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Eskisehir Osmangazi University Faculty of Medicine Students' Knowledge Levels about Botulinum Toxin: Survey Study

Eskişehir Osmangazi Üniversitesi Tıp Fakültesi Öğrencilerinin Botulinum Toksini Hakkında Bilgi Düzeyleri: Anket Çalışması

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Abstract

The aim of the study is to evaluate the knowledge and awareness level of medical students through a questionnaire about botulinum toxin, which is widely used in medicine. The correct answer(s) of each question is explained at the end of the questionnaire thus it is aimed to encourage students to learn more about the subject by providing necessary information. The study is a cross-sectional descriptive study conducted by Google survey method to Osmangazi Medical Faculty students in the 2020-2021 academic year. Of the 404 students who responded the survey, 53 were 1st grade, 103 were 2nd grade, 50 were 3rd grade, 64 were 4th grade, 68 were 5th grade and 68 were 6th grade students. The questionnarie contains eight questions and the correct answer to each question is ten points. In questions with more than one correct answer, the weighted average score of each correct answer is calculated by division of ten to the number of correct answers. The total score of the questionnarie is eighty points. The average scores of the first to sixth grades were 38.87, 41.21, 56.75, 56.59, 60.66 and 62.95 respectively. According to the results of our study the level of knowledge of medical students about Botulinum toxin increases with the grade and both the level of knowledge and awareness about Botulinum toxin are at an acceptable level.

Keywords: Botulinum toxin; medical school; student; knowledge level; survey

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Özet

Tıpta kullanımı çok yaygın olan Botulinum toksininin tıp fakültesi öğrencileri arasında bilinirlik ve farkındalık düzeyinin bir anket çalışması üzerinden değerlendirilmesi planlanmıştır. Anket sonunda her sorunun doğru yanıtı/yanıtları açıklanmış olup, öğrencilere gerekli bilgiler verilerek bu konuda daha fazlasını öğrenmeye teşvik etmek amaçlanmıştır. Çalışma 2020-2021 öğretim yılı içinde Osmangazi Tıp Fakültesi öğrencilerine Google anket yöntemi uygulanarak gerçekleştirilmiş kesitsel tanımlayıcı bir çalışmadır. Ankete yanıt veren 404 öğrencinin 53'ü 1. sınıf, 103'ü 2. sınıf, 50'si 3. sınıf, 64'ü 4. sınıf, 68'i 5. sınıf ve 68'i de 6. sınıf öğrencisidir. Sekiz soruluk bu anket çalışmasında her sorunun doğru yanıtı 10 puan olarak belirlenmiş; anket, toplamda 80 puan üzerinden değerlendirilmiştir. Birden fazla doğru yanıtı olan sorularda sorunun değeri doğru yanıt sayısına bölünerek; her bir doğru şıkkın ağırlık puanı hesaplanmıştır. Puan ortalamaları birinci sınıf öğrencilerinden başlayarak sırasıyla 38,87; 41,21; 56,75; 56,59; 60,66 ve 62,95 olarak hesaplanmıştır. Sınıfla beraber Botulinum toksini bilgi düzeyinin de arttığı gözlenmektedir. Çalışmamızın sonucuna göre tıp fakültesi öğrencilerinin Botulinum toksini hakkındaki bilgi düzeyleri ve farkındalıkları kabul edilebilir seviyededir.

Anahtar Kelimeler: Botulinum toksini; tıp fakültesi; öğrenci; bilgi düzeyi; anket

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1. Introduction

Botulinum toxin (BT) is a neurotoxic protein produced by Clostridium botulinum, a gram-positive anerobic spore bacterium, and is also one of the most toxic biological substances known.

Although BT stands out as a cosmetic application today, its use in medicine is becoming widespread. It is also used in the treatment of hyperactive nerve disorders, including excessive sweating, chronic pain and some allergy symptoms, treatment of muscle spasticity and some other muscle diseases1. Its first use in medicine was described by Alan Scott as an alternative to surgery in the treatment of strabismus and blepharospasm2.

Although BT is generally considered safe, complications may occur; they are usually mild and temporary. The most common complications are ecchymosis, injection into the wrong muscle group or spreading from the injection site causing temporary paralysis of unwanted muscles. Other complications include asymmetry, muscle weakness, eyelid/eyebrow ptosis and difficulty in swallowing3,4 and they can be prevented largely by the practitioner's mastery of anatomy.

Medical students should learn all aspects of the medicine to practice along the evidences, guidelines, and ethics after their graduation. Besides they have an unnamed responsibility to inform and guide their environment in medical matters. Therefore, in this study we aimed to determine the knowledge and awareness levels of medical students about BT and its scope of application and to evaluate the differences according to the grades.

2. Material and method

The study was approved by Eskisehir Osmangazi University (ESOGÜ) non-interventional clinical research ethics committee (decision # 18.02.2020/19). The study is a cross-sectional and descriptive study. BT information questionnaire prepared with "Google surveys" were mailed to Osmangazi Medical Faculty students of 2020-2021 academic year. A total of 1582 students received the questionnaire.

The survey consists of 8 questions of 10 points each. The questions # 2 and 7 have multiple correct answers. For questions with multiple correct answers, 10 points is divided by the number of the correct answers thus the weight score of each correct option is calculated. The survey is evaluated on a total of 80 points.

Statistical Analysis

The distribution of each continuous variable was tested for normality using the Shapiro-Wilk test and is expressed as median value (%25_%75). Non-normally distributed variables were performed using the Kruskal Wallis test. A p-value <0.05 was considered significant. All analyses were performed using the SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA).

3. Results

Of the 1582 students, 407 answered the survey. The grade levels and the number of responding students are presented in Table 1.

Table 1. Distribution of total number of students in ESOGÜ Faculty of Medicine and number of students who answered the survey to the classrooms.

Grade level	Number of students	Number of students who answered the survey	Participation rate
1	306	53	%17,32
2	290	103	%35,51
3	278	52	%18,7
4	235	64	%27,23
5	239	67	%28,03
6	234	68	%29,05
Total	1582	407	%25,72

Table 2. TIP FAKÜLTESİ ÖĞRENCİLERİNİN BOTULİNUM TOKSİNİ İLGİLİ BİLGİ DÜZEYLERİNİ ÖLÇME ANKETİNE VERDİKLERİ CEVAPLARIN DAĞILIMI

STUDENTS' ANSWERS TO THE SURVEY

		1.SINIF (1st grade)	2.SINIF (2nd grade)	3.SINIF (3rd grade)	4.SINIF (4th grade)	5.SINIF (5th grade	6.SINIF (6th grade)
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Botulinum toksini nedir? **What is botulinum toxin?**	Bir tür dolgudur. It is a kind of filler.	31 (%58,5)	50 (%48,5)	9 (%18)	15 (%23,4)	12 (%18,2)	7 (%10,3)
	Bir tür zehirdir* It is a kind of poison.	25 (%47,2)	59 (%57,3)	44 (%88)	56 (%87,5)	60 (%90,9)	65 (%95,6)
	Bilmiyorum I don't know	2 (%3,8)	3 (%2,9)	1 (%2)	0 (%0)	1 (%1,5)	0 (%0)
	Yüzün bazı bölgelerindeki istenmeyen kırışıklardan kurtulmak* Treatment of facial rhytids	51 (%96,2)	98 (%95,1)	50 (%100)	62 (%96,9)	65 (%98,5)	67 (%96,5)
	Şaşılık* Strabismus	19 (%35,8)	15 (%14,6)	12 (%24)	32 (%50)	38 (%57,6)	46 (%67,6)
	Servikal distoni* Cervical dystonia	9 (%17)	14 (%13,6)	14 (%28)	25 (%39,2)	40 (%60,6)	47 (%69,1)

BT hangi endikasyonlarda kullanılabilir? **Which are the indications of BT?**	Migren* Migraine	13 (%24,5)	20 (%19,4)	12 (%24)	27 (%42,2)	27 (%40,9)	34 (%50)
	Blefarospazm* Blepharospasm	5 (%9,4)	9 (%8,7)	6 (%12)	16 (%25)	44 (%66,7)	48 (%70,6)
	İdrar kaçırma* Urinary incontinance	16 (%30,2)	17 (%16,5)	14 (%28)	28 (%43,8)	28 (%42,4)	42 (%61,8)
	Hemifasial spazm* Hemifacial spasm	9 (%17)	13 (%12,6)	14 (%28)	29 (%45,3)	39 (%59,1)	49 (%72,1)
	Aşırı terleme* Hyperhydrosis	21 (%39,6)	29 (%28,2)	26 (%52)	39 (%60,6)	42 (%63,6)	49 (%72,1)
	Cerebral palsili çocuklarda* Children with cerebral palsy	6 (%11,3)	9 (%8,7)	8 (%16)	14 (%21,9)	31 (%47)	51 (%75)
	Geceleri diş sıkma/gıcırdatma* Bruxism	21 (%39,6)	34 (%33)	18 (%36)	43 (67,1)	36 (%54,5)	47 (%69,1)
	Bilmiyorum I don't know	5 (%9,4)	8 (%7,8)	1 (%2)	1 (%1,6)	3 (%4,5)	4 (%5,9)
Botulinum toksini vücutta nereye etki eder? **Where does botulinum toxin**	Tüm vücuttaki kas ve sinirlere To all muscles and nerves all over the body	1 (%1,9)	5 (%4,9)	1 (%2)	1 (%1,6)	4 (%6,1)	5 (%7,4)
	Uygulandığı bölgedeki kas ve sinirlere* To the muscles and nerves in the	50 (%94,3)	96 (%93,2)	50 (%100)	64 (%100)	66 (%100)	66 (%97,1)

affect in the body?	injection area						
	I don't know	4 (%7,5)	6 (%5,8)	0 (%0)	0 (%0)	0 (%0)	0 (%0)
Botulinum toksininin moleküler yapısı nedir? **What is the molecular structure of botulinum toxin?**	Protein* Protein	13 (%24,5)	52 (%50,5)	29 (%58)	43 (%67,2)	42 (%63,6)	48 (%70,6)
	Lipit Lipid	9 (%17)	12 (%11,7)	1 (%1)	1 (%1,6)	1 (%1,5)	2 (%2,9)
	Karbonhidrat Carbohydrate	1 (%1,9)	4 (%3,9)	0 (%0)	0 (%0)	1 (%1,5)	0 (%0)
	Mineral Mineral	2 (%3,8)	4 (%3,9)	1 (%2)	0 (%0)	0 (%0)	0 (%0)
	Bilmiyorum I don't know	33 (%62,3)	44 (%42,7)	19 (%38)	23 (%35,9)	22 (%33,3)	19 (%27)
Botulinum toksininin etki mekanizması nedir? **What is the mechanism of action of botulinum toxin?**	Sinaptik aralıktaki nörotransmitterleri parçalar. Breaks down neurotransmitters in the synaptic range.	11 (%20,8)	13 (%12,6)	6 (%12)	6 (%)	2 (%3)	2 (%2,9)
	Nöronları zehirleyerek sinirsel iletimi engeller. Inhibits neuronal transmission	10 (%18,9)	15 (%14,6)	0 (%0)	3 (%)	2 (%3)	1 (%1,5)
	Nöronların mitokondrilerini baskılayarak enerjisiz bırakır Suppresses the mitochondria of	2 (%3,8)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	0 (%0)

	neuronal cells						
	Sinir uçlarından asetil kolin salınımını engeller* inhibits the release of acetylcholine from nerve endings	26 (%49,1)	54 (%52,4)	42 (%84)	50 (%78,1)	61 (%92,4)	64 (%94,1)
	Bilmiyorum I don't know	12 (%22,6)	26 (%25,2)	4 (%8)	10 (%15,6)	4 (%6,1)	2 (%2,9)
Botulizm nedir? **What is botulismus?**	Yiyecekler ile Clostridum botulinum bakteri toksinin alınmasıyla oluşan enfeksiyon hastalığı* An infectious disease caused by ingestion of Clostridum botulinum bacterial toxin with food	16 (%30,2)	23 (%22,3)	36 (%72)	44 (%68,8)	55 (%83,3)	56 (%82,4)
	Kasların spastik kasılı kalmasıyla oluşan durum Condition caused by spastic contraction of the muscles	7 (%13,2)	20 (%19,4)	7 (%14)	17 (%26,6)	18 (%27,3)	11 (%16,2)
	Çok soğuk havalarda yüz kaslarının felciyle karakterize durum Condition characterized by paralysis of facial muscles in very cold weather	5 (%9,4)	7 (%6,6)	1 (%2)	3 (%4,7)	0 (%0)	0 (%0)
	Bilmiyorum I don't know	32 (%60,4)	57 (%55,3)	6 (%12)	6 (%9,4)	2 (%3)	3 (%4,4)

Tıbbi ve kozmetik Botulinum toksini uygulaması kimlere yapılamaz? **To whom cannot be applied medical and cosmetic Botulinum toxin?**	18-65 arası herkese Anyone aged between 18-65	1 (%1,9)	2 (%1,9)	0 (%0)	1 (%1,6)	1 (%1,5)	2 (%2,9)
	Hamilelik-Emzirme dönemi yaşayanlara* During pregnancy and breastfeeding*	27 (%50,9)	64 (%62,1)	36 (%72)	38 (%59,4)	35 (%53)	42 (%61,8)
	Çocuklara Children	19 (%35,8)	52 (%50,5)	20 (%40)	19 (%29,7)	24 (%36,4)	12 (%17,6)
	Kas hastalığı olanlara* For those with muscle diseases*	26 (%49,1)	64 (%62,1)	28 (%56)	29 (%45,3)	33 (%50)	24 (%35,3)
	Bilmiyorum I don't know	15 (%28,3)	17 (%16,5)	7 (%14)	15 (%23,4)	13 (%19,7)	10 (%14,7)
Kozmetik Botulinum toksini uygulamasını kimler yapabilir? **Can it be used in cosmetic Botulinum toxin use?**	Plastik, Rekonstrüktif ve Estetik cerrahi uzmanı, Dermatoloji uzmanı* Plastic, Reconstructive and Aesthetic surgery specialist, Dermatology specialist	49 (%92,5)	92 (%89,3)	50 (%100)	61 (%95,3)	65 (%98,5)	60 (%88,2)
	Bütün sağlık çalışanları All healthcare workers	1 (%1,9)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	1 (%1,5)
	Herhangi bir branştan bir hekim A physician of any specialty	1 (%1,9)	0 (%0)	1 (%2)	5 (%7,8)	5 (%7,6)	15 (%22,1)
	Güzellik salonunda çalışan estetisyenler Estheticians working in beauty centers	5 (%9,4)	13 (%12,6)	9 (%18)	8 (%12,5)	2 (%3)	0 (%0)

	Bilmiyorum I don't know	5 (%9,4)	8 (%7,8)	0 (%0)	1 (%1,6)	0 (%0)	0 (%0)
	Ortalama puan **Average score**	38,87	41,21	56,75	56,59	60,66	62,95

Table 2 shows the percentage of correct answers for each question according to the grade level. The average scores of the students for each question and for total according to their grades are shown in Table 3.

Table 3. Students' averages of points in each question according to their grade

	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Total
1st grade	4,24	3,11	9,33	2,16	4,15	2,92	4,19	8,77	38,87
2nd grade	5,29	2,42	9,12	4,46	5,04	1,74	4,8	8,34	41,21
3rd grade	8,26	3,38	9,9	5,76	8,07	7,11	5,33	8,94	56,75
4th grade	8,2	4,92	9,92	6,48	7,58	6,41	4,41	8,67	56,59
5th grade	8,58	5,96	9,7	6,27	9,03	7,54	4,25	9,33	60,66
6th grade	9,26	7,06	9,56	6,99	9,34	8,16	4,49	8,09	62,95

Each question is evaluated on 10 points and the maximum score that can be obtained is 80.

According to the statistical analysis results, there is a significant difference between the scores of the students from different grades in questions 1 and 2 ($P<0.001$). There is no statistical difference between graders for question # 3. In the 4th, 5th, 6th questions, graders 1 and 2 differed significantly from other grades ($P<0.001$). There is no statistical difference between the grades in questions #7 and 8. The 1st and 2nd graders differed significantly from other classes in total scores ($P<0.001$).

4. Discussion

Botulinum toxin is a neurotoxic protein produced by Clostridium botulinum, a gram-positive anaerobic spored bacterium, and is one of the most toxic biological substances known5.. Of the seven serotypes, only species A and B are medically used6,7,8. Other species are much rarer and often cause animal diseases. Botulinum neurotoxin causes flaccid neuroparalysis by preventing the release of acetylcholine neurotransmitter from the axon ends at the neuromuscular junction9.. The toxin shows its effect by breaking down key proteins necessary for nerve activation. First, it binds to the neuronal cells then it is taken into a vesicle through receptor-mediated endocytosis9. The vesicle becomes acidic as it moves through the cell membrane into the cell, and pushes of the toxin along the vesicle membrane towards cell cytoplasm5. Once toxin enters the cell cytoplasm, it divides the SNARE proteins (proteins that mediate vesicle fusion) and leads to paralysis by interfering nerve signals4. The disease caused by this toxin has been called botulism.

BT, which stands out with its cosmetic facial rejuvenation usage in written and social media, and it is usually confused with fillers. In the first question of the survey, students were asked whether BT was toxin (poison) or filler. The lowest average score in this question belonged to 1st graders with 4.24 (correct answer rate 47.2%). The average score increased to 5.29 in 2nd graders (correct response rate 57.3%), without a statistical difference between these two grades. The correct response rate and average score of the first question showed a raise from the 3rd graders to the 6th graders. Most of the 6th students knowed BT is a toxin. The average scores of 3rd to 6th graders differed significantly from 1st and 2nd graders. As the result of the question is in the basic curriculum of 2nd and 3rd years of medical school, 3rd graders and superiors are expected to be familiar with the subject. Depending to the timing of the survey, some of the 2nd graders may not have had the opportunity to process this issue yet.

The second question in the survey covers the areas of clinical use of BT rather than the mechanism of action or structural properties of the toxin. 96% of 1st grade students know that BT is used for cosmetic purposes, but their information about other clinical usage areas were low. This question was answered more accurately by 4th graders and above because they are more familiar with the various clinical usage of BT based on the compulsory clinical courses and internships from the 4th grade. The largest proportional increase of a subject under this question was the blepharospasm treatment (from 9.4% to 70.6%) which is a very common treatment method extensively discussed Ophthalmology internship. This subject had a higher marking rate in the 5th and 6th graders than in previous classes. The least known application of BT was in migraine treatment (50%). The average scores of this question were not different between 1st, 2nd, and 3rd graders, but they differed significantly from 4th, 5th, and 6th graders. The proportional increase in the right answers of this option with the class level, show that students use the information they gained from previous classes and make healthier assessments. In another BT awareness level survey applied on a hundred dental college students in Chennai, India, only 50% of students knew that toxin injection was effective in reducing facial rhytids; in our study, this rate (97.2%) was higher11.

In the third question, independent from the grade level, all students stated that the toxin have the paralytic effect solely in the area of injection; there was no statistical difference between classes.

In the fourth, fifth and sixth questions, the molecular structure of BT, mechanism of action and botulismus disease were asked as an academic knowledge. In the fourth question, the average score of the 1st and 2nd graders were lower than in other classes and statistically not different from each other. There was a significant difference between 3rd, 4th, 5th and 6th graders from 1st and 2nd graders. This subject is in the curriculum of physiology and pharmacology which are thought in the second and third years of medical school therefore 3rd graders and above are expected to had the physiologic and

pharmacologic properties of BT. Again, depending to the timing of the survey, some of the 2nd graders may not have learned this subject yet. The 3rd graders and above replied the fourth, fifth and sixth questions with high scores without a statistical difference between them. More comprehensive information and increasing awareness about BT is an not a surprising finding for upper grades of medical school students.

In the seventh question, the students were asked to whom BT can be applied. Unlike many drugs BT can be used even in the pediatric age group especially in spasticity and has been approved for use by the American Health and Food Organization in several indications 12. In contrast, the pregnancy category of BT is C and its use in pregnancy is not recommended if the potential benefit to the pregnant woman is greater than the potential harm to the fetus13. BT injections are contraindicated in patients with progressive muscle diseases, such as Myasthenia-Gravis and Eaton-Lambert syndromes, as it can aggravate the symptoms of the disease14,15 Although many students replied correctly, this question had the lowest average scores in all grades and there was no statistical difference between classes. The reason may depend on the content of the basic curriculum; it usually covers the general aspects of mechanisms, indications and contraindications. In a similar survey study, Imam et al showed that only 2/3 of the students thought that BT injections may not be safe during pregnancy or breastfeeding.

The eighth question is related to the legislation and is not included in the curriculum. In this question the students were asked who could administer BT injections. Cosmetic filler and Botox injections are often identified with youth and beauty. When there is not enough supervision by the lawmakers, these kinds of applications are prone to abused by several occupational groups other than physicians. Everyday we witness various news in the media about a BT/filler disaster performed in beauty centers or even in hairdressers. In 03.08.2015 of the Ministry of Health of the Republic of Turkey released an article - numbered 23590821/180/1423- about BT injections. The article states that “The training of facial cosmetic procedures are given in plastic, reconstructive and aesthetic surgery and dermatology departments in our country therefore only these specialists are allowed to perform of cosmetic injection procedures in the facial area. In other words, to perform botulinum toxin injections for facial cosmetic procedures, it is an obligation to have been trained in these specialties as well as having the title of Doctor of Medicine. Without these conditions, it is not possible for non-physicians to engage in professional activities in the field of medicine based on the knowledge or documents obtained from various courses... " 17.. It is also stated that BT injections can be performed by the relevant branch physicians for various clinical indications such as cervical dystonia and spasticity. In this question of the survey, some of the students answered that beauticians may also perform this medical practice. Despite the recent reports of complications or even deaths because of the under the counter cosmetic practices which are carried out in beauty centers; it is interesting and worrisome that a physician candidate can accept a medical practice performed by non-physicians. To overcome this erroneous disbelief, it should be emphasized more frequently in the clinical courses that all kinds of medical procedures should be performed by health personnel who are specialized in the relevant specialty and who can cope with the possible complications. A similar misconception was highlighted in the publication of Imam et al. In his survey, although 66% of the 386 female medical students emphasized that the toxin may have significant side effects and/or complications, 32.4% stated that BT can be sold and applied without a prescription16.

5. Conclusion

Compared to the 1st and 2nd grade students, which are the basic classes of the faculty, the knowledge and awareness levels of the other classes are higher. Botulinum toxin has been included in the curricula of various basic and clinical branches especially in the physiology and pharmacology courses in the 2nd and 3rd grades general surgery, neurology, plastic surgery, and ophthalmology in the upper grades. Besides, the intense interest of media

to noninvasive procedures such as BT may draw attention and accentuate the awareness levels of medical students. However, the variety of complications and contraindications should be underlined, and it should be emphasized that any medical procedure whether it is cosmetic or not, should be performed by physicians not by other professions.

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