



Depression and Anxiety States of Patients Followed in Pituitary Polyclinic

Hipofiz Polikliniğinde Takip Edilen Hastaların Depresyon ve Anksiyete Durumları

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ABSTRACT

Objective: Individuals with pituitary disease are susceptible to the development of depression and anxiety because of interventional therapies, such as surgery and radiotherapy (RT), and long-term medical care (due to hyper or hypofunction). The aim of this study was to assess the quality of life, depression, and anxiety levels of patients in remission from different etiologies of pituitary pathology and to determine the impact of this condition on the disease, treatment approach, and other factors.

Methods: The Beck Depression and Anxiety Inventory was administered to sixty patients and thirty healthy individuals. The parameters of the patient group, including the etiology of pituitary pathology, surgical and radiotherapeutic history, hormonal failure status, and replacement therapy, were recorded.

Results: The patient group's depression and anxiety scores were significantly higher than those of the control group. In the patient group, there was no significant difference in depression and anxiety levels between those who underwent surgery and those who did not, and between those who received RT and those who did not. Furthermore, depending on pituitary adenoma functionality [functional pituitary adenoma and non-functional pituitary adenoma], hormonal secretion type (growth hormone excess, prolactin hormone excess, cortisol hormone excess, etc.), and hormone replacement treatment. There was no significant difference between the levels of depression and anxiety.

Conclusion: In our study, the presence of pituitary disease due to any etiology was associated with elevated levels of depression and anxiety. Our findings that patients with pituitary adenomas had increased levels of depression and anxiety may have implications for the long-term care of these patients. Although well-being in terms of pituitary illness is ensured in the follow-up of these patients, an effort should be made to reduce depression and anxiety. Comprehensive mental evaluation and psychotherapy should be incorporated into the treatment plan if necessary.

Keywords: Pituitary diseases, pituitary adenoma, hypopituitarism, quality of life, depression, anxiety

ÖZ

Amaç: Hipofiz hastalığı olan bireyler, cerrahi ve radyoterapi gibi girişimsel tedaviler ve uzun süreli tıbbi bakım (hiper veya hipofonksiyon) nedeniyle depresyon ve anksiyete gelişimine yatkındır. Bu çalışmanın amacı, hipofiz patolojisinin farklı etiolojilerinden remisyondaki hastaların yaşam kalitesi, depresyon ve anksiyete düzeylerini değerlendirmek ve bu durumun hastalığa, tedavi yaklaşımına ve diğer faktörlere etkisini belirlemektir.

Yöntemler: Altmış hasta ve otuz sağlıklı bireye Beck Depresyon ve Anksiyete Envanteri uygulandı. Hasta grubunun hipofiz patolojisinin etiolojisi, cerrahi ve radyoterapi öyküsü, hormonal yetmezlik durumu ve replasman tedavisi gibi parametreleri kaydedildi.

Bulgular: Hasta grubunun depresyon ve anksiyete puanları kontrol grubuna göre anlamlı derecede yüksekti. Hasta grubunda ameliyat olan ve olmayanlar, radyoterapi alan ve almayanların depresyon ve anksiyete düzeyleri arasında anlamlı fark yoktu. Ayrıca hipofiz adenomunun fonksiyonelliğine (fonksiyonel hipofiz adenom ve non-fonksiyonel hipofiz adenom), hormon yaymasına (büyüme hormonu fazlalığı, prolaktin hormon fazlalığı, kortizol hormonu fazlalığı, vb.) ve hormon replasman tedavisine bağlı olarak değişiklik yapılabilir.

Sonuç: Çalışmamız herhangi bir etiolojiye bağlı hipofiz hastalığının varlığı, yüksek düzeyde depresyon ve anksiyete ile ilgili olacaktır. Hipofiz adenomlu hastalarda depresyon ve anksiyete düzeylerinin arttığına dair bulgularımız, bu hastaların uzun süreli bakımı üzerinde anlamlar taşıyabilir. Bu hastaların takibinde hipofiz eğitiminin başarısı sağlanmakla birlikte, depresyon ve anksiyetenin azaltılmasına yönelik çaba gösterilmelidir. Gerekirse kapsamlı zihinsel değerlendirme ve psikoterapi tedavi planına dahil edilmelidir

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INTRODUCTION

Pituitary adenomas are the third most common central nervous system tumors after gliomas and meningiomas (1). Its overall prevalence is estimated to be 17% (2). They are classified as functional pituitary adenomas (FPA) and non-functional pituitary adenomas (NFPA) according to their hormone secretory capacity. Depending on the type of hormone secreted, it is classified as prolactin, growth hormone (GH), adrenocorticotrophic hormone (ACTH), or thyrotropin (TSH) producing adenomas. 15-54% of pituitary adenomas (3). 32-66% of FHAs are adenomas that secrete prolactin, 8-16% secrete GH, 2-6% secrete ACTH, and approximately 1% secrete TSH (3). Although histologically benign, they have many endocrine effects that cause significant morbidity and mortality. FPAs brings a number of complications due to hormone excess. FPA can affect many systems, such as hypercortisolism (Cushing's disease), excess GH (acromegaly), and excess prolactin hormone (prolactinoma). NFPA do not cause symptoms associated with hormone hypersecretion. Although patients may be asymptomatic, they may present with compression symptoms associated with an enlarged mass, such as pituitary hormone deficiency and visual impairment. In both FPAs and NFPA, the adenoma itself may cause one or more hormone deficiencies with the effect of mass compression, which may not be reversible after surgery. Similarly, pituitary adenoma excision may cause various complications associated with surgery, including isolated or panhypopituitarism.

In the long-term follow-up of patients with pituitary adenomas, non-pituitary intracranial mass, or isolated pituitary insufficiency, deterioration in the quality of life is expected (4-6). This situation can be caused by various factors such as radiotherapy (RT), pituitary surgery, pituitary hormone deficiency, or excess (7). In many patients with pituitary adenoma, symptoms such as sleep disorders, anxiety, and depression that were present before surgery may continue in the post-surgical period (8,9). Various studies have been conducted to evaluate the state of depression and anxiety in patients with hormonally functional and NFPA. In a recent systematic review of the neuropsychological status assessment of pituitary adenomas, impairment in quality of life in Cushing's disease was reported as 40%, with the prevalence of psychiatric disorders reaching 77% and 63% in acromegaly. These disorders are mostly depression, but psychosis and anxiety are frequently observed (10). As a result, it has been shown that the quality of life of patients with pituitary pathology is impaired, which increases depression and anxiety levels (11). We measured the depression and anxiety levels of patients with pituitary pathology who were followed in our center.

MATERIALS AND METHODS

In our study, 60 patients were being followed up in the pituitary polyclinic of our center for any pituitary disease. Thirty healthy individuals who applied to the check-up outpatient clinic for control purposes who did not have a known chronic disease and did not use drugs were included in the study as the control group.

Patients who received the same dose of hormone replacement therapy for at least six months were included in the study. Patients without clinical signs of adrenal insufficiency or glucocorticoid excess under glucocorticoid replacement were included in our study. The serum-free T4 (FT4) level was maintained in the upper

half of the reference range for the optimal dose in patients receiving L-thyroxine therapy due to TSH deficiency (central hypothyroidism). Patients with an appropriate fT4 range and no clinical symptoms of hypothyroidism were included in this study. Regarding gonadotropin deficiency, treatment was planned according to fertilization requests in men. Patients receiving different forms of testosterone replacement or gonadotropin replacement generally aim to maintain the total testosterone level at the lower limit (280-300 ng/dL). Women with gonadotropin deficiency were treated with preparations containing conjugated estrogen or estradiol valerate. Optimal dose planning for patients using desmopressin (d-DVAP) for antidiuretic hormone deficiency was performed according to the patient's urine output, serum sodium level, and weight monitoring. Patients whose urine output could be controlled under desmopressin therapy and whose serum sodium level was within the normal range were included in the study.

The patients were informed about the study during their routine polyclinic examinations, and those who wanted to participate voluntarily were asked to complete the Beck depression and Beck anxiety inventory. The Turkish version developed by Hisli (12) was used in the validity and reliability study. The demographic characteristics of the participants, history of surgery due to pituitary pathology, and RT (conventional or gamma-knife) were questioned, and the drugs they used were recorded. All patients with pituitary hormone deficiency received hormone replacement therapy at the same dose for at least 6 months.

It was planned to evaluate the symptoms and severity of depression using the Beck Depression Inventory Form. The Beck Depression Inventory Form, a 21-item self-reporting questionnaire in which each item is scored on a scale of 0-3, was used to assess the presence and severity of depression. Scores between 0 and 9 were considered average, 10 to 18 indicated mild symptoms of depression, 19 to 29 indicated moderate depression, and 30 to 63 was considered a sign of severe depression.

"Beck Anxiety Inventory Form was used to determine anxiety levels, which is also a 21-item self-reporting questionnaire with each item scored from 0 to 3. Those scoring 0-21 had mild anxiety, 22-42 had moderate anxiety, and those scoring 43-63 had severe anxiety."

This study was approved by the Gazi University Faculty of Medicine Ethics Committee (approval number: 563). All participants were informed about the study, and a written consent form was obtained.

Statistical Analysis

SPSS 22.0 (SPSS Inc. Chicago, USA) computer package program was used for statistical data analysis. Categorical variables are presented as numbers and percentages, and continuous variables are presented as median (minimum-maximum value). The Shapiro-Wilk test was used to evaluate the normal distribution of variables. The Mann-Whitney U test was used for comparative analyses between the two groups for variables that did not fit the normal distribution. The chi-square test was used for categorical variables among independent groups. The statistical significance level was set as $p < 0.05$.

RESULTS

The median age of the pituitary patient group participating in the study was 45 (20-73), and 50% of them were female. The median age

of the control group was 43 (25-72), and 70% were women. There was no statistically significant difference between the two groups according to age ($p=0.11$) and gender ($p=0.07$) (Table 1).

The study included 16 patients with acromegaly (26.7%), 1 with Cushing's disease (0.6%), 7 with prolactinomas (11.7%), 21 with NFPA (35%), 11 with non-pituitary masses consisting of 8 craniopharyngiomas and 3 Rathke cleft cysts (18.3%), and 4 patients with isolated pituitary hormone deficiency (6%). Surgery was performed in 47 patients because of pituitary mass. Gamma-knife treatment was applied to 27 patients in addition to surgery. Thirty-one patients received glucocorticoids, 40 levothyroxine, 11 gonadal hormones, 4 desmopressin, and 2 GH replacements.

Depression [10.5 (0-43) and 5 (0-17); $p<0.01$] and anxiety [9.5 (0-38) and 5 (0-24); $p=0.01$] scores were found to be significantly higher than those in the control group. When the patients who received gamma-knife treatment were compared with those who did not, no statistically significant difference was found in their depression [9.5 (0-18) and 11 (0-43); $p=0.25$] and anxiety levels [8.5 (0-38) and 13.5 (1-38); $p=0.46$]. Similarly, no statistically significant difference was observed between the patients who underwent pituitary surgery and those without a history of surgery regarding depression and anxiety levels [depression [10 (0-43) and 14 (0-27); $p=0.39$] and anxiety levels [9 (0-38) and 22 (1-38); $p=0.14$]. In addition, there was no significant difference between depression and anxiety levels when patients who underwent surgery only and those who underwent surgery and RT were compared ($p=0.40$ and $p=0.87$) (Table 2).

When patients with FPA and patients with NFPA were compared, no significant difference was found between depression and anxiety levels ($p=0.62$ and $p=0.13$). When patients with FPA were evaluated according to their hormonal secretion status, no significant difference was found between depression and anxiety levels. There

was no significant difference in Beck Depression and Anxiety levels between those who received glucocorticoid replacement and those who did not ($p=0.79$ and $p=0.85$). Similarly, there was no significant difference between Beck Depression and Anxiety levels between those who received levothyroxine replacement and those who did not ($p=0.17$ and $p=0.15$).

DISCUSSION

In our study, the depression and anxiety levels of patients with pituitary disease were found to be higher than those of the control group, but it was observed that this situation was not related to the surgery or RT process. Although there are many studies in the literature based on clinical, laboratory, treatment, and remission criteria due to pituitary pathologies, fewer studies reflect these patients' depression and mental and emotional well-being. Studies have shown in different publications that there is a deterioration in the quality of life in people with pituitary disease (11,13). Pituitary adenomas may cause deterioration in the quality of life and increase depression and anxiety levels during the nature of the disease or in the post-treatment period. For example, in Cushing's syndrome caused by pituitary ACTH-secreting tumors, it has been shown in many publications that hypercortisolism itself causes deterioration in the quality of life and an increase in depression and anxiety levels in patients who undergo surgery, RT, and/or medical treatment (14,15). According to the results of a study conducted with patients with CS from Türkiye, it was found that patients who were not in remission had a higher level of depression than the control group who were in remission (16).

According to the results obtained from studies on the quality of life in patients with pituitary adenoma, it can be said that the quality of life is impaired not only in those with active disease but also after a long period of biochemical cure (5,17). The comparative evaluation

Table 1. Demographic characteristics and depression and anxiety levels of patients and healthy controls

	Patient, (n=60)	Healthy control, (n=30)	p-value
Age (years)	45 (20-73)	43 (25-72)	0.11
Female (n, %)	30 (50)	21 (70)	0.07
Beck Depression Score	10.5 (0-43)	5 (0-17)	0.006
Beck Anxiety Score	9.5 (0-38)	5 (0-24)	0.012
History of operation (n, %)	47 (78.3)		
Radiotherapy (n, %)	27 (45.0)		
Glucocorticoid replacement (n, %)	31 (51.6)		
Levothyroxine replacement (n, %)	40 (66.6)		
Gonadal hormone replacement (n, %)	11 (18.3)		
Desmopressin replacement (n, %)	4 (6.7)		
Growth hormone replacement (n, %)	2 (3.3)		

Table 2. Effect of surgery and radiotherapy on depression and anxiety levels in the pituitary group

	Surgery (-), (n=11)	Surgery (+), (n=43)	p-value	RT (-), (n=28)	RT (+), (n=26)	p-value
Age (years)	46 (20-73)	45 (20-71)	0.53	46 (20-73)	45 (20-71)	0.87
Beck Depression Score	14 (0-27)	10 (0-43)	0.39	11 (0-43)	9.5 (0-18)	0.25
Beck Anxiety Score	22 (1-38)	9 (0-38)	0.14	13,5 (1-38)	8.5 (0-38)	0.46

Surgery (-): Patients without surgical history, Surgery (+): Patients with surgical history, RT (-): Patients without radiotherapy, RT (+): Patients with radiotherapy.

of FPA and NFPA determined that impairment in quality of life was observed at different rates. For example, patients with acromegaly have more body pain and physical dysfunction and, therefore, more deterioration in quality of life than patients with NFPA and patients with prolactinoma (18). In the same study, patients with Cushing's syndrome were associated with higher anxiety levels than patients with NFPA, and it was found that they had more physical dysfunction (18). In similar studies conducted in patients with prolactin-secreting pituitary adenoma, it has been shown that there is an inverse relationship between prolactin level and quality of life, and quality of life deteriorates even in patients with normal prolactin levels (19). It has been shown in various studies that patients with panhypopituitarism have similarly impaired quality of life. In particular, GH deficiency has been associated with a decrease in quality of life, which has been accepted as an important measure of the effectiveness of GH replacement therapy (20). Deterioration in quality of life is affected by different factors, such as the etiology of the disease, the treatment used, the severity of hypopituitarism, and incomplete treatment (18,21).

Our study found that patients with pituitary pathology had higher depression and anxiety levels than healthy volunteers. However, this difference was not associated with other factors that may affect anxiety and depression levels, such as hormonal secretion status, history of surgery, RT, and hormone replacement therapy.

Study Limitations

The major limitation of our study was the retrospective design. An important limitation was the highly heterogeneous nature of the study group, which consisted of both functional and non-functional tumors. Due to the limitations and the many affecting factors, a general conclusion can be drawn from our study that concerns all types of patients who can be seen in the pituitary polyclinic rather than a specific result.

CONCLUSION

In our study, it was observed that the presence of pituitary pathology due to any cause was associated with higher depression and anxiety levels.

Our findings regarding increased levels of depression and anxiety in patients with pituitary adenomas may be important for the long-term management of these patients. In the follow-up of these patients, well-being in terms of pituitary disease is ensured, but it should be aimed to improve depression and anxiety levels and provide a better quality of life. If necessary, detailed psychiatric evaluation and psychological counseling should be included in the treatment.

Ethics

Ethics Committee Approval: This study was approved by the Gazi University Faculty of Medicine Ethics Committee (approval number: 563).

Informed Consent: All participants were informed about the study, and a written consent form was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Concept: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Design: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Data Collection or Processing: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Analysis or Interpretation: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Literature Search: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T., Writing: A.B., M.M.Y., A.T., A.T.S., A.E.A., M.A., M.A.K., İ.Y., F.B.T.

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