

Duration of untreated psychosis and the long-term course of schizophrenia

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Summary – This study examines the relationship between duration of untreated psychosis (DUP) and long-term symptomatic and social outcome in 205 patients with schizophrenia, whose parents are member of a consumer organisation. We found only a tendency that longer DUP was related to negative symptoms, but no relation to other outcome domains. The results of this study do not support antipsychotic intervention at the earliest sign of psychosis in order to 'protect the brain'. © 2000 Éditions scientifiques et médicales Elsevier SAS

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INTRODUCTION

Recently, projects have been set up to achieve early detection and intervention in schizophrenia [4, 10, 11]. These projects are based on the association between duration of untreated psychosis (DUP) and outcome. Liebermann et al. [5] assumed that ongoing (or recurrent) psychosis might lead to a degenerative process manifested by persistent morbidity, treatment resistance, and clinical deterioration. If psychosis is neurotoxic, then it is likely that a longer DUP is associated with poorer outcomes in a variety of domains. The clinical importance is that DUP is one of the few prognostic factors that can be influenced. Nevertheless, DUP may not be independent of 'fixed markers' [6] such as mode of onset, premorbid functioning and gender.

DUP was found to be significantly associated with some aspects of short-term outcome: time to remission and level of remission [8] and time to relapse [3]. One

study found an association between extremely long DUP and level of negative symptoms at long-term outcome [13].

Data concerning the relationship of DUP and long-term outcome in several domains are lacking. It will take many years before results from prospective longitudinal studies of the relationship between DUP and long-term outcome will be available. This study reports a retrospective study in the relationship between the extensive range of DUP and long-term outcome in several domains.

We expected to demonstrate an effect of DUP on outcome as we intended to compare the effects of extremely short vs very long DUP on several domains of long-term outcome.

SUBJECTS AND METHODS

A questionnaire was published in the monthly magazine of family members for patients with schizophrenia.

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Family members were asked the year and month in which psychotic symptoms first appeared in their relatives. The symptoms were defined as: 1) delusions (individual convictions which are not concordant with reality, for example, thought reading or paranoid delusions); 2) hallucinations (sensory experiences – hearing, sight, smell, etc. – without a concrete stimulus); or 3) disorganisation (strange or incomprehensible verbal expressions or behaviour). Family members were also asked the year and month in which antipsychotic medication was first administered, and the year and month that the first psychotic episode ended. With this information we calculated DUP and duration of the first psychotic episode. We investigated the following outcome-measures: positive symptoms and negative symptoms during the last half-year in three categories (depending on the interference with daily functioning: none, mild, severe), the number of psychotic episodes, the number of psychiatric admissions and the number of compulsory admissions, the time to remission during treatment with an antipsychotic drug, the support in housing, any regular activities and vocational adjustment (hours regular activities in a week: no activities, day activity centre, hobbies, volunteer job, education, paid job).

Family members of patients with schizophrenia revealed information about 205 patients. The patients were predominantly male (71%), had a mean age of 31.9 years (SD 8.8), an age of onset of 21.1 years (SD 4.4), and a time between onset of first psychotic episode and moment of survey of 11.1 years (SD 7.9). The mean number of psychotic episodes was 3.58 (SD 4.34), while 15.4% of the patients were chronically psychotic. The mean number of admissions was 3.40 (SD 7.60). Fourteen patients were never treated with antipsychotic medication, 71 patients had a DUP shorter than three months, and 73 patients had a DUP longer than 16 months (mean five years, five months).

In order to control for a possible response bias we compared demographic and admission characteristics of patients in our group with those of an extensive survey of a random sample of 1000 members (with a response rate of 70%) of the same family association [12].

Data analysis

Data were analysed with SPSS. Patients were divided into two extreme groups: DUP shorter than three months ($N = 71$), and patients with DUP longer than

16 months ($N = 73$). The middle group was expelled from analysis. The extreme groups were compared with multiple χ^2 in this exploratory study.

We compared extremely short versus extremely long DUP on social, vocational and symptomatic long-term outcome to find even small effects. We assumed that if family members thought the DUP shorter than three months we could safely define that group as having a short DUP and that if family members thought the DUP to be longer than 16 months we could define that group as having a long DUP. We assumed that the reliability of the retrospective assessment of DUP is too poor to analyse the intermediate group with a DUP between three and 16 months.

RESULTS

Two hundred and seven questionnaires were returned. Two questionnaires could not be used because of incompleteness.

We compared patients with a DUP of three months or less ($N = 71$, mean DUP 14 days) with patients with a DUP of 16 months or longer ($N = 73$, mean DUP 5.5 years). There were no significant differences (χ^2) between these extreme groups on any of the outcome measures (table 1).

There was a tendency for long DUP to be associated to negative symptoms. This relationship was not statistically significant.

The characteristics of the representative population of Schene and Van Wijngaarden did not differ from our population on: mean age of the patients (34 years, SD 10 years vs 31.9 years, SD 8.8 years), gender (69.1% male vs 71% male), age of onset of psychotic symptoms (22.9 years vs 21.1 years), mean amount of time since onset of the disorder (10.6 years vs 11.1 years), number of admissions (3.8 vs 3.4), and percentage with one or more involuntary admissions (58.7% vs 59.2%).

DISCUSSION

We found no relationship between short and long DUP and ten-year outcome. The tendency between DUP and negative symptoms is in accordance with Waddington's study [13], in which extreme DUP (mean 17.1 years, SD 12.8) was associated with negative symptoms. If we had found an effect of DUP on long-term outcome, even then this effect could not be attributed to the timing of initiating treatment since DUP is

Table 1. Comparison between short and long DUP.

	χ^2	DF	P-value
Positive symptoms	1.99	2	0.37
Negative symptoms	5.52	2	0.06
Number of psychotic relapses	10.05	10	0.44
Number of admissions	12.17	14	0.59
Number of compulsory admissions	4.74	7	0.69
Time to remission during treatment with antipsychotic drugs	46.35	42	0.30
Support in housing	0.01	1	1.0
No activities	0.19	1	0.66
Day activity centre	9.89	13	0.70
Hobbies	12.54	16	0.71
Voluntary work	10.28	14	0.74
Education	12.97	8	0.11
Paid job	9.23	8	0.32

possibly related with insidious onset of psychosis, which is a poor prognostic factor on its own [14].

The study has some drawbacks. The reliability of the diagnosis was not assessed. Nevertheless, there are arguments in favour of the representative nature of the study population. The studied population has an age of onset and a long-term course that is comparable with other populations with schizophrenia [1, 2]. Moreover, the family association focuses on relatives of patients with schizophrenia. The primary diagnosis, made by health professionals and reported by the respondents, was schizophrenia for 87.6%, chronic psychosis for 4.8%, manic-depressive disorder for 4.5% and other disorders for 3.1% in the survey of Schene and Wijngaarden [12]. Another drawback is the predominance of male patients. This resembles the predominance of males in the representative sample in Schene and Wijngaarden's survey [12] and points to the over-representation of family members of male patients in this family association. Moreover, members of advocacy groups tend to be better educated and less likely to be members of a minority group, and tend to have relatives that are more severely ill.

These biases could limit the generalizability of our findings. As the population we studied resembles a random sample of the same family association, it is likely that patients from responding families and from non-responding families are comparable.

How can we explain the lack of long-term consequences of long DUP, while short-term differences were documented by other studies? It is possible that there are only short-term effects of variation in DUP. Current positive symptoms are a better predictor of independent living than DUP more than ten years ago.

Also, current negative symptoms are a better predictor of activities and vocational outcome than DUP more than ten years ago. Another explanation could be that DUP is no predictor of outcome in a population with a predominance of males. The results of this study do not support an aggressive pharmacologic intervention at the earliest sign of psychosis in order to 'protect the brain'. We are aware of three other findings that weaken the hypothesis of psychosis as a neurotoxic process. Wyatt et al. [15] found no difference in long-term outcome between patients who used placebo in clinical trials and patients treated with active medication. Bleuler [1] found that there is usually a plateau in the progression of schizophrenia after the first five to ten years. Finally, a more acute and florid presentation of psychosis is associated with a better prognosis. Nevertheless, there are also findings that support the hypothesis of psychosis as a neurotoxic process [3, 7-9].

Although our results do not support a relationship between DUP and several domains of outcome, we think that early detection and intervention is still desirable to diminish the suffering of patients and their families during the early phase of schizophrenia. However, more investigation is needed before recommendations about programmes for early detection and treatment of psychosis can be made.

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