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Effect of paralysis of the abdominal wall muscles by botulinum A toxin to intraabdominal pressure: an experimental study

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Intraabdominal pressure;
Botulinum A toxin;
Abdominal muscles;
Abdominal wall defects;
Experimental study

Abstract

Purpose: To show the effect of botulinum A toxin–induced paralysis of abdominal muscles on intraabdominal pressure.

Material and Methods: Fifteen Sprague-Dawley rats were divided into 2 groups. An abdominal skin incision was done, and 2 catheters were placed for the pressure monitoring and saline infusion. Saline solution was given to the abdomen until reaching to a pressure level of 9 cm H_2O and 6 mm Hg in pressure device, and the amounts of injected saline were recorded. Then intraabdominal saline was drained. Two milliliters (5 U/mL) botulinum A toxin was applied to the abdominal muscles in group 2. Saline was injected at the same points in same amounts in group 1. After 3 days, catheters were placed, and the saline volumes needed to obtain the same pressure levels were recorded for each rat. Spontaneous motor unit potential (MUP), single MUP analysis and interference patterns of the muscles, respiratory rates, and vascular pressure measurements were recorded before and after botulinum toxin (Botox) injections.

Results: Mean intraabdominal saline volumes in the first and third days were 63.8 and 64.4 mL in group 1 and 67.6 and 80.6 mL in group 2, respectively. Mean MUP amplitude and duration of the rectus muscles in group 2 (17.1 μV and 1.47 milliseconds) were significantly lower than those of group 1 (187 μV and 4.9 milliseconds) in the third day. There were no pathological changes in respiratory rates and pressure measurements before and after Botox injections.

Conclusion: This pilot experimental study showed that local injection of botulinum A toxin causes paralysis in abdominal wall muscles, increases the intraabdominal volume, and decreases the pressure, and this application may be used as an adjunct in abdominal wall closure in selective cases.

Increased abdominal pressure (IAP) after complete primary repair of abdominal wall defects such as gastroschisis, omphalocele, ventral hernia, and congenital diaphragmatic hernia is a great problem affecting the success of the operation, morbidity, and mortality. One of the problems

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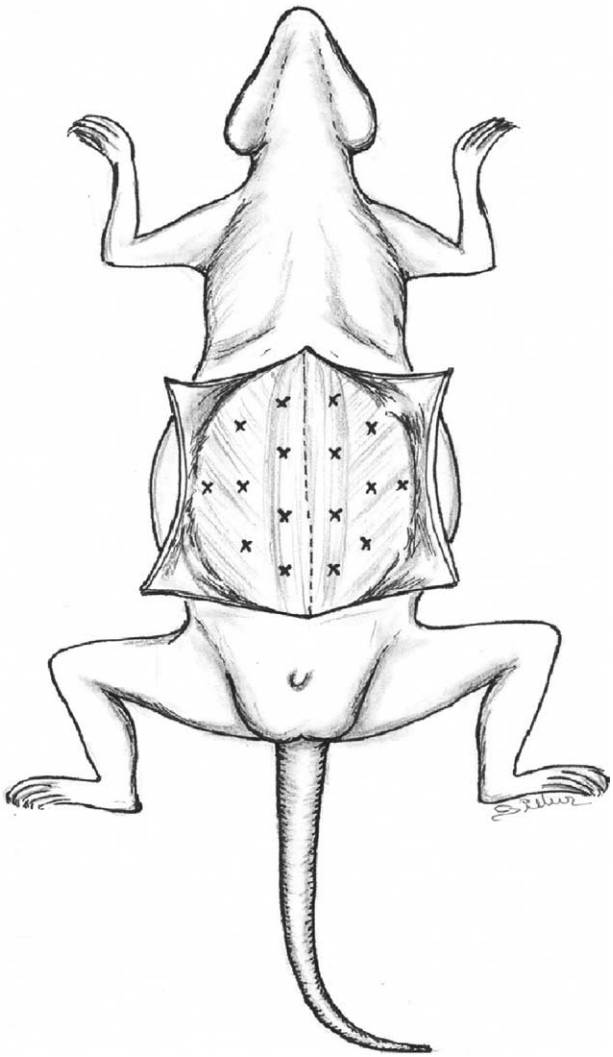

Fig. 1 A schematic view of the injection sites.

caused by IAP is the elevation and immobilization of the diaphragm which leads to respiratory distress, whereas the other is circulatory collapse resulting from the compression of inferior vena cava. To achieve this problem, staged operations were performed by using skin coverage, and large ventral hernias were created, or different methods such as silo techniques were applied.

Techniques such as application of progressive pneumoperitoneum; transverse division of the rectus muscles; using skin and muscle flaps, silastic, or other prosthetic materials; and abdominal wall stretching were used to enlarge the abdomen and to decrease the abdominal pressure (AP) [1]. Primary closure of the abdomen is the first aim of the operator by using these mentioned techniques. Moreover, postoperative muscle paralysis by using a nondepolarizing neuromuscular blocking agent was done to avoid IAP [2].

Botulinum toxin type A (Botox-A) is a muscle paralytic agent which is used in spasmodic dysphonia, strabismus, blepharospasm, oromandibular dystonia, cranioservical dystonia, torticollis, hemifacial spasm, focal hand dystonia, and anismus [3].

In this experimental study, we aimed to show the effect of botulinum toxin injection to abdominal muscles of the rats and whether it may be a useful method for decreasing the intraabdominal pressure by increasing the intraabdominal volume as a result of muscle paralysis.

1. Material and methods

A total of 15 Sprague-Dawley rats weighing 280 ± 20 g were included to the study. The animals were housed under standardized conditions and were fed standard rat chow and allowed water ad libitum. The study was approved by the Ethical Committee of the Medical Faculty, and experiments were performed in the animal research laboratory of Kirikkale University.

The animals were divided into 2 groups. Group 1 was consisting of 5 rats which served as the control group. Group 2 was the study group consisting of 10 rats. Respiratory rates were recorded, and pressure measurements were done by femoral artery catheterization (Data Acquifation, Biopac, Santa Barbara, CA). After 4 hours' starvation, intramuscular ketamine hydrochloride injection was done (50 mg/kg) (Ketalar, Eczacıbaşı, İstanbul, Turkey). After shaving and preparing the abdominal skin with 10% povidone-iodine solution, an abdominal 2-cm skin incision was done, and catheter (1.6 × 203 mm) of the intracompartmental pressure monitor system (Stryker, Kalamazoo, Mich) was introduced to the abdominal space with a depth of 3 cm through linea alba and secured with 4-0 silk suture material. Saline solution was given to the abdomen by a similar catheter until reaching to a pressure level of 9 cm H_2O which was corresponding 6 mm Hg in device (the device has a ±3.4 mm Hg error margin; we started to measure after 4 mm Hg), and volumes of the saline solution were recorded for each rat. After completing the measurements, the abdomen was emptied. Botulinum toxin (Botox, Allergan, Dublin, Ireland) was applied to the abdominal muscles at 16 different points (right, left, upper and lower quadrants, and rectus muscles) as a total of 2 mL (5 U/mL) by 26-gauge needles in group 2 (Fig. 1). Saline was injected at the same points in same amounts in the control group (group 1). Catheters were

Table 1 Mean intraabdominal saline volumes of the groups in the first and third days and percent differences (mean ± SEM)

	Group 1	Group 2
First day (mL)	63.8 ± 5.3	67.6 ± 6.4
Third day (mL)	64.4 ± 5.5	80.6 ± 6.1[a]
% Difference	1 ± 2.0	21 ± 3.7[b]

[a] Statistically higher in group 2 than group 1 ($P = .002$).
[b] Statistically significant difference between first and third days' values in group 2 ($P = .005$).

Table 2 The mean MUP amplitude and duration of the abdominal rectus muscles in group 1 and 2 (mean, min-max)

	Rectus muscles	
	Group 1	Group 2
First day		
MUP (μV)	193.4 (52-612)	186.9 (67-566)
Duration (ms)	5.2 (1.5-16.3)	5.7 (2.0-15.4)
Third day		
MUP (μV)	187.0 (50-592)	17.1[a] (5-49)
Duration (ms)	4.9 (1.8-14.7)	1.47[b] (0.2-6.0)

[a] Significantly lower than both first-day value in group 2 and third-day value in group 1 ($P < .05$).

[b] Significantly lower than group 1 value ($P < .05$).

removed, and incisions were closed with 4-0 silk suture material by continuous suturing.

After 3 days, respiratory rates and tension measurements were recorded, and all the rats were prepared as described previously.

All electromyographic (EMG) tests were performed with a Keypoint 4C (Dantec, Skovlunde, Denmark) EMG machine with the same examiner performing the test throughout the study. EMG activity was amplified using differential amplifier filter (bandpass 10 Hz to 10 kHz) monitored on a storage oscilloscope. EMG signals were recorded by using concentric needle electrodes. They were summed and integrated for qualification (motor unit potential [MUP]; with a very weak voluntary contraction, the needle EMG electrode records activity from single motor units. These action potentials are called MUPs (4) single MUP analysis, and interference patterns of muscles were recorded, respectively.

The EMG activity of the bilateral rectus abdominis and biceps muscles, which represent the muscles of the extremity and trunk, served as an index of botulinum toxin. EMG activity was recorded from groups 1 and 2 when animals were resting, when muscles were minimally contracted, and during continuous activity.

Saline was given to the abdomen of the rats, and volumes needed to obtain the same pressure levels (9 cm H_2O and 6 mm Hg in pressure device; Stryker) were recorded for each rat. After emptying the abdomen, the catheters were removed, and incisions were closed with 4-0 silk suture material.

Mann-Whitney U test was used in comparing the groups, and Wilcoxon signed rank test was used within the groups. The significance level was accepted as $P < .05$.

2. Results

First and third days' saline volumes were compared between the groups and within the groups. First days' volume was considered as 100, and the volume changes were measured according to this volume as percentage. Mean intraabdominal saline volumes of group 1 in the first and third days were 63.8 and 64.4 mL, respectively. The difference (1%) between the first and third days' saline volumes of group 1 was not statistically significant ($P = .461$). Mean intraabdominal saline volumes were 67.6 and 80.6 mL, respectively, in group 2 after botulinum toxin injection. There was a statistically significant difference (21%) between the first and third days' saline volumes of group 2 ($P = .005$). The difference between the saline volumes of groups 1 and 2 saline volumes on the third day was statistically significant ($P = .002$). The results are shown in Table 1.

The mean MUP amplitude of group 1 was 193.4 μV (52-612 μV), with a duration of 5.2 milliseconds (1.5-16.3 milliseconds) in the beginning and 187 μV (50-592 μV), with a duration of 4.9 milliseconds (1.8-14.7 milliseconds) after saline injection. The mean MUP amplitude of the abdominal rectus muscles in group 2 was 186.9 μV (67-566 μV), with a duration of 5.7 milliseconds (2.0-15.4 milliseconds) in the beginning, and 17.1 μV (5-49 μV), with a duration of 1.47 milliseconds (0.2-6.0 milliseconds) after botulinum toxin injection (Table 2).

In group 1, EMG activity could be seen, whereas there was little EMG activity in group 2 on the third day. Fig. 2 shows examples of EMG recording during single MUPs shown in normal, abnormal rectus muscles, and normal biceps muscle in Botox-injected rat in group 2.

Fig. 3 shows the normal MUP activity compared with normal MUPs after saline injection.

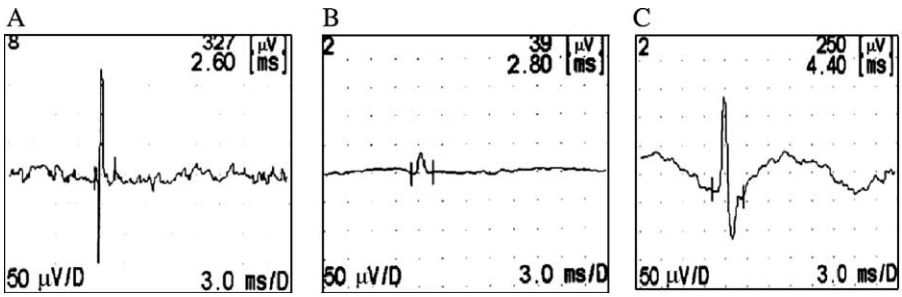

Fig. 2 Normal MUPs from minimally contracted rectus muscles before Botox injection (A), abnormal MUPs from minimally contracted rectus muscles after Botox injection (B), normal MUPs from minimally contracted biceps muscles from Botox injected rat in group 2 (C).

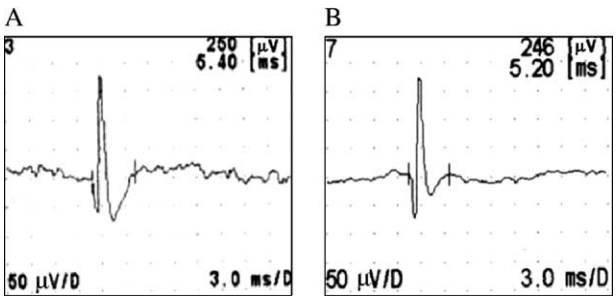

Fig. 3 Normal MUPs from minimally contracted rectus muscles before (A) and after (B) saline injection in group 1.

In group 1, the episodes of interference pattern of the rectus muscles were followed by continuous activity of some MUPs which was absent in group 2.

Respiratory and heart rates and pressure measurements were done. There was no significant difference between groups and in groups during procedure.

3. Discussion

Increased intraabdominal pressure after primary closure of gastroschisis and omphalocele or other abdominal wall defects is a problem. Especially in gastroschisis, it is sometimes hard to place the structures which have to be returned to the abdomen because of the visceroabdominal disproportion.

Increase in AP leads to diaphragmatic elevation, cardiorespiratory compromise, and intraabdominal organ hypoperfusion, including the kidneys and the gastrointestinal tract [4]. Gastric, vesical, and intraabdominal pressure monitoring was developed to maintain a safe closure and to avoid compartment syndrome [5,6]. Therefore, the basic aim of the surgeon is the closure of the defect without increasing the AP.

Abdominal muscles are the important components of the abdominal wall. Some of the preventive measures against the pressure are related with the elimination of the muscle activity. Many techniques or methods were developed and used to achieve this problem.

Lafer [7] described a method of dividing the rectus muscles transversely at the level of the umbilicus. They used this method in 2 gastroschisis patients and managed to close the defect with skin only by adding decompressing gastrostomy to the procedure. Later, this method was developed by Savage and Davey [8]. They performed a wide transverse division of the abdominal musculature by dividing both recti abdominis muscles and the lateral abdominal muscles as far as the anterior axillary line.

All previously described methods were planned to close the defect in small abdomen, and all were creating a ventral hernia and necessitating a second operation.

In 1948, Gross [9] reported the usefulness of the staged technique for the closure of small abdominal cavities. Meeker and Snyder [10] reported ventral hernia creation by skin closure in diaphragmatic defects.

Denmark and Georgeson [2] used a nondepolarizing neuromuscular blocking agent in 17 patients whose gastroschisis had been closed primarily. Paralysis continued for an average of 2 days, and mechanically assisted ventilation was continued for a mean of 3 days. They also used vigorous abdominal stretching in the operation. They suggested that using nondepolarizing neuromuscular blocking agent with vigorous abdominal stretching is helpful in avoiding the complications associated with increased AP.

In cases in which primary closure is not possible, there are other techniques or methods such as using silo, spring-loaded silo in gastroschisis, or Surgisis (Cook Surgical, Bloomington, IL) in hernia defects [11,12]. In addition, closure of umbilical port by using umbilical cord is reported by Bianchi and Dickson [13] without anesthesia. Similarly, Sandler et al [14] reported a plastic sutureless abdominal wall closure in gastroschisis. In their method, the defect is covered by umbilical cord, and Tegaderm dressings (3M Australia, Bumble, NSW) reinforce the defect.

Botulinum neurotoxin is produced by-gram negative anaerobic bacterium, *Clostridium botulinum*. The neurotoxin is synthesized in 7 different serotypes, and serotype A is the most potent [15]. Botulinum neurotoxin acts selectively on peripheral cholinergic nerve endings; it also inhibits transmitter release from preganglionic and postganglionic cholinergic nerve endings of the autonomic nervous system [15].

We found that botulinum A toxin injection to abdominal muscles of the rats increased intraabdominal volume which therefore decreased the pressure. If used in clinical cases, botulinum A toxin may gain popularity because it does not have a systemic effect, unlike the nondepolarizing neuromuscular blocking agents, and the patient will not need continuous ventilatory assistance for days. As we did not investigate the respiratory dynamics in detail such as vital capacity or other measures, our study has a limitation in this aspect, but according to the measurements on respiratory rates and pressure measurements, we observed that botulinum toxin did not effect these parameters.

Another benefit of botulinum A toxin injection may be avoiding ventral hernia and also a staged operation. Return of the muscle activity in 4 to 10 months is another advantage of the described study as abdominal wall dynamics will not be changed by dividing the muscles and the other components.

Botulinum toxin may be very useful as an adjunct in silo techniques and also in traumatic abdominal wall defects as well by decreasing the pressure.

Even after elective operations such as cholecystectomy or gastric procedures, AP increases postoperatively. Duggan and Drummond [16] reported that upper-lower abdominal and lower intercostal muscles have phasic respiratory activity during expiration after upper abdominal surgery, and this phasic pattern of muscle activity directly affects AP and breathing. Moreover, reduced lung volume is caused by

the result of this activity because of the insertion of the muscles at the lower rib cage and displaced diaphragm. In another study, they investigated the changes in abdominal muscle activity after upper abdominal surgery in the first 24 hours. They found a 3- to 5-times increase in the activity of the each group's abdominal muscles during inspiration when compared with the preoperative values. This increase also occurred in the expiration phase [17].

In the light of these studies, we see that tight closure of the abdomen may not be the only problem alone. Botulinum A toxin paralyzes the muscles, and therefore, these inspiratory or expiratory activities may be prevented in the patients postoperatively. Except the respiratory rates, we do not know how the respiratory dynamics will be affected by the possible use of botulinum toxin. As previously mentioned, our study has a limitation on the respiratory effects of the abdominal wall paralysis. This requires further studies searching the possible changes in vital capacity, hemodynamics, PaO_2, and the respiratory functional tests or other parameters.

This pilot experimental study shows that local injection of botulinum A toxin causes paralysis in abdominal wall muscles, increases the volume, and decreases the pressure, and this application may be used as an adjunct in abdominal wall closure in selective cases. Clinical application may be tried after the evaluation of the respiratory studies, and the minimal required dosages determined by the abdominal wall muscle pressure studies.

Acknowledgments

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References

[1] Schuster SR. Omphalocele, hernia of the umbilical cord and gastroschisis. In: Ravitch MM, Welch KJ, Benson CD, et al, editors. Pediatric surgery (3rd ed, vol 2). Chicago: Year Book Med; 1979. p. 778-801 [Chapter 77].

[2] Denmark SM, Georgeson KE. Primary closure of gastroschisis. Facilitation with postoperative muscle paralysis. Arch Surg 1983;118:66-8.

[3] Shaari CM, Sanders I. Quantifying how location and dose of botulinum toxin injections affect muscle paralysis. Muscle Nerve 1993;16:964.

[4] Oh SJ. Anatomical and physiological basis for electromyography studies. In: Oh SJ, editor. Clinical electromyography nerve conduction studies. 2nd ed. Baltimore: Williams and Wilkins; 1993. p. 4-6.

[5] Engum SA, Kogon B, Jensen E, et al. Gastric tonometry and direct intraabdominal pressure monitoring in abdominal compartment syndrome. J Pediatr Surg 2002;37:214-8.

[6] Lacey SR, Carris LA, Beyer III AJ, et al. Bladder pressure monitoring significantly enhances care of the infants with abdominal wall defects: a prospective clinical study. J Pediatr Surg 1993;28(10):1370-4.

[7] Lafer DJ. Rectus muscle transection for visceral replacement in gastroschisis. Surgery 1968;63:988-90.

[8] Savage JP, Davey RB. The treatment of gastroschisis. J Pediatr Surg 1971;6:148-52.

[9] Gross RE. A new method for surgical treatment of large omphaloceles. Surgery 1948;24:277.

[10] Meeker IA, Snyder WH. Surgical management of diaphragmatic defects in the newborn infant. Am J Surg 1962;104:196.

[11] Kidd JN, Levy MS, Wagner CW. Staged reduction of gastroschisis: a simple method. Pediatr Surg Int 2001;17(2-3):242-4.

[12] Oelschlager BK, Barreca M, Chang L, et al. The use of small intestine submucosa in the repair of paraesophageal hernias: initial observations of a new technique. Am J Surg 2003;186:4-8.

[13] Bianchi A, Dickson AP. Elective delayed reduction and no anesthesia: minimal intervention management for gastroschisis. J Pediatr Surg 1998;33:1339-40.

[14] Sandler A, Lawrence J, Meehan J, et al. A plastic sutureless abdominal wall closure in gastroschisis. J Pediatr Surg 2004;39(5):738-41.

[15] Coffield JA, Considine RB, Simpson LL. The site and mechanism of action of botulinum neurotoxin. In: Jankovic J, Hallett M. editors. Therapy with botulinum toxin. New York: Marcel Dekker; 1994. p. 3.

[16] Duggan JE, Drummond GB. Abdominal muscle activity and intra-abdominal pressure after upper abdominal surgery. Anesth Analg 1989;69:598-603.

[17] Duggan JE, Drummond GB. Activity of lower intercostal and abdominal muscle after upper abdominal surgery. Anesth Analg 1987;66:852-5.