

First Episode Psychosis: The Relation Between Symptoms, Initial Treatment, and Clinical Response



Eren YILDIZHAN¹, Ahmet TÜRKCAN², Sibel İNAN³, Zehra ERENKUŞ⁴, Özhan YALÇIN⁵,
Ayten ERDOĞAN⁶

SUMMARY

Objective: It was aimed to explore the relationship of clinical psychopathology and treatment response with “duration of untreated psychosis” (DUP) and “duration of untreated illness”(DUI) in 15-20 years old (mean age: $17,34 \pm 1.69$) inpatients in Turkey.

Method: Mood disorders with psychotic features were grouped as affective psychoses (18 patients, mean age: $17,28 \pm 1,75$); schizophrenia, schizophreniform disorder and other psychotic disorders were grouped as non-affective psychoses (25 patients, mean age: $17,38 \pm 1,68$). 43 patients (11 females, 32 males) were evaluated for acute treatment response with Positive and Negative Syndrome Scale – PANSS and Clinical Global Impressions Scale –CGI.

Results: Mean DUP was determined as $6,5 \pm 12,4$ weeks, mean DUI was determined as $37,8 \pm 49,8$ weeks. For the affective psychosis (AP) group; mean DUP was $1,9 \pm 1,2$ weeks, mean DUI was $24,6 \pm 37,1$ weeks, for the non-affective psychosis (NAP) group; mean DUP was $9,8 \pm 15,5$ weeks, mean DUI was $47,3 \pm 55,9$ weeks. Treatment response was better for the non-affective psychosis group and for the patients who had earlier access to treatment. Shorter DUP and DUI was related with better PANSS negative symptom severity at the time of the discharge.

Conclusion: Better treatment response related with shorter DUP and DUI reveals the significance of early treatment for the disease prognosis.

Key words: Psychotic disorders, Age of Onset, Prodromal Symptoms, Psychopharmacology, Adolescent Psychiatry

INTRODUCTION

Since early diagnosis and treatment can have a significant effect on the course of disease in psychotic disorders, this represents a promising field. The prodromal period is when preliminary symptoms of psychotic disorder are seen and when suspicions regarding the possibility of disease begin to develop, even though there is no certainty regarding diagnosis. This period is important in terms of permitting early diagnosis and early treatment of psychotic disorder, providing clues concerning

early identification of recurrences and identifying high-risk individuals. “Duration of untreated psychosis” (DUP), which comprises the period from the first onset of psychotic symptoms to commencement of appropriate antipsychotic drug therapy, is thought to be a factor in the clinical course of the disease and in response to treatment (Wyatt 1995, Ho et al. 2000, Black et al. 2001, Moller 2001). “Duration of untreated illness” (DUI) is defined as the sum of the prodromal period and DUP. It has been suggested that DUI can predict

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¹Psychiatrist, Trabzon Ataköy Mental Hospital, Psychiatry, Trabzon, ²Psychiatrist, Bakırköy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Forensic Psychiatry, İstanbul, ³Psychiatrist, Gaziantep Şehit Kamil State Hospital, Psychiatry, Gaziantep, ⁴Bahçeşehir University, Statistics, İstanbul, ⁵Psychiatrist, Bakırköy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Child and Adolescent Psychiatry, İstanbul, ⁶Prof., in Child and Adolescent Psychiatry, Bakırköy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, İstanbul and Düzce University Medical Faculty, Düzce, Turkey.

e-mail: erenyildizhan@hotmail.com

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the course of disease and response to treatment better than other factors (Malla et al. 2006).

Chronological age, racial differences, sex, marital status, socioeconomic status, level of education, age at onset of disease, level of functioning before the disease, pattern of onset of disease, diagnosis, continuity of antipsychotic therapy, family history of psychiatric disease, and insight are all potential factors that can confuse the relation between DUP and prognosis (Perkins et al. 2005, Baldessarini et al. 2013, Capdevielle et al. 2013).

In current diagnostic systems, some psychotic syndromes that cannot be associated with substance use or any organic cause are classified within the diagnostic group including schizophrenia and similar psychotic disorders; others are classified as affective disorders, including depression with psychotic features, bipolar disorder with psychotic features, and mood disorders not otherwise specified. The distinction between the group classified with a diagnosis of mood disorder (considered affective psychoses) and the other group (considered non-affective psychoses) is basically at the phenomenological level. However, this Kraepelinian dichotomy is also seen in variations in clinical course (Van Os et al. 2003). Studies investigating clinical course have reported higher recurrence rates and full remission rates in cases with affective psychosis than in cases with non-affective psychosis, and there are also differences between these two groups in terms of prodromal period (Ivleva et al. 2009).

While the presence of prodrome in affective psychoses is controversial, it has been suggested that mood lability, hyper-reactivity, destructive behavior, and increased psychomotor activity during the course are prodromal period characteristics (Ivleva et al. 2009). Increased energy and an increase in goal-directed activity emerge as characteristics of psychotic mania prodrome, and mild psychotic symptoms are expected at the end of this prodromal period. Depressive mood, suicidal ideation, mood swings, difficulty in concentration, disruption in relationships, fatigue and energy loss, obsessions and compulsions, and physical agitation are thought to be symptoms specific to mania prodrome, rather than schizophrenia (Correll et al. 2007).

There are overlaps between schizophrenia and the prodromes of affective psychoses; symptoms such as scepticism, suspiciousness, experiences including hallucination, ambivalence, insomnia, and a decrease in academic or occupational functioning may be seen in both affective psychosis prodrome and in schizophrenia prodrome (Ivleva et al. 2009).

When conditions defined as prodromal symptoms of schizophrenia and premorbid characteristics result in psychosis, final diagnosis may be psychotic disorders other than schizophrenia. Therefore, these features are not unique to schizophrenia. In a 1-year follow-up study, Yung et al. (2003) observed that

psychosis developed in 40.8% of a group described as high-risk. Since patients' diagnoses included schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, and major depression with psychotic features, they stated that prodromal symptoms predicted progression to psychosis but did not predict what type of psychotic disorder might develop. These findings explain why several studies of first episode psychosis have not been limited to schizophrenia but have been designed to include other psychotic disorders.

Examination of studies including both affective and non-affective psychoses reveals a focus on the relation between clinical characteristics of psychotic disorder at time of first presentation for treatment and DUP. Studies have reported a correlation between long DUP and negative symptoms at first presentation (Perkins et al. 2005). General psychopathology at initial presentation, positive symptoms, and level of functioning have generally been found to be not correlated with DUP (McGorry et al. 1996, Verdoux et al. 1998, Perkins et al. 2005). The majority of studies show that short DUP is associated with better response to antipsychotic therapy. Also considering studies including affective psychotic disorders, short DUP has been found to be correlated with an improvement in global psychopathology and a positive response to treatment (McGorry et al. 1996, Verdoux et al. 1998). Some studies including both affective and non-affective psychotic disorders have determined no correlation between DUP and response to treatment (Norman et al. 2001).

Despite the recent studies of the clinical effect of DUP in first episode non-affective psychotic disorders in Turkey performed by Üçok et al. (2004, 2006, 2011), there are no qualitative, prospective studies concerning the clinical course of first episode psychosis while also including affective psychotic disorders other than schizophrenia in hospitalized young adult patients. Since chronological age is a factor that affects treatment response and disease prognosis, studies involving adolescents can provide valuable information (Bottlender et al. 2000, Craig et al. 2000, Drake et al. 2000, Bottlender et al. 2003, Addington et al. 2004, Levine and Rabinowitz 2010). The main purposes of this study were to assess first prodromal and first psychotic symptoms in patients hospitalized for treatment under the category of first episode psychotic disorder; to determine DUP and DUI; and to analyze the relation between DUP, DUI, clinical presentation and response to treatment.

METHOD

Sampling and Design

Patients hospitalized for treatment due to first episode psychosis at the Adolescents and Young Adult Psychiatry Clinic

in Bakırköy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Istanbul, Turkey, over a 1-year period (01.03.2011-01.03.2012) were evaluated. Inclusion criteria were being in first psychotic episode, literacy, having given informed consent, and age no greater than 20 years old.

The definition of first episode psychosis comprises patients with at least one psychotic symptom, no psychotic disorder associated with general medical condition, and never having entered remission since onset of psychotic episode (Loebel et al. 1992, Verdoux et al. 1998). The requirement that patients should not have received sufficient treatment was imposed for inclusion. Sufficient treatment was defined as use of 6 mg/day haloperidol or equivalent antipsychotic drug for 6 weeks or more (Woods 2003). Patients meeting criteria for substance abuse or substance dependence or who were compatible with a diagnosis of psychotic disorder caused by substance use according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), (American Psychiatry Association, 1994) and patients with severe congenital cognitive disability that prevents psychiatric interview were excluded. Nicotine use disorders were not defined as exclusion criteria.

Bakırköy Training and Research Hospital ethical committee approval was granted for the study.

Before enrollment, the patient and family were informed about the study, and 'informed consent forms' were signed. One patient who did not give informed consent and four patients discharged at the request of their families before the end of the normal therapeutic duration were not included in the study.

MATERIALS

Sociodemographic Data Form: Initial symptoms of disease, duration of these symptoms and calculated DUI and DUP were recorded on a sociodemographic data form.

The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I): This advanced diagnostic scale is based on DSM diagnostic criteria adapted for DSM-IV (First et al. 1999). It is evaluated by the interviewer and contains seven diagnostic groups. The Turkish version has been validated (Çorapçıoğlu et al. 1999). In this study, the scale was employed to determine DSM-IV diagnoses of patients over 18 years old.

Positive and Negative Syndrome Scale (PANSS): This Likert-type scale is evaluated by the interviewer. It measures positive and negative psychopathology in schizophrenia and general psychopathology. It consists of 30 items: 7 for positive symptoms, 7 for negative symptoms and 16 for general symptoms. It was developed by Kay et al. (1987) and the Turkish-language

version of the form has been validated (Kostakoğlu et al. 1999). Although this scale was developed for schizophrenia, it has also been administered to patients diagnosed with bipolar disorder with psychotic features and major depression with psychotic features in studies of first episode psychosis (Verdoux et al. 1998, Perkins et al. 2005).

Clinical Global Impressions (CGI): Developed by Guy et al. (1976) for the purpose of assessing the clinical course of psychiatric diseases, this three-dimensional scale can be applied to patients of all ages (Forkmann et al. 2011). The first section (Clinical Global Impressions – Disease Severity) assesses disease severity at time of completion on a scale of 1 to 7: 1=Normal, not at all ill; 2= Borderline mentally ill; 3= Mildly ill; 4= Moderately ill; 5= Markedly ill; 6= Severely ill; 7= Extremely ill. The second part (Clinical Global Impression – Improvement) serves to assess how much the patient has changed relative to baseline on a scale of 1 to 7: 1= Very much improved; 2= Much improved; 3= Minimally improved; 4= No change; 5= Minimally worse; 6= Much worse; 7= Very much worse. In this study, the severity section was applied based on the first interview at treatment onset upon hospitalization and the improvement section was applied at discharge. Patients in the affective psychosis group and the other patients were compared in terms of severity of disease at first presentation and level of improvement at discharge. The third part of the scale is the Clinical Global Impression – Side Effects section calculated on a scale of 4. This part was not used in this study.

Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version-Turkish Version (K SADS-PL-T): Turkish validation for this scale was performed in 2004. K-SADS-PL-T is a structured interview chart used to assist diagnostic assessment and applied to patients aged under 18 years old (Ambrosini et al. 2000, Gökler et al. 2004). In our study it was used to determine DSM-IV symptoms in patients under 18 years old.

Application

Patients were interviewed twice: once at initial hospitalization and once at discharge. All interviews and scales were administered by the same individual (first author, Eren Yıldızhan), as soon as possible after hospitalization and at discharge, in two sessions lasting approximately half an hour. Onset of first prodromal symptoms and first psychotic symptoms were determined at interview with patients and family as described by Loebel et al. (1992). Patients and their families were asked when they first became aware of behavioral changes. A list of symptoms on a form developed by Perkins et al. (2000, 2004) for the purpose of recording the onset of psychotic syndrome was employed for determining which initial symptoms were present. In deciding which symptoms should be coded,

a Turkish translation of the form, produced by us, was employed. In certain cases when it was not possible to determine which of two symptoms appeared first, both were recorded among the initial symptoms. DUP was taken as the period between onset of first psychotic symptoms to the beginning of treatment, and DUI as onset of first prodromal symptoms indicating a deviation from normal to the beginning of treatment (Loebel et al. 1992). Short/long DUP and short/long DUI values were determined by dividing DUP and DUI along their respective median points.

Statistical analysis

Findings were analyzed on "SPSS 16.0 for Windows" software. The Mann-Whitney U test was used to compare non-parametric quantitative data and the Wilcoxon signed-rank test to analyze repeated data. The chi square was used to compare qualitative data, with Fisher's exact test where appropriate, and Spearman correlation analysis was used to analyze relations between scale scores and duration of disease. Significance was set at $p < 0.05$.

RESULTS

Sociodemographic characteristics

Forty-three patients with a mean age of 17.34 ± 1.69 (minimum: 14 years old, maximum: 19 years old) were identified as meeting the study criteria. Eleven (25.6%) subjects were female and 32 (74.4%) male.

Diagnostic Distribution

For descriptive diagnostic purposes, patients were grouped into affective psychosis and non-affective psychosis groups. Bipolar disorder, manic episode, major depression with psychotic features, and other psychotic mood disorders not

otherwise classified were grouped in the affective psychosis group. Schizophrenia, schizophreniform disorder, psychotic disorder not otherwise classified, and brief psychotic disorder were grouped in the non-affective psychosis group (Table 1).

We established that 18.6% of patients had previously used antipsychotic medication and that 14% were still using them. Dose and length of use were not at a sufficient level to merit sufficient treatment in any case.

Analysis of the Scales

The affective and non-affective psychosis groups were compared both before and after treatment in terms of Clinical Global Impression scale and PANSS positive, negative, general psychopathology and total scores.

When patients with affective and non-affective psychosis were compared in terms of Global Impression Scale, no significant difference was observed in terms of severity of disease at time of presentation or level of improvement measured at discharge.

Post-treatment PANSS positive subscale scores in the affective psychosis group were significantly lower than those in the non-affective psychosis group (mean score for all patients 20.0 ± 9.1 , mean score in the affective psychosis group 15.0 ± 7.6 , and mean score in the non-affective group 23.7 ± 8.5 , $z = -3.09$, $p = 0.002$). Post-treatment PANSS negative subscale scores in the affective psychosis group were also significantly lower than those in the non-affective psychosis group ($z = -2.84$, $p = 0.004$) (mean for all patients was 15.4 ± 7.1 , mean score in the affective psychosis group was 12.0 ± 5.5 and mean score in the non-affective group was 17.9 ± 7.1) (Table 2).

Pre- and post-treatment PANSS subscale scores were analyzed for all patients and for the affective and non-affective psychosis groups separately. A significant decrease in post-treatment PANSS general scores was determined in all patients ($z = -5.71$, $p = 0.000$), in the affective psychosis group ($z = -3.72$, $p = 0.000$), and in the non-affective psychosis group ($z = -4.37$, $p = 0.000$). Similar analysis of PANSS positive scores revealed a significant decrease for all patients at the end of treatment ($z = -3.59$, $p = 0.000$). A significant decrease was observed in PANSS positive scores in the affective psychosis group ($z = -3.10$, $p = 0.000$), but no significant difference was determined at the end of treatment in the non-affective psychosis group ($z = -1.61$, $p = 0.106$). A significant decrease was observed post-treatment in PANSS negative scale scores in all patients ($z = -5.24$, $p = 0.000$), in the affective psychosis group ($z = -3.59$, $p = 0.000$), and in the non-affective psychosis group ($z = -3.73$, $p = 0.000$). Mean PANSS scores are shown in Table 2. Due to the small sample size, we did not investigate whether there was any difference between the groups in terms of decreases in PANSS scores.

Table 1. Distribution of DSM-IV-TR diagnoses

Diagnosis	n (11 female, 32 male)	%
Affective psychosis		
Bipolar disorder manic episode, psychotic	9 (3 female, 6 male)	20.9
Major depressive disorder, psychotic	8 (2 female, 6 male)	18.6
Mood disorder, nos	1 (0 female, 1 male)	2.3
Non-affective psychosis		
Schizophreniform disorder	17 (6 female, 11 male)	39.5
Psychotic disorder, nos	5 (0 female, 5 male)	11.6
Schizophrenia	2 (0 female, 2 male)	4.7
Brief psychotic disorder	1 (0 female, 1 male)	2.3

(nos: not otherwise specified)

Table 2. PANSS measurements at presentation and after treatment

	All patients	Affective Psychosis	Non- Affective Psychosis	Mann Whitney U	
	Mean $\pm$ s.d.	Mean $\pm$ s.d.	Mean $\pm$ s.d.	z	p
PANSS Scale Scores					
PANSS General-Pre-Treatment	40.5 $\pm$ 8.6	42.7 $\pm$ 9.5	38.9 $\pm$ 8.3	-1.31	0.187
PANSS Positive-Pre-Treatment	25.8 $\pm$ 7.5	25.1 $\pm$ 8.9	26.3 $\pm$ 6.5	-1.24	0.213
PANSS Negative-Pre-Treatment	28.5 $\pm$ 5.6	29.2 $\pm$ 6	28 $\pm$ 5.6	-0.98	0.323
PANSS General-Post-Treatment	12.6 $\pm$ 4.0	11.6 $\pm$ 3.7	13.4 $\pm$ 4.3	-1.30	0.190
PANSS Positive-Post-Treatment	20.0 $\pm$ 9.1	15.0 $\pm$ 7.6	23.7 $\pm$ 8.5	-3.09	0.002*
PANSS Negative-Post-Treatment	15.4 $\pm$ 7.1	12 $\pm$ 5.8	17.9 $\pm$ 7.1	-2.84	0.004*
PANSS General Pre/Post (Wilcoxon Signed Ranks Test)	z= -5.71 p= 0.00+	z= -3.72 p= 0.00+	z= -4.37 p= 0.00+		
PANSS Positive Pre/Post (Wilcoxon Signed Ranks Test)	z= -3.54 p= 0.00+	z= -3.10 p= 0.00+	z= -1.61 p= 0.10+		
PANSS Negative Pre/Post (Wilcoxon Signed Ranks Test)	z= -5.24 p= 0.00+	z= -3.59 p= 0.00+	z= -3.73 p= 0.00+		

* p<0.05 Mann Whitney U test

+ p<0.05 Wilcoxon signed ranks test

PANSS: Positive and Negative Syndrome Scale

Daily doses of antipsychotics during hospitalization were compared by converting these into haloperidol-equivalent doses. Mean daily haloperidol-equivalent dose used by patients was 17.3 ± 8.5 mg. No significant difference was determined in terms of antipsychotic doses between affective psychosis and non-affective psychosis groups (18.7 ± 8.9 mg; 16.2 ± 8.2 mg) ($z=-1.13$, $p=0.258$).

First Symptoms

All symptoms on the list of symptoms described by Perkins et al. (2000) were inquired during the investigation of first symptoms. These are defined as dysphoric mood, sleep disturbance, ideas of reference, suspiciousness, thought disorder, perceptual abnormalities, deterioration in functioning, social withdrawal, avolition, decreased expression of emotion, decreased experience of emotion, hallucinations, delusions, disorganized thought process, disorganized behavior, and other symptoms. When all the patients were assessed together, the most common first symptom was dysphoric mood (37.2%). This was followed by ideas of reference (23.2%) and social withdrawal (23.2%). In the affective psychosis group, the most common first symptom was again dysphoric mood (45%), followed by sleep disturbance (25%) and ideas of reference (20%). In the non-affective psychosis group, the most common first symptom was social withdrawal (34.7%), followed by dysphoric mood (30.4%) and ideas of reference (26%).

Analysis of the study sample for DUP and DUI

Mean DUI in the study sample was 37.8 ± 49.8 weeks and mean DUP 6.5 ± 2.4 weeks. Mean DUI in the affective psychosis group was 24.67 ± 37.1 weeks, compared to 47.32 ± 55.9 weeks in the non-affective psychosis group. DUI was significantly shorter in the affective psychosis group ($p=0.018$, $z=-2.37$). Mean DUP in the affective psychosis group was 1.9 ± 1.2 weeks, and 9.8 ± 15.5 weeks in the non-affective psychosis group. DUP was also shorter in the affective psychosis group ($p=0.013$, $z=-2.48$), (Table 3). No significant relation was determined between DUP and DUI and length of hospitalization.

Short and long DUP and DUI were determined on the basis of median values. A median value of 20 weeks was calculated for DUI. $DUI \leq 20$ weeks was defined as "short DUI" and $DUI > 20$ weeks as "long DUI." Median value for DUP was calculated as 2 weeks, and $DUP \leq 2$ weeks was defined as "short DUP" and $DUP > 2$ weeks as "long DUP." Fifteen of the patients with affective psychosis were in the short DUP and 13 were in the long group, while 13 patients were in the short DUI group and 5 were in the long DUI group. Ten of the patients with non-affective psychosis were in the short DUP group and 15 were in the long DUP group, while 9 were in the short DUI group and 16 were in the long DUI group.

Table 3. Relation between DUP, DUI and being affective psychosis

	All Patients	Affective Psychosis	Non-Affective Psychosis	Mann Whitney U	
	Mean $\pm$ s.d.	Mean $\pm$ s.d.	Mean $\pm$ s.d.	z	p
DUI	37.84 $\pm$ 49.82	24.67 $\pm$ 37.31	47.32 $\pm$ 55.99	-2.37	0.018*
DUP	6.56 $\pm$ 12.42	1.94 $\pm$ 1.22	9.88 $\pm$ 15.54	-2.48	0.013*

* p<0.05 Mann Whitney U test

Table 4. Relation between PANSS measurements and DUI

	SHORT DUI ($\leq$ 8 weeks)	LONG DUI ($>$ 8 weeks)	Mann Whitney U	
	Mean $\pm$ s.d.	Mean $\pm$ s.d.	Z	p
PANSS Scale Values				
PANSS General-Pre-Treatment	41.7 $\pm$ 10.3	40.0 $\pm$ 8.4	-0.58	0.560
PANSS Positive-Pre-Treatment	22.7 $\pm$ 4.2	27.0 $\pm$ 8.2	-1.45	0.147
PANSS Negative-Pre-Treatment	26.1 $\pm$ 5.3	29.4 $\pm$ 5.7	-1.65	0.097
PANSS General-Post-Treatment	11.2 $\pm$ 4.2	13.2 $\pm$ 4.1	-1.46	0.142
PANSS Positive-Post-Treatment	16.0 $\pm$ 7.7	21.6 $\pm$ 9.3	-1.80	0.071
PANSS Negative-Post-Treatment	11.5 $\pm$ 5.0	16.9 $\pm$ 7.3	-2.49	0.013*

* p<0.05 Mann Whitney U test

PANSS: Positive and Negative Syndrome Scale

Table 5. Relation between PANSS measurements and DUP

	SHORT DUP ($\leq$ 2 weeks)	LONG DUP ($>$ 2 weeks)	Mann Whitney U	
	Mean $\pm$ s.d.	Mean $\pm$ s.d.	z	P
PANSS Scale Values				
PANSS General-Pre-Treatment	40.0 $\pm$ 9.8	41.1 $\pm$ 7.9	-0.55	0.582
PANSS Positive-Pre-Treatment	24.6 $\pm$ 7.4	27.3 $\pm$ 7.6	-1.44	0.148
PANSS Negative-Pre-Treatment	29.0 $\pm$ 6.5	27.9 $\pm$ 4.8	-0.39	0.695
PANSS General-Post-Treatment	12.1 $\pm$ 4	13.3 $\pm$ 4.4	-0.85	0.390
PANSS Positive-Post-Treatment	17.3 $\pm$ 7.6	23.5 $\pm$ 9.9	-1.92	0.054
PANSS Negative-Post-Treatment	13.2 $\pm$ 5.5	18.2 $\pm$ 8.1	-2.31	0.021*

* p<0.05 Mann Whitney U test

PANSS: Positive and Negative Syndrome

Length of hospitalization was greater in the affective psychosis group (29.61 $\pm$ 9.66) than in the non-affective group (24.4 $\pm$ 7.94) ($z=-1.97$, $p=0.048$). When patients with affective psychosis were divided into long and short DUP subgroups, no significant difference was determined between the two in terms of length of hospitalization.

Relation between DUI and psychopathology

The association between PANSS measurements at time of hospitalization and at discharge and the length of DUI was investigated. No significant difference was determined in terms of PANSS scores between the short and long DUI groups ($p>0.05$). When 8 weeks (instead of 20 weeks) was used as a cut-off point to divide long and short DUI groups, PANSS negative symptom scores were significantly lower in patients with DUI of less than 8 weeks ($z=-2.49$; $p=0.013$) (Table 4)

Relation between DUP and psychopathology

PANSS negative symptom scores at discharge were significantly lower in patients with DUP less than 2 weeks ($z=-2.31$, $p=0.021$) (Table 5).

DISCUSSION

Determination of first symptoms, DUP, DUI

The most common first symptom in the affective psychosis group was dysphoric mood, while social withdrawal was most common in the non-affective psychosis group. These findings are in line with the study of first episode psychosis done by Perkins et al. (1999), in which they determined dysphoric mood and social withdrawal as the most common first symptoms.

Mean DUP for the patients evaluated was 6.5 weeks and mean DUI was 37.8 weeks. In terms of previous studies examining patients presenting on an out-patient basis, there are studies reporting mean DUP of 29 months and mean DUI of 46.4 months. These values are considerably higher than those in our study. The fact that our study involved patients requiring hospitalization for treatment may be one probable reason for the difference between the durations determined in our and other studies. Üçok et al. (2003, 2005) determined short DUP of 8.6 months in their studies of patients hospitalized for treatment in Turkey. The fact that our study was performed with adolescents may also represent a factor

shortening DUP and DUI. One of the powerful aspects of our study is that it involved individuals in middle and late adolescence. The finding that mean DUP and DUI levels in the affective psychosis group are significantly shorter compared to the non-affective psychosis group is compatible with research by McGorry et al. (1996) reporting a shorter prodrome in non-schizophrenia psychotic disorders.

Relation between DUP and DUI and psychopathology

No difference was determined in terms of pre-treatment symptoms at PANSS analysis between affective psychosis group and non-affective psychosis group. However, examination of the PANSS subscales revealed a milder severity of symptoms post-treatment in the affective psychosis group. Previous literature also shows that affective psychosis patients have better response to treatment (Peralta and Cuesta 2007). The lack of any significant decrease in PANSS positive scores in the non-affective psychosis group suggests that positive symptoms resist treatment in this group.

According to Perkins et al. (2005), the use of median value in the dichotomization of DUP and DUI is superior to dichotomization based on mean, because when division is performed on the basis of means, patients at the extremes have a much greater effect on data. Extreme group analysis is the technique that reduces loss of data in this area to a minimum (Ho et al. 2000). In this technique, the sample is divided into more than one group and analysis is performed between the two groups at the extremes. This was not employed in this study due to the insufficient sample size.

Since there is as yet no consensus on the point at which DUP or DUI can be regarded as “long,” points other than the median can also be used in dichotomization (Perkins et al. 2005). While investigating the relation between DUI and PANSS, in addition to division from the median point, we also defined long and short DUI on the basis of the 8-week cutoff point and added this to the analysis. While no difference was determined between DUI and negative symptom scores on PANSS at a cutoff point of 20 weeks, we determined that DUI of more than 8 weeks was associated with higher negative symptoms at discharge. This suggests that improvement in negative symptoms was more pronounced in a specific patient group that started treatment very early. Analysis of negative symptom scores on PANSS and DUP revealed no significant difference between patients with long or short DUP in terms of severity of negative symptoms at initial presentation. However, severity of negative symptoms at discharge was lower in the short DUP group. In line with our results, meta-analysis by Perkins et al. (2005), who showed a significant correlation between DUP and negative symptoms measured at initial presentation, reported a greater improvement in negative symptoms with treatment in patients with

short DUP. Studies by Addington (2004) (mean DUP =13.9 years) and Scully (1997) (mean DUP =17.1 years), who demonstrated that long DUP was associated with severe negative symptoms and cognitive dysfunction, differ from ours in that their DUP were extremely long. There is a possibility that differences between mean DUP in samples may affect results (Barnes 2000). There are studies from Turkey reporting no association between DUP and improvement in negative symptoms in patients hospitalized for initial episode psychosis, but the DUP in those studies were, again, longer than ours (Üçok 2003).

McGorry et al. (1996) showed, in a sample consisting of both affective and non-affective psychotic disorders (21.5% affective psychosis), a slower improvement in psychotic symptoms in patients with DUP of more than 4 weeks compared to other patients, and also reported a greater severity of symptoms in these patients post-treatment. When all patients in our study were evaluated together, short DUP and DUI were correlated with a post-treatment improvement in negative symptoms. Due to the small sample size, however, affective and non-affective psychosis groups could not be analyzed separately on the basis of division into long and short DUP and DUI groups.

Differences between the groups evaluated in this study determined with PANSS were not pronounced in the CGI scale. The reason for this may be the fact that PANSS reflects clinical appearance in a more detailed manner.

Although differences were determined between daily doses of haloperidol-equivalent antipsychotic treatment (minimum 5 mg, maximum 40 mg), no significant difference was determined in terms of antipsychotic dose between the affective and non-affective psychosis groups. Mean antipsychotic doses were 17.3 ± 8.5 mg, higher than those in the study by Üçok et al. (2003) involving first episode patients hospitalized for treatment in Turkey. Our study sample largely consisted of patients with a severe onset of disease and requiring relatively swift hospitalization for treatment, and this may explain the differences in antipsychotic doses.

The difference in length of hospitalization in the affective and non-affective psychosis groups was analyzed by dividing DUP and DUI into long and short periods, but no significant difference was determined. Since mean length of hospitalization in our study was 26.5 days (minimum 15 days, maximum 54 days), it may be classified as a study measuring acute treatment response (Üçok 2003, Levine and Rabinowitz 2010, Szymanski et al. 1996, Malla et al. 2002, Harrigan et al. 2003, Addington et al. 2004). When we compared two groups established solely on the basis of compatibility or incompatibility with a diagnosis of affective psychosis, independent of DUP and DUI, mean length of hospitalization was higher in

the affective psychosis group (mean 29.6 days compared to 24.4 days). This difference may derive from the antidepressants and mood stabilizers used in the treatment of patients with affective psychosis demonstrating their effects later than antipsychotics.

Limitations

Diagnostic groups could not be compared independently due to the small sample size. Since our study evaluated treatment response after a mean 4 weeks of hospitalization for treatment, it only provides data for rapid response to treatment, but none concerning long-term response. The small sample size did not permit the possibility of excluding various confounders such as gender, previous psychiatric history, and family psychiatric history.

Conclusions and recommendations

Studies examining other factors affecting the association between DUI/DUP and prognosis which are capable of providing data concerning longer follow-up and long-term prognosis are now needed. Studies involving larger samples and evaluating the effects of DUP, DUI and prognosis will assist in determination of type and intensity of psychosocial and biological treatments, especially in prodromal cases. Studies investigating findings exhibited by patients during DUP may assist clinicians in predicting the type of disorder that develops subsequently. Long DUP and DUI being associated with high severity of post-treatment negative symptoms highlights the importance of early intervention. Negative symptoms are the symptoms most resistant to treatment in psychotic disorders, but it may be possible to intervene in this area with early diagnosis. It may be possible to achieve more definitive data regarding the course of psychotic disease with the exclusion of various confounders in epidemiological studies involving larger samples. Comparative studies of high risk cases with or without treatment will contribute to the determination of the clinical significance of DUI and its effect on prognosis.

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