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Research Article

Botulinum Toxin and its Effect on Depression

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Abstract

Objectives: This study aimed to evaluate the relationship between depression in patients who regularly undergo botulinum toxin (BoNT) treatment.

Methods: This is a retrospective, single center, observational study. For the individual information form of the study, the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were filled up by the participants, in addition to data on their age and gender. Patients who had undergone BoNT treatment for aesthetic purposes on the upper face at least once a year for the last 5 years were compared with those who had never undergone BoNT treatment.

Results: The study group consisted of 50 male and 50 female patients. When the mean ages of patients who had undergone BoNT and those who had not were analyzed, no statistically significant difference was found between the two groups (p=0.871). It was determined that the BDI and BAI of those who had regular BoNT were lower than those who had never undergone BoNT.

Conclusion: The mechanism of action of BoNT on depression is not fully known, it is considered that BoNT injection in the upper facial area, mainly when performed by experienced specialists, may constitute a new approach to treating depression.

Keywords: Beck depression inventory, Beck anxiety inventory, botulinum toxin, depression

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The skin is the largest organ of our body and plays a significant role in communicating with the external world. Furthermore, having healthy skin plays an essential role in maintaining the physical and mental health of individuals. Sometimes having primary dermatological diseases or believing that one's appearance is aesthetically displeasing can increase the risk of depression, raise anxiety levels, and lead to stigma in social circles.[1] Depression is one of the most common mental disorders. The relationship between changes in the skin and depression is known. Therefore, there are many studies in the literature from different disciplines like dermatology and psychiatry on this topic. It is reported that both surgical and non-surgical cosmetic procedures have a positive effect on patients' quality of life.[2]

Botulinum toxin is a presynaptic neurotoxin that causes skeletal muscle paralysis by inhibiting calcium-mediated acetylcholine release at motor nerve endings, and it is widely used in the cosmetic field.[3] Moreover, in recent years, there have been studies suggesting that the effects of botulinum toxin (BoNT) could be utilized in the treatment of depression. It is believed that muscle manipulations leading to more positive facial expressions may result in more positive emotional states in affected individuals.[4]

The aim of this study is to evaluate the depression scale between individuals who regularly receive BoNT injections for aesthetic purposes and patients who have never received BoNT injections.

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Methods

Between April and July 2023, all clients who presented to the Ulaş Güvenç Private Clinic and agreed to participate in the study were included, provided they were at least 18 years old and did not have any systemic or psychiatric diseases. The inclusion criteria for the study were having had a BoNT injection for aesthetic purposes in the upper facial area at least once a year for the past five years or never having received a BoNT injection before. In the prepared individual information form, participants filled in details about their age and gender, as well as completing the Beck Depression Inventory and Beck Anxiety Inventory.

All procedures performed in studies involving human participants were in accordance with the ethical standarts of the institutional and/or national research committee and with 1964 Declaration of Helsinki and its later amendments or comparable ethical standarts.All patients provided written informed consent prior to enrollment.

Beck Depression Inventory (BDI)

The Beck Depression Inventory, developed by Beck et al. in 1961 to assess the vegetative, emotional, cognitive, and motivational symptoms observed in depression, underwent a Turkish validity and reliability study conducted by Hisli et al. in 1989.[5] The scale consists of 21 questions based on a four-point Likert scale, with each question being evaluated on a score range of 0-1-2-3. Participants are asked to choose the statement that best describes how they felt, including the day they marked the scale, over the past week. The possible scores on the scale range from 0 to 63. The scale is interpreted as 0-9 indicating minimal mood disturbance, 10-16 mild depression, 17-29 moderate depression, and 30-63 severe depression. The Cronbach Alpha reliability coefficient of the scale was found to be 0.74. [6] In our study, the Cronbach Alpha coefficient was calculated as 0.860.

Beck Anxiety Inventory (BAI)

The Beck Anxiety Inventory was developed by Beck et al. in 1988 to determine the frequency of anxiety symptoms experienced by an individual. The validity and reliability study for its use in Turkey was conducted by Ulusoy and colleagues in 1998. The inventory consists of 21 items, each rated between 0 and 3. From the 21 items on the inventory, a total score ranging from 0 to 63 can be obtained, with an increasing total score indicating heightened anxiety symptoms. Scores from the Beck Anxiety Inventory are interpreted as follows: 0-7 points indicate no signs of anxiety; 8-15 points indicate mild anxiety; 16-25 points indicate moderate anxiety, and 26-63 points indicate severe anxiety. In Ulusoy et al.'s 1998 study, the Cronbach alpha value of the inventory was found to be 0.85. In this research, the Cronbach Alpha value for the inventory was determined to be 0.93.[7] In our study, the Cronbach Alpha coefficient was calculated as 0.877.

Statistical Analysis

Normality controls for continuous measurements were tested with the Shapiro Wilk test. The Student t-test was used to determine intergroup differences for continuous measurements. Descriptive statistics are given as mean and standard deviation values. The Pearson Chi-square test was utilized to determine differences between categorical variables. Descriptive statistics for these are given as numbers and percentages. The Pearson correlation analysis was used to determine the relationship between continuous measurements. Statistical significance was set at $p<0.05$.

Results

A total of 100 participants were included in the study, consisting of 50 women (50.0%) and 50 men (50.0%). The average age of the participants was calculated as 34.6±8.5. Additionally, when examining the average age of women and men, it can be said that there is no statistically significant difference between them, indicating homogeneity ($p=0.625$). The average age of women was calculated as 34.2±9.0, and for men, it was 35.1±8.2. Moreover, when examining the average age based on whether or not they had previously received BoNT, no statistically significant difference was found ($p=0.871$). The average age of those who had not previously undergone the procedure was 34.8±9.8, and for those who had, it was 34.5±7.2 (Table 1). Comparisons of scale scores by groups and genders were made, and statistically significant differences were observed only for

Table 1. Descriptive statistics of the participants

	Number	Percentage
Gender		
Female	50	50.0
Male	50	50.0
Beck depression inventory		
Minimal	32	32.0
Mild mood disturbance	28	28.0
Borderline clinical depression	35	35.0
Severe depression	5	5.0
Beck anxiety inventory		
No anxiety	39	39.0
Mild anxiety	31	31.0
Modarate anxiety	25	25.0
Severe anxiety	5	5.0

BDI and BAI scores between those who underwent the procedure and those who did not (all p values <0.001). It was found that the BDI and BAI scores of those who regularly underwent BoNT were lower than those who had never had it. Descriptive statistics (mean and standard deviation) and p-values are given in Table 2.

The relationship between the BDI and BAIscores and the age variable was also investigated, and it was determined that there is no statistically linear relationship between them (respectively, r=0.033, p=0.77; r=0.041, p=0.683). However, we can say that as the Beck depression scale score increases, the Beck anxiety scale scores also increase linearly (r=0.645, p<0.001).

In addition, whether the categorized scores of the BDI and BAIcaused any action was examined, and the differences were found to be statistically significant (respectively, p values; <0.001 and 0.002). Differences in terms of each scale's categories have also been investigated. For the BDI, differences in all categories other than those with only mild mood disorders were found to be significant (all p-values p<0.05). When examining the BAI, differences between groups without anxiety and those with severe anxiety were found to be significant (p-values p<0.05). Descriptive statistics (number and percentage) and p-values related to comparisons between BDI and BAI scores and groups are given in Table 3.

Table 2. Comparisons in terms of scale scores

	Beck depression inventory	Beck anxiety inventory
Group		
BoNT - (n=50)	19.9±8.1	14.8±8.7
BoNT + (n=50)	10.0±6.4	8.7±6.7
p	<0.001	<0.001
Gender		
Female	15.6±9.1	13.4±9.8
Male	14.3±8.5	10.1±6.2
p	0.476	0.051

Botulinum toxin (BoNT).

Discussion

Botulinum toxin is a presynaptic neurotoxin that causes dose-dependent weakness or skeletal muscle paralysis by inhibiting calcium-mediated acetylcholine release at motor nerve endings, and is a potent biological toxin produced by Clostridium botulinum.[3] Beyond its cosmetic benefits, when applied in aesthetic medicine as BoNT, it not only enhances emotional well-being and improves social and psychological behaviors, but also reduces anxiety and depressive mood.[8,9]

Depression is one of the most common mental disorders affecting approximately 280 million people worldwide and is one of the leading causes of disability.[10] Symptoms include feelings of sadness, irritability, or emptiness, as well as a persistent depressive mood accompanied by a loss of interest and energy. Despite effective treatments with antidepressant drugs and psychotherapy, about one-third of patients still suffer from chronic and/or treatment-resistant depression after multiple treatment trials.[11]

Outside of its cosmetic use, botulinum toxin is known to be used for migraines, hyperhidrosis, and certain neurological diseases. The first case series on the efficacy of botox on depression was presented in 2006.[12] In recent years, studies on the efficacy of BoNT application on psychiatric symptoms have been increasingly featured in the literature.

Table 3. Comparisons of categorical levels of scale scores

	BoNT – (n=50)		BoNT + (n=50)		p
	Number	Percentage	Number	Percentage	
Beck depressioninventory					
Minimal	3	6.0	29	58.0	<0.001
Mild mood disturbance	14	28.0	14	28.0	
Borderline clinical depression	28	56.0	7	14.0	
Severe depression	5	10.0	0	0.0	
Beck anxiety inventory					
No anxiety	11	22.0	28	56.0	0.002
Mild anxiety	19	38.0	12	24.0	
Modarate anxiety	15	30.0	10	20.0	
Severe anxiety	5	10.0	0	0.0	

Botulinum toxin (BoNT).

Some of these studies suggest that BoNT applications, primarily for aesthetic purposes, alleviate aesthetic concerns, which in turn have a positive effect on anxiety and depression.[13-15]

In a review by Qian et al., they suggested that the varying results in the literature on depression and botox could be due to differences in dosage and the gender of the participants.[16] The underlying mechanism for the positive effect of BoNT application on depression is not fully understood. According to the facial feedback hypothesis, which dates back to the 19th century with Charles Darwin and William James, the facial expression of emotions produces proprioceptive feedback signals that can sustain and amplify the expressed emotions. Through facial regulation, an initially semi-cognitive, cool emotion can be transformed into a warmly felt emotional experience.[17] Through BoNT injections that relax the eyebrow muscles, not only does it give the face a less negative/more positive expression, but it can also interrupt the described feedback loop, thus leading to a less negative/more positive emotional state.[18] Beyond its cosmetic benefits, when applied in aesthetic medicine, the treatment appears to enhance emotional well-being, improve social and psychological behaviors, and reduce irritability as well as depressive and anxious moods.[9] These effects might contribute to the popularity of treating upper face mimic lines with BoNT injections in aesthetic medicine. There are experimental evidences suggesting that aesthetic purposes of upper face BoNT treatment can modulate the perception and processing of emotional stimuli, including the activation of the amygdala, a key brain structure in the processing of negative emotions.[19] Excessive activation of the amygdala is associated with negative emotions (e.g., anger, anxiety, depression, and fear). A potential mechanism of BoNT's effect is by blocking the release of acetylcholine to synapses, thereby reducing the activation of the amygdala, which has a positive effect on mood.[20] There are also theories suggesting that a small amount of BoNT, which can enter the systemic circulation, might reduce the activation of the amygdala.[21]

In our study, we found a significant decrease in anxiety and depression scales among those who regularly received BoNT treatments compared to those who never did. While these results support the literature, limitations of our study were its retrospective nature and the small number of patients.

Conclusion

Considering the study findings and related literature, it is thought that regular BoNT application in our study might be associated with lower levels of depression and anxiety. There is a strong need for new treatment approaches beyond the routine treatment models used for depression. While the mechanism of action of BoNT treatment on depression is not fully understood, upper face BoNT injections, especially when done by experienced hands, might introduce a new approach to depression treatment. While it is thought that BoNT applications might have a place in the treatment of depression, more extensive and advanced studies are needed to come to a definitive conclusion.

Disclosures

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standarts of the institutional and/or national research committee and with 1964 Declaration of Helsinki and its later amendments or comparable ethical standarts.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

References

1. Picardi A, Pasquini P, Abeni D, et al. Psychosomatic assessment of skin diseases in clinical practice. Psychother Psychosom 2005;74:315-22.
2. Sommer B, Zschocke I, Bergfeld D, Sattler G, Augustin M. Satisfaction of patients after treatment with botulinum toxin for dynamic facial lines. Dermatol Surg 2003;29:456–60.
3. Brunton LL, Lazo JS, Parker KL. Goodman & Gilman's Tedavinin farmakolojik temeli. Süzer Ö, Akın D, Süzer AH, Dedeoğlu BD, Küçükhüseyin C. (Çevirenler) 1. Baskı, İstanbul: Nobel Matbaacılık, 2009;225-30.
4. Davis JI, Senghas A, Brandt F, Ochsner KN. The effects of BOTOX injections on emotional experience. Emotion 2010;10:433–40.
5. Beck AT, Ward C, Mendelson M, Mock J, Erbaugh J. Beck depression inventory (BDI). Arch Gen Psychiatry 1961;4(6):561-71.
6. Hisli N. The validity and reliability of Beck Depression Inventory for university students. Psikoloji dergisi 1989;7:3-13.
7. Ulusoy M, Şahin NH, Erkmen H. Turkish version of the Beck Anxiety Inventory: Psychometric properties. J Cogn Psychother 1998;12:163-72.
8. Lewis MB, Bowler PJ. Botulinum toxin cosmetic therapy correlates with a more positive mood. J Cosmet Dermatol 2009;8:24–6.
9. Sykianakis D, Stratigos A, Chatziioannou A, Christodoulou C. Botulinum toxin type A treatment is associated with improved social and psychological behavior: A retrospective study. J Cosmet Dermatol 2022;21:142–8.
10. Bovin MJ, Marx BP, Weathers FW, et al. Psychometric properties of the PTSD checklist for diagnostic and statistical manual of mental disorders–fifth edition (PCL-5) in veterans. Psychol Assess 2016;28-11:1379.

11. Shelton RC, Osuntokun O, Heinloth AN, Corya SA. Therapeutic options for treatment-resistant depression. CNS drugs 2010;24:131-61.
12. Singh GC, Hankins MC, Dulku A, Kelly MB. Psychosocial aspects of botox in aesthetic surgery. Aesthetic Plast Surg 2006;30(1):71-6.
13. Magid M, Keeling BH, Reichenberg JS. Neurotoxins: expanding uses of neuromodulators in medicine–major depressive disorder. Plast Reconstr Surg 2015;136:111–9
14. Schwartz GE, Fair PL, Salt P, Mandel MR, Klerman GL. Facial muscle patterning to affective imagery in depressed and nondepressed subjects. Science 1976;192:489–91.
15. Burgen AS, Dickens F, Zatman LJ. The action of botulinum toxin on the neuro-muscular junction. J Physiol 1949;109:10–24.
16. Qian H, Shao F, Lenahan C, et al.Efficacy and Safety of Botulinum Toxin vs. Placebo in Depression: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Front Psychiatry2020;4:11.
17. Al Abdulmohsen T, Kruger TH. The contribution of muscular and auditory pathologies to the symptomatology of autism. Med Hypotheses 2011;77:1038-47.
18. Heckmann M, Teichmann B, Schröder U, Sprengelmeyer R, Ceballos-Baumann AO. Pharmacologic denervation of frown muscles enhances baseline expression of happiness and decreases baseline expression of anger, sadness, and fear. J Am Acad Dermatol 2003;49:213–6.
19. Havas DA, Glenberg AM, Gutowski KA, Lucarelli MJ, Davidson RJ. Cosmetic use of botulinum toxin-a affects processing of emotional language. Psychol Sci 2010;21:895–900.
20. Baumeister JC, Papa G, Foroni F. Deeper than skin deep—The effect of botulinum toxin-A on emotion processing. Toxicon 2016;118:86–90.
21. Hennenlotter A, Dresel C, Castrop F, Ceballos-Baumann AO, Wohlschläger AM, Haslinger B. The link between facial feedback and neural activity within central circuitries of emotion-new insights from botulinum toxin-induced denervation of frown muscles. Cereb Cortex 2009;19:537–42.