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Chapter 1.5

Improvement of subjective well-being and enduring symptomatic remission, a 5-year follow up of first episode schizophrenia

Pharmacopsychiatry

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Improvement of subjective well-being and enduring symptomatic remission

Abstract

**Introduction** The aim of this prospective study was to compare the predictive validity of early improvement of subjective experience and early improvement of rater-assessed symptoms on enduring symptomatic remission (ESR) status during 5 years follow.

**Methods** 110 Consecutively admitted patients suffering from a first episode of schizophrenia or related disorders were investigated. We defined early improvement of subjective well-being as a delta-score of the total Subjective Well-being under Neuroleptics scale-20 item version (SWN-K) at admission and after 6 weeks treatment. The severity of psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) at admission, 6 weeks, 6-months, 3 and 5 years after admission. Enduring symptomatic remission (ESR) was defined as complying to the symptomatic remission criteria at PANSS assessment at 6 months and 5 year and continuing this state between 6 months and 5 year follow up. Paired-samples and independent t-test were used to compare means.

**Results** Patients with ESR (n=30) had a higher mean improvement of subjective well-being during early treatment as assessed with the SWN-K than those without ESR (n=74) (p=0.004). Early symptomatic improvement as assessed with the PANSS was not related to ESR (p=0.95).

**Discussion** Early improvement of subjective well-being is related to ESR in first episode schizophrenia or related disorders.
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Introduction

The proposed remission criteria (Andreasen et al 2005) for patients with schizophrenia consist of two components: a symptom-based criterion (low scores on diagnostically relevant symptoms; including the following PANSS items: delusions, unusual thought content, hallucinatory behaviour, mannerisms and posturing, blunted affect, social withdrawal, lack of spontaneity) and a time criterion (duration of 6 months). These criteria have clinical validity (van Os et al 2006), although further research is required (Lambert et al 2006). Early functional, symptomatic and subjective well-being improvement was found to predict remission during two-year follow up (Lambert et al 2006). Identifying predictors of remission that are potentially amenable is clinically relevant. Modifying such predictors might influence the long-term course of the disorder.

Subjective well-being as assessed by patients is only partly related to severity of psychopathological symptoms as assessed by clinically trained raters (Naber 1995). Since subjective well-being is directly related to quality of life we can not rely only on clinicians based assessments (Wehmeier et al 2007). Moreover subjective well-being is an important factor in choice of medication and medication adherence (Karow et al 2006, 2007, Kay et al 1987, Lambert et al 2007).

We hypothesized that subjective early improvement is related to enduring symptomatic remission (ESR). We compared the predictive validity concerning ESR status of patient based assessment of early treatment effects with those of clinically trained raters.

Methods

Subjects

Patients were eligible for the study if 1) they were diagnosed as having schizophrenia or a related disorder using DSM IV-R criteria, 2) were in need of inpatient treatment because they were actively symptomatic and had severe social dysfunction, and 3) had an age between 15 and 28 years. Patients with drug-related psychoses who needed detoxification were excluded. The local review board approved the study, and written informed consent was obtained from all subjects.
Assessments

To assess subjective well-being we used the Subjective Well-being under Neuroleptics scale – 20 item version (SWN-K) (Naber 1995). This is a self rating scale referring to the subjective experience in the past 7 days. For instance the following statements are presented to patients: I am full of energy and life, I feel very comfortable with my body, I feel powerless and exhausted, My thinking is difficult and slow. Patients are asked to mark the appropriate response on a 6 point scale from “not at all” to “very much”. The answers of negatively formulated items are recoded. The total score ranges from 20-120, higher scores implying higher subjective well-being. The majority of patients are able to complete the SWN-K in a reliable and consistent manner (de Haan et al 2002, Naber 1995). We defined early improvement of subjective well-being as a delta-score of the total SWN-K score at admission and after 6 weeks treatment.

The severity of psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) (Kay et al 1987) at admission, 6 weeks, 6-months, 3 and 5 years after admission based on information collected in a semi-structured interview (SCI-PANSS) by trained and clinically experienced raters not involved with collection of data concerning subjective experience.

The intra class correlation coefficient for the positive, negative, and general psychopathology subscales were 0.91, 0.84 and 0.76, respectively. We defined early improvement of psychopathology as the delta of the PANSS scores at admission and after 6 weeks treatment.

Remission of psychopathology was assessed according to the criteria of Andreasen et al (2005). When a patient met the symptom based criteria we evaluated whether this situation continued until the following assessment. This evaluation was based on the assessment of the professional caregiver who rated the psychopathological state each half year till the end of 5 year follow-up. Enduring symptomatic remission (ESR) was defined as complying to the symptomatic remission criteria at PANSS assessment at 6 months and 5 year and continuing this state between 6 months and 5 year follow up.

Paired-samples and independent t-test were used to compare means.

Results

We included 110 patients, mean age at admission 21.1 (SD 2.8), 93 male, with a DSM-IV-R diagnosis of schizophrenia (n=69), schizoaffective disorder (n=16), schizophreniform disorder (n=19), delusional disorder (n=2) and psychotic disorder
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For all 110 patients admission and 6 weeks follow-up data were available, thereafter 4 patients were lost to follow-up, 2 died by suicide. In the total group we found the following mean improvement during early treatment: in SWN-K total scores: 6.1 (SD = 6.3, t(109)=-4.5, p<0.001); in total PANSS scores: 14.9 (SD=18.5, t(109)=7.7, p<0.001); in PANSS positive subscale scores: 5.1 (SD=6.7, t(109)=7.3, p<0.001); in PANSS negative subscale scores: 3.5 (SD=6.1, t(109)=5.4, p<0.001); and in PANSS general subscales scores: 6.3 (SD=9.6, t(109)=6.4, p<0.001).

The mean total PANSS scores at baseline were 84.7 (SD= 20.3) and 6 weeks after admission 69.8 (SD = 17.8).

Percentages of patients meeting symptomatic remission criteria were 3.8% at admission; 19.2% at 6 weeks after admission; 44.2% at 6 months after admission and 37.5% at 5 years after admission. Thirty patients (27.3%) were in ESR.
The mean improvement of SWN-K total scores during early treatment in patients with ESR (12.0, SD=13.6, n=30) was significantly higher than in those without ESR (3.6, SD = 13.0, n=74, t(103)=-2.9, p=0.004).

The mean improvement of PANSS total scores during early treatment in patients with ESR (15.1, SD=13.9, n=30) was not significantly different from those without ESR (14.8, SD = 20.0, n=74) (t(103)=-0.6, p=0.95). Neither was the mean improvement of positive, negative and general subscales of the PANSS during early treatment for patients with ESR significantly different from those without ESR (p values varying from 0.53 to 0.97).

Patients with ESR had lower mean PANSS total scores 6 weeks after admission than patients without ESR (64.4, SD= 16.9 versus 71.8, SD = 17.8), this finding did not reach statistical significance (p=0.07).

We found no significant gender and age effect on the total score of the SWN-K: 17 women had a mean total SWN-K score of 78.9 (SD = 13.2), 93 men had a total SWN-K score at admission of 75.7 (SD = 16.3) (p=0.5); age at admission was not related to total score SWN-K score (pearson correlation -0.06, p=0.5).

Although we found that early symptomatic improvement was related to reaching symptomatic remission criteria at 6 weeks and 6 months after admission, this relationship did not hold when we used our stringent criteria for ESR: symptomatic remission should be continued 4 ½ year afterwards.

We did not find significantly different results for patients with a diagnosis of schizophrenia (n=69) versus patients with other psychotic disorders (n=41).

**Discussion**

The results of our study suggest that early improvement of subjective well-being is related to ESR, whereas early improvement in severity of symptoms as assessed by clinically trained raters is not related to ESR. Early improvement of subjective well-being might be related to medication adherence during follow-up and by that to enduring symptomatic remission (Wehmeier et al 2007). However, we found no relation between subjective well-being and with long term medication adherence in our sample (de Haan et al 2007). Early improvement of subjective well-being might be a sensitive marker of the ability to recover. The subjective experience of improvement during early treatment might identify a group of patients with a better prognosis. Whether interventions that aim to improve subjective well-being in the early treatment phase have long term consequences is unknown. Lambert et al (2007) found that complete remission in the first 3 months of the study defined as symptomatic, functional, and subjective well-being remission predicted complete
remission in schizophrenia in the course of 24 months follow-up. The absence of a relation between early symptomatic improvement and ESR we found in our study was unexpected. Reasons for this finding could be unreliable assessment of early symptomatic improvement or unreliable assessment of symptomatic remission or both. However since the inter-rater reliability of the PANSS assessment is good and since the assessment of ESR is done by the professional caregiver in close contact with patients we think that problems with reliability of the assessments do not explain our findings.

Furthermore one might question the applicability of the SWN-K in patients with first episode schizophrenia. Obviously, using self-report scales in patients with schizophrenia has its limitations. However, Naber (1995) found in 216 patients with schizophrenia that only 4% of the patients were inconsistent in their ratings. In order to determine the reliability of patient’s assessment with the SWN-K the difference between the item scores on the positively and the negatively formulated items was computed. The SWN-K consists of 20 items, divided in 10 positive and 10 negative formulated items, describing each complaint in a positive and a negative manner.

The mean absolute difference between the positively and the negatively formulated items of the SWN-K at admission and 6 weeks after admission were respectively 0.69 (SD 0.49) and 0.66 (SD 0.50) (de Haan et al 2002). Only 1 patient at T1 and 3 patients at T2 had a mean difference of 2 or more. This means that patients produce mean different scores of about a half between the 6 possible responses when they assess their subjective experience on items describing each complaint in a positive and a negative manner. Therefore we think that the applicability of the SWN-K in the patients we included is good.

Although we found that early symptomatic improvement was related to reaching symptomatic remission criteria at 6 weeks and 6 months after admission, this relationship did not hold when we used our stringent criteria for ESR: symptomatic remission should be continued 4 ½ year afterwards.

However, patients with ESR had lower mean PANSS total scores 6 weeks after admission at a trend level, so reaching a less symptomatic state in early treatment may be related to ESR. Further studies are needed. In conclusion, early improvement of subjective well-being is related to ESR in first episode schizophrenia or related disorders.
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