Chemical components separation with the use of botulinum toxin A: A critical review for correction of ventral hernia

Yuri Justi Jardim1,3; Gustavo Heluani Antunes de Mesquita1; Leonardo Zumerkorn Pipek1; Kayo Augusto de Almeida Medeiros1; Barbara Justo Carvalho1; Leandro Ryuchiiuamoto1; Diego Ramos Martines3; Fernanda Nii1; Daniel Reis Waisberg1; Alberto Meyer2

1Faculty of Medicine FMUSP, University of Sao Paulo, Brazil
2Department of Gastroenterology, University of Sao Paulo, Brazil
3Department of Global Health and Social Medicine, Harvard Medical School, USA

Abstract

Background: Ventral hernias are prevalent results in abdominal surgeries and may represent a surgical challenge in complex cases, mainly due to tension in the abdominal wall musculature. The failure of surgical correction may lead to a more morbid treatment for the patient, in addition to a considerable socioeconomic impact. In order to have a lower risk of complications, the use of Botulinum Toxin A (BTA), may be a preoperative alternative to reduce abdominal wall tension by causing sustained and reversible paralysis. This critical review of the literature proposes to evaluate the adjacent use of BTA in surgical corrections of ventral hernias.

Methods: Using the PubMed database, the keywords ‘ventral hernia’, and ‘botulinum toxin’ were searched using the Boolean operator AND. Articles were selected based on their relevance and updated information. The outcomes of interest included the change in ventral hernia defect width and in lateral abdominal wall muscle length, pain, hernia recurrence and complications.

Results: A total of 20 articles from 2009 to 2018 were found. We excluded some articles due to irrelevant technique, use of animal models and lack of outcome data. Reduction of the abdominal wall thickness increasing it’s length, less perioperative pain, hernia reduction and the correction with less tension were observed after the use of BTA injection. No complications occurred during applications.

Conclusion: The use of BTA seems to be a promising alternative in the management of ventral hernias due to the capacity of reducing tension in the abdominal wall. Given the complexity of such cases, however, more studies are necessary to determine the efficacy of this method.
Introduction

In abdominal surgery 28% of patients can develop ventral hernia [1]. In order to correct this hernia defects there are some techniques described such as Anterior Component Separation (ACS), The Posterior Component Separation (PCS), Progressive Preoperative Pneumoperitoneum (PPP), mesh reinforcement, and optimal suturing techniques for large incisional hernias.

In this type of procedures, is frequent high recurrence rates, ranging from 12%–54% [2]. Failure in the correction of hernia defect generates higher costs to the health care system, greater morbidity to the patient and more complexity in reconstructive surgical technique.

The success of surgical approach of the hernia depends on a variety of factors, such as the technique employed, the patient’s comorbidities, and the size of the hernia defect. The European Hernia Society (EHS) establishes large incisional hernias (W3) according with the diameter of 10 cm or larger [3]. In these conditions, it’s more difficult to repair without tension, which is fundamental for myofascial closure of the abdominal wall, what increases the risk of recurrence.

In this context, there are some techniques used to approach a first incisional hernia repair relieving tension. The ACS technique described by Ramirez et al. permits fascial repositioning through lateral stretching, restoring the integrity of the abdominal wall [4]. However, we find in the literature significant rates of recurrence associated with this procedure. Another technique used is the PCS, which increases the size and assures fascial closure; and it was most recently described in the treatment of large ventral hernia defects [5-7].

In more complex cases, these techniques alone are not sufficient to guarantee the closure of the hernia defect, with the appropriate tension. To achieve a lower risk of complications other techniques can be used, such as PPP and the placement of expanding tissues on the abdominal wall [8]. Following the same principle, a recent proposal is the preoperative application of Botulinum Toxin A (BTA), a neurotoxic protein produced by Clostridium botulinum, for hernia correction, in order to relax and stretch the musculature.

BTA has been used in medical practice for treatment of a great variety of conditions. It’s preoperative application, can induce a sustained and reversible flaccid muscular paralysis helping the closure of the abdominal wall, which should help to lower the recurrence rate [1,2,9].

Abdominal wall reconstruction may benefit of the use of Botox injections to help in the abdominal components separation. The objective of this study was to conduct a critical review of the literature on the use of BTA in the surgical correction of Ventral Hernia.

Methods

Eligibility criteria

The study population was patients undergoing ventral hernia repair. The intervention was administration of BTA as an adjunct to surgical hernia repair. The primary quantitative outcomes of interest included the decrease in ventral hernia defect width and the increase inlateral abdominal wall muscle length following BTA injection. Secondary outcomes of interest included pain, hernia recurrence, complications, length of stay, and length of follow-up.

Literature search

This critical review of the literature was performed using the PubMed database to search for published articles to include studies evaluating the effects of Botox on ventral hernias. The keywords ‘ventral hernia’ and ‘botulinum toxin’ were searched using the Boolean operator AND.

Results

A total of 20 articles from 2009 to 2018 were found. These articles were selected based on their relevance and updated information (Figure 1, Table 1).

Discussion

The incisional hernia is often common delayed complication following laparotomies surgeries. Some comorbidities such as diabetes, obesity, male sex, advanced age, incision type, immunosuppression therapy, wound infection and pulmonary complications are considered risk factors for incisional hernia development [10]. Closure of the abdominal wall with low tension with the use of mesh is the standard treatment for correcting this type of hernia [5]. Tension in the sutured area is commonly associated with ischemia in the abdominal wall, that can result in great probability of recurrence of the hernia defect. In large hernia cases, complementary techniques to stretch the abdominal wall are necessary in order to guarantee success of the surgical approach.

BTA is a therapeutic complementary treatment to decrease the suture tension and consequently the hernia recurrences rate. The flaccid muscular paralysis, provoked by this neurotoxin, takes effect from two days after application and lasts for 6–9 months [10]. It reduces the thickness of the abdominal wall, increasing its length, allowing hernia reduction and therefore allowing closure with less tension.

In a 2014 clinical trial of male trauma patients with hernia secondary to open abdomen management, Ibarra-Hurtado TR et al. showed that left muscle thickness mean reduction was 1 ± 0.55 cm (p < 0.001), right muscle thickness mean reduction was 1.00 ± 0.49 cm (p < 0.001), left muscle length mean increase was 2.44 ± 1.22 cm (p < 0.001), and right muscle length mean increase was 2.59 ± 1.38 cm (p < 0.001) [1].

With a similar approach, Farooque F et al. in a prospective pilot study in 2016, showed that post-BTA preoperative computed tomography showed a significant increase in mean length of lateral abdominal wall: 18.5 cm pre-BTA to 21.3 cm post-BTA (P = 0.017) with a mean unstretched length gain of 2.8 cm per side (range 0.8-6.0 cm) [11].

A 2016 prospective evaluation of 27 patients undergoing elective complex ventral hernia laparoscopic repair, conducted by Elstner KE et al. found similar positive results demonstrating an increase in mean length of the lateral abdominal wall from 15.7 cm pre-BTA to 19.9 cm post-BTA (p < 0.0001), with mean unstretched length gain of 4.2 cm/side (range 0-11.7 cm/side [12].

The injections of BTA minimizes the forces of traction on the area of closure during postoperative recuperation and the period of scarring of the operative wound. This promotes adequate perfusion to the area of the scarring, reducing postoperative morbidity, including pain, increasing the chances of successful primary closure of the incisional hernia [13,14].
A systematic review and meta-analysis of botulinum toxin for management of ventral hernia done by Weissler JM et al in 2017, showed significant hernia width reduction (mean = 5.79 cm; n = 29; p < 0.001) and lateral abdominal wall muscular lengthening (mean = 3.33 cm; n = 44; p < 0.001) following BTA applications [8].

The advantage of the combination of abdominal wall reconstruction with the use of BTA is the minimal tension and protection of the sutures in the postoperative phase, what reduces the risk of recurrence, pain, and complications [1,5,8,10-13,15-17].

**Tables**

**Table 1: Included studies and characteristics.**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Design</th>
<th>Number of patients</th>
<th>Primary Outcome</th>
<th>Secondary outcome</th>
<th>BTA dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zendejas B et al. [9]</td>
<td>2013</td>
<td>retrospective</td>
<td>n = 22</td>
<td>It was observed reduction in muscle thickness and increase in muscle length on both sides. Left muscle thickness presented a mean reduction of 1 ± 0.55 cm (p &lt; 0.001). Right muscle thickness presented a mean reduction of 1.00 ± 0.49 cm (p &lt; 0.001). Left muscle length presented a mean increase of 2.44 ± 1.22 cm (p &lt; 0.001). Right muscle length presented a mean increase of 2.59 ± 1.38 cm (p &lt; 0.001).</td>
<td>Patients used less analgesia and reported less pain and, there was no difference in postoperative complications</td>
<td>300 Units</td>
</tr>
<tr>
<td>Ibarra-Hurtado TR et al. [1]</td>
<td>2014</td>
<td>prospective</td>
<td>n=17</td>
<td>Increase in mean length of lateral abdominal wall from 18.5 cm pre-BTA to 21.3 cm post-BTA (P = 0.017) with a mean unstretched length gain of 2.8 cm per side (range 0.8-6.0 cm).</td>
<td>No recurrences at mean follow-up of 49 months were observed</td>
<td>500 units (250 each side)</td>
</tr>
<tr>
<td>Farooque F et al. [11]</td>
<td>2016</td>
<td>prospective</td>
<td>n=8</td>
<td>Increase in mean length of the lateral abdominal wall from 16.7 cm pre-BTA to 19.9 cm post-BTA (p &lt; 0.0001), with mean unstretched length gain of 4.2 cm/side (range 0-11.7 cm/side)</td>
<td>All hernias were surgically corrected with mesh with no early recurrence.</td>
<td>300 Units</td>
</tr>
<tr>
<td>Elstner KE et al. [12]</td>
<td>2016</td>
<td>prospective</td>
<td>n=27</td>
<td>Increase in mean length of lateral abdominal wall from 18.5 cm pre-BTA to 21.3 cm post-BTA (P = 0.017) with a mean unstretched length gain of 2.8 cm per side (range 0.8-6.0 cm).</td>
<td>No early recurrences.</td>
<td>Most patients received a total dose of 300 units</td>
</tr>
<tr>
<td>Ibarra-Hurtado TR et al. [13]</td>
<td>2009</td>
<td>prospective</td>
<td>n=12</td>
<td>Pre BTA mean defect width of 13.9 cm; mean reduction was 5.25 cm (p &lt; 0.001).</td>
<td>All hernias were surgically corrected with mesh with no early recurrence.</td>
<td>500 units (250 each side)</td>
</tr>
<tr>
<td>Zielinski MD et al. [14]</td>
<td>2013</td>
<td>retrospective</td>
<td>n=18</td>
<td>Increase in mean baseline abdominal wall length from 16.4 to 20.4 cm per side (p &lt; 0.0001) and the increase in mean transverse length of the unstretched anterolateral wall muscles of 4.0 cm/side (range 0-11.7 cm/side).</td>
<td>Reported rates of complications (67%), and mortality (11%)</td>
<td>300 units</td>
</tr>
<tr>
<td>Bueno-Lledó J et al. [15]</td>
<td>2017</td>
<td>retrospective</td>
<td>n=45</td>
<td>Mean reduction of 16.6% of the volumes of the incisional hernia(VIH)/abdominal cavity(VAC) ratio after (PPP) and BTA (p &lt; 0.05).</td>
<td>No complications occurred during the BT administration</td>
<td>500 units</td>
</tr>
<tr>
<td>Elstner KE et al. [16]</td>
<td>2017</td>
<td>prospective</td>
<td>n=32</td>
<td>Increase in mean baseline abdominal wall length from 16.4 to 20.4 cm per side (p &lt; 0.0001) and the increase in mean transverse length of the unstretched anterolateral abdominal wall muscles of 4.0 cm/side (range 0-11.7 cm/side).</td>
<td>No hernia recurrences.</td>
<td>300 Units</td>
</tr>
<tr>
<td>Rodriguez-Acevedo O et al. [17]</td>
<td>2017</td>
<td>prospective</td>
<td>n=56</td>
<td>In this study was obtained an increase in mean lateral abdominal wall length from 16.1 cm to 20.1 cm per side, a mean gain of 4.0 cm/side (range 1.0-11.7 cm/side) (p &lt; 0.0001), and the unstretched mean length increase was 8.0 cm of the lateral abdominal wall.</td>
<td>One patient presented with a new fascial defect 26 months post-operative.</td>
<td>300 or 200 units depending on the patient</td>
</tr>
<tr>
<td>Bueno-Lledó J et al. [15]</td>
<td>2018</td>
<td>retrospective</td>
<td>n=70</td>
<td>Mean reduction of 16.6% of the volumes of the incisional hernia(VIH)/abdominal cavity(VAC) ratio after (PPP) and BTA was obtained (p &lt; 0.05).</td>
<td>No complications occurred during the BT administration.</td>
<td>500 Units</td>
</tr>
</tbody>
</table>
Conclusion

A number of aspects of the closure of ventral incisional hernias remain controversial; among these is the use of botulinum toxin A. This paper describes a critical review, involving the application of BTA in the correction of ventral hernia defects. BTA seems to reduce the tension of the sutures in the postoperative phase, improving the patient’s outcomes. But given the complexity of such cases, however, more studies are necessary to determine the efficacy of this method.

References