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COMPARISON OF PATIENTS WITH AND WITHOUT AGORAPHOBIA PANIC DISORDER AND THE CLINICAL EFFECT OF AGORAPHOBIA ON PANIC DISORDER

AGAROFOBİLİ VE AGAROFOBİSİZ PANİK BOZUKLUĞU HASTALARININ KARŞILAŞTIRILMASI VE AGAROFOBİNİN PANİK BOZUKLUĞU ÜZERİNE KLİNİK ETKİSİ

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Abstract

Panic Disorder (PD) is an anxiety disorder characterized by spontaneous and unexpected panic attacks. Agoraphobia is the fear of being in a place or setting where escaping or receiving help may be difficult in case of a panic attack. Studies on the effect of the relationship between agoraphobia and PD on the disease process have shown that patients with PD accompanied by agoraphobia have earlier disease onset, more severe symptoms, a higher rate of comorbidity and chronicity, and a more negative prognosis in general. The purpose of this study was to compare sociodemographic and clinical characteristic of panic disorder patients with and without agoraphobia. The sample of the study consists of 100 patients who have applied to the psychiatry clinic of the Lutfi Kirdar Kartal Training and Research Hospital and who have been diagnosed with only PD or PD with agoraphobia by clinical interview (SCID-I) based on the DSM-IV. The sociodemographic data form, Clinical Global Impression Scale (CGIS), Global Assessment Scale (GAS), Beck Depression Inventory (BECK-D), Beck Anxiety Inventory (BECK-A), and Panic and Agoraphobia Scale were used for all patients. The incidence of agoraphobia accompanying PD was found to be 44% in our study. The PD with agoraphobia group had significantly worse results compared to the PD without agoraphobia group in terms of CGIS, GAS, and BECK-A scores. Also, the PD with agoraphobia group had a higher mean total PAS score and higher mean agoraphobic avoidance, anticipatory anxiety, disability, and functional avoidance (health concerns) sub-scale scores.

Keywords: panic disorder; agoraphobia, incidence; clinical effect

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Özet

Panik Bozukluğu (PB) kendiliğinden ve beklenmedik panik nöbetleri ile giden bir anksiyete bozukluğudur. Panik ataklarının diğer hastalıklara eşlik etmesinin bu hastalıklardaki tedavi yanıtını olumsuz yönde etkilemekle beraber semptom şiddetini, komorbidite oranlarını ve intihar riskini arttırdığı da gösterilmiştir. Agorafobi, kaçınmanın güç olabileceği ya da panik nöbet halinde yardımın gelemeyebileceği yerler ya da durumlarda bulunmaktan korku duymaktır. Agorafobi ile PB ilişkisinin hastalık sürecine yönelik etkisi üzerine yapılan çalışmalarda Agorafobinin eşlik ettiği PB hastalarında hastalık başlangıç yaşının daha erken, epizodların daha uzun, belirtilerin daha şiddetli, eştanıların ve kronikliğin daha sık olduğu ve genel olarak prognozun daha olumsuz seyrettiği gösterilmiştir. Lütfi Kırdar Kartal Eğitim ve Araştırma Hastanesi psikiyatri polikliniğini ziyaret eden 100 hasta başta sadece PB veya agorafobili PB olarak tanı almıştır. Agorafobili olan PB grubunda KGİ, İGD, BECK-A puanları agorafobi olmadan PB grubundan anlamlı olarak daha olumsuz sonuçlar göstermekteydi. Buna karşılık iki grubun BECK-D puanları ise benzerdi. Ayrıca agorafobili olan grupta ortalama PAÖ toplam puanı ile panik atağı özellikleri, agorafobi/kaçınma davranışı, beklenti anksiyetesi, yeti yitimi ve sağlık konusunda endişe alt başlıkları puan ortalamaları da karşılaştırma grubuna göre daha yüksekti. Bizim çalışmamızda örneklem PB hastalarından oluşmakta olup PB'na eşlik eden Agorafobi sıklığı %44 olarak belirlenmiştir. Bu çalışmada agorafobi ile birlikte olan ve olmayan panik bozukluğu hastalarının sosyodemografik ve klinik özelliklerinin karşılaştırılması amaçlanmıştır.

Anahtar Kelimeler: *panik bozukluk; agarofobi; sıklık; klinik etki*

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1. Introduction

Panic Disorder (PD) is an anxiety disorder characterized by spontaneous and unexpected panic attacks. It was included as a separate diagnosis category in DSM-III (1980) for the first time, and it has been one of the most intensively studied anxiety disorders since then (Cackovic & Adigun, 2018). Among all anxiety disorders, PD causes the highest number of emergency visits, and patients have overall reduced functionality and quality of life (Taylor, 2006). The PD prevalence has been studied around the world based on the DSM-IV criteria, and consistent results have been obtained. Its prevalence in 12 months has been found to be %0,2-1,1 (Demyttenaere et al., 2004). While epidemiological studies from the United States have shown a higher life-time prevalence than the rest of the world, it has been found to have a prevalence of %1,4-2,9 around the world (Weissman et al., 1997). While PD is a disorder characterized by panic attacks, panic attacks may be seen associated with many other psychiatric disorders or general medical conditions other than PD. This has been taken into account in DSM-V, and panic attack has not been coded as a mental disorder; it has instead been included as a marker which is not limited to PD or agoraphobia and could be added to other diagnoses within DSM-V (Craske et al., 2010). It has been shown that panic attacks which accompany other disorders negatively affects treatment response, as well as increasing symptom severity, comorbidity rate and suicide risk (Craske et al., 2010). A recent epidemiological study assessing the relationship between panic attack and PD based on the framework set forth by DSM-V has reported a life-time panic attack prevalence of %13.2 and the same study has shown that about %80 of PD patients have an additional psychiatric disorder (De Jonge et al., 2016). PD is most commonly accompanied by major depression, which has a life-time prevalence of %50-60 (Hirschfeld, 2001; Chen et al.,2010). Additionally, the presence of physiological symptoms which characterize panic attack is also associated with other medical conditions accompanying PD. Cardiovascular disease occur two times more commonly and asthma occurs six times more commonly in PD patients compared to those without an anxiety disorder (Hasler et al., 2005). Also, PD has been found to occur 1.5-2 times more commonly in conditions such as respiratory tract diseases (asthma, chronic obstructive pulmonary disease), heart diseases (hypertension, coronary artery disease), diabetes, and irritable bowel syndrome, which may be associated with PD's symptomatology (Meuret et al., 2017). This shows the bilateral relationship between PD and medical conditions associated with PD.

Agoraphobia is the fear of being in a place or setting where escaping or receiving help may be difficult in case of a panic attack. Whereas it used to be defined as the fear of open spaces; today, the definition of agoraphobia has been expanded to include the fear of being alone, the fear of using public transport, the fear of waiting in a queue, or the fear of being in crowded places. With the arrival of DSM-V, agoraphobia is no longer considered under PD as in PD with and without agoraphobia, but included as a separate diagnosis category (Craske et al., 2010). There is a close and reciprocal relationship between agoraphobia and PD. Agoraphobia may accompany PD at varying rates in the general population and in a clinical sample. In the general population, %33-50 of PD cases are accompanied by agoraphobia, while this rate may be higher in clinical samples (approximately %75) (Tukel, 2002). A prospective longitudinal study targeting an adolescent/young adult sample (representing what is considered to be the high-risk age range for psychopathology development) found a much higher incidence when DSM-IV rules requiring agoraphobia to be diagnosed within the context of panic disorder were not used, compared to when they were (5.3 percent versus 0.6 percent) (Wittchen et al., 2008). Studies on the effect of the relationship between agoraphobia and PD on the disease process have shown that patients with PD accompanied by agoraphobia have earlier disease onset, more severe symptoms, a higher rate of comorbidity and chronicity and a more negative prognosis in general (Warshaw et al., 1994; Keller et al., 1994; Wittchen et al.,2008). In addition, the effect of agoraphobia on oxidative stress in panic disorder has been

studied and it was found that the oxidative stress and damage to the anti-oxidative mechanism are significantly higher in the group with agoraphobia (Gul et al., 2013). According to a study presenting a 3-year follow-up of PD patients, %75 of the PD patients without agoraphobia experienced improvement in panic symptoms, while only %25 of the PD patients with agoraphobia experienced improvement in panic symptoms (Francis et al., 2007). The purpose of this study was to compare sociodemographic and clinical characteristic of PD patients with and without agoraphobia.

2. Materials and Methods

2.1. Participants

The sample of the study consists of 100 patients who have applied to the psychiatry clinic of the Lutfi Kırdar Kartal Training and Research Hospital between January, 2017 and January, 2018, who have been diagnosed with only PD or PD with Agoraphobia by clinical interview (SCID-I) based on the DSM-IV. The ethics committee approval of this study was obtained. The sociodemographic data form, Clinical Global Impression Scale (CGIS), Global Assessment Scale (GAS), Beck Depression Inventory (BECK-D), Beck Anxiety Inventory (BECK-A), and Panic and Agoraphobia Scale were used for all patients. The PD with agoraphobia group (44 patients) and the PD without agoraphobia group (56 patients) were compared in terms of sociodemographic and clinical characteristics. The inclusion criteria were being between the ages of 18 and 65, being diagnosed with PD based on the DSM-IV criteria, being literate and the exclusion criteria were having a severe mental or physical disorder which might obstruct the interview, having alcohol/substance use disorder, having a general medical condition which might cause PD due to its physiological effects, giving verbal and written informed consent regarding participation in a research.

2.2. Data Collection Tools:

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

SCID-I is the structured clinical interview for DSM-IV axis I disorders. It was developed to allow for a standard administration of the diagnostic assessment, thereby increasing the diagnosis validity and reliability, making it easier to evaluate DSM-IV diagnosis criteria, and studying symptoms in a systematic manner (First et al., 1997). SCID-I was adapted to Turkish and tested for reliability by Corapcıoglu et al. (1999).

2.2.2. Global Assessment Scale

The patient's lowest level of social, occupational and mental functionality is determined based on the patient's status in the last week. It is rated from 1 (lowest) to 100 (highest) with 0 representing inadequate information (Endicott et al, 1976).

2.2.3. Clinical Global Impression Scale

It is a scale evaluating in general the severity of any disease or the improvement of disease symptoms. The clinician rates the severity or improvement of the disease between 0 (not ill) and 7 (very severe) depending on his/her own overall experience concerning the disease in question (Guy, 1976).

2.2.4. Beck Depression Inventory (BDI)

BDI is a 21-item scale evaluating the signs and symptoms of depression and scored as the sum of the answers. Each item is rated between 0 and 3; higher scores indicate severer disease. Total score is the sum of the scores and interpreted as following: 0 - 10: no depression, 11 - 17: mild depression, 18 - 23: moderate depression, ≥24: severe depression (Beck et al., 1961; Hisli, 1988, Tegin, 1980).

2.2.5. Beck Anxiety Inventory (BAI)

BAI is a 21-item self-report scale, which is defined as the generalized symptoms of anxiety the subject experienced in the last week. The highest score of BAI is 63 (0 - 7: minimal anxiety, 8 - 15: mild anxiety, 16 - 25: moderate anxiety, 26 - 63: severe anxiety) (Beck et al., 1988; Ulusoy, 1993).

2.2.6. Panic and Agoraphobia Scale

Developed by Bandelow (1998), the scale measures the severity of illness in patients diagnosed with panic disorder (with or without agoraphobia) by considering panic attacks, agoraphobic avoidance, anticipatory anxiety, disability, and functional avoidance (health concerns) (Bandelow, 1995). It is available in both clinician-administered and self-rating formats. It has five sub-scales. Each item is rated from 0 to 4. Thirteen out of fourteen items are included in the calculation. The scale was tested for validity and reliability in Turkish (Tural et al., 2000).

2.3. Statistical Analysis

Statistical analyses were conducted by Statistical Package for Social Sciences (SPSS)-Version 11. Student t test, Mann-Whitney U and Chi square were used for statistical analyses. The cutoff point for statistical significance was $p< 0.05$ and the confidence interval was assumed as 95%.

3. Results

PD was accompanied by agoraphobia in 44 patients (%44) other 56 patients (%56) were diagnosed as PD without agoraphobia. There was no significant difference between the groups in terms of age, sex, marital status, education, place of birth and residence, age of PD onset, and total duration of disease (Table 1)

Table 1: Comparison of Sociodemographic Variables of the Participants

	PD-with agoraphobia (n=44, %44)	PD-without agoraphobia (n=56, %56)	χ2	p
Sex				
Female	29 (65.9)	36 (64.2)	0.029	0.866
Male	15 (34.09)	20 (35.71)	0.811	0.715
Marital status				
Married	33 (75.0)	36 (64.2)	0.869	0.351
Non-married or Single	11 (25)	20 (35.71)	0.318	0.401
Place of birth				
Village	9 (20.4)	17 (30.35)	0.794	0.372
Town	35 (79.54)	39 (69.64)	0.634	0.432
Place of residence				
Village	5 (11.3)	12 (21.4)	1.128	0.288
Town	39 (88.63)	44 (78.57)	1.323	0.543
	Mean (SD)	**Mean (SD)**	**t/u**	**p**
Age	33.5 (10.9)	29.5 (10.5)	1.859 [t]	0.065
Education (years)	6.7 (2.9)	7.7 (3.2)	1.615 [t]	0.109
Age of onset	30.1 (10.7)	28.1 (10.0)	0.962 [t]	0.338
Duration of disease (months)	40 (67.4)	16.3 (23.0)	1.698 [z]	0.058
Number of siblings	5.1 (2.3)	5.2 (2.5)	0.063 [z]	0.950
Number of comorbidities	2.4 (1.3)	2.0 (1.0)	0.546 [z]	0.585

Chi-square test, [t]Student t test, [z]Mann-Whitney U test

When the study sample was compared in terms of CGIS score, the PD with agoraphobia group had a score of 3.9, the PD without agoraphobia had a score of 3.2, PD with agoraphobia group had significantly low scores compared to the PD without agoraphobia group (p<0.001). When the study sample was compared in terms of GAS score, the PD with agoraphobia group had a score of 56.7, the PD without agoraphobia had a score of 62.7, PD with agoraphobia group had significantly low scores compared to the PD without agoraphobia group (p<0.001). When the study sample was compared in terms of BECK-D scores, the PD with agoraphobia group had a score of 20.8, the PD without agoraphobia had a score of 18.1, there was not found any statistically significant difference between the two groups (p=0.162). When the study sample was compared in terms of BECK-A scores the PD with agoraphobia group had a score of 40, the PD without agoraphobia had a score of 29.7, PD with agoraphobia group had significantly low scores compared to the PD without agoraphobia group (p=0.002). When the study sample was compared in terms of PAS total scores the PD with agoraphobia group had a score of 27, the PD without agoraphobia had a score of 17.9 the PD with agoraphobia group had a higher mean total PAS score and higher mean agoraphobic avoidance (p<0.001), anticipatory anxiety (p<0.001), disability (p<0.001) and functional avoidance (health concerns) (p=0.026) sub-scale scores (Table 2).

The PD with agoraphobia group had significantly low scores compared to the PD without agoraphobia group in terms of CGIS, GAS, and BECK-A scores. However, the groups had no significant difference in terms of BECK-D scores. Also, the PD with agoraphobia group had a higher mean total PAS score and higher mean agoraphobic avoidance, anticipatory anxiety, disability, and functional avoidance (health concerns) sub-scale scores (Table 2).

Table 2: Findings obtained from data collection tools

	PD-with agoraphobia (n=44, %44) Mean (SD)	PD-without agoraphobia (n=56, %56) Mean (SD)	t/u	p
CGIS	3.9	3.2	5.798 [z]	<0.001
GAS	56.7	62.7	6,890 [z]	<0.001
BECK-D	20.8	18.1	1.405 [t]	0.162
BECK-A	40	29.7	3.090 [z]	0.002
PAS	27	17.9	13.638 [t]	<0.001
PAS - panic attacks	6.0	5.4	2,241 [z]	0.025
PAS-agoraphobic avoidance	6	0.5	4.419 [z]	<0.001
PAS - anticipatory anxiety	4	3.1	4.497 [z]	<0.001
PAS - disability	5	3.5	6.155 [z]	<0.001
PAS - functional avoidance	5	4.5	2,226 [z]	0.026

[t]Student t test, [z]Mann-Whitney U Test
Clinical Global Impression Scale (CGIS), Global Assessment Scale (GAS), Beck Depression Inventory (BECK-D), Beck Anxiety Inventory (BECK-A), Panic and Agoraphobia Scale (PAS)

4. Discussion

While some studies on the prevalence of agoraphobia determine the general prevalence of agoraphobia due to its close relationship with PD, some other studies focus on the prevalence of agoraphobia without any association with PD (Goodwin et al., 2005). The sample of our study consisted of PD patients and the incidence of agoraphobia accompanying PD was found to be 44%. This rate was higher compared to the epidemiological study where the prevalence rate was found to be 3.7% for PD without agoraphobia, 1.1% for PD with agoraphobia, and 22% for agoraphobia (Kessler et al., 2006). The prevalence of agoraphobia accompanying PB is known to be higher in clinical settings compared to population-based studies, and the prevalence of agoraphobia found in our study was consistent with this phenomenon (Tukel, 2002). This high prevalence in clinical samples compared to the general population seems to be associated with the fact that PD patients with agoraphobia more commonly seek treatment.

While the mean age of PD onset was found to be about 24 in previous studies, the age of disease onset was found to be early 20's for PD with agoraphobia and late 20's for PD without agoraphobia (Borwin Bandelow & Michaelis, 2015). In our study, the age of disease onset was found to be 30.1 in PD patients with agoraphobia and 28.1 in PD patient without agoraphobia. The age of disease onset was found to be slightly higher than previous studies, and the effect of agoraphobia on the age of disease onset was not consistent with previous studies.

A noteworthy common finding of studies on the subject is the 2-4 times higher prevalence of PD among women (Kessler et al., 1994; Eaton et al., 1994; Joyce et al.,1989). It is also reported that PD accompanied by agoraphobia

is more severe (higher difficulty in breathing, sensation of fainting and suffocating) and more likely to have a chronic course in women, and avoidance symptoms associated with agoraphobia are more severe (Yonkers et al., 1998; Turgeon et al., 1998; Sheikh et al., 2002). 65% of the PD patients in our study were female, which supports the higher prevalence among women found in previous studies. However, no significant difference was found between genders in terms of whether or not PD was accompanied by agoraphobia.

The PD with agoraphobia group in our study had significantly worse results in clinical global impression, functionality level, and anxiety scores compared to the PD without agoraphobia group. However, whether or not PD was accompanied by agoraphobia did not lead to a significant difference in depression scores. Our results were similar to previous reports suggesting that the presence of agoraphobia is a predictor of poor prognosis with reduced functionality, increased symptom severity, and chronic course in PD cases (Keller et al., 1994; Warshaw et al., 1994; Weissman et al., 1997; Kikuchi et al.,2005; Carpiniello et al., 2010). While there are studies reporting different results regarding the relationship between depression and whether or not PD is accompanied by agoraphobia, our study seems to support those which suggest that there is not significant relationship between depression and agoraphobia presence (Kikuchi et al., 2005). In a recent study assessing suicide risk in primary care patients suffering from panic disorder, it was demonstrated that suicide ideation was not rare in this patient group (25%), while no relationship could be found between the presence of agoraphobia and suicide risk (Teismann et al., 2018). The present study has certain limitations. The reliability and validity studies of the two scales we used were not performed (Global Assessment Scale, Clinical Global Impression Scale). It is a cross-sectional study based on patients seeking help from pyschiatry clinic. Longitudinal studies are needed to clarify the relationship between panic disorder and agoraphobia with depression and anxiety level. The reciprocal relationship between agoraphobia and PD continues to be relevant today. Changes in diagnosis categories affect the epidemiological studies on these disorders as well, which leads to different results regarding such intertwined clinical pictures. As well as reporting findings regarding the prevalence, coexistence, and clinical manifestation of these conditions, it is expected to be improved with more comprehensive studies based on updated classifications.

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