Frequency of hiccups: increased frequency: 44/67 (66%)	**At least one first-degree relative affected:** 8/67 (12%)
Painful hiccups: 59/67 (88%)	**Emetophobia:** 33/67 (49%)
Difficulty swallowing solid foods: 14/67 (21%)	**Effortful vomiting:** 43/63 (68%)
Difficulty swallowing liquids: 14/67 (21%)	**Perception of delayed esophageal transit:** 34/67 (51%)
Foods and/or drinks avoidance: always: 26/67 (39%); often: 23/67(34%); sometimes: 8/67 (12%); never/rarely: 10/67 (15%)	
Social avoidance: always: 6/67 (9%); often: 12/67 (18%); sometimes: 16/67 (24%); rarely: 17/67(25%); never: 16/67 (24%)	
Self-reported global impact on QoL (scale 0-10): 9-10: 35/67 (52.2%); 7-8: 29/67 (43.3%); 5-6: 3/67 (4.4%)	

Clinical assessment questionnaire of 67 patients

RESULTS

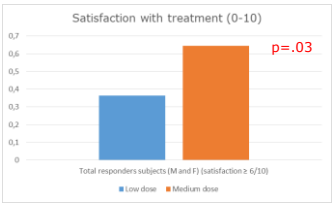


Figure 1. Satisfaction with treatment (1-month follow-up) between low and medium dose in all patients, male and females. Statistically significant difference (p=0.03) in satisfaction with medium dose.

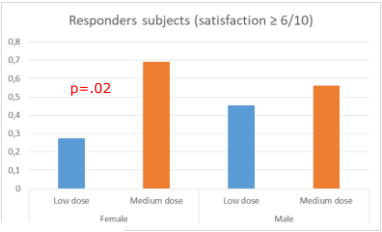


Figure 2. Treatment response to low and medium dose at 1-month follow-up: comparison between males and females. Statistically significant difference (p=0.02) in females treated with medium dose.

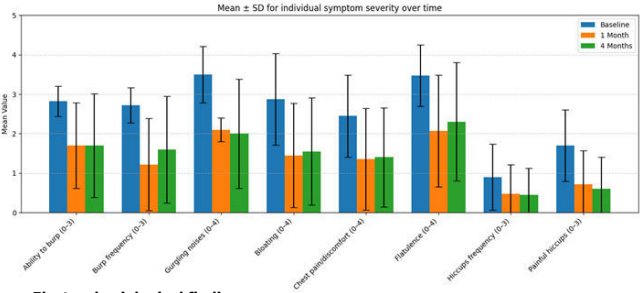


Figure 3. Among the 40 patients who completed all three assessments, including individuals from both dose groups, a significant and sustained reduction in overall symptom severity was observed (all items show a statistically significant (p≤.0001) difference between baseline and both 1 month and 4 months timepoints).

ADVERSE EFFECTS	ADVERSE EFFECT SEVERITY (low dose vs medium dose) 1: minimum; 2: mild; 3: moderate; 4: severe	ADVERSE EFECT DURATION (low dose vs medium dose)
•Dysphagia: 83% •Hoarseness: 25% •Acid reflux: 18% •Exertional dyspnea: 6% •Injection site pain >24 hours post-treatment: 3%	•Low dose: median severity 1 (IQR: 1-2) •Medium dose: median severity 2 (IQR: 1-3)	•Low dose: median duration 30 days (IQR: 14-30) •Medium dose: median duration 30 days (IQR: 21-30)

Electrophysiological findings

- ↑ difficulty in burping: ↑ tonic basal activity – peak amplitude (r = 0.28, p = 0.02); mean amplitude (r = 0.29, p = 0.02)
  ↑ CP EMG pause - mean amplitude (r = 0.26, p = 0.03); area under the curve (r = 0.25, p = 0.04)
- ↑ burp frequency: : ↑ tonic basal activity – peak amplitude (r = 0.25, p = 0.04)
- ↑ gurgling noises: ↑ tonic basal activity – area under the curve (r = 0.26, p = 0.04)
- ↑ flatulence: ↑ squeezing - duration (r = 0.28, p = 0.02)
- ↑ squeezing: ↓ chest pain/discomfort (r = −0.26, p = 0.03), hiccup frequency (r = −0.32, p = 0.01), painful hiccups (r = −0.25, p = 0.04)

CONCLUSIONS

The treatment leads to an important and sustained reduction in symptoms severity, with higher doses showing enhanced benefits in female patients. Adverse effects were generally mild and transient. Regarding electrophysiological findings, higher tonic basal activity and reduced relaxation during the swallowing-related EMG pause were associated with more severe impairment in belching and lower treatment response, pointing to a hypertonic or less modulable muscle profile. Further exploration of sex-related differences, dose optimization, long-term clinical outcomes, as well as comparison of different procedural techniques will be essential.

References

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