Intragastric botulinum toxin injection: Is it the solution to all gastric ailments?

Irritable bowel syndrome, dyspepsia and gastroparesis are common functional gastrointestinal disorders associated with very complex and poorly understood underlying etiology. The burden of such disorders on the healthcare systems across the globe is staggering due to the highly variable clinical presentations, and the lack of highly effective medical or surgical interventions. Obesity, on the other hand, is a chronic metabolic illness associated with several comorbidities and an enormous economic and quality of life burden. Over the last decade, endoscopic bariatric therapies emerged as safe and effective therapies to induce weight loss on the short and intermediate terms, however, long term sustainability of weight loss remains variable. Maintaining the weight loss has been observed in multidisciplinary programs with close patient follow up.

Over the last two last decades, endoscopy continued to play an increasing role in the management of gastroparesis, enhancing gastric emptying through pyloric directed therapies, including transpyloric stenting, pyloric dilations, intrapyloric botulinum toxin injection (IPBI) and eventually gastric peroral endoscopic myotomy (G-POEM). The clinical results of such interventions, especially G-POEM, appear to be encouraging, which highlights pylorospasm as one of the fundamental pathologic contributors to this disease.

Intrapyloric botulinum toxin injection (IPBT) has been used for gastroparesis patients to enhance gastric emptying. Several early pilot studies revealed a positive impact of IPBI on both patient reported outcomes and on gastric emptying. Nevertheless, two randomized controlled studies reported that findings were not statistically significant compared to the controls.[1,2] Over the course of the last decade, many clinicians continued to find refuge in IPBI for treating refractory gastroparesis, particularly those with frequent hospital admissions, failure to thrive and prior positive response to IPBI.

The use of intragastric botulinum toxin injection (IGBT) for weight loss is more recent than its use in gastroparesis and also shows similar promise. In a recent systematic review and meta-analysis, IGBT in adequate doses (≥ 200 U) and multiple injections across the gastric various regions, was found to be effective in reducing weight when combined with diet control.[3] The exact mechanism for weight loss is unclear but is believed to be related to prolonging gastric half-emptying time.

In this issue of the Saudi Journal of Gastroenterology (SJG), two articles highlight the use of botulinum toxin in gastric disorders. In the first, Santucci NR et al.[4] reports on the outcomes of combined IPBI and balloon dilation in dyspepsia patients with and without delayed gastric emptying. In this retrospective study the authors included a total of 79 patients with dyspepsia and 83 controls. After propensity score matching for age, sex, and duration of symptoms, 63 patients were included in each group. It was reported that 76% of the cases showed partial or complete symptom improvement compared with 49% of the controls within 12 months follow up (p = 0.004). Interestingly, younger children tended to respond more favorably to the intervention compared to adults (p = 0.08).

Two previous studies have reported a pooled response rate of 67% with IPBT alone.[5,6]

Gastroparesis symptoms wax and wane and some of the perceived improvement may be related to natural fluctuations in disease course. The questions remain: what level of evidence do we need to see for wider adoption of IPBT in refractory gastroparesis patients? Despite the lack of consensus around the use of IPBT in gastroparesis and functional dyspepsia, there is a growing body of literature that continues to support its use. A recent randomized, blinded, sham-controlled trial comparing G-POEM to sham in patients with refractory gastroparesis was halted halfway through after the mid-point interim analysis showed a dramatic response in G-POEM compared to the sham arm.[7] Although it is hard to discern the added benefit of dilation to botulinum toxin injection, it is plausible that there is an additive effect to the concurrent use of both therapies. The improvement in gastric emptying that happens after pyloric-directed therapies is clear and concrete, and drives the credibility of all such therapies. The combined techniques of both balloon dilation and
botulinum injection in specific age groups appears safe and effective in alleviating upper gastrointestinal symptoms related to gastroparesis or dyspepsia, according to this study, although this remains mainly based on non-randomized, observational data.

A second article in this issue of SJG by Tayyem RM et al. compares the safety and efficacy of endoscopic intragastric botulinum toxin injection (EIBT) versus endoscopic planned gastric balloon (EPGB) placement, in achieving weight loss, with up to 6 months follow up. This was a prospective case-matched study of 176 patients who underwent either EIBT or EPGB, with 88 patients included in each arm. The main outcome of the study was weight loss, but additional endpoints included adverse events rates and quality of life. At 6-month follow up, EPGB was associated with greater absolute weight loss, but was associated with longer procedure duration and higher post procedure complication rates. The quality of life (QoL) assessments were no different at the end of the study. Interestingly, percent excess weight loss (%EWL) was higher in the EIBT, raising some questions about the main difference in the baseline characteristics of the 2 groups, where the baseline weight of the EPGB group was significantly heavier that the EIBT group. Hence, the absolute weight loss was higher in the first group but the %EWL was higher in the latter. This is an impressive study and the observations derived from it reflect the safety and potential efficacy of botulinum toxin in inducing and maintaining weight loss in the short term. Nonetheless, we see the fundamental question of the efficacy of EIBT better answered in a blinded, randomized clinical trial in the future, bereft of the inherent shortcomings that observational data.

Long-term maintenance of weight lost following endoscopic weight loss therapy can be hard to demonstrate. Conservative modalities result in 4-8% weight loss, however, 90% relapse within 5 years. Surgical bariatric procedures were shown to be more favorable in terms of achieving long-term weight loss. Maintenance of weight loss is crucial in attaining the beneficial effects of weight reduction including resolution of comorbidities and improvement in QOL. The use of botulinum toxin to induce delays in gastric emptying and satiety leading to weight loss remains very intriguing and worthy of continued exploration.

The two studies published in this issue of SJG add to the growing body of literature accentuating the role of botulinum toxin in gastric disorders. Nonetheless, the question that needs to be addressed is where in the clinical management of obesity and gastroparesis can we fit the role of botulinum toxin? Clearly, we need more evidence before embracing it for regular use. The elephant in the room remains the placebo effect, a deficiency that can only be overcome by randomized, blinded, sham-controlled trials. Until then, the judicious use of botulinum toxin on a case-by-case basis appears to be safe and efficacious.

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How to cite this article: AlLehibi AH, Al-Haddad M. Intragastric botulinum toxin injection: Is it the solution to all gastric ailments? Saudi J Gastroenterol 2022;28:247-9.