Comorbid Anxiety Disorders in Schizophrenia: The Relationship between Sociodemographic and Clinical Characteristics

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DOI: 10.5350/DAJPN2010230103t

ÖZET

Şizofrenide anksiyete bozuklukları eştanısı: sosyodemografik ve klinik özellikler ile ilişkisi

Amaç: Bu araştırmada, şizofreni tanılı hastalarda anksiyete bozukluğu eştanısının araştırılması, anksiyete bozukluğu olan ve olmayan şizofreni hastalarının sosyodemografik özellikler ve klinik özellikler açısından karşılaştırılması amaçlanmaktadır.

Yöntem: Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi Psikotik Bozukluklar Tedavi Eğitim ve Araştırma Merkezi tarafından takip edilen, DSM-IV TR'ye göre şizofreni tanılı 105 hasta bu çalışmaya dahil edilmiştir. Katılımcılara sosyodemografik veri formu, DSM-IV Eksen I Bozuklukları İçin Yapılandırılmış Klinik Görüşme Ölçeği (SCID-I), Pozitif ve Negatif Sendrom Ölçegi (PANSS), Hamilton Anksiyete Değerlendirme Ölçeği (HAM-A) ve Barnes Akatizi Ölçeği (BAÖ) görüşmeci tarafından uygulanmıştır.

Bulgular: Olguların %23,80'inde (n=25) herhangi bir anksiyete bozukluğu saptanmazken, %47,61'inde (n=50) birden fazla anksiyete bozukluğu, %4,76'sında (n=5) panik bozukluğu, %0,95'inde (n=1) obsesif kompulsif bozukluk, %0,95'inde (n=1) agarofobi, %4,76'sında (n=5) sosyal anksiyete bozukluğu, %14,28'inde (n=15) özgül fobi ve %2,85'inde (n=3) başka türlü adlandırılamayan anksiyete bozukluğu bulunmuştur. Anksiyete bozukluğu olan ve olmayan olgular arasında cinsiyet, yaş, aile öyküsü, şizofreni alt tipi, alkol ve madde kullanım öyküsü ve kendine zarar verici davranış, patolojik ebeveynin varlığı, bir ebeveynin yokluğu, PANSS-pozitif, PANSS-negatif, PANSS-genel ve PANSS-total puanları açısından istatistiksel olarak anlamlı farklılık saptanmamıştır. Okul fobisi veya başka bir fobinin varlığı ve çocuklukta kötü muamele öyküsü anksiyete bozukluğu olan olgularda, anksiyete bozukluğu olmayan olgulara göre anlamlı derecede daha fazla bulunmuştur.

Sonuç: Bu sonuçlar şizofrenide anksiyete bozukluğu eştanısının önemini vurgulamakta, tedavi yaklaşımlarında yeni arayışları gündeme getirmektedir.

Anahtar kelimeler: Şizofreni, anksiyete bozukluğu, eştanı

ABSTRACT

Comorbidity of anxiety disorders in schizophrenia: relationship with sociodemographic and clinical variables

Objective: In this study, we aimed to investigate the frequency of comorbidity of anxiety disorders and schizophrenia and to assess its relation with sociodemographic and clinical variables

Methods: One hundered five patients diagnosed as having schizophrenia according to DSM-IV were recruited from Bakırköy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery, Treatment Education and Research Center for Psychotic Disorders. The data from the participants were collected using sociodemographic data form, Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition, Positive and Negative Syndrome Scale (PANSS), Hamilton Anxiety Rating Scale (HAM-A), Barnes Akathisia Rating Scale (BARS). The collected data has been evaluated by using SPSS 10.0.

Results: Among the participants, 23,80% (n=25) had no anxiety disorders whereas 47,61% (n=50) had diagnosis for more than one anxiety disorder; 4,76% (n= 5) had panic disorder, 0,95% (n=1) had obsessive-compulsive disorder, 0,95% (n=1) had agorophobia, 4,76% (n=5) had social anxiety disorder, 14,28% (n=15) had special phobia, and 2,85% (n=3) had anxiety disorder otherwise unspecified as comorbid diagnosis along with schizophrenia. Anxiety symptoms were more frequent in patients with a story of childhood separation anxiety, school phobia and childhood maltreatment.

Conclusion: These results emphasize the importance of screening for comorbid anxiety disorders in the prognosis and treatment of schizophrenia and display the need for new contemporary treatment modalities.

Key words: Schizophrenia, anxiety disorder, comorbidity

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Date of acceptance:
February 28, 2010

INTRODUCTION

Although it has been established that anxiety plays a significant role in the psychopathology of schizophrenia information with regard to the emergence of anxiety symptoms and disorders in schizophrenia is inadequate. There are a limited number of studies that evaluate the role of anxiety in psychotic disorders and

the relation of anxiety with psychotic symptoms. One reason for this may be the difficulty of structuring criteria for a psychiatric diagnosis in a hierarchical order; the disorder that may be at the bottom, hierarchically, may not be added as a comorbid diagnosis to the basic diagnosis (1).

There are also some issues in terms of evaluation. Criteria developed for measuring the anxiety level in the non-psychotic population, i.e. the Hamilton Anxiety Rating Scale, the Yale-Brown Obsession Compulsion Rating Scale, are not specific for schizophrenia (2). Some studies have suggested that anxiety in schizophrenic patients might be associated with both positive (3) and negative (4) symptoms. In addition, extrapyramidal symptoms that develop secondary to neuroleptic treatment may also be comorbid with anxiety symptoms (5).

Epidemiologically, many studies show that anxiety disorders increase in schizophrenic patients. In clinical and epidemiological studies, a diagnosis of comorbid anxiety disorders in schizophrenic patients is reported to be over 60%. In the study conducted by Goodwin et al. to investigate the frequency of anxiety disorders in 60 hospitalized schizophrenic patients, the rate of obsessive compulsive disorder (OCD) was reported to be 5.4%, panic disorder 7.1%, social phobia 8.2%, agoraphobia 8.2% and specific phobia 13.60% (6). In a study conducted with 32 schizophrenic patients followed up in an outpatient clinic, Tibbo et al., reported that the rate of panic disorder is 3.3%, social phobia 13.3%, diffuse anxiety 16.7% and agoraphobia 16.7% (7). In the study conducted by Pallanti et al. with 80 schizophrenic patients followed up in an outpatient clinic, the rate of obsessive-compulsive disorder was 22.5%, panic disorder 13.8%, social phobia 36.3%, post-traumatic stress disorder (PTSD) 1.3%, generalized anxiety 2.5 % and agoraphobia 3.8% (8).

While anxiety-related symptoms are often seen in schizophrenic patients, it is not clear which anxiety symptoms are related to the disorder and whether or not these symptoms affect the functioning. Anxiety symptoms in schizophrenia increase the severity of both the positive and negative symptoms and cause deterioration in patients' ability to function (1,7,9,10). Anxiety symptoms or disorders in schizophrenic patients are significant, as they increase the risk of recurrence and suicide and impair social and professional functions and quality of life (11-14).

The objective of this study is to investigate comorbid anxiety disorder in patients diagnosed as schizophrenia according to the DSM IV-TR, and to compare schizophrenic patients, with and without anxiety disorder, in terms of sociodemographic and clinical characteristics.

METHODS AND MATERIALS

Participants

One hundred and five patients, who were followed up in the Treatment Education and Research Center for Psychotic Disorders of the Bakırköy Prof. Dr. Mazhar Osman Research and Training Hospital, diagnosed as schizophrenia according to the DSM-IV-TR included in the study. Those patients with severe physical or neurological diseases, alcohol or substance abuse disorders, who have received ECT within last 6 months, and cases with higher scores on the Barnes Akathisia Rating Scale were excluded. The study was approved by the ethics committee of Bakırköy Prof. Dr. Mazhar Osman Research and Training Hospital and all participants signed written informed consent.

Scales

1. Sociodemographic data form: Questions on patients' childhood history [presence of pathological parents (anxious, overprotective or unable to provide adequate care); history of maltreatment, i.e., violence, abuse; absence of one parent due to separation or death; presence of school phobia or another phobias] were added to the sociodemographic data form used to evaluate sociodemographic characteristics, past and current conditions of the diseases, diagnosis and the treatments administered, comorbid diagnosis, family histories, and legal issues of the patients.
2. Structured Clinical Interview Scale for the DSM-IV Axis I Diagnosis (SCID-I) is a clinical interview

structured by First et al. for DSM-IV Axis I Disorders in 1997 (16). SCID I was developed to increase the validity of the diagnosis and to investigate symptoms systematically by providing standard diagnostic evaluations and by facilitating the screening of reliability of the diagnosis and DSM-IV diagnostic criteria. Adaptation and reliability studies of SCID-I for Turkey were conducted by Özkürkçügil et al. in 1999 (17). SCID-I determines whether an Axis I diagnosis is present or not at any time (lifelong prevalence) and the presence or absence of disorder symptoms within the last month (17).

3. The Positive and Negative Syndrome Scale (PANSS) is a semi-structured clinical interview scale developed by Kay et al. and includes 30 items and a seven-point severity rating (18). Seven of thirty psychiatric parameters belong to the positive symptoms subscale, seven parameters belong to the negative symptoms subscale and the remaining sixteen parameters belong to the general psychopathology subscale. Turkish reliability and validity studies of the scale were conducted by Kostakoğlu et al. (19).
4. The Hamilton Anxiety Rating Scale (HAM-A). This scale was developed by Hamilton in 1959. It includes 14 questions on psychological and physical symptoms (20). It provides five Likert-type measurements. This scale determines the anxiety level and symptom distribution and measures the severity variances. Turkish validity and reliability studies of the scale were conducted by Yazıcı et al. in 1998 (21). A cutoff point was not calculated in the study conducted in Turkey.
5. The Barnes-Akathisia Rating Scale (BAS or BARS) is a scale widely used for evaluating akathisia in patients receiving antipsychotic treatment (22). It includes diagnostic criteria for pseudoakathisia and mild, intermediate and severe akathisia. The scale measures both observed movements and subjective restlessness experience.

Statistical Evaluation:

In this study, statistical analysis was conducted using an SPSS for Windows 10.0 program. The T test was used for the independent groups in comparing demographic characteristics and disease-related characteristics; and chi-square and Fisher exact tests were used to compare qualitative data. Results were assessed at a significance level of $p<0,05$.

RESULTS

Twenty-five of the patients were female (23.8%) and 80 were male (76.2%). The patients' ages ranged from 21 to 56 years. Age range was determined at 22-52 for females and 21-56 for males. While general average age was 35.08 (SD ±8.29) years, the average age for females was 35.77 (SD ±8, 30) years and the average age for males were 34.85 (SD ±8, 33) years. The education levels of the patients were classified according to eight years compulsory education course. There were 46 patients who graduated from primary school, or did not complete primary school (43.8%); 28 patients were high-school graduates or completed a high-school equivalency program (26.7%); and 31 patients were university graduates (29.5%). Eighty-one of the patients (77.1%) were single, 15 (14.3%) were married and 9 of them (8.6%) were widowed or divorced.

The patients included in this study were grouped as those who had been diagnosed with comorbid lifelong and current anxiety disorder , according to the structured Clinical Interview Guideline for the DSM-IV Axis I Disorders (SCID-I), and those who had not been diagnosed with the disorder. No anxiety disorder was determined for 23.80% of the cases (n=25). More than one anxiety disorder was determined for 47.61% of the cases (n=50). Panic disorders were determined for 4.76% of the cases (n=5); obsessive compulsive

Table 1: Frequency of anxiety disorder in cases included into the study

Anxiety Disorders	% (n)
More than one anxiety disorder (Mixed type)	47,61 (50)
Social anxiety disorder	4,76 (5)
Specific phobia	14,28 (15)
Panic disorder	4,76 (5)
Obsessive-compulsive disorder	0,95 (1)
Unspecified anxiety disorder	2,84 (3)
Agoraphobia	0,95 (1)

Table 2: Comparison of patients (with and without comorbid lifelong and current anxiety disorder) in terms of history of schizophrenia in family, subtype of schizophrenia, alcohol and substance abuse and self-destructive behavior.

	Anxiety Disorder					
	Absent		Present			
Characteristics	**n**	**%**	**n**	**%**	**Chi-square**	**p**
Family history					0,01	0,930
Present	11	44,0	36	45,0		
Absent	14	56,0	44	55,0		
Subtype of schizophrenia					0,05	0,808
Paranoid	14	56,0	47	58,8		
Non paranoid	11	44,0	33	41,3		
Alcohol, substance abuse history						-
Present	2	8,0	8	10,0		
Absent	23	92,0	72	90,0		
Self-destructive behavior						-
Present	3	12,0	11	13,8		
Absent	22	88,0	69	86,3		

Table 3: Comparison of patients (with and without comorbid lifelong and current anxiety disorder) in terms of family characteristics.

	Anxiety Disorder					
	Absent		Present			
Characteristics	**n**	**%**	**n**	**%**	**Chi-square**	**p**
Pathological parent					2,62	0,105
Present	5	20,0	30	37,5		
Absent	20	80,0	50	62,5		
Parent death, divorce					3.32	0,068
Present	2	8,0	20	25,0		
Absent	23	92,0	60	75,0		
Presence of school phobia or another phobia					12,07	0,001*
Present	1	4,0	33	41,3		
Absent	24	96,0	47	58,8		
Maltreatment history during childhood					4,94	0,026*
Present	2	8,0	24	30,0		
Absent	23	92,0	56	70,0		

* : $p < 0.05$ significance level

disorder for 0.95% of the cases (n=1); agoraphobia for 0.95% of the cases (n=1); social anxiety disorder for 4.76% of the cases (n=5); specific phobia for 14.28% of the cases (n=15); and unspecified anxiety disorders were determined for 2.85% of the cases (n=3). None of our cases met the posttraumatic stress disorder and generalized anxiety criteria alone, but they were included in the cases having more than one anxiety disorder (Table 1).

No significant correlation was determined between anxiety disorders, gender and age in schizophrenia ($p>0.05$). The number of high-school graduates was significantly higher among patients with comorbid anxiety disorder diagnosis ($p<0.05$).

No statistically significant difference was found regarding familial schizophrenia history, subtype of schizophrenia, alcohol and substance abuse history and self-destructive behavior for patients with or without anxiety disorders(Table 2). The presence of a pathological parent (anxious, overprotective or unable to provide adequate care) and the absence of a parent due to separation or death did not contribute to a statistically significant difference in cases, with or without anxiety disorder (Table 3).

Table 4: Comparison of patients (with and without comorbid lifelong and current anxiety disorder): PANSS scores.

	Anxiety Disorder				
	Absent		Present		
	Mean	SD	Mean	SD	p
PANSS positive	12,88	5,95	12,20	4,33	0,534
PANSS negative	17,60	5,80	17,44	5,41	0,898
PANSS general	31,28	7,38	31,81	6,25	0,723
PANSS total	61,76	16,08	61,21	12,91	0,862

The incidence of school phobia or other phobias and a history of childhood maltreatment were significantly higher in patients with anxiety disorder than in patients without anxiety disorder ($p<0.05$) (Table 3).

No statistically significant variation was found in terms of disease duration, treatment duration and number of hospitalizations, for patients with or without anxiety disorder. No statistically significant difference was found in patients with or without anxiety disorder, in terms of PANSS-positive, PANSS-negative, PANSS-general and PANSS-total scores (Table 4).

DISCUSSION

Our study indicated that 86.2% of the patients with a diagnosis of schizophrenia met the anxiety disorder criteria. Almost half the patients (47.61%) met the criteria for more than one anxiety disorder. This rate is higher than in the literature. But variables like national differences in standards of life, rehabilitation and support systems should be taken into consideration as factors in this disparity. In a study conducted by Huppert et al. on 32 schizophrenic or schizoaffective patients, researchers found a comorbid anxiety disorder diagnosis in 9 patients (28.1%); one patient had 3 comorbid anxiety disorder diagnoses (3.1%); and a diagnosis of four comorbid anxiety disorders was determined for one patient (3.1%). More than one anxiety disorders for a total of 34.37% of the patients were determined (10). In the study conducted by Seedat et al. on 70 schizophrenic patients, 22.9% of them (16 patients) received at least one anxiety disorder diagnosis and four (5.7%) of these patients received two or more anxiety disorder diagnoses (5). In our study, 4.76% of the patients met the social phobia criteria. This percentage is similar to that reported by Seedat et al. (5). A number of studies report a rate for social phobias as 13.3% and 37.5% (7, 10, 23-25).

Panic disorders found in 4.76% of the participants met the DSM-IV SCID criteria. This rate is also consistent with the studies conducted by Tibbo et al. and Braga et al. (7, 23). In another study, 19 out of 40 (47.5%) schizophrenic patients experienced panic attacks.

Fourteen of the patients met the panic disorder criteria. Panic attacks for 7 of 19 developed spontaneously and were not due to a state of fear, delusion or paranoid thoughts (26). The frequency of OCD (obsessive-compulsive disorder) was 0.95% in our study and it is too low to compare with other reports, where OCD rates increased to 4.3% to 37.5% (5, 10, 23, 27, 28). OCD was determined in 23 patients (31.5%) in the study conducted in Turkey by Üçok et al. on 73 schizophrenic patients followed in an outpatient clinic (29). In our study, there were no patients diagnosed solely with generalized anxiety disorder. But 11 patients meeting generalized anxiety disorder criteria (10.47%) were found in the mixed group. This is consistent with other studies in the literature (5, 7, 10, 23, 24). In our study, no patient met the PTSD diagnosis. PTSD was not reported in the study conducted by Huppert et al. on 32 patients diagnosed with schizophrenia and schizoaffective disorder (10). The rate of PSTD was reported to be 4.3% in the study conducted on 70 schizophrenia patients followed in an outpatient clinic (5).

Agoraphobia was determined in 0.95% of the participants and this rate is lower than the that reported in the previous studies. While this rate was 1.9% in the study conducted by Braga et al., it was 13.7% in

the study conducted by Tibbo et al. (7, 23). Specific phobia was determined in 14.28% of the patients. Given the presence of patients who also had specific phobia diagnosis in the mixed group, this rate is higher. Incidence of unspecified anxiety disorder was 2.85% for the patients in our study. This rate is lower than the one reported in Braga's study (23).

In our study, no significant correlation was determined for patients with comorbid lifelong and current anxiety disorder diagnosis in terms of gender and age. Our study is consistent with the literature (23, 24). However, in the study conducted by Lysaker et al. on 128 patients with schizophrenia and schizoaffective disorder, findings indicated females were exposed to sexual trauma more often (75%) than males (46%); anxiety scores in the females were higher (9). In our study, the rate of high-school graduates who had comorbid lifelong and current anxiety disorder was significantly higher than the rate of high-school graduates who did not comorbid lifelong and current anxiety disorder. The literature contains limited data on this. The limited number of patients in the study, and the higher education levels of the cases compared to our groups could be a factor in this discrepancy. In patients with a comorbid lifelong and current anxiety disorder diagnosis and without such a diagnosis, no significant difference was found regarding familial schizophrenia history, schizophrenia subtype, alcohol and substance abuse and self-destructive behavior for patients with or without comorbid lifelong and current anxiety disorder diagnosis. One study's results indicated that alcohol abuse was higher in schizophrenic patients with comorbid panic disorder (30). In our study, for patients with and without comorbid lifelong and current anxiety disorder diagnosis, there was no significant variation in terms of the presence of pathological parental characteristics like overprotectiveness, anxiety or to the inability to provide adequate care or the absence of one of the parents due to separation or death. The incidence of school phobia or another phobia and a history of childhood maltreatment were found to be higher in the patients with comormid lifelong and current anxiety disorder diagnosis compared to the patients without comorbid anxiety disorder diagnosis. These results are consistent with the limited number of studies in the literature (13, 30). Studies indicate that many schizophrenic patients are exposed to trauma during premorbid period and after diagnosis. But the correlation between trauma symptoms and positive and negative symptoms in schizophrenia is not fully known. A recent study's results indicated that 68 out of 81 schizophrenic patients experienced at least one traumatic event and two-thirds of them had suffered clinically significant trauma symptoms (31).

In our study, no statistically significant difference was found between patients with and without morbid anxiety disorder diagnosis regarding PANSS scores. In most studies, while positive and negative symptom scores were higher in schizophrenic patients with comorbid anxiety disorder, a significant correlation could not be established between positive and negative symptoms and comorbid anxiety disorder (1, 7, 10). In a study conducted in Turkey, positive symptoms were higher in schizophrenic patients with panic symptoms (32).

There are several limitations of this study which are: Being a cross-sectional study, failing to apply the scales for specific anxiety disorders (and therefore providing no determination of detailed characteristics related to them); and, particularly, failing to exclude cases where an antidepressant agent is present.

CONCLUSION

The results obtained from our study indicate that the comorbid anxiety disorder diagnosis is high in schizophrenic patients. In our study, anxiety disorders were higher in schizophrenic patients exposed to maltreatment during childhood and with incidences of school phobia or another phobia. In brief, suicidal attempt, suicidal thought and depressive symptoms markedly increase in patients with anxiety symptoms or comorbid anxiety disorder, and anxiety symptoms cause quality of life deterioration. These results emphasize the importance of determining anxiety symptoms and comorbid anxiety disorders in the clinical prognosis and treatment of schizophrenia and propose new research in treatment approaches for the agenda.

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