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ORIGINAL ARTICLE

Influence of duration of untreated psychosis on the short-term outcome of drug-free schizophrenia patients

MARIYAMMA PHILIP, BN GANGADHAR, JAGADISHA, LATHA VELAYUDHAN, D.K. SUBBAKRISHNA

ABSTRACT

Western studies in the recent past have suggested that reducing the duration of untreated psychosis (DUP) is associated with better control of symptoms of schizophrenia. The present investigation attempts to assess the influence of duration of untreated psychosis and other predictors on the outcome of schizophrenia, six weeks after the treatment. Data of 45 DSM-IV schizophrenia patients (Mean age 31 ± 9.2; 27 males) who were treated for the first time formed the sample. Based on the clinical notes in files two psychiatrists independently rated the outcome at 6-8 weeks of neuroleptic treatment. The inter rater agreement was good. Improved and unimproved groups did not differ on any variables except the duration of untreated psychosis. Duration of untreated psychosis was longer in the unimproved group. In a logistic regression model, only duration of untreated psychosis emerged as a significant predictor (OR= 0.9854, with 95% CI= 0.9717 – 0.9993; p=0.039). DUP affects acute outcome in schizophrenia.

Key words: Acute outcome, DUP, Logistic Regression, Predictors, Psychosis, Schizophrenia.

INTRODUCTION

Studies, all from the West, in the recent past have suggested that reduction of duration of untreated psychosis (DUP) is associated with better control of symptoms/ outcome of Schizophrenia. Many authors have argued that reducing the time between onset of psychosis and institution of treatment may result in substantially improved outcomes for schizophrenia and related disorder (McGlashan & Johannessen, 1996; McGorry et al, 1996). It has also been suggested that psychosis itself may have toxic effects on brain (Grace, 1991; Wyatt, 1991).

Most of the retrospective studies found the outcome to be correlated with shorter duration of psychosis before first treatment. Fenton & McGlashan (1987) described a subgroup of 23 patients who, after a period of inpatient treatment sustained good outcome without maintenance medication for an average of 15 years. Compared to the rest of the sample (n=140), these patients had shorter period of untreated psychosis. Lo & Lo (1977) in a ten year retrospective follow-up of 133 patients in China found the outcome to be correlated with shorter duration of untreated psychosis.

In a prospective study, Loebel et al (1992) found that DUP predicted time to remission and also the level of remission in a group of predominantly drug naïve schizophrenic and schizoaffective patients. The influence of DUP on time to remission was independent of gender and diagnosis. Similar results were reported by Robinson et al (1999). Szymanski et al (1996) in their follow-up data on 36 patients with drug naïve schizophrenia reported that longer DUP was associated with less change in positive symptoms. This was independent of age, gender, or baseline severity of symptoms.

However, some studies have found no relationship between DUP and outcome. Craig et al (2000) followed up patients with psychosis of various diagnostic groups for 24 months after first admission; patients were split into three groups on the basis of length of DUP in each diagnostic group. In no case, was DUP significantly related to the likelihood of attaining a remission. Ho et al (20001) in their six-month follow up report of 74 drug naïve first episode schizophrenics found no significant relationship between DUP and *post hoc* estimates of time to remission or level of symptoms. After reviewing the indirect and direct evidences of relationship between DUP and outcome Norman & Malla (2001) conclude that there is evidence suggesting a relationship between DUP and initial response to treatment, although robustness of such findings is yet to be established. Though there is no definitive evidence as to whether reduction of DUP will alter the course of schizophrenia for better, this issue has considerable public health importance.

While studying the influence of DUP on the outcome, one needs to consider other predictors of outcome of Schizophrenia also. A number of socio-demographic, clinical, pre-morbid and biological factors have also predicted the outcome. Male gender, low socioeconomic status, family history of schizophrenia, low IQ, longer duration of past psychosis etc., were predictors of poor outcome across a number of follow-up studies (McGlashan, 1986). However, despite the knowledge of such factors, the prediction of outcome in schizophrenia has remained a challenging task and is generally poor. One of the well established facts and consistent finding about outcome of schizophrenia is that patients from developing countries including India, have better outcomes than those from the developed countries (Lieberman, 1996; Lipton & Cancro, 1995). Given the low psychiatrist-to-population ratio and difficulties in reaching a psychiatrist, it is unlikely that patients from developing countries have shorter DUP than those

from the developed countries. .There is a need to study the influence of DUP on outcome of schizophrenia in the Indian context, hence this study.

MATERIALS & METHODS

Forty-five never-treated schizophrenia patients, fulfilling DSM-IV criteria (APA, 1994), who were treated under one unit, formed the sample. Apart from demographic details their Positive and Negative Syndrome Scale (PANSS) scores were available before treatment. Mean age of the patients was 31 (±9.2) years. 60 % of the subjects were males and socioeconomic status of half of the subjects was medium. All were literate, had minimum of seven years schooling and hence presumably had normal IQ. Over half (53%) of the subjects were unmarried. Family history of psychosis assessed clinically was present in one- third of the subjects (35.6%). The mean duration of psychosis was four years and the mean age at onset 27(±8.1) years. Mean PANSS score of the subjects was 87(±18.7).

The response to treatment was assessed on the basis of information available in the charts approximately at six weeks after the commencement of therapy, by two psychiatrists separately. The raters were blind to all clinical details except the progress notes documented between 6-8 weeks. The outcome was assessed on a five-point scale, based on the progress notes entered in the file. Inter-rater reliability was established and Kappa was 0.611(p = .001). The above outcome variable was converted into dichotomous, unimproved (no improvement; mild improvement) and improved (moderate improvement; remission; recovery), and the inter-rater reliability statistic Kappa was better (0.692, p = .001). For subsequent analyses this was the classifying variable. Data was analyzed with Chi-square test, t-test and Logistic regression and all the statistical analyses were carried out in SPSS (Version 11.0). The level of significance was fixed at 0.05.

TABLE I : Comparison between improved and unimproved groups

Variables	Unimproved No.	%	Improved No.	%	c^2	p
Sex						
Male	6	54.5	18	63.6		
Female	5	45.5	10.	36.4	.317	.574
SES						
Low	6	54.5	12	42.9		
Middle	5	45.5	15	536	.728	.695
High			1	3.6		
Marital Status						
Never Married	4	36.4	16.	57.1	1.365	.243
Ever Married	7	63.6	12	42.9	1.365	.243
Family History for Schizophrenia						
Absent	6	54.5	19	67.9		
Present	5	45.5	9	32.1	.608	.435

RESULTS

Demographic variables were compared between the two outcome groups - unimproved & improved (Tables I and II). The two groups were comparable on all variables except one. Duration of Untreated Psychosis (DUP) of two outcome groups differed significantly. "Unimproved" group had longer duration as compared to the "improved" group.

MULTIVARIATE ANALYSIS

Binary logistic regression using forward stepwise method was applied using the dichotomous outcome, "Unimproved" and "Improved". The following variables were entered – age, sex, SES, education, marital status, duration of psychosis, age at onset, family history and PANSS score. The model evolved contains duration of untreated psychosis and the odds ratio is 0.9854, with 95% CI (0.9717 – 0.9993), (p = 0.039). As duration of untreated psychosis increases, the chance of improvement decreases. The overall correct prediction rate is 69 % and the R^2 is 44 %, i.e., duration of untreated psychosis explains 44 % of the variation in the outcome variable.

DISCUSSION

This study consisted of 45 drug naïve (never-treated) schizophrenia patients. Their outcomes were assessed by two psychiatrists, and the inter rater reliability/ agreement was good and significant. Results of this investigation are similar to the previous findings (Fenton & McGlashan , 1987; Loebel et al, 1992; Szymanski et al,1996). DUP was found to predict the outcome significantly however; none of the socio-demographic factors seem to be significant predictors of the outcome. The observation that DUP emerged as a significant variable in both univariate and multivariate analyses confirms that the result obtained is not an artifact as the multivariate analysis takes into account the covariation, among different variables measured in the study.

The merits of the present study are that all patients were treated as in-patients, the same psychiatrist team treated them and the same diagnostic criteria were uniformly used. Two independent psychiatrists who were blind to all variables except the progress notes did the assessment of acute outcome. This study however, also has limitations in that the outcome was not assessed on any

TABLE 1 : Comparison between improved and unimproved groups

Variables	Unimproved		Improved		P
	Mean	SD	Mean	SD	
Age (Years)	31.18	10.69	31.61	8.53	.897
Education (Years)	8.55	4.50	9.89	5.46	.473
DUP (months)	81.82	65.69	37.50	45.41	.021
Age at onset (years)	25.64	9.11	28.29	7.48	.355
PANSS Score	87.64	21.85	87.50	17.33	.984

structured instrument. Also, only acute outcome measure was obtained for the study. Assessment of DUP involves retrospective recall of time of onset of psychosis, which has the usual problem of recall bias from patient. In the current study all patients were accompanied by a relative, who had lived with the patient from a time before the onset of psychosis. In this study, only the socio-demographic variables were included. We suggest that the future studies include variables such as pre-morbid adjustment, perinatal complications, neurological soft signs and subtypes of schizophrenia.

Earlier studies suggested better outcome in schizophrenia in India than in the West. The patients in this study had an average DUP of four years, which is considerably more than that reported in the literature from the West 1.3 years and 3.2 years (Robinson et al, 1999; Szymanski et al, 1996). It is conceivable that the reported better outcome for Schizophrenia in India is unlikely to be because of shorter DUP. It may hence suggest some other inherent advantage in our population yet to be identified. However, instituting treatment earlier gives further advantage and can make the outcome in our people even brighter. In summary, in our population of schizophrenia too, longer duration of untreated psychosis predicts poor acute outcome.

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MARIYAMMA PHILIP, *B.N. GANGADHAR, JAGADISHA, LATHA VELAYUDHAN, D.K. SUBBAKRISHNA, Depatments of Biostatistics & Psychiatry, NIMHANS, Bangalore-560029, India

* **Correspondence**