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Severe Botulism after Intragastric Botulinum Toxin-A Injection: A Case Series

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Abstract

Intragastric botulismus toxin-A (BoNT-A) is one of the new approaches in the treatment of obesity. We aimed to contribute to the literature by presenting the clinical features, laboratory findings and treatment responses of iatrogenic botulism cases due to intragastric BoNT-A administered in our clinic. All detailed medical information was obtained by accessing the medical records of the patients who were hospitalized and followed up and treated between September 2022 and December 2022, and the diagnosis of A.05.1 Botulism was entered according to ICD-10, and whose clinical findings were compatible with botulism disease and who underwent intragastric BoNT-A application beforehand. These records were obtained by examining this information. 10 patients who developed botulism after intragastric BoNT-A application between 01/09/2022 and 28/02/2023 were followed up in our clinic. All of the patients were women. The mean age was 35. The mean hospital stay was 9 days. Only 1 of our cases required intensive care. Good response to treatment was accepted as a complete or near-complete improvement in the clinical findings of the patients and all of them had a good response to treatment. Intragastric BoNT-A administration is a procedure that requires careful indication with a profit/loss calculation considering the potential side effects. In addition, attention should be paid to dilution rates and dose amounts.

Keywords

Intragastric Botulismus Toxin-A, Botulism, Single Fiber Electromyography

1. Introduction

Obesity is becoming one of the most significant health problems with its increasing incidence all over the world [1] [2]. Today, surgical treatments of obes-

ity (gastric band and bypass, etc.) are the most effective approach for weight loss, but involve invasive and risky techniques [1] [3]. These invasive techniques have guided researchers to develop new endoscopic treatment modalities in this patient group who already have comorbid factors due to the risk they entail. Intra gastric botulismus toxin-A (BoNT-A) administration is a new treatment method developed with this mindset. By implementing this method, it is aimed to reduce the surgical risks, to eliminate the bad results of the surgery and to provide medical assistance to many patients who are at risk of mortality and morbidity due to obesity. With this indication, intra-gastric BoNT-A has come to the fore as a viable option due to its potency and longevity, and has been widely used in animal experiments and then in clinical practice, thanks to the safety information obtained from these studies [4] [5].

BoNT-A preparations are a pharmaceutical used to treat many diseases such as dystonia and migraine. The success and safety of treatment in such diseases have paved the way for the registered and unregistered use of this treatment in many areas [6]. BoNT varies from brand to brand in terms of the presence of complex proteins and excipients. This difference also determines the effectiveness and side effect profile of the molecule. BoNT neurotoxin has not yet been approved for obesity and its side effect profile needs to be determined in unusual applications such as intragastric application [7] [8].

Accurate and standardized reporting of adverse events of any method and medication contributes to the correct determination of the safety profile of a method or medicinal product and, in this respect, to the treatment of patients. In this study, we present a series of botulismus cases due to intragastric BoNT-A administration, who applied to a neurology department of a 3rd level healthcare institution within 6 months, to question the reliability of the current method, to determine the factors related to safety, and we aimed to draw attention to how this complication should be managed.

2. Materıal and Method

Patients who were followed up with a diagnosis of A.05.1 Botulism according to ICD-10 in the neurology service between September 2022 and December 2022 were identified by retrospective screening method. The files of 13 patients who met these criteria were examined. 3 patients were excluded from the study because botulism due to intragastric injection did not occur. All demographic and clinical information of the 10 patients included in the study were recorded by file scanning method.

3. Results

The age range of the patients was 28 - 40 years. 100% of the patients were female. All patients included in the study had a history of intragastric botulismus injection before the development of symptoms. Detailed clinical characteristics of the patients are mentioned below (**Table 1**).

Table 1. Demographic and clinical features of cases.

Variables	Age	Sex	Symptoms	Symptom duration	The time between administration and symptom onset	EMG findings	Response to treatment	Hospitalisation duration
Case 1	35	Female	Fatique Hoarsenes Diplopia	4 days	6 days	Repetetive EMG: Normal Single fiber EMG: NMJD	Evident	4 days
Case 2	28	Female	Dysphagia	6 days	5 days	Repetetive EMG: Normal Single fiber EMG: Normal	Evident	16 days
Case 3	38	Female	Weakness, Hoarseness Dyspnea Dysphagia	2 days	1 days	Repetetive EMG: Normal Single fiber EMG: NMJD	Complete	4 days
Case 4	31	Female	Weakness Dysphagia	10 days	5 days	Repetetive EMG: Normal Single fiber EMG: Normal	Complete	3 days
Case 5	40	Female	Diplopia	5 days	5 days	Repetetive EMG: Normal Single fiber EMG: Normal	Complete	7 days
Case 6	35	Female	Diplopia Dysphagia Dyspnea Fatique	6 days	3 days	Repetetive EMG: Normal Single fiber EMG: Normal	Complete	4 days
Case 7	34	Female	Diplopia Dyspnea Weakness	4 days	1 days	Repetetive EMG: Normal Single fiber EMG: Normal	Evident	29 days
Case 8	40	Female	Diplopia Weakness	13 days	5 days	Repetetive EMG: Normal Single fiber EMG: Normal	Complete	3 days
Case 9	36	Female	Diplopia Fatique	5 days	5 days	Repetetive EMG: Normal Single fiber EMG: NMJD	Complete	11 days
Case 10	34	Female	Diplopia Chewing Diffuculty	5 days	4 days	Repetetive EMG: Normal Single fiber EMG: Normal	Complete	9 days

EMG; Electromyography, NMJD; Neuromuscular junction.

3.1. Case 1

A 35-year-old female patient presented with symptoms of fatigue, hoarseness and double vision. Her symptoms were present for 4 days. The patient had

intragastric BoNT-A administration 10 days prior. The patient's neurological examination and the Repetitive Electromyography (EMG) performed were within normal limits. Motor end plate dysfunction was detected on Single Fiber EMG. Botulismus antitoxin administration at the appropriate dose and supportive treatment was initiated for the patient. After 4 days of follow-up, the patient was discharged with a normal neurological examination and almost complete improvement in her symptoms.

3.2. Case 2

A 28-year-old female patient presented with the symptom of dysphagia. The patient, whose symptoms were present for 6 days, had been administered intragastric BoNT-A 13 days prior due to obesity. In her neurological examination, the patient's bilateral gag reflex could not be detected, and her Repetitive and Single Fiber EMG were within normal limits. Supportive treatment and antitoxin administration were initiated for the patient. During the follow-up of the patient, her saturation decreased due to aspiration of her salivation and it was decided to follow him in the intensive care unit. The patient started to be administered pyridostigmine treatment. The patient, whose saturation improved with oxygen support and antibiotherapy, and whose swallowing and gag reflexes returned, was followed up in the service with pyridostigmine and supportive treatment. Following 18 days of hospitalization, the patient was discharged to use pyridostigmine 4 × 1 with an 80% improvement in symptoms.

3.3. Case 3

A 38-year-old female patient presented with lethargy, difficulty in chewing, hoarseness, dyspnea, and dysphagia. The patient had intragastric BoNT-A administration 2 days prior. The patient's symptoms were increasing at the end of the day. In her neurological examination, bilateral ptosis developed in the eye strain test and motor strength in the neck flexor muscles was 4/5. Denervation potentials were detected in places as a result of the needle EMG, and the repetitive EMG of the patient was within normal limits, but the findings of motor endplate dysfunction were discovered in the Single Fiber EMG. The patient started to be administered supportive treatment, antitoxin administration and pridostigmine 3 × 1 treatment. On the 3rd day of treatment, the patient's neurological examination returned to normal. After 5 days of follow-up, the patient was discharged in good health.

3.4. Case 4

A 31-year-old female patient presented with symptoms of lethargy for 10 days, fatigue when talking and difficulty in swallowing. The patient had intragastric BoNT-A administration 15 days prior. The patient's neurological examination, repetitive and Single Fiber EMG were within normal limits. The patient started to be administered antitoxin therapy. After 5 days of follow-up, she was dis-

charged in good health.

3.5. Case 5

A 40-year-old female patient presented with a symptom of double vision for 5 days. It was learned that he had intragastric BoNT-A administration 10 days prior. In the neurological examination of the patient, there was bilateral ptosis in the fatigue test. The patient started to be administered botulismus antitoxin therapy. Repetitive EMG was within normal limits, but Single Fiber EMG showed motor endplate dysfunction. The patient was discharged in good health following 20 days of hospitalization.

3.6. Case 6

A 35-year-old female patient presented with the symptoms of diplopia, dysphagia, shortness of breath, and fatigue. The patient's symptoms were present for 6 days, intragastric BoNT-A was administered 9 days prior due to obesity. The patient started to be administered pyridostigmine and antitoxin therapy. During the follow-up of the patient, a significant improvement was detected in the examination. The patient was followed up for 4 days and was discharged in good health.

3.7. Case 7

A 34-year-old female patient presented with the symptoms of double vision, shortness of breath, and lethargy. In her neurological examination, motor power was 4/5 in the proximal upper extremities. Her Repetitive and Single Fiber EMG results were within the normal limits. The patient reported that her symptoms began after intragastric BoNT-A administration 4 days prior. Anti-toxin and pyridostigmine started to be administered to the patient. She was discharged with partial improvement after 29 days of follow-up.

3.8. Case 8

A 40-year-old female patient presented with the symptom of diplopia and lethargy. She had intragastric BoNT-A done 18 days prior. Neurological examination was normal. Repetitive and Single Fiber EMG were normal. The patient started to be administered supportive treatment and pyridostigmine. On the 3rd day of the follow-up, complete recovery was observed in the patient. The patient was discharged in good health.

3.9. Case 9

A 36-year-old female patient presented with symptoms of diplopia and fatigue. Her symptoms started 5 days after intragastric BoNT-A administration and she had been complaining about these symptoms for 5 days. Neurological examination was normal. Repetitive EMG was within normal limits, but Single Fiber EMG had neuromuscular junction dysfunction. The patient started to be admi-

nistered supportive treatment and antitoxin treatment and was discharged with full recovery after 11 days of follow-up.

3.10. Case 10

A 34-year-old female patient had double vision and chewing difficulties for 5 days. She had had intragastric BoNT-A administration 4 days before her symptoms started. The patient's neurological examination, tender and repetitive EMG were normal. Antitoxin therapy was initiated, and the patient's symptoms completely resolved.

4. Discussion

In this study, we aimed to draw attention to the potential risks of the method by presenting our experience of botulism in patients who received intragastric BoNT-A. To our knowledge, this case series is the first to report cases of botulism associated with intragastric BoNT-A. Intragastric BoNT-A has the effect of slowing gastric motility and causing an earlier sensation of fullness, resulting in weight loss in obese patients [9]. The first case of this technique was reported by Rollnik [10] in 2003. Some subsequent studies have reported conflicting results, some being effective and some being ineffective [11]-[15]. The reason why this technique came to the fore was the life-threatening nature of morbid obesity, and bariatric surgery methods used in the surgical treatment of morbid obesity were difficult-to-apply techniques with many complications. In addition, this technique was considered important in this patient group in terms of both shortening the time until surgery and reducing surgical risks by supporting weight loss in patients during this period [16] [17].

Botulism, on the other hand, is a potentially fatal paralytic disease primarily caused by toxins from the anaerobic, spore-forming bacterium Clostridium botulinum. If this disease is not recognized and treated within the appropriate time, it may result in respiratory failure and death. Botulinum toxin is a potent neurotoxin produced by Clostridium botulinum is classified as serotype A-G, however, serotype A is the only agent currently commercially available. By inhibiting alpha motor neurons and acetylcholine release in all parasympathetic and cholinergic postganglionic sympathetic neurons, it reduces lethargy of striated and smooth muscle and hyperactivity of glands, but all these effects are dose-dependent [18]. BOTOX (crystalline toxin type A, molecular weight [MW] 900 kD, Allergan Inc, Irvine, Calif) is licensed to treat blepharospasm, strabismus, cervical dystonia, glabellar lines, and primary axillary hyperhidrosis. A typical clinical application ranges from 4 to 20 units for cosmetic purposes to 300 units for therapeutic purposes. Myobloc/Neurobloc (toxin type B, Solstic Neurosciences, Malvern, Pa) [19].

The expansion of registered and unregistered applications of botulinum toxins has resulted in widespread use. Although the exact human lethal dose of crystalline botulinum toxin A is unknown, extrapolation from primate studies suggests

that the approximate intravenous or intramuscular human lethal dose is 40 U/kg. Cosmetic injection-induced botulism is a type of botulism that has gradually emerged due to the growth of cosmetic medicine in recent years. It differs from other forms of botulism (food-borne, infant, and wound) in that patients receive direct injections of the botulinum toxin without experiencing Clostridium botulinum infection. However, specific diagnostic and treatment modalities for cosmetic injection-induced botulism have not been clarified. Clinical experience is the main way to diagnose and treat botulism [19]. One of the reasons why the side effects of botulismus toxins applied for cosmetic purposes are under-reported and unknown is that this toxin is used in many cosmetic conditions by many disciplines, either registered or unregistered, but its side effects are on the neurological systems. Therefore, this agent can be used uncontrollably and its side effects cannot be followed up precisely, thus posing a potential risk to the health of patients. BoNT-A is one of the most potent neurotoxins in human history. Therefore, iatrogenic botulismus is a very remarkable complication in medical practice. Many cases have been reported on this subject so far. These adverse events were generally related to the amount of titration and number of injections [20]-[24].

The mechanism of action of intragastric BoNT-A is acetylcholine-mediated inhibition of gastric antral motility, which delays gastric emptying and also causes a feeling of early satiety. The interesting aspect is that it is less invasive and has fewer expected side effects than other obesity surgery procedures [25]. Although research on this treatment modality has not proven its effectiveness, it encourages the method due to these aspects. But there are studies that contradict this information [26] [27] [28] [29]. The heterogeneous feature of the method in terms of dose, injection site and number of injections also affects the results on effectiveness and reliability. The general opinion about the application is that it can be beneficial in selected patients and reduces body weight by 14%. However, this effect is expected to last for two months [30].

The cases we presented were botulism cases that developed due to intragastric botulismus toxin A application, administered by our clinic in the last 6 months. Considering our previous experiences, the increase in these cases in the last 6 months compared to the time period we mentioned was a remarkable observation from our perspective. Since the method of intra-gastric application of botulinum toxin A is a novel method, this caused us to believe that the current method of administration could potentially be effective in creating iatrogenic botulism, and our cases were reported to the pharmacovigilance unit. If we examine the characteristics of our cases; The mean duration of symptoms with the procedure was 4 days. The incubation period of botulism varies from 6 hours to 8 days [30]. Therefore, the time from the procedure to the symptom onset may vary from case to case. The most common symptoms were double vision, lethargy, fatigue, and difficulty chewing. Generally, the response to treatment was positive. We think that the most significant factor in the response to treatment is the ability to provide antitoxin therapy quickly and effectively [31] [32] [33]. The

average length of stay was 9 days. One patient was followed up in the intensive care unit. The mean age of the patients was 35 years and all were female patients. It was quite remarkable that all of our cases consisted of female patients. This may be due to the fact that women possess less muscle mass than men [34]. Baseline EMGs of the patients showed neuromuscular junction dysfunction at a rate of 30%. EMG was found to be normal in 70% of the patients. None of our patients had any other chronic diseases or drug use.

No side effects of this method were reported in the studies. However, neuromuscular symptoms related to botulismus toxin application have been reported in procedures performed with other indications. Therefore, these side effects are expected to occur following intragastric botox application. However, when we reviewed the literature, we did not encounter any systemic botulism cases due to intragastric BoNT-A [4] [19]. Therefore, the cases we present are the first of their kind in this respect. This may be due to the unregistered nature of these transactions and the lack of a multidisciplinary approach. Therefore, our study is important because it includes cases seen in a neurological clinic on this subject. It is important to address this emergency by presenting these cases that we have observed within a short time. We think that the explanation for the systemic side effects of a local administration method is likely the local uptake of high and intense doses and the passage of toxins into the systemic circulation [35].

Due to the volume injected at each puncture site and the proximity of the cholinergic nerve endings, serious side effects may occur with this method. In addition, studies have shown that the effectiveness of the method depends on the toxin dose. Therefore, it is thought that using a higher dose would not be appropriate [11]. In other words, paying attention to the amount of dilution and low dose administration is a way of thinking that will reduce side effects without reducing the effectiveness of intragastric BoNT-A administration. In addition, the correct transport and storage conditions should be observed. Furthermore, it is recommended to use the product within 4 hours after dilution, it should not be frozen and should be used within this period [36].

The limitations of our study are small sample size, the lack of a control group, the lack of information about the dosages of the neuromodulators used, the type of neuromodulator used, the clinical areas injected, and our retrospective design. Consequently, the method should not be seen as having no side effects. Randomized controlled studies are needed to determine the reliability of the method. In addition, we believe that the method should be standardized in the most reliable way, again with the dose, dilution rate and injection sites. In addition, all cosmetic applications of BoNT-A should be regulated and closely followed. Patients should be informed of potential side effects before and after administration. On top of this, clinicians should be careful about the follow-up of potential side effects and awareness of the antitoxins used in the treatment of generalized botulism, the application methods, doses and the importance placed on early antitoxin applications should be increased.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Torralvo, F.J.S., Pedreño, L.V., Marín, M.G., *et al.* (2021) Endoscopic Intragastric Injection of Botulinum Toxin a in Obese Patients on Bariatric Surgery Waiting Lists: A Randomised Double-Blind Study (IntraTox Study). *Clinical Nutrition*, **40**, 1834-1842. https://doi.org/10.1016/j.clnu.2020.10.008

[2] ASGE Bariatric Endoscopy Task Force and ASGE Technology Committee, Abu Dayyeh, B.K., Edmundowicz, S.A., Jonnalagadda, S., *et al.* (2015) Endoscopic Bariatric Therapies. *Gastrointestinal Endoscopy*, **81**, 1073-1086. https://doi.org/10.1016/j.gie.2015.02.023

[3] Elder, K.A. and Wolfe, B.M. (2007) Bariatric Surgery: A Review of Procedures and Outcomes. *Gastroenterology*, **132**, 2253-2271. https://doi.org/10.1053/j.gastro.2007.03.057

[4] Zargaran, D., Zoller, F., Zargaran, A., *et al.* (2022) Complications of Cosmetic Botulinum Toxin a Injections to the Upper Face: A Systematic Review and Meta-Analysis. *Aesthetic Surgery Journal*, **42**, 327-336. https://doi.org/10.1093/asj/sjac036

[5] Boon Harold Tan, K. (2007) Aesthetic Medicine: A Health Regulator's Perspective. *Clinical Governance: An International Journal*, **12**, 13-25. https://doi.org/10.1108/14777270710725364

[6] Li, Y., Liu, T. and Luo, W. (2021) Botulinum Neurotoxin Therapy for Depression: Therapeutic Mechanisms and Future Perspective. *Frontiers in Psychiatry*, **12**, Article 584416. https://doi.org/10.3389/fpsyt.2021.584416

[7] Chiu, S.Y., Burns, M.R. and Malaty, I.A. (2021) An Update on Botulinum Toxin in Neurology. *Neurologic Clinics*, **39**, 209-229. https://doi.org/10.1016/j.ncl.2020.09.014

[8] Dressler, D. (2021) Clinical Pharmacology of Botulinum Toxin Drugs. In: Whitcup, S.M. and Hallett, M., Eds., *Botulinum Toxin Therapy*, Springer, Cham, 93-106. https://doi.org/10.1007/164_2019_273

[9] Finucane, M.M., Stevens, G.A., Cowan, M.J., *et al.* (2011) National, Regional, and Global Trends in Body-Mass Index Since 1980: Systematic Analysis of Health Examination Surveys and Epidemiological Studies with 960 Country-Years and 9·1 Million Participants. *The Lancet*, **377**, 557-567. https://doi.org/10.1016/S0140-6736(10)62037-5

[10] Rollnik, J.D., Meier, P.N., Manns, M.P. and Göke, M. (2003) Antral Injections of Botulinum a Toxin for the Treatment of Obesity. *Annals of Internal Medicine*, **138**, 359-360. https://doi.org/10.7326/0003-4819-138-4-200302180-00026

[11] Foschi, D., Lazzaroni, M., Sangaletti, O., Corsi, F., Trabucchi, E. and Bianchi Porro, G. (2008) Effects of Intramural Administration of Botulinum Toxin a on Gastric Emptying and Eating Capacity in Obese Patients. *Digestive and Liver Disease*, **40**, 667-672. https://doi.org/10.1016/j.dld.2008.02.040

[12] Topazian, M., Camilleri, M., Enders, F.T., *et al.* (2013) Gastric Antral Injections of Botulinum Toxin Delay Gastric Emptying But Do Not Reduce Body Weight. *Clinical Gastroenterology and Hepatology*, **11**, 145-150. https://doi.org/10.1016/j.cgh.2012.09.029

[13] Bang, C.S., Baik, G.H., Shin, I.S., *et al.* (2015) Effect of Intragastric Injection of Botulinum Toxin a for the Treatment of Obesity: A Meta-Analysis and Meta-Regression. *Gastrointestinal Endoscopy*, **81**, 1141-1149. https://doi.org/10.1016/j.gie.2014.12.025

[14] Bustamante, F., Brunaldi, V.O., Bernardo, W.M., *et al.* (2017) Obesity Treatment with Botulinum Toxin-A Is Not Effective: A Systematic Review and Meta-Analysis. *Obesity Surgery*, **27**, 2716-2723. https://doi.org/10.1007/s11695-017-2857-5

[15] De Moura, E.G.H., Ribeiro, I.B., Frazão, M.S.V., *et al.* (2019) EUS-Guided Intragastric Injection of Botulinum Toxin a in the Preoperative Treatment of Super-Obese Patients: A Randomized Clinical Trial. *Obesity Surgery*, **29**, 32-39. https://doi.org/10.1007/s11695-018-3470-y

[16] Wolfe, B.M., Kvach, E. and Eckel, R.H. (2016) Treatment of Obesity: Weight Loss and Bariatric Surgery. *Circulation Research*, **118**, 1844-1855. https://doi.org/10.1161/CIRCRESAHA.116.307591

[17] Simpson, S.A., Shaw, C. and McNamara, R. (2011) What Is the Most Effective Way to Maintain Weight Loss in Adults? *BMJ*, **343**, d8042. https://doi.org/10.1136/bmj.d8042

[18] Michael Cherington, M. (2004) Botulism: Update and Review. *Seminars in Neurology*, **24**, 155-163. https://doi.org/10.1055/s-2004-830901

[19] Zong, C., Chen, Z.Y., Liu, W.H. and Li, G.S. (2021) Botulism Due to Cosmetic Injection of Botulinum Toxin: Five-Year Experience. *Plastic and Reconstructive Surgery*, **148**, 335e-337e. https://doi.org/10.1097/PRS.0000000000008173

[20] Ghasemi, M., Norouzi, R., Salari, M. and Asadi, B. (2012) Iatrogenic Botulism after the Therapeutic Use of Botulinum Toxin-A: A Case Report and Review of the Literature. *Clinical Neuropharmacology*, **35**, 254-257. https://doi.org/10.1097/WNF.0b013e31826248b8

[21] Coban, A., Matur, Z., Hanagasi, H.A. and Parman, Y. (2010) Iatrogenic Botulism after Botulinum Toxin Type A Injections. *Clinical Neuropharmacology*, **33**, 158-160. https://doi.org/10.1097/WNF.0b013e3181d479e0

[22] Crowner, B.E., Torres-Russotto, D., Carter, A.R. and Racette, B.A. (2010) Systemic Weakness after Therapeutic Injections of Botulinum Toxin A: A Case Series and Review of the Literature. *Clinical Neuropharmacology*, **33**, 243-247. https://doi.org/10.1097/WNF.0b013e3181f5329e

[23] Varghese-Kroll, E. and Elovic, E.P. (2009) Contralateral Weakness and Fatigue after High-Dose Botulinum Toxin Injection for Management of Poststroke Spasticity. *American Journal of Physical Medicine & Rehabilitation*, **88**, 495-499. https://doi.org/10.1097/PHM.0b013e3181a5b056

[24] Howell, K., Selber, P., Graham, H.K. and Reddihough, D. (2007) Botulinum Neurotoxin A: An Unusual Systemic Effect. *Journal of Paediatrics and Child Health*, **43**, 499-501. https://doi.org/10.1111/j.1440-1754.2007.01122.x

[25] Elder, K.A. and Wolfe, B.M. (2007) Bariatric Surgery: A Review of Procedures and Outcomes. *Gastroenterology*, **132**, 2253-2271. https://doi.org/10.1053/j.gastro.2007.03.057

[26] Shapiro, R.L., Hatheway, C. and Swerdlow, D.L. (1998) Botulism in the United States: A Clinical and Epidemiologic Review. *Annals of Internal Medicine*, **129**, 221-228. https://doi.org/10.7326/0003-4819-129-3-199808010-00011

[27] García-Compean, D. and Maldonado Garza, H. (2008) Intragastric Injection of Botulinum Toxin for the Treatment of Obesity. Where Are We? *World Journal of Gastroenterology*, **14**, 1805-1809. https://doi.org/10.3748/wjg.14.1805

[28] Topazian, M., Camilleri, M., De La Mora-Levy, J., *et al.* (2008) Endoscopic Ultrasound-Guided Gastric Botulinum Toxin Injections in Obese Subjects: A Pilot Study. *Obesity Surgery*, **18**, 401-407. https://doi.org/10.1007/s11695-008-9442-x

[29] Bustamante, F., Ottoboni Brunaldi, V., Bernardo, W.M., *et al.* (2017) Obesity Treatment with Botulinum Toxin-A Is Not Effective: A Systematic Review and Meta-Analysis. *Obesity Surgery*, **27**, 2716-2723. https://doi.org/10.1007/s11695-017-2857-5

[30] Gui, D., Migrone, G. and Valenza, V. (2006) Effect of Botulinum Toxin Antral Injection on Gastric Emptying and Weight Reduction in Obese Patients: A Pilot Study. *Alimentary Pharmacology & Therapeutics*, **23**, 675-680. https://doi.org/10.1111/j.1365-2036.2006.02773.x

[31] Tacket, C.O., Shandera, W.X. and Mann, J.M. (1984) Equine Antitoxin Use and Other Factors That Predict Outcome in Type A Foodborne Botulism. *The American Journal of Medicine*, **76**, 794-798. https://doi.org/10.1016/0002-9343(84)90988-4

[32] Chang, G.Y. and Ganguly, G. (2003) Early Antitoxin Treatment in Wound Botulism Results in Better Outcome. *European Neurology*, **49**, 151-153. https://doi.org/10.1159/000069073

[33] Sandrock, C.E. and Murin, S. (2001) Clinical Predictors of Respiratory Failure and Long-Term Outcome in Black Tar Heroin-Associated Wound Botulism. *Chest*, **120**, 562-566. https://doi.org/10.1378/chest.120.2.562

[34] Coban, A., Matur, Z., Hanagasi, H.A. and Parman, Y. (2010) Iatrogenic Botulism after Botulinum Toxin Type A Injections. *Clinical Neuropharmacology*, **33**, 158-160. https://doi.org/10.1097/WNF.0b013e3181d479e0

[35] Garner, C.G., Straube, A., Witt, T.N., Gasser, T. and Oertel, W.H. (1993) Time Course of Distant Effects of Local Injections of Botulinum Toxin. *Movement Disorders*, **8**, 33-37. https://doi.org/10.1002/mds.870080106

[36] Coté, T.R., Mohan, A.K., Polder, J.A., Walton, M.K. and Braun, M.M. (2015) Botulinum Toxin Type A Injections: Adverse Events Reported to the US Food and Drug Administration in Therapeutic and Cosmetic Cases. *Journal of the American Academy of Dermatology*, **53**, 407-415. https://doi.org/10.1016/j.jaad.2005.06.011