



Response to Letter to the Editor Re: “EUS-Guided Intra-gastric Injection of Botulinum Toxin A in the Preoperative Treatment of Super-Obese Patients: a Randomized Clinical Trial”

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Thank you for your interest in our randomized controlled trial of EUS-guided intra-gastric injection of botulinum toxin A (BTX-A) in super obese patients [1]. We agree that injection of botulinum toxin A is a very controversial topic and we are happy to answer your questions.

First, Regarding a BTX-A Injection

On page three of the article in the left column, we briefly described that 40 units of BTX-A were injected in five different regions with a total of 200 BTX-A units injected per patient. Then, in the right column, we describe the injections in further detail. First, 12 microinjections containing 10 units of BTX-A were performed at respective points: four microinjections at 3 cm from the pyloric sphincter (region 1), repeated twice in the direction of gastric cardia (region 2 and 3), at 2 cm intervals, followed by four injections performed around the gastric cardia (region 4), and four injections in the region of the greater curvature (region 5).

To clarify, we divided the injection region as follows:

Region 1 - Four microinjections with 10 BTX-A units each were performed at the cardinal points 3 cm from the pyloric sphincter.

Region 2 - Four microinjections with 10 BTX-A units each were performed in the anterior wall of the stomach.

Region 3 - Four microinjections with 10 BTX-A units each were performed in the posterior wall of the stomach.

Region 4 - Four microinjections with 10 BTX-A units each were performed around the gastric cardia.

Region 5 - Four microinjections with 10 BTX-A units each were performed in the proximal portion of the greater gastric curvature.

Second, Regarding Injection Sites

The mechanisms for weight loss following endoscopic therapies are thought to be multifactorial. Specifically, the primary mechanisms include decreasing gastric accommodation and delaying gastric emptying. While the fundus is an important location for an endoscopic procedure that focuses primarily on affecting accommodation, procedures that focus on gastric emptying should target the areas with high concentration of *Cajal* cells since they create the bioelectrical slow wave potential that leads to contraction of the smooth muscle [2, 3]. BTX-A is thought to delay gastric emptying by blocking acetylcholine resulting in temporary paralysis. The literature on BTX-A injection for obesity has reported various locations of the injection, including the antrum, body, and fundus [4–6]. In our study, we target the location of BTX-A injection in the area with the highest concentration of *Cajal* cells that serve as a gastric pacemaker (given its possible effect on gastric emptying). These include the junction between the fundus and gastric body, followed by the greater curvature and the pylorus [7–10]. In our study, to further confirm the accuracy of BTA-X

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injection (which should be injected into the muscular layer where *Cajal* cells are located), an endoscopic ultrasound was used to ensure that the needle tip was in the correct layer.

Third, Regarding the Use of BTX-A in Obesity

We agree that we cannot conclude that “the findings of this study suggest that the practice should be abandoned” with just our randomized study done in super obese patients (BMI > 50 kg/m²). This has already been included in the discussion section. Based on our study, we have concluded that “Intra-gastric injection of BTX-A does not appear to be an effective endoscopic treatment for preoperative weight loss in super-obese patients”. Nevertheless, our group recently published a systematic review and meta-analysis [11] based on randomized controlled trials (evidence 1A) comparing BTX-A versus saline injections in obese patients (BMI > 30 kg/m²), which showed no statistical difference in the amount of weight loss between the two groups. In this systematic review, our conclusion was “The available literature demonstrates that BTA therapy alone is not effective for the primary treatment of obesity.”

As critical appraisal is important for clinical research, we are appreciative of your commentary on our study. We look forward to collaborating with you and Obesity Surgery in the future.

Author Contributions IBR, DTHdM, and EGHdM wrote the response letter and approved the final draft of this manuscript.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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