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Chemical abdominal wall release using botulinum toxin A: A personal view

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Abstract:

INTRODUCTION: Botulinum Toxin A (BTA) has gained increasing interest in hernia surgery, especially when dealing with complex ventral hernias. The goal of using BTA is the preoperative reduction of the transverse hernia diameter achieving a higher primary fascial closure rate, avoiding a potential additional component separation. However, high evidence data are sparse and the treatment protocols of BTA and patient selection are heterogeneous. In this article, we review the most recent literature; discuss indications for BTA, the ideal patient selection, and available BTA protocols. Also, we provide our own data and discuss the potential future role of BTA in treating complex ventral hernias.

MATERIALS AND METHODS: We reviewed the available literature and analyzed our own data from patients with complex ventral hernias undergoing preoperative BTA application retrospectively. We present our BTA protocol and measured abdominal wall muscle and hernia parameters before BTA application and before surgery using CT scans.

RESULTS: In total 22 patients with a median diameter of the incisional hernias of 11.75 cm (IQR 10.9–13.4) were included in our study. BTA administration was performed 4 weeks prior to surgery. In CT scans a significant reduction of the thickness and an elongation of the lateral abdominal wall muscle compartment were seen in all patients. Also, the transverse hernia diameter decreased in all cases from median 11.8 cm (IQR 10.9–13.4) pre-BTA to 9.1 cm (IQR 7.6–10.2) presurgery. Primary fascial closure was achieved in all cases with additional component separation in three cases.

CONCLUSION: BTA administration in the lateral abdominal wall muscle compartment is a helpful tool to simplify surgery of complex ventral hernias. It has a visible effect on the muscle parameters in the CT scans and subsequently may increase the rate of primary fascial closure. Further multicenter studies are necessary to gain data with higher evidence.

Keywords:

Botulinum toxin A, BTA, ventral hernia

Introduction

Botulinum Toxin A (BTA) is a neurotoxic protein produced by clostridium botulinum and has managed to gain clinical importance beyond beauty medicine. For at least a decade BTA became an adjunct tool for hernia surgeons when it comes to complex abdominal wall hernias,^[1] especially when the “complexity” of the hernia is defined by its diameter. The reason for using BTA is justified by the potential avoidance of component separation (CS)

techniques and their negative impact on peri- and postoperative complications^[2] and truncal and spinal stability.^[3] Sparing e.g., the transversus abdominis muscle from transection during transversus abdominis muscle release (TAR) maintains its important role in the abdominal wall physiology. BTA also enables higher rates of primary fascial closure (PFC), which should be the primary goal in ventral hernia repair considering the positive effect on the quality of life.^[4]

The paralyzing effect of BTA on the treated abdominal wall muscles reaches a maximum at 2 weeks after topical administration and declines gradually after 2–3 months.^[5-7]

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Several clinical studies investigated the effect of BTA on abdominal wall muscle parameters using computed tomography (CT) scans demonstrating a significant reduction of the transverse hernia defect and lateral abdominal wall muscle thickness, a significant elongation of lateral abdominal wall muscles enabling a primary fascial closure in most cases avoiding additional component separation techniques.^[8-17]

As mentioned above, the main goal of using BTA is PFC without additional adjunct procedures, such as progressive pneumoperitoneum (PPP) or CS. In a recent propensity-scored matched analysis in patients with massive, complex abdominal wall hernias, and severe loss of domain, preoperative BTA application improved the PFC rate significantly with lower wound infection rates.^[18-20] However, many studies demonstrated that PFC was achieved with BTA in combination with an additional component separation,^[18,19,21-24] diminishing the pure effect of BTA alone. Only a few studies compared BTA application alone compared to CS in incisional hernias >10cm showing significant advantages in the BTA group regarding PFC, complications and length of hospital stay.^[25]

Considering that BTA reaches its maximum paralyzing effect after 2 weeks,^[5-7] timing of BTA application seems of somewhat importance. Timing concepts in the available literature differ, ranging from surgery day up to 6 weeks before surgery.^[8-14,26] Administration of BTA is mostly done using ultrasound,^[9,10,12-14,26] rarely using electromyography.^[8] The injection volume, units, and concentration of BTA administration is characterized by a large heterogeneity ranging from 300 up to 500 units of BTA^[8-14,26] with a concentration ranging from 2 up to 100 units/ml.^[9-14,26] Ultrasound-guided injections are either administered on three^[10-14] or five^[8,9,26] locations per side, at which it does not seem to be important if BTA has been injected in two or three muscle layers.^[3] Also, BTA seems to decrease the level of postoperative pain, highlighting its direct analgetic effect in ventral hernia repair.^[14]

However, scientific evidence is still low with level 3 and 4 statements and no conclusive recommendations in the most recent guidelines.^[27] Therewith, the use of BTA still relates to personal experience and patient selection. In this article, we would like to share our personal experience and view on using BTA in complex abdominal wall repair highlighting pitfalls as well as technical tips and tricks.

Indication for Botulinum Toxin A in Ventral Hernia Patients

The most important aspect of having optimal effect of BTA application is elaborated and justified patient

selection. The ideal cut-off horizontal diameter for ventral hernia patients who might benefit from preoperative BTA is thought to be 10cm and above. We generally see the indication of BTA quite generously in patients with hernias of 8cm diameter and above. Some may argue that defects up to 10cm are sufficiently closed by an open Reeves-Stoppa sublay repair alone in most cases. However, especially in the epigastric and periumbilical parts, the reconstruction of the linea alba in these borderline cases may be challenging and sometimes only possible with some degree of tissue tension or bridging. Therewith, we try to make such challenging cases as easy as possible and use preoperative BTA in patients with 8cm hernia diameter. Additionally, hernias with criteria of complexity^[11] may benefit from preoperative BTA application. Preoperative assessment of the hernia should be supported by the CT scan of the abdomen,^[28,29] which gives valuable information about the anatomy of the abdominal wall, the exact hernia diameter, hernia content, and the abdominal wall muscle conditions of the patient. For example, contracted lateral abdominal wall muscles may be a good indicator for maximum benefit from preoperative BTA application. In patients with long-standing laparostomas and/or muscle calcification in the CT scan, PFC may be challenging or even impossible even in smaller hernias. This is the reason, why we use BTA in such patients in hernias <8cm too. In contrast, identifying patients with atrophic or fibrotic rectus muscles may predict intraoperative difficulties during the retro-rectus repair. Also, only minimal elongated lateral abdominal wall muscles after BTA administration may indicate a suboptimal effect. Also, demonstrating the CT scans to the patients seems extremely helpful for consenting the patients and explaining why they benefit from a BTA application.

Botulinum Toxin A Application Protocol and Technical Considerations

All hernia patients in our institution are routinely enrolled in the Herniated registry.^[30] As only cases of routine hernia surgery are documented in the Herniated Registry, an ethical approval for analyzing the patients was not necessary. All patients are consented separately for the preoperative BTA application according to our protocol since BTA using for abdominal wall muscles is still an off-label use in Switzerland. Before BTA application all patients underwent a CT scan of the abdomen. We measured the hernia diameter, length, and thickness of the lateral abdominal wall muscles at the level of the 4th lumbar vertebra in centimeters before BTA application and before surgery. According to the time-depending maximum muscle relaxation effect of BTA,^[5-7] we defined the optimal time point for the application 4 weeks prior to surgery. The BTA application is performed by our collaborating

radiologists using ultrasound guidance. The costal margin, the iliac crest line, the medial clavicular line, the anterior axillary line, and the medial axillary line are defined [Figure 1]. The five infiltration points are marked too. The BTA (Allergan) is prepared undiluted, in total 20 ml (200 IE Botulinum Toxin A). Per side 100 IE of BTA are injected, 2ml (20 IE) on each of the five marked points under ultrasound guidance. The transversus abdominis muscle is reached first with the needle tip. The 2 ml (20 IE) of BTA are injected with slow retraction of the needle, passing the transversus abdominis, internal oblique, and external oblique muscle, equally distributing the 20 IE BTA to all three muscle layers [Figure 2]. One day before surgery the second CT scan of the abdomen was made to objectively evaluate the effect of the BTA application on the hernia diameter as well as the muscle shape, length, and thickness.

Results

Between January 2018 and December 2019, 22 patients (7 female) with large or complex incisional hernias received

preoperative BTA and were subsequently operated in our hernia center and retrospectively analyzed. The median diameter of the hernias was 11.75 cm (IQR 10.9–13.4). Patients with hernias <8 cm received BTA too, when muscle calcification was visible in the CT scan ($n = 2$) or a laparostoma was present ($n = 3$). Measurements revealed a pre-BTA median hernia diameter of 11.8 cm (IQR 10.9–13.4) and a presurgery median hernia diameter of 9.1 cm (IQR 7.6–10.2), resulting in an average reduction of the hernia diameter of 2.7 cm or 23%. On the right side the median muscle length of the lateral abdominal wall compartment was 14.6 cm (IQR 13.2–19.2) before BTA and median 18.5 cm (IQR 13.5–20.4). The median muscle thickness of the right lateral abdominal wall compartment was 2.6 cm (IQR 2.0–3.0) prior to BTA and median 1.8 cm (IQR 1.3–2.3) prior to surgery. On the left side, the median pre-BTA muscle length was 14.7 cm (IQR 12.5–16.1.) and median 17.2 cm (IQR 14.0–18.1) before surgery. The muscle thickness on the left was median 2.8 cm (IQR 2.0–3.2) before BTA application and median 2.0 cm (IQR 1.6–2.4) before surgery. This results in BTA-induced extension of the lateral abdominal wall muscles

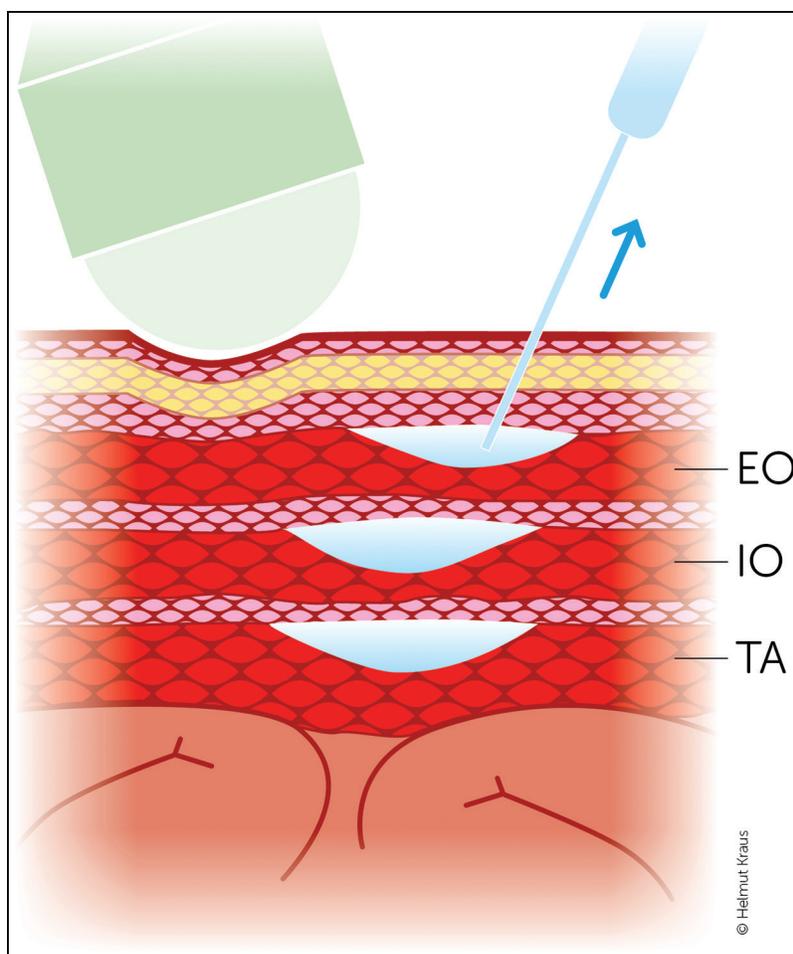


Figure 1: Injection of Botulinum Toxin A is performed under ultrasound guidance. The needle tip is advanced until it reaches the transversus abdominis muscle (TA), while pulling the needle slowly back, depots of Botulinum Toxin A are administered in all three muscle layers of the lateral abdominal wall: external oblique muscle (EO), internal oblique muscle (IO), and transversus abdominis muscle (TA)

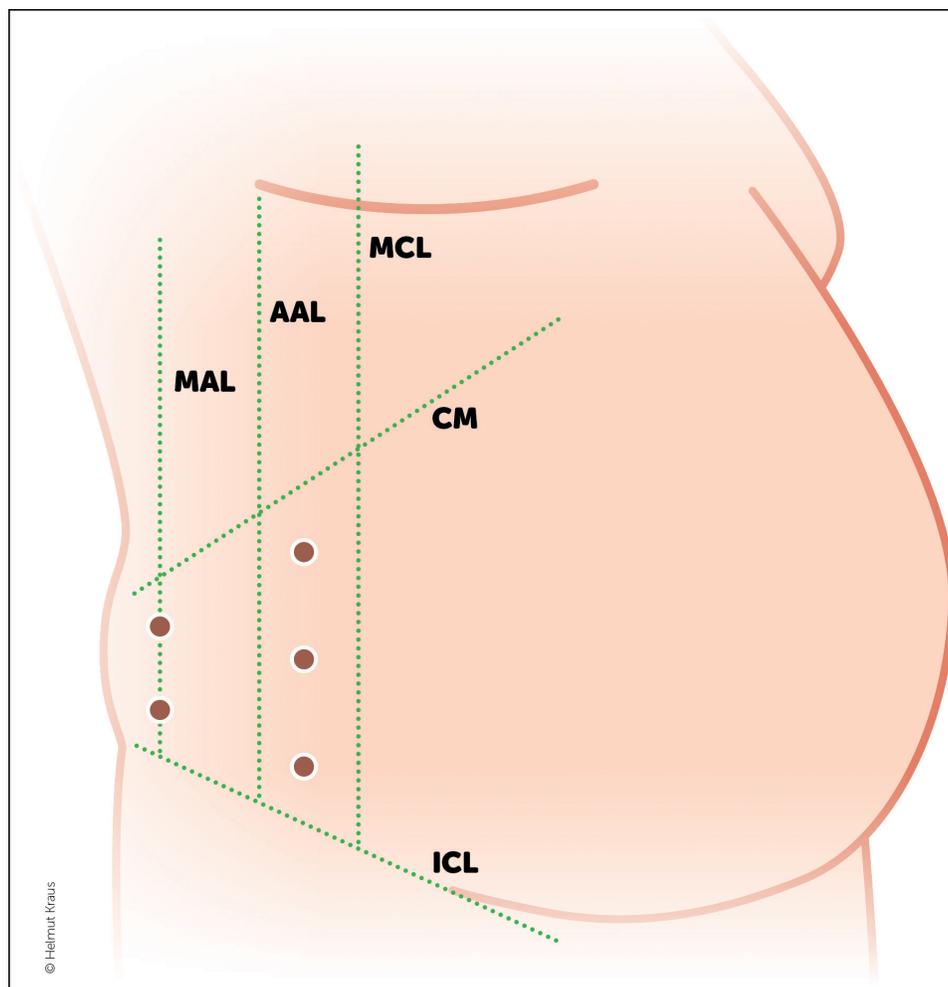


Figure 2: Preferred five BTA infiltration points of the lateral abdominal wall

of 27% (3.9 cm) on the right and 17% (2.5 cm) on the left. The thickness of the lateral abdominal wall muscle compartment was reduced from median 2.6 cm to 1.8 cm on the right and from median 2.8 cm to 2.0 cm on the left.

BTA was administered median 29 days before surgery (IQR 27–34). Duration of surgery was median 139 min (IQR 103–152). Primary fascial closure was achieved in all 22 patients. Additional CS was necessary in three patients. Median age of patients at the time of surgery was 62 years (IQR 57–71). The median length of hospital stay was 6 days (IQR 5–7). No major postoperative complications according to the Clavien-Dindo-classification occurred.^[31]

Summary and Outlook

In our patient collective, we could demonstrate that preoperative BTA application into all three lateral abdominal wall muscles seems to have a beneficial effect for our patients. The objective measurements of the abdominal wall anatomy revealed a reduction of the

transverse hernia diameter, as well as a reduction of the muscle thickness and elongation of the lateral abdominal wall muscle compartment following the BTA application. The PFC was achieved in all patients, however, in three cases additional CS was necessary.

In our experience, we use BTA rather generously than restrictive, trying to simplify the operation as much as possible and to downstage the complexity of the hernia first and foremost by its diameter. Patient satisfaction seems to be high and pain levels are generally low, compared to patients without BTA application,^[14] highlighting the direct analgetic effect of BTA.

Since BTA application is far away from being standard clinical practice, there are some limitations to our data. Like many other studies, our results are hampered by the fact that a control group is missing, and the study was not designed as a randomized controlled trial (RCT) to gain higher levels of evidence. Likewise, additional adjunct techniques such as CS were necessary in a few cases to achieve PFC, masking the true effect of BTA alone. In some cases, the complexity

of hernias may have been overestimated resulting in an unneeded application of BTA. This may contribute to the fact that in some comparative studies BTA application showed no benefit when compared to patients without BTA. Therewith the independent and original effect of BTA remains unclear in some clinical scenarios.

However, performing case series analysis or case-control studies is the very beginning of gaining data and may be reasonable, since these studies are the inevitable fundamentals of every RCT. In our patient collective, the effect of BTA seems to be quite variable. In some patients, the effect differed on one side compared to the other in the same patient, which highlights the role of the BTA applicant, who must follow a clear predefined protocol with a sustainable quality of BTA application. There may be some variability in the quality of BTA application, which certainly affects the effect of BTA on the muscle. However, it is sometimes difficult to predict, which patients benefit most from BTA since the effect on the muscle seems to be subject to a certain variability. BTA cannot prevent additional CS in some cases, which may be explained by the fact that some stiffness of the abdominal wall is generated by calcified or fibrotic muscle structures. This is certainly the case for patients with laparostoma, open abdomen, or visible calcification in the CT scans. Here we are applying BTA even in smaller hernias, since primary fascial closure may be difficult even in smaller hernias under such conditions.

In future research, we need multicenter studies to gain more valuable data. We have to clarify, which amount of BTA units in which dilution concentration has the best effect, and where we have to administer the BTA. Also, we need larger patient populations to better identify the patient collective, which benefits most from the BTA application. In addition, it is still unclear by which degree BTA avoids component separation. Here we certainly need well-designed trials comparing BTA vs. non-BTA in complex ventral hernias.

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Conflicts of interest

Dr. Henry Hoffmann is an Associate Editor of *International Journal of Abdominal Wall and Hernia Surgery*. The article was subject to the journal's standard procedures, with peer review handled independently of this Associate Editor and their research groups.

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