A Case Matched Comparison between Endoscopic Intragastric Botulinum Toxin-A Injection and Conventional Weight Loss Program

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Article

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Abstract

Introduction

Mild obesity can progress to more extreme forms of obesity if untreated, thus deserves early intervention. A new revolutionary treatment for mild obesity utilizes injecting the stomach with Botulinum Toxin-A. The study aimed to evaluate the efficacy and safety of endoscopic intragastric Botulinum Toxin-A injection for weight loss in patients with mild obesity compared to diet and exercise alone.

Methods

Patients with mild obesity were recruited into a prospective case-matched study. The therapeutic group received Botulinum Toxin-A gastric injections in addition to dietary advice and regular exercise. The control group only received dietary advice and regular exercise. The measured outcomes were weight loss, quality of life, early satiety, procedure cost, and procedure complications.

Results

A total of 250 patients (matched for age, sex, weight, and comorbidities) were equally divided. Patients were followed up for a mean of six months. Mean weight loss was better in the BTA group compared to the control group (10.8 versus 4.3 kg, P<0.001). Both groups enjoyed a comparable improvement in quality of life. No significant complications were observed in the series. The average cost per procedure was $1037 US dollars.

Conclusions

Endoscopic intragastric Botulinum Toxin-A injection can be beneficial in treating mild obesity. It is minimally invasive, cost-effective, and without serious side effects.

Introduction

Over the last two decades, there has been an increased awareness of obesity and its related comorbidities which has contributed to prosperity of weight loss techniques and interventions. Bariatric surgery has established itself as a cornerstone in the management of individuals suffering from severe and extreme obesity. However, individuals suffering from mild obesity are lacking a gold standard treatment up to date. The presence of several approaches to manage mild obesity including endoscopic and pharmacological interventions with variable success rates and outcomes may indicate the need to further investigate the topic and find out a more effective approach to treat mild obesity. Furthermore, genetic, social, psychological, and behavioral factors are important players in the development of obesity which needs consideration at the time when deciding the most appropriate weight loss intervention.

Botulinum toxin-A (BTA) is a neurotoxin produced by the Gram-positive, anaerobic bacterium Clostridium botulinum. Though it is one of the most toxic substances in the world, BTA injection has been used to
treat several disease conditions. BTA acts by decreasing acetylcholine release at the neuromuscular junction, thus inhibiting the muscular contractions of smooth and striated muscles. BTA can help people with certain pain disorders and abnormal muscle twitching. Perhaps BTA most well-known use is in cosmetic field to paralyze the facial muscles which in turn smooth out facial wrinkles. It was also shown that BTA is effective in the treatment of some diseases concerned with the gastrointestinal smooth muscles such as achalasia and chronic anal fissure.

Previous studies suggested that BTA injected into the stomach could be used to induce weight loss as it can slow the gastric emptying, provoke the feeling of bloating, induce early satiety, and decrease of body weight. Its main advantage would be the absence of serious adverse events in contrast to other treatments. However, there are a few studies that do not support the use of intragastric BTA for weight reduction.

Because previous studies evaluating BTA as a treatment for obesity showed contradicting results, this prospective study was designed with its main objective to evaluate the efficacy and safety of endoscopic intragastric BTA injection in the treatment of mild obesity compared to the conventional method of diet and exercise.

**Materials And Method**

A prospective case matched study was performed between June 2021 and May 2022. The study was approved by the university ethical committee. All patients were given full information about the study and a signed consent was obtained. Included patients were adults (18–65 years old) with mild obesity (body mass index 25–35 kg/m\(^2\)). Pregnant and lactating women, patients with myopathy or neuromuscular disorder, patients who were hypersensitive to BTA and patients who were shown to have peptic ulcer disease during endoscopy were excluded. Patients received thorough counselling by a specialist dietician. Weight and height were recorded before the procedure and weight was recorded monthly for six months. Percent excess weight loss (%EWL = weight loss / excess weight) was calculated at the end of treatment. A body mass index (BMI) of 25 kg/m\(^2\) was used to calculate the excess weight.

Minor and major complications related to the treatment were recorded during the procedure and at each visit. Minor complications included nausea, vomiting, abdominal pain, and minor upper gastro-intestinal bleeding. Major complications include death, major upper gastro-intestinal bleeding, injury to upper gastro-intestinal organs, muscle weakness, double vision, dysphagia, and allergic reactions to BTA (chest pain, dyspnoea, pyrexia, arthralgia, skin rash).

The procedure cost was recorded as total cost including material used (midazolam, BTA, endoscopic injection needle), endoscopy time, and doctors’ fees. Satiety was assessed using a Licker scale one-five (one = normal appetite, five = complete loss of appetite). Scores > two were considered indicators of early satiety. The quality of life (QoL) was measured using SF-36 tool.

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Procedure

After ten hours of fasting, patients were admitted to endoscopy suite to have upper gastro-intestinal endoscopy under conscious sedation. 300 units of Clostridium botulinum type A toxin-haemagglutinin complex were diluted in 50 ml of 0.9% saline. BTA injections were administered using a standard seven French endoscopic injection needle. Injections were administered into the gastric antrum, cardia and fundus under direct endoscopic visualization.

Diet And Follow-up

BTA group patients were observed for about one hour after the procedure then they were discharged on Proton Pump Inhibitor (PPI), anti-emetics and pain killers. They were instructed to take liquid diet for one week to be followed by a reduced calorie diet.

Patients of both groups were instructed to take reduced calorie diet advised by the dietician (1200–1500 Kcal/day). Patients were also encouraged to walk daily for 30–45 minutes. Patients were reviewed in the bariatric outpatient clinic monthly for six months to measure their weights and to report occurrence of side effects.

Ethics Ethical approval of the study was granted by the Hashemite University Ethics Committee. All methods were performed in accordance with the relevant guidelines and regulations. Informed consent was obtained from all participants and/or their legal guardians. In addition, this study has been performed in accordance with the Declaration of Helsinki.

Data Collection And Statistical Analysis:

Data was collected using Excel sheets (version 2010, Microsoft, USA). Statistical analysis was performed using SPSS software (version 25, SPSS Inc., USA). Quantitative continuous variables were expressed as mean with standard deviations (SD). Continuous data were compared using Student’s t-test with confidence interval (CI) of 95%. Categorical data were compared using Chi-Square. P-values less than 0.05 were considered statistically significant.

Data Availability:

The datasets generated and/or analysed during the current study are not publicly available as the data is owned by The Hashemite University, but are available from the corresponding author on reasonable request.

Results
Demography and Baseline characteristics

A total of 250 patients were recruited in the study. Table-1 shows that both groups were matched for age, sex, BMI and comorbidities.

Weight Loss

Weight loss at a mean follow-up of six months was in favor of BTA as shown in Table-2. The weight parameters differences between BTA group and control group was statistically significant, including weight (79.7 versus 84.5 kg, P < 0.001), weight loss (10.8 versus 4.3 kg, P < 0.001), BMI (27.6 versus 29.3 kg/m2, P < 0.001), BMI loss (3.8 versus 1.5 kg/m2, P < 0.001), and %EWL (57.5% versus 29.7%, P < 0.001).

Satiety Score

Early satiety was reported in the majority of patients who received BTA (n = 103, 82.4%).

Procedure Cost

The average cost of the procedure was $1037 (SD $186).

Quality Of Life

The improvement in the QoL between both groups was similar as shown by comparable SF36 scores (85.5 vs. 84.3, P = 0.61).

Complications

No major complications were recorded during the endoscopic or during the six-month follow up period. A minority of the patients (n = 11, 8.8%) complained of mild gastric upset (nausea, vomiting and abdominal pain) that settled quickly in less than 24 hours.

Discussion

Up to authors' knowledge, this study is the largest prospective study evaluating endoscopic intragastric BTA injection to 125 mildly obese patients. It showed that BTA had a clear effect on appetite and provided an average weight loss of 10.8 kg which is similar to other studies 13, 14.

The importance of appetite control and early satiety is a well known factor for the success of any weight loss program. For example, one of the main mechanisms of weight loss after sleeve gastrectomy is the reduction of ghrelin hormone level thus decreasing appetite. In our study, 82.4% of patients reported...
reduction in their appetite. Gui et al proposed that gastric motility may play a role in appetite modification after BTA injection. Normal gastric motility depends on antral contractility. Reduced antral contractility following BTA injection appears to prolong gastric emptying which in turn may reduce appetite. In addition, BTA injection into gastric fundus which is a major area responsible for ghrelin production may further help suppressing gastric production of the hunger hormone.

The reported ineffectiveness of BTA in weight reduction in a few studies could be due to the fact that BTA was used on patients with extreme obesity. The weight loss shown in our study suggests that intragastric BTA is more suitable for patients with mild obesity i.e. class one (as per World Health Organization classification, BMI 25–35 kg/m²).

The considerable weight loss in patients of both groups guaranteed that they enjoyed improvement in their QoL.

BTA was shown to be a safe procedure as there were no reported serious side effects and only 8.8% developed minor complications.

The study shortcomings include the lack of randomization. Therefore, large randomized studies are needed to conclusively demonstrate the effectiveness of intragastric BTA for weight loss. Moreover, further studies are needed to assess the long term results of BTA treatment.

In summary, our experience was generally in favor of using intragastric injection of BTA. It showed that intragastric BTA was effective in the treatment of mild obesity with an average weight loss of 10.8 kg. It also demonstrated that intragastric BTA is a minimally invasive and cost-effective procedure costing $1037 per procedure. In addition, it is a safe procedure without a record of serious side effects.

References


**Tables**
Table 1. Baseline characteristics†

<table>
<thead>
<tr>
<th>Group</th>
<th>BTA (n=125)</th>
<th>Control (n=125)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (SD)</td>
<td>36.0 (10.8)</td>
<td>37.7 (13.8)</td>
<td>0.28</td>
</tr>
<tr>
<td>Number of females (%)</td>
<td>94 (75%)</td>
<td>88 (70%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Initial weight kg (SD)</td>
<td>90.9 (13.4)</td>
<td>88.8 (10.2)</td>
<td>0.16</td>
</tr>
<tr>
<td>Excess weight kg (SD)</td>
<td>18.4 (8.5)</td>
<td>16.8 (4.7)</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI kg/m² (SD)</td>
<td>31.3 (2.8)</td>
<td>30.8 (1.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Comorbidity Prevalence (%)</td>
<td>17 (14%)</td>
<td>19 (15%)</td>
<td>0.72</td>
</tr>
<tr>
<td>SF36 score 0-100 (SD)</td>
<td>49.2 (20.9)</td>
<td>53.1 (17.8)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

† Values are means (SD) unless otherwise indicated. SD = standard deviation
BMI = Body Mass Index

Table 2. Weight loss, early satiety, and procedure complications at 6 months follow up†

<table>
<thead>
<tr>
<th></th>
<th>BTA</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight kg (SD)</td>
<td>79.7 (11.1)</td>
<td>84.5 (10.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI kg/m² (SD)</td>
<td>27.6 (3.1)</td>
<td>29.3 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight loss kg (SD)</td>
<td>10.8 (9.1)</td>
<td>4.3 (4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI loss kg/m² (SD)</td>
<td>3.8 (3.1)</td>
<td>1.5 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>%EWL (SD)</td>
<td>57.5 (51.7)</td>
<td>29.7 (38.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

† Values are means (SD) unless otherwise indicated. SD = standard deviation
%EWL = Percent Excess Weight Loss, BMI = Body Mass Index