

# Hemifasiyal Spazm ve Blefarospazm Hastalarında Botulinum Toksin Enjeksiyonu Tedavisi Sonrası Depresyon ve Anksiyete Durumunun Değerlendirilmesi

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## Özet

**Amaç:** Botulinum toksin tedavisi (BTT) alan hemifasiyal spazm (HS) ve blefarospazm (BS) hastalarında mevcut klinik duruma bağlı oluşan depresyon ve anksiyete durumunun, hastalık süresi ve yaşla ilişkisi ve tedavi sonrası parametlerdeki değişimin araştırılması amaçlandı.

**Gereç ve yöntem:** Araştırmaya 125 hemifasiyal spazm, 14 blefarospazm hastası, 70 sağlıklı gönüllü kişi kontrol grubu olarak alındı. Hasta ve kontrol grubuna Beck depresyon, Beck anksiyete ölçekleri uygulandı. BTT tedavisinden 4 hafta sonra hasta grubuna test tekrarlandı.

**Bulgular:** Kontrol grubuna göre tedavi öncesi vaka grubunun Beck anksiyete ve Beck depresyon ölçekleri puanı daha yüksekti. Hem HS hastalarında hem de BS hastalarında tedavi sonrası Beck anksiyete ve Beck depresyon skorları düşüş gösterdi. Gruplar arasında blefarospazm grubunda, tedavi sonrası Beck anksiyete puanları hemifasiyal spazm grubundan istatistiksel anlamlı olarak daha düşük bulundu. Vaka grubunda hastalık süresi arttıkça depresyon ölçek puanı da artmaktaydı. İleri yaş hastalarda anksiyete ve depresyon skorlarının daha düşük olduğu gözlemlendi. BTT tedavisi ile hastaların Beck depresyon ve Beck anksiyete puanlarında iyileşme gözlemlendi.

**Sonuç:** HS ve BS hastalığı yüz kaslarında fiziksel sorunlara yol açtığı için hastaların aynı zamanda fonksiyonel durumları ve duyu durumunu da olumsuz etkilemektedir. Bu hastalığa genellikle anksiyete ve/veya depresyon eşlik etmektedir. BT tedavisi HS ve BS hastalarında fonksiyonel kas sorunlarını düzelterek hastalığın tedavisinin yanında duyu durum üzerine de olumlu etkiler sağlamakta ve hastalığa bağlı anksiyete ve depresyon bulgularını da düzeltmektedir.

**Anahtar Kelimeler:** Hemifasiyal Spazm, Blefarospazm, Anksiyete ve Depresyon

# Assessment of Depression and Anxiety After Botulinum Toxin Injection Treatment in Patients with Hemifacial Spasm and Blepharospasm

## Abstract

**Objective:** The aim of this study was to investigate the relationship between depression and anxiety due to the current clinical situation, disease duration and age, and the change in post-treatment parameters in patients with hemifacial spasm (HS) and blepharospasm (BS) receiving botulinum toxin therapy (BTT).

**Materials and methods:** 125 hemifacial spasm patients, 14 blepharospasm patients and 70 healthy volunteers were included in the study as control group. Beck depression and Beck anxiety scales were applied to the patient and control groups. The test was repeated in the patient group 4 weeks after BTT treatment.

**Results:** The Beck anxiety and Beck depression scale scores of the case group were higher before treatment compared to the control group. Beck anxiety and Beck depression scores decreased after treatment in both HS and BS patients. Among the groups, the post-treatment Beck Anxiety score in the blepharospasm group was statistically significantly lower than in the hemifacial spasm group. The depression scale score increased with increasing disease duration in the case group. Anxiety and depression scores were lower in older patients. Beck depression and Beck anxiety scores of the patients improved with BTT treatment.

**Conclusion:** Since HS and BS cause physical problems in the facial muscles, it also negatively affects the functional status and emotional state of the patients. This disease is often accompanied by anxiety and/or depression. After CT treatment, functional muscle problems are corrected in HS and BS patients, providing positive effects on mood as well as the treatment of the disease and correcting the anxiety and depression findings related to the disease.

**Keywords:** Hemifacial Spasm, Blepharospasm, Anxiety and Depression

## Introduction

Hemifacial spasm (HS) is a movement disorder characterized by irregular, tonic-clonic seizures of the muscles innervated by the facial nerve on the same side<sup>1</sup>. The most common cause of this clinical disorder is compression of the facial nerve for any reason and possible vascular structural abnormalities in the brainstem<sup>2</sup>. Furthermore, HS can also develop following peripheral facial paralysis (PFP) secondary to trauma<sup>3</sup>. Blefarospazm (BS) is a type of focal dystonia originating in the basal ganglia manifested by involuntary contractions of the muscles around the eyes<sup>3</sup>. Although their pathophysiologies are different, both clinical conditions result in contraction of the orbicularis oculi muscle and involuntary closure of the eyelid. Since these two types of focal dystonia directly lead to involuntary contractions in the patient's facial muscles, they result in social anxiety disorder, withdrawal, and secondary anxiety and depressive mood in the patient<sup>3</sup>. Botulinum toxin injection

treatment (Botox) is routinely applied in 3-4 month periods as part of the medical treatment in such cases of focal dystonia<sup>4</sup>. The fact that there is improvement in the facial muscles for up to 3-4 months following the Botulinum toxin injection treatment applied in such clinical conditions somewhat alleviates patients' anxieties at the conclusion of the treatment. In our study, we aimed to determine the anxiety and depressive mood that will arise in the patients under our follow up who are diagnosed with HS/BS, as well as the relationship of this condition with the disease duration and patients' ages as well as the changes in the post-treatment anxiety and depression scores.

### **Materials and Methods**

The study was conducted in accordance with all procedures, ethical principles, and Helsinki pursuant to the decision of Van Yüzüncü Yıl University Hospital Clinical Research Ethics Committee (Date: 21.09.2022, Decision No.: 03).

After obtaining the approval from our hospital's ethics committee, a total of 139 cases were included from the adult individuals, diagnosed with focal dystonia (hemifacial spasm and blepharospasm patients), aged between 18-65, who have applied to our dystonia clinic for the botulinum toxin treatment (BTT) applied as part of each 3–4-month treatment period. The demographic data of the patients to be included in the study, such as age, gender, marital status, and occupational information, were recorded. In addition to these, patient information such as disease duration, presence of comorbidities, and duration of treatment were obtained and afterwards the patients filled out the Beck Anxiety Scale (BAS) and Beck Depression Scale (BDS) questionnaires prior to Botulinum toxin injection treatment, and these questionnaires were then filled out again after the treatment during the 1-month clinical follow-up visit, where their neurological examinations were also checked.

Patients with malignancy, history of use of medications that may cause dystonia, those with a prior diagnosis of depression or anxiety undergoing psychiatric follow-up and treatment, individuals under 18 and over 65 years of age were determined as exclusion criteria.

Botox preparation of botulinum toxin type A, which is one of the three different preparations (Dysport, Botox-Allergan, Nabota) approved by the FDA in our country and licensed and approved by the Turkish Ministry of Health, is available in vial form in the market. In our study, we used the Botox preparation of the toxin. The medication was diluted with 2.5 ml of 0.9% saline solution before use.

Beck anxiety inventory: Beck Anxiety Score (BAS) is a self-assessment scale consisting of 21 items used to measure the level and severity of anxiety symptoms. Each item is assigned with a score between 0 and 3, resulting in a total score ranging from 0 to 63. The total scores of the test are

interpreted as follows: 0-7 minimal anxiety, 8-15 mild anxiety, 16-25 moderate anxiety, and 26-63 severe anxiety. Validity and reliability study for the Turkish adaptation was conducted by Ulusoy et. Al<sup>5</sup>.

Beck depression scale: Beck depression score (BDS) is used to determine the risk in terms of depression and measure the level and severity of depressive symptoms. Beck depression scale is developed by Beck et. al. in 1961<sup>6</sup>. It is a self-assessment scale consisting of 21 items administered to measure the level and severity of depression symptoms. This questionnaire form consisting of 21 questions is used to assess the Beck depression score. The patients were asked to select the option from these questions that best suited their own conditions. This test is scored using a four-point Likert scale. Each item assigned with a score between 0 and 3, and the sum of these scores results in a total score ranging from 0 to 63. According to the scores obtained using the scale developed by Beck et. al. (1996), depression levels are classified as follows: 0-13 points indicate no depression, 14-19 points indicate mild depression, 20-28 points indicate moderate depression, and 29-63 points indicate severe depression. The reliability and validity study of the scale in the Turkish culture was conducted by Hisli<sup>7</sup>.

Data were analyzed using SPS 24.0. In the study, tests of normality were conducted by calculating kurtosis (a measure of the peakedness of a frequency distribution curve) and skewness (a measure of the lack of symmetry of a probability distribution of a real-valued random variable). As a result, parametric tests were used in the comparative tests and correlational test. Chi-squared test was used for the relationship between categorical variables and groups, independent samples t-test was used for comparing groups, and Pearson correlation test was used for the relationship.

## Results

Of the patients included in the study, 69 (49.6%) were male and 70 (50.4%) were female. There were 26 (37.1%) male and 44 (62.9%) female participants in the control group. The youngest patient was 19 years old, and the oldest was 78 years old, and the mean age of all patients was 49.93 years. The mean age of the control group was 39.16 years. In terms of occupation, the highest percentage in the group with “HS” disease were homemakers (45.6%) and pensioners (17.6%). Similarly, in the group with “BS” disease, homemakers (42.9%) and pensioners (28.6%) were also the most prevalent. However, there was no significant difference between the two disease types in terms of occupation groups ( $\chi^2(6) = 2.976, p = .812$ ).

Demographic data and the analysis of intergroup variables, disease duration, patients' ages, duration of the treatment administered, and the pre- and post-botox treatment BAS and BDS scores, are detailed in Table 1 and Table 2.

**Table 1.** Demographic data, Analysis of inter-group variables

		Group				Chi-squared	p
		Btx		Control			
		n	%	n	%		
Sex	Male	69	49,6	26	37,1	2,933	,087
	Female	70	50,4	44	62,9		
Marital status	Single	14	10,1	20	28,6	10,378	,001*
	Married	125	89,9	50	71,4		
Occupation	Homemaker	63	45,3	38	54,3	19,483	,003*
	Pensioner	26	18,7	5	7,1		
	Self-Employed	5	3,6	7	10,0		
	Student	8	5,8	6	8,6		
	Public	13	9,4	12	17,1		
	Unemployed	11	7,9	0	0,0		
	Worker	13	9,4	2	2,9		
Comorbidity	No	75	54,0	54	77,1	10,593	,001*
	Yes	64	46,0	16	22,9		

**Table 2.** The Descriptive Statistics and Normality Test for the Entire Cohort

	Minimum	Maximum	Mean	ss	Skewness	Kurtosis
Disease duration (years) (n=139)	1,00	20,00	8,22	3,97	,540	,540
Age (N=189)	18,00	78,00	46,32	13,57	-,283	-,647
BAS-1 (n=189)	0,00	55,00	13,52	11,47	1,055	,685
BDS-1 (n=189)	0,00	55,00	10,97	10,94	1,341	2,007
Duration of treatment (years) (n=139)	1,00	10,00	4,14	2,24	,213	-,898
BAS-2 (n=139)	2,00	35,00	11,25	6,08	1,189	1,369
BDS-2 (n=139)	0,00	40,00	9,95	6,80	1,447	2,943

**BAS-1:** Pre-treatment Beck anxiety score, **BDS-1:** Pre-treatment Beck depression score, **BAS-2:** Post-treatment Beck anxiety score, **BDS-2:** Post-treatment Beck depression score

Mean of pre-treatment Beck anxiety score (BAS-1) and Beck depression scores (BDS-1) of the patients in the case group administered with Botox treatment was significantly higher than those of the control group. ( $p < 0,05$ ). (Table-3).

**Table 3.** Analysis of Case and Control Group BAS-1 and BDS-1 scores

	Group				t	p
	Case		Control			
	Mean	ss	Mean	ss		
BAS-1	18,55	10,85	3,51	2,90	15,293	,000*
BDS-1	15,59	10,67	1,80	2,13	14,668	,000*

While the post-treatment Beck anxiety ve Beck Depression scores manifested decrease in both cases groups (HS, BS), the mean of post-treatment Beck anxiety score (BAS-2) scores with HS as disease type was significantly lower than those of patients with BS as disease type ( $p < 0,05$ ) (Table-4). There was no significant different in terms of other variables.

**Table 4.** Sub-Group Analysis of Anxiety and Depression Scores in the Case Group

	Disease type				t	p
	HS		BS			
	Mean	ss	Mean	ss		
BAS-1	18,05	10,89	23,07	9,65	-1,653	,101
BDS-1	15,54	10,67	16,07	11,02	-0,177	,859
BAS-2	10,75	5,87	15,71	6,24	-2,980	,003*
BDS-2	9,85	6,72	10,79	7,63	-0,484	,629

There is a statistically significant difference between the initial measurement of BAS score and the post-treatment second measurement, and the BAS score has decreased in the second measurement. There is a statistically significant difference between the first measurement of BDS score and the post-treatment second measurement, and the BDS score has decreased in the second measurement (Table-5). Regression is observed in the anxiety and depression score points of post-treatment patients.

**Table 5.** Pre-Treatment and Post-Treatment Scores in the Case Group

	Pre-Treatment Score (initial measurement)		Post-Treatment Score (second measurement)		t	p
	Mean	ss	Mean	ss		
BAS	18,55	10,85	11,25	6,08	11,165	,000*
BDS	15,59	10,67	9,95	6,80	11,292	,000*

Age, duration of treatment, and BDS-1 scores also increase as the disease duration increases in the correlation test results among the variables of the case group receiving botulinum toxin treatment

(Table-6). As the age increases, the disease duration is prolonged, and the BAS-1 score decreases. As the duration of treatment is increased, the BDS-1 scores also increase.

**Table 6.** Case Group Analysis of Variables

		Disease duration (years)	Age	Duration of treatment (years)	BAS-1	BDS-1	BAS-2	BDS-2
Disease duration (years)	r	1	,495**	,783**	,164	,204*	,048	,046
	p		,000	,000	,053	,016	,573	,588
Age	r		1	,474**	-,186*	-,071	-,168*	-,137
	p			,000	,028	,404	,048	,109
Duration of treatment (years)	r			1	,157	,205*	,068	,081
	p				,064	,015	,426	,343
BAS-1	r				1	,761**	,722**	,585**
	p					,000	,000	,000
BDS-1	r					1	,677**	,855**
	p						,000	,000
BAS-2	r						1	,760**
	p							,000
BDS-2	r							1
	p							

### Discussion:

Blepharospasm is a disease characterized by involuntary contractions of the orbicularis oculi muscle and is presented with continuous or intermittent eyelid closures. The condition is referred to as a type of focal dystonia originating from a disorder in the basal ganglia<sup>8</sup>. Hemifacial spasm, on the other hand, is characterized by tonic-clonic contractions involving half of the face, including the orbicularis oculi and other facial innervated muscles. Although the symptoms and subjective impairment of both diseases are clinically similar, hemifacial spasm is not associated with basal ganglion dysfunction but rather arises from irritation of the peripheral facial nerve<sup>8</sup>. Medical treatment of dystonia is challenging in clinical practice. Currently, Botulinum toxin type A treatment applications have been widely accepted for many types of hyperkinetic movement disorders, including HS and BS. Better results are obtained with Botulinum toxin type A treatment applications for both mentioned clinical conditions compared to medical treatments<sup>4</sup>.

Our cohort mainly consisted of patients with HS spasms. HS is typically seen in middle-aged women and occurs in the 5<sup>th</sup> decade of life<sup>9</sup>. 50.4% of our patients were female, with a mean age of 46.32 years. The most common cause of HS is the relationship between the facial nerve at the root entry zone in the brainstem and pathological vascular structures in this area<sup>10</sup>. In our

patients, while the inquiry in terms of possible comorbidity or ischemic vascular disorder revealed a comorbidity in 46% of cases with hypertension identified in 40 patients as part of the medical history interview, Type 2 Diabetes Mellitus was identified in 24 patients. The magnetic resonance imaging of the brain of the patients revealed no ischemic-vascular or tumoral formation were identified in the brainstem and facial nerve exit zone.

The mean BAS-1 and BDS-1 scores of the patients prior to the Botox treatment were higher compared to the control group. The mean post-treatment BAS-2 scores of patients with HS as disease type were significantly lower compared to those with BS as disease type. It was observed that the frequency of anxiety decreased even further after botulinum toxin treatment in HS patients compared to the BS group. While blepharospasm is reported to be more common in some psychiatric disorders, such as obsessive-compulsive disorder (OCD), it is not certain that the etiology and clinical findings of the disease are directly associated with psychiatric disorders<sup>10</sup>. The emergence of involuntary movements in facial muscles in both BS and HS can indirectly affect the patients' interpersonal communication negatively and lead to depressive mood and feelings of stigma in the patient<sup>11,12</sup>. Self-stigmatization can result in decreased self-esteem and reduced quality of life<sup>12</sup>. In a study of HS patients, visual symptoms and social inhibition due to involuntary movements in the face were observed in 41% of the patients<sup>13</sup>. In rural areas and traditional societies, these involuntary movements in the face will sometimes be misinterpreted which are expressed as causes of anxiety and depression in the patients<sup>11</sup>. Especially in HS patients, since voluntary facial movements exacerbate facial spasms, impairment in vision and speech and even, in more severe cases, mental functions may be affected as a result of these symptoms<sup>14</sup>. These issues can affect the patient's perception and relationship with the external world, leading to secondary social anxiety and sometimes feelings of shame<sup>14</sup>. In furtherance of this information, the anxiety and depression scores of our HS patients were higher than those of the normal population.

Previous studies have mentioned a higher prevalence of OCD and depressive symptoms in blepharospasm patients<sup>10</sup>. Additionally, the social and physical barriers related to these conditions are other reasons of the underlying psychopathology. Another study conducted on patients with blepharospasm and hemifacial spasm also yielded similar results<sup>15</sup>. It is observed in the blepharospasm group that psychiatric symptoms were significantly more prevalent. Likewise, in our cohort, the anxiety and depression scores were found to be higher in BS patients compared to the normal population, similar to the HS patient group.

There is a statistically significant difference between the first measurement (Pre-treatment) and the second measurement (Post-treatment) of BAS and BDS scores, and the BAS and BDS



scores have decreased in the second measurement. A regression was observed in the anxiety and depression score points of post-treatment patients. Furthermore, in correlation analyses among variables in the group receiving Botox treatment, it was found that as the disease duration increased, age, duration of treatment, and BDS-1 scores also increased, and it is considered that factors such as the necessity of continuous hospital visits and long-term treatment concerns have a negative effect on depressive mood as the current process becomes chronic. The fact that observing an increase in BDS-1 scores as the duration of treatment increases during the chronic process in parallel to increased disease duration, it is considered that patients continuing the current treatment for a long time during the chronic phase of the disease and living with the disease anxiety may be a contributing factor to such increase.

### **Conclusion**

In conclusion, anxiety and depression may be more prevalent in HS and BS patients compared to the normal population. Since these conditions involve involuntary contractions of the muscles around the eyes and facial nerves, they can negatively impact the patients both in terms of health and social anxiety, triggering anxiety and depressive mood in the long term. Long-term follow-up and well-managed treatment can not only improve patients' physical well-being but also help protect them from potential concerns, worry, anxiety, and depressive mood associated with the disease from a mental perspective.

From our perspective, recording the severity of HS and BS disease in patients and providing a more detailed description of treatment response could have made the study more understandable and informative.

**Ethical Committee Approval:** The study was conducted in accordance with all procedures, ethical principles, and Helsinki pursuant to the decision of Van Yüzüncü Yıl University Hospital Clinical Research Ethics Committee (Date: 21.09.2022, Decision No.: 03).

**Patient Consent:** Detailed informed consent of the patients were obtained in accordance with the Helsinki Declaration.

**Peer Review:** Reviewed by both the editorial board and off editorial board individuals.

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**Note:** The preliminary data of the current study, evaluated with a smaller number of patients, were presented as an oral presentation at the "3<sup>rd</sup> International and 7<sup>th</sup> Medicine and Treatment Congress" held in Bafra/Turkish Republic of Northern Cyprus between September 21-25, 2022.

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