Patients' perspectives. Subjective experiences and attitudes of patients with recent onset schizophrenia

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Summary
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**Background**: This thesis discusses research into the perspective of patients with recent-onset schizophrenic disorders:

(Part I) The opinion of patients about the beginning of the disorder and the treatment.

(Part II) The prospects of patients in connection with the postponement of treatment.

The experiences of patients with the treatment:

(Part III) Subjective experiences.

(Part IV) Obsessive-compulsive symptoms as a possible side-effect of antipsychotic medication.

**Method**: Review of the literature, retrospective and prospective studies.

**Results**: (Part I) More than half of the patients realize at the first manifestation of psychotic symptoms that they are suffering from a mental disorder. Yet it usually takes months before they acknowledge the need for psychiatric treatment.

Patients give priority to the following aspects of the treatment: information, calm and safe possibilities for hospitalization, help in their own environment, and individual consultations.

(Part II) The idea that shortening the duration of untreated psychosis improves the prognosis was not substantiated by our research.

(Part III) Subjective experiences of patients can be determined in a reliable way. Subjective non-well-being is related to higher D₂ receptor occupancy by antipsychotic medication. D₂ receptor occupancy between 60%-70% results in optimal subjective experience.

(Part IV) Obsessive-compulsive symptoms frequently occur during use of clozapine. There are provisional indications that treatment with olanzapine can in the longer term be associated with increased severity of obsessive-compulsive symptoms in comparison to treatment with risperidon.

**Conclusion**: Research into the perspective of patients with recent-onset schizophrenia yields clinically relevant findings.
The following pages give a summary of the findings and limitations of the research described in this thesis.

Part I. Attitudes of patients concerning psychosis and treatment

Chapter 1.1. Attitudes of patients concerning the first psychotic episode and the start of treatment

*Findings:*

56 successively hospitalized patients with recent-onset schizophrenic disorders were asked about: their ideas regarding the disorder at the moment they first manifested psychotic symptoms; their opinion about the need for psychiatric treatment; their perception of the role of others in bringing about psychiatric treatment; suggestions for getting treatment underway at an earlier point.

Approximately 57% of the patients realized at the first manifestation of psychotic symptoms that they were suffering from a mental disorder. Before treatment was started, approximately two-thirds of the patients were of the opinion that psychiatric treatment was unnecessary. It took an average of 8 months before patients recognized the need for treatment. A majority of the patients (91%) considered the role of others essential in bringing about the treatment. Patients attributed delay in treatment chiefly to themselves.

*Limitations:*

- The group that we studied consisted largely of young men, 78% of whom had at some time used drugs. This limits the possibility of generalizing from our findings. We studied no patients who had never been hospitalized, no older patients, and only a few women.
- The retrospective character of the research implies that the answers obtained to our questions could have been influenced by memory defects, later experiences or the current psychiatric state. Prospective research, which is free of these problems, is not available at present. However, research into the attitudes of patients at the moment when they first experience psychotic symptoms is not feasible.

Chapter 1.2. Preferences for treatment during a first psychotic episode

*Findings:*

For an optimal treatment it is necessary to know which aspects of the care are considered important by patients and family members. Ten patients, ten family members and ten professional caregivers compiled a list of 42 statements about desirable elements in the treatment of a first psychotic episode. 99 patients, 100 family members and 263 caregivers ranked these 42 statements. We found a striking agreement between the rankings of the statements by patients, family members and caregivers. All the groups considered information about the disorder and the treatment to be especially important. Yet significant differences
emerged between the groups that we studied. Patients placed a higher priority than caregivers on the following aspects of the treatment of a first psychosis: rapid help in their own environment by a family doctor or psychiatrist, the creation of a quiet, safe environment, a short waiting period for hospitalization, and individual consultations.

Limitations:
- From the ranking of the statements it cannot be inferred that respondents consider statements with a lower priority to be unimportant.
- The respondents’ judgment of priority could be influenced by later experiences.
- The similarity found between the groups of respondents could be caused by the selection of respondents. The active involvement of family members and caregivers in the treatment of patients with psychotic disorders is probably above average, considering their presence at a congress on schizophrenia.
- Preferences for treatment during other phases of the disorder have not been studied.

Part II. Duration of untreated psychosis and outcome

Chapter 2.1. Course of schizophrenia; Pathogenetic hypotheses concerning schizophrenia; Duration of untreated psychosis and outcome

Findings:
- The course of schizophrenia in the years after the first hospitalization is heterogeneous and for a large number of patients unfavorable.
- There are indications that, in addition to an early developmental disorder, schizophrenia involves a progression of brain defects around the time that the disorder sets in. This underscores the importance of further research into the relation between early treatment after the development of psychotic symptoms and the prognosis.
- Studies have repeatedly found a relation between the duration of untreated psychosis and the outcome of schizophrenia. This link was found in groups of patients to whom other unfavorable prognostic factors applied in varying degrees. Yet in a number of recent studies no relation was found between the duration of untreated psychosis and the outcome of schizophrenia (Craig et al. 2000; Ho et al. 2000; Hoff et al. 2000; Barnes et al. 2000). Moreover, in view of the contradictory research results it is not yet clear to what extent the duration of untreated psychosis is dependent on other prognostic factors that cannot be influenced. For this reason it is not yet possible to determine whether shortening the duration of untreated psychosis favorably affects the prognosis.

Limitations:
- Data available up to now are derived mainly from correlation research.
- Studies in this area are difficult to compare owing to the lack of generally
accepted criteria for identifying the beginning of psychotic symptoms and the start of adequate treatment. It is unclear, for example, whether the start of adequate treatment should be defined as the start of treatment with antipsychotic medication or whether it is (also) a matter of the start of psychosocial and psychotherapeutic interventions.

Chapter 2.2. Early intervention, social functioning and psychotic relapse in patients with recent-onset schizophrenic disorders

*Findings:*
After an early intensive treatment of 133 young patients with recent-onset schizophrenic disorders, the social functioning and the frequency of psychotic relapse were assessed retrospectively. Two-thirds of the patients who had undertaken no activities at the time of their hospitalization were involved in structured activities after 12 months of outpatient treatment. One-fifth of the patients experienced a relapse within one year. Early intensive intervention combined with treatment with antipsychotic medication was found in these cases to be associated with an improvement in social functioning and a relatively low percentage of relapse in the period of 1 year.

*Limitations:*
- This was an uncontrolled retrospective study.
- A follow-up period of a year is not sufficient to yield a picture of the course of recent-onset schizophrenia.

Chapter 2.3. Duration of untreated psychosis and the long-term course of schizophrenia

*Findings:*
The relation between the duration of untreated psychosis and the course of psychopathology and social functioning in the longer term was studied retrospectively in 205 patients with schizophrenic disorders. These were patients whose parents belonged to an organization for family members of patients with schizophrenia. No relation was found between the duration of untreated psychosis and the course over an average of 11 years.

*Limitations:*
- The reliability of assessing the duration of untreated psychosis a considerable time after the development of the first psychosis is unknown.
- The findings cannot be generalized for the entire population of patients with schizophrenic disorders because we studied a select group of patients (mainly men, information obtained from members of an organization for family members of patients with schizophrenia).
Chapter 2.4. Duration of untreated psychosis and the outcome of schizophrenia: delay in intensive psychosocial treatment versus delay in treatment with antipsychotic medication

Findings:
We investigated the relation between delay in treatment with medication, delay in intensive psychosocial treatment and the outcome of schizophrenia. The outcome was measured an average of 6 years after the development of the first psychotic symptoms, in a cohort of 88 patients. Both delay in treatment with medication and delay in intensive psychosocial treatment were related to negative symptoms 6 years after the development of the first psychosis. Delay in intensive psychosocial treatment was related to the number of months that patients were hospitalized in a psychiatric institution. Delay in intensive psychosocial treatment remained related to negative symptoms when correction was made for the age at which the first psychosis developed, sex, and duration of the psychotic symptoms during treatment. Delay in intensive psychosocial treatment may have consequences for the long-term course.

Limitations:
- Retrospective study.
- Over-representation of young men in the group we studied.
- The relation between delay in intensive psychosocial treatment and outcome with regard to negative symptoms can be influenced by sociocultural and/or psychopathological characteristics.

Part III. Subjective experience of patients with schizophrenia related to antipsychotic medication

Chapter 3.1. Introduction

Findings:
Subjective experiences of patients during use of antipsychotic medication have received relatively little attention in research and in clinical practice. With the development of a new generation of antipsychotic medication and the rediscovery of the importance of low doses of selective D2 antagonists there has been increased interest in the subjective experiences of patients during treatment with antipsychotic medication. Attention has shifted from combating psychotic symptoms to improving the quality of life. Patients’ subjective feelings of non-well-being during the use of antipsychotic medication are related to non-compliance with medication. Considering that medication non-compliance increases the chance of a psychotic relapse, “the subjective experiences of patients during the use of antipsychotic medication” are very likely also relevant for the course of schizophrenia.

Limitations:
The relation between subjective experiences and therapy compliance in the use of antipsychotic medication has been found almost without exception in studies
in which it was clear to the patients that a link was being sought between the use of antipsychotic medication and subjective experiences. This means that the relation between subjective experiences and therapy compliance could be explained by patients’ ideas about antipsychotic medication.

Chapter 3.2. Psychometric properties of the Subjective Well-being under Neuroleptics Scale (SWN) and the Subjective Deficit Syndrome Scale (SDSS)

Findings:
Psychometric properties of the SWN and the SDSS were studied at admission and after stabilization on antipsychotic medication in 105 successively hospitalized patients with recent-onset schizophrenic disorders. Both before and after stabilization of their disorder, the patients proved capable of reliably assessing their subjective experiences with the SWN. The SWN is particularly sensitive to changes in medication or dosage. The concurrent validity of SWN and SDSS is good, indicating that both instruments measure the same concept. The short version of the SWN has psychometric properties equal in quality to those of the original version.

Chapter 3.3. Subjective experience and striatal dopamine D₂ receptor occupancy in patients with schizophrenia stabilized on olanzapine or risperidone

Findings:
Study was made of the relation between subjective experience and dopamine D₂ receptor occupancy as determined with [¹²³I]IBZM SPECT in 22 patients with schizophrenic disorders stabilized during treatment with olanzapine or risperidone. Subjective experience, depressive symptoms and negative symptoms were found to be related to the degree of D₂ receptor occupancy. There were virtually no extrapyramidal symptoms in the group studied.

Limitations:
From our research it cannot be concluded that there is a causal relation between increase in D₂ receptor occupancy and negative subjective experience.

Chapter 3.4. Subjective experience and D₂ receptor occupancy in patients with schizophrenia, treated with low dose Olanzapine or Haloperidol; a randomized double-blind study

Findings:
In a randomized double blind study 24 patients with schizophrenia received olanzapine 7.5 mg/day or haloperidol 2.5 mg/day for 6 weeks. Preliminary evidence was found that a level of D₂ receptor occupancy between 60% and 70% is optimal for subjective experience of patients with recent onset schizophrenia. We found substantial interindividual variation in D₂ receptor occupancy at fixed low-dose haloperidol and olanzapine. Olanzapine 7.5mg
showed neither superior subjective response nor superior efficacy over haloperidol 2.5 mg. Haloperidol needs to be individualy titrated in the very low dose range to reach optimal occupancy and olanzapine needs to be dosed higher than 7.5 mg for most patients with recent onset schizophrenia.

Limitations:
Most of the included patients used antipsychotic medication before study entry, probably altering their D2 binding capacity. Half of the patients used oxazepam as adjunctive medication.

Part IV. Obsessive-compulsive Symptoms associated with antipsychotic medication in patients with schizophrenia

Chapter 4.1. Obsessive-Compulsive Symptoms and antipsychotic medication in patients with schizophrenia

Findings:
Obsessive-compulsive symptoms occur relatively frequently in patients with schizophrenia. Patients with schizophrenia who exhibit obsessive-compulsive symptoms probably have a worse prognosis and specific neuropsychological function disorders. Case reports and a few retrospective studies tentatively indicate a relation between use of certain antipsychotic medications and the development or exacerbation of obsessive-compulsive symptoms.

Limitations:
There is no agreement about the criteria for demarcating psychotic symptoms from obsessive-compulsive symptoms. Much of the data about the prevalence of OCS is based on studies of select clinical populations.

Chapter 4.2. Clozapine and obsessions in patients with recent-onset schizophrenia and other psychotic disorders

Findings:
A retrospective cohort study of young patients with recent-onset schizophrenic disorders (n=121) investigated the increase or the development of obsessions during treatment with clozapine and during treatment with other antipsychotic medications. Also studied was whether the addition of selective serotonin reuptake inhibitors (SSRIs) to the antipsychotic medication lessened the obsessive-compulsive symptoms. Patients who used clozapine were found to develop obsessive-compulsive symptoms or experience an increase in those already present more frequently than patients who used other antipsychotic medication. After a lowering of the clozapine dosage and an addition of SSRIs the obsessive-compulsive symptoms decreased in less than half of the patients.

Limitations:
- Because this was a retrospective cohort study, the findings have to be seen as tentative indications.
- It is possible that obsessions remain when psychotic symptoms are treated successfully.
- The finding could also be explained by differences between the group of patients treated with clozapine and the group that received other antipsychotic medication.
- Because obsessive-compulsive symptoms may decrease spontaneously, no conclusions can be drawn from the favorable reaction of some patients to SSRIs.

Chapter 4.3. Obsessive-compulsive symptoms during treatment with olanzapine and risperidone, a prospective longitudinal study of 113 patients with recent-onset schizophrenia or related disorders

Findings:
In a prospective study no difference was found in the occurrence and severity of obsessive-compulsive symptoms between patients who were randomized for olanzapine or risperidone (n=36). In the group that was already receiving olanzapine or risperidone before admission and that continued with this medication for 6 weeks during hospitalization (n=55) more severe obsessive-compulsive symptoms occurred in patients treated with olanzapine. A relation was found between the duration of the treatment with olanzapine and the severity of the obsessive-compulsive symptoms.

Limitations:
- Considering the open and only partly randomized nature of the study, the results are tentative in character.
- The reliability and validity of the DSM-IV diagnosis OCD and the reliability and validity of the instrument used (Y-BOCS) are unknown for patients with schizophrenia.