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CAN COMORBID BIPOLAR DISORDER BE ASSOCIATED WITH ATYPICAL DEPRESSION IN PATIENTS WITH SOCIAL ANXIETY DISORDER?

SOSYAL ANKSİYETE BOZUKLUĞU HASTALARINDA BİPOLAR BOZUKLUK EKTANISI ATİPİK DEPRESYON İLE İLİŞKİLİ OLABİLİR Mİ?

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Abstract

Social anxiety disorder (SAD) is one of the most common psychiatric disorders and frequently co-exists with other psychiatric conditions, primarily with mood disorders. MD is the most common psychiatric comorbidity in patients with SAD, and the association of anxiety disorders and bipolar disorder with atypical depression, which is included in diagnostic guidelines for MD as a subgroup, has been well established. The present study aims to determine if SAD patients with comorbid atypical depression or bipolar disorder show differences in terms of symptomatology and disease course compared to SAD patients without bipolar disorder. We hypothesize that social phobia patients may have subgroups within themselves and the processes of these subgroups may be different from those of known SAD patients. In this study a retrospective chart review was performed for patients who had applied to the Psychiatry Outpatient Unit, Kartal Research and Training Hospital, during a 7-month period in 2018. The study had a retrospective design. A total of 82 patients diagnosed with Social Anxiety Disorder based on a SCID-I interview for DSM-IV were included in the study. Of the 82 SAD patients, 16 patients (19.5%) had also co-existing BPD. All SAD patients with comorbid BPD had at least one major depressive episode history, while 15 (93.7%) SAD patients with comorbid BPD exhibited atypical features in at least one episode. Thus, we identified an association between SAD/BPD and atypical depression and discussed the importance of this co-occurrence in terms of clinical evaluation.

Keywords: social anxiety disorder; atypical depression; comorbidity; bipolar disorder

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Öz

Sosyal Anksiyete Bozukluğu (SAB) en yaygın görülen psikiyatrik rahatsızlıklardan biri olup başta duygudurum bozuklukları olmak üzere diğer psikiyatrik hastalıklarla ile sıklıkla birlikte görülmektedir. SAB olan kişilerde Major Depresyon (MD) görülme sıklığının yüksek olması her iki hastalığa bağlı antidepresan kullanımına yaygınlığına sebep olmaktadır. SAB'na en sık eşlik eden psikiyatrik rahatsızlık olan MD tanı kılavuzlarında bir alt grubu olarak belirlenen Atipik Depresyonun daha önceki çalışmalarda Anksiyete Bozuklukları ve Bipolar Bozukluk (BPB) ile olan ilişkisi ortaya konulmuştur. Atipik Depresyonun SAB ile de komorbid olarak daha sık görüldüğünü belirten yayınlar olmakla birlikte bu birlikteliğin Atipik Depresyonun tanı kriterlerinden olan "başkaları tarafından kabul görmemeye duyarlılık"ın SAB'ndaki psikopatolojinin temelinde de yer almasının rol oynadığı düşünülmektedir. SAB'na komorbid olarak BPB sıklığındaki yükseklik hastalık seyri ve tedavi düzenlenmesi açısından daha dikkatli olmayı gerektirmektedir. Bu çalışmaya alınan kişiler; Kartal Eğitim ve Araştırma Hastanesi Psikiyatri Polikliniği'ne 2018 yılı içinde, 7 ay boyunca ayaktan takip edilen poliklinik hastaları arasından dosya taraması şeklinde alınmıştır. Çalışmamız retrospektif olarak yapılmıştır. Çalışmaya alınan kişilere, klinik görüşme (SCID-I) ile DSM-IV'e göre Sosyal Anksiyete Bozukluğu tanısı almış 82 kişi dâhil edilmiştir. Çalışmamızda SAB ile BPB birlikteliği araştırılmış olup, depresif epizodların BPB eşlik eden hastalarda daha fazla olmak üzere çoğunlukla Atipik özellik taşıdığı saptanmıştır. SAB-BPB ve Atipik Depresyon ilişkisi ortaya konulmuş olup bu birlikteliğin sebepleri klinik değerlendirmedeki önemi tartışılmıştır.

Anahtar Kelimeler: *sosyal anksiyete bozukluğu; atipik depresyon; ektanı; bipolar bozukluk*

1. Introduction

Social anxiety disorder (SAD), also known as social phobia, is characterized by a number of symptoms such as blushing, sweating, shaky hands, and fear of being humiliated in social or performance situations. SAD is one of the most prevalent psychiatric conditions with an estimated 12-month prevalence of 3% to 7% among adults in the US and a life-time prevalence of 5% to 12% (Grant et al., 2005; Kessler et al., 2005). The reported prevalence rates in developed countries are generally comparable, while the disorder appears to be less common in developing countries (Stein et al., 2010). According to the Turkish Mental Health Profile survey, the estimated prevalence of social phobia in Turkish women and men is 2.3% and 1.1%, respectively (Kılıç, 1988). The risk factors for SAD include female gender, family history of SAD, and behavioral restrictions or shyness during early childhood. Patients with SAD may also suffer from a variety of psychiatric disorders, mainly phobic disorders and other anxiety disorders, but also from affective disorders, alcohol use disorder, eating disorder, and schizophrenia. Approximately 19.5% to 32% of patients with SAD suffer from major depressive disorder (Huppert, 2009; Ohayon & Schatzberg, 2010), while 3% to 21.2% have been reported to have bipolar disorder as a comorbid condition (Koyuncu et al., 2014; Perugi et al., n.d.; Van Ameringen, Mancini, Styan, & Donison, 1991). Comorbid mood disorders are associated with the presence of more severe manifestations of social anxiety disorder and dysfunction in patients with SAD (Aderka et al., 2012). In one study patients with comorbid mood disorders in SAD were found to present with more severe social anxiety symptoms compared to those without comorbid conditions (Fracalanza, McCabe, Taylor, & Antony, 2014).

MD is the most common psychiatric comorbidity in patients with SAD, and the association of anxiety disorders and bipolar disorder with atypical depression, which is included in diagnostic guidelines for MD as a subgroup, has been well established. In comparison to other types of major depression, atypical depression occurs more commonly in women, and is associated with early disease onset, prolonged disease duration, frequent depressive episodes, high suicide risk, and severe symptoms (Blanco et al., 2012; Posternak & Zimmerman, 2002; Thase, Carpenter, Kupfer, & Frank, 1991). It has been suggested that patients with unipolar depression who have atypical features should be closely monitored for development of bipolar disorder during the course of the disease, and atypical depression may even represent a transitory form between unipolar depression and bipolar disorder. Although some studies suggest a more frequent co-occurrence of atypical depression and SAD, this might be due to the fact that one of the diagnostic criteria for atypical depression (i.e. interpersonal rejection sensitivity) is also an underlying factor in the psychopathology of SAD (Parker, 2007). On the other hand, presence of atypical depression in SAD was associated with more severe symptoms and earlier onset of disease. It has been suggested that co-existence of atypical depression in a patient with SAD should alert the clinician for possible worsening in functions and development of bipolar disorder during the course of the disease (Koyuncu et al., 2015).

The hypothesis of our study is that SAD patients with comorbid atypical depression or bipolar disorder may show differences in terms of symptomatology and disease course compared to SAD patients without bipolar disorder. We believe that social phobia patients may have subgroups within themselves and the processes of these subgroups may be different from those of known SAD patients.

2. Methods

In this study, a retrospective chart review was performed for patients who had applied to the Psychiatry Outpatient Unit, Kartal Research and Training Hospital. The data were obtained cross-sectionally according to time in 7 months period. The study had a retrospective design. A total of 82 patients diagnosed with Social Anxiety Disorder based on

a SCID-I interview for DSM-IV were included in the study

All interviews were performed by a physician. Demographic characteristics and clinical features (such as depressive episode with life-long atypical features) were assessed using a semi-structured interview. In the assessment of atypical features, if the DSM-IV criteria for atypical depression were met for at least one major depressive episode during the lifetime of the patient, then depressive episodes with no such features were also accepted as "positive/atypical features present". The inclusion criteria were being between the ages of 18 and 65, being diagnosed with SAD based on DSM-IV, being literate, not having schizophrenia or other accompanying psychotic disorders, not having severe mental or physical disorder which may impair the interview process, not having alcohol/substance dependence, not having a general medical condition which may mimic SAD due to its physiological effects.

2.1. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

SCID-I is a structured clinical interview for DSM-IV Axis I disorders. It provides a standardized diagnostic evaluation that improves the diagnostic reliability, increases the validity of the diagnosis by facilitating systematic screening of diagnostic criteria, and allows for a systematic assessment of symptoms (First, Spitzer, Gibbon, & Williams, 1997). The adaptation and validity studies for the Turkish version were performed by Çorapçıoğlu et al. (Çorapçıoğlu, Aydemir, Yildiz, Esen-Danaci, & Koroglu, 1999).

2.2. Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS), Version 21. Fisher's exact test, independent sample t-test and Chi square were used for statistical analysis. The statistical significance level was set at $p < 0.05$ with 95% confidence interval.

3. Results

Overall, there were 56 male (68.3%) and 26 female (31.7%) participants in the study groups, with a mean age of 27.6 years (± 6.2 y). The study groups were comparable in terms of age, gender, and educational level, while SAD patients with comorbid BPD were more likely to be married ($p=0.046$). Seven patients (8.5%) had no comorbidities, while 34 (41.5%) had one, 37 (45.1) had two, and 4 (4.9%) had three comorbidities. Of the 82 SAD patients, 59 (71.9%) had major depression, 16 (19.5%) had BPD, 10 (12.2%) had obsessive-compulsive disorder, 6 (7.3%) had alcohol and psychoactive substance use disorder, 5 (6.1%) had specific phobias, 2 (2.4%) had panic disorder and generalized anxiety disorder, and 1 (1.2%) had an eating disorder as a life-time comorbidity. None of the patients had any psychotic or somatoform disorders. Of the 16 patients with comorbid BPD, 1 (1.2%) BPD 1 patient, 2 (2.4%) BPD 2 patients, and 13 (15.9%) BPD 3 patients exhibited antidepressant-induced hypomanic shift. All SAD patients with comorbid BPD had at least one major depressive episode history, while 15 (93.7%) SAD patients with comorbid BPD exhibited atypical features in at least one episode. In contrast, of the 59 patients with (at least one) MDE history in the control group, 34 (57.6%) were found to have atypical features in at least one episode.

4. Discussion

SAD patients with or without comorbid bipolar disorders were not significantly different in term of age and gender, which indicates that the two groups were comparable in terms of sociodemographic characteristics.

Compared to previous reports, a slightly higher proportion of the patients were found to have comorbid major depression and bipolar disorder (Huppert, 2009; Ohayon & Schatzberg, 2010). It appears that inclusion of hypomanic episodes triggered by antidepressant medications, which are commonly used in SAD patients, in the bipolar spectrum disorders according to DSM-IV may partially account for the difference observed. Also, the presence of at least one depressive episode in all SAD patients with comorbid BPD as well as the high occurrence of major depression in those without comorbid BPD are indicative of the overlap between SAD and depressive symptoms. The recent understanding suggests that hypomania-mania in patients receiving antidepressant treatment due to a diagnosis of unipolar depression represents a misdiagnosis, and that these patients should be regarded as having bipolar disorder (Chun & Dunner, 2004). In our study, hypomanic shift due to antidepressant use was observed in a high proportion of the patients (15.9%), who were considered to have BPD, and this requires close attention with regard to BPD after initiation of treatment for SAD. In a recent meta-analysis on pharmacotherapy for SAD patients, selective serotonin re-uptake inhibitors (SSRIs), although not very efficacious, showed the highest activity among all pharmacotherapies tested in the study, and these medications also represent the most frequently prescribed antidepressants for major depression (Williams et al., 2017). Separate and combined use of SSRIs in the treatment of both for SAD and depressive disorders may help explain high rates of drug-related hypomania and mania, as suggested by our findings.

Alcohol use disorder has been increasingly diagnosed in patients with SAD as well as patients with other anxiety disorders (Polo, Alegría, Chen, & Blanco, 2011). Several hypotheses have been suggested to explain the link between SAD and alcohol use including the tension relief theory (CONGER, 1956), stress response dampening (Sher & Levenson, 1982), and self-treatment hypothesis (Khantzian, 1985). In contrast with 24% of patients reported to have comorbid alcohol use disorder in previous studies, the corresponding figure was 7.3% in the present study (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). Although this percentage is lower than previous reports, it is comparable to previous rates of comorbidity

identified in other studies from Turkey (Koyuncu et al., 2014), and we believe that this is associated with the sociocultural characteristics of the general population.

Atypical depression, a subtype of major depression, is believed to occur in 15% to 40% of patients with major depression (Benazzi, 1999; Łojko & Rybakowski, 2017; Singh & Williams, 2006). In our study, atypical features among SAD patients without comorbid BPD experiencing a major depressive episode were more common than previously reported. In another study from Turkey, atypical depression was reported in 19.6% of the subjects. As compared to other patients with depression, individuals with atypical features tend to have earlier disease onset as well as more severe and protracted disease course, leading to the assumption that atypical depression represents another form of depression (Ağargün, Kara, Kıncır, & Bilgin, 1996). Several studies have investigated the role of hereditary and genetic factors in patients with atypical depression (Pilowsky et al., 2006). Also, atypical depression has been linked with bipolar 2 and bipolar spectrum disorders (Angst, Gamma, Sellaro, Zhang, & Merikangas, 2002). The high incidence of atypical features in SAD patients with co-existing BPD supports the close relationship between the presence of Atypical Depression and depressive episode of BPD as suggested in previous studies (Akiskal & Benazzi, 2005). In addition to the "rejection sensitivity" criterion, which is believed to predispose individuals to co-existent SAD and atypical depression, its higher occurrence in individuals with co-existing BPD requires a further explanation beyond that provided by this criterion (Parker, 2007). Although the presence of atypical features of major depression in patients with SAD has not attracted much attention in the past, a high incidence of co-existing SAD-BPD and atypical features was noted in our study. Similar to the factors indicating the co-existence of BPD and atypical depression, further studies may shed light on this association in individuals with SAD.

One limitation of our study is that the SAD patients were not assessed with respect to the co-existence of avoidant personality disorder (APD). Alpert et al. (1997) found a higher occurrence of atypical depressive features and a higher risk of social function disorder in patients diagnosed with both SAD and APD (Alpert et al., 1997). In another study, Sanderson et al. (1994) reported that APD frequently co-existed with psychiatric disorders such as panic disorder, atypical depression, and body dysmorphic disorder (Sanderson, Wetzler, Beck, & Betz, 1994). Social phobia patients who also meet the crit eria for APD have been found to experience more severe social dysfunction and depressive comorbidity (Schneier, Spitzer, Gibbon, Fyer, & Liebowitz, 1991). Currently, whether the marked presence of atypical depressive features in SAD patients is a coping strategy for anxiety or represents a phenomenon of genetic predisposition is not fully elucidated. In this context, further studies, which also include APD patients, are warranted to determine whether atypical depressive features are predictive of genetic predisposition.

Table 1.

	SAD with BD (n=16)	SAD without BD (n=66)	p
+Age, mean (SD)	27.3 (5.7)	27.6 (6.3)	0.826
++Gender, females, n (%)	4 (25.0)	22 (33.3)	0.520
++Marital status, married, n (%)7 (43.8)	12 (18.2)	0.046*F	
+++Major Depresyon	16 (100)	43 (65)	0.040*
+Education, mean (SD)	12.8 (2.3)	13.1 (2.4)	0.683
+++Atypical features in MDE** n (%)	15 (93.8)	34 (57.6)	0.007
Lifetime comorbidity, n (%)			
Any psychotic disorder	0 (0.0)	0 (0.0)	N/A
+++Obsessive-compulsive disorder	2 (12.5)	8 (12.1)	1.000
+++Generalized anxiety disorder	0 (0.0)	2 (3.0)	1.000
+++Panic disorder	0 (0.0)	2 (3.0)	1.000
+++Simple phobia	1 (6.3)	4 (6.1)	1.000
Post traumatic stress disorder	0 (0.0)	0 (0.0)	N/A
+++Alcohol or substance abuse	0 (0.0)	6 (9.1)	0.592
Somatoform disorder	0 (0.0)	0 (0.0)	N/A
+++Eating disorder	0 (0.0)	1 (1.5)	1.000
+++Any anxiety disorder (except SAD)	3 (18.8)	15 (22.7)	1.000

N/A: Not Analyzed, +Student t test, ++ Chi Square test +++Fischer's Exact test, **: Oranlar MDE öyküsü olan hastalar arasında atipi öyküsü olanların oranıdır (The figures represent the rate of patients with atypical features among those with MDE history.)

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