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Association between subjective well-being and depressive symptoms in treatment-resistant schizophrenia before and after treatment with clozapine

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Abstract

Background: We examined the relationship between subjective well-being and depressive symptoms in patients with treatment-resistant schizophrenia before and after treatment with clozapine to contribute to the growing body of research regarding the determinants of patients' perspective of their own well-being in schizophrenia.
Methods: Forty patients with treatment-resistant schizophrenia were comprehensively evaluated for subjective well-being, schizophrenic symptoms, and depressive symptoms before and 8 weeks after the initiation of treatment with clozapine. Correlation analysis and Fisher's *z*-transformation statistics were performed.
Results: There were significant improvements in all Positive and Negative Syndrome Scale (PANSS) factor scores and Beck Depression Inventory (BDI) score over the treatment period ($P < .05$). Before clozapine administration, the subjective well-being score had significant negative correlations with the PANSS depression factor score ($P < .05$) and the BDI score ($P < .05$). After clozapine treatment, the subjective well-being score still had significant negative correlations with the PANSS depression factor score ($P < .05$) and the BDI score ($P < .05$) and no new associations emerged with treatment. Fisher's *z*-transformation statistics revealed that the correlations between the subjective well-being score and the depression score were not significantly different before and after clozapine treatment.
Conclusions: These results indicate that depressive symptoms are significantly associated with low subjective well-being in patients with treatment-resistant schizophrenia. The association was equally significant before and after treatment with clozapine, suggesting that the relationship does not change with clozapine treatment, even when depressive symptoms improve significantly, and that there may be a common pathophysiological basis for depressive symptoms and the subjective appraisal of well-being in schizophrenia.

1. Introduction

Subjective well-being is a major component of the quality of life (QOL) of patients with schizophrenia, and it has been reported that subjective well-being has a strong impact on drug compliance and achieving remission in schizophrenia [1,2]. Therefore, a comprehensive evaluation of patients' perceptions of their own well-being is crucial in order to improve their treatment compliance and functional outcome.

Since the concept of QOL was introduced in schizophrenia research, there have been efforts to identify clinical factors that are most likely to play a major role in determining subjective well-being [3]. With regard to psychopathology, a number of reports have shown that depressive symptoms are strongly related to subjective well-being [4–8], while positive and negative symptoms are only moderately correlated with it [3–9], suggesting that the detection and appropriate treatment of depressive symptoms in schizophrenia patients may affect the perception of their own well-being.

However, previous studies of the association of depressive symptoms with subjective well-being mainly focused on the cross-sectional relationship in stable patients and the results may not be generalizable to other patient groups, such as treatment-resistant inpatients characterized by a high level of positive symptoms and poor functioning [10]. Moreover, it is unclear whether clozapine administration can change the relationship between depressive symptoms and subjective well-being in patients with treatment resistance.

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Hence, the purpose of the present study was to examine the relationship between subjective well-being and depressive symptoms in patients with treatment-resistant schizophrenia before and after treatment with clozapine, in order to contribute to the growing body of research regarding the determinants of patients' perspective of their own well-being in schizophrenia.

2. Materials and methods

2.1. Subjects

The study protocol was approved by the local ethics committee, and all procedures used in the study were conducted in accordance with international ethical standards, Declaration of Helsinki. Forty patients (23 men, 17 women) who met the Diagnostic and Statistical Manual of Mental Disorders Fourth edition (DSM-IV) criteria for schizophrenia were enrolled. The diagnoses were established using the Structured Clinical Interview for DSM-IV [11]. Informed consent was obtained from all subjects after a full explanation of the study procedure. All patients were required to have documented treatment-resistant status, as defined by the absence of clinically significant improvement observed using at least two different classes of antipsychotics at adequate dosage (equivalent to 1000 mg/day of chlorpromazine), during a minimum treatment period of 6 weeks. Patients had a mean age of 33.0 ± 8.1 years and a mean duration of illness of 10.0 ± 7.2 years. The mean number of years of education was 13.9 ± 2.1.

2.2. Clozapine administration and clinical assessments

All patients started receiving clozapine under open-label conditions and were assessed for subjective well-being and psychopathology before and 8 weeks after the initiation of treatment with clozapine.

Patients discontinued their previous antipsychotics before entering the study, and clozapine was initiated at either 12.5 or 25 mg/day. The dose was titrated by attending psychiatrists, according to the clinical condition and tolerability of each individual patient. The mean daily dose of clozapine at the end of the treatment period was 260.0 ± 73.3 mg.

Subjective well-being was assessed using the Subjective Well-being under Neuroleptics Scale (SWN) [12]. The SWN is a questionnaire that has been used to assess the subjective well-being and QOL of patients with schizophrenia [13–17]. The SWN consists of 20 items with a 6-point Likert scale response format and it measures the well-being of patients from their own perspective [12]. Previous studies have shown sufficient internal consistency and construct validity of the SWN [12–14]. The scale has been increasingly used in different populations of patients with schizophrenia [13–17].

Symptoms of schizophrenia were assessed using the Positive and Negative Syndrome Scale (PANSS) [18]. The PANSS is a 30-item instrument that measures positive, negative, and general psychopathology symptoms and each of the items is scored on a 7-point Likert-type scale (1 = absent and 7 = extreme) representing increasing levels of psychopathology. Before enrolling patients in the study, the rater was sufficiently trained to administer the PANSS using the Structured Clinical Interview for the PANSS [19]. A five-factor model of the PANSS was used based on evidence from the factor analysis studies [20,21]. The factors were positive, negative, cognitive/disorganized, depression, and excitement. The severity of illness was also assessed using the Clinical Global Impression Scale of Severity (CGI-S) [22]. The Beck Depression Inventory (BDI) [23] was also used for the evaluation of depressive symptoms. All rating scales were administered at the time of study entry (baseline) and at the end of week 8 of clozapine administration.

2.3. Statistical analysis

Pearson's correlation analysis between subjective well-being and clinical symptoms before and after treatment with clozapine was performed. The significance of the differences between the correlations was analyzed using Fisher's z-transformation statistics. For all analyses, the level of statistical significance was defined as $P < .05$ (two-tailed).

3. Results

The demographic and baseline clinical characteristics of the subjects are presented in Table 1. The mean PANSS total score was 94.0 ± 19.8, suggesting a marked severity of illness. Table 2 shows the intercorrelations between the SWN score and clinical variables before clozapine administration. The SWN score had no significant correlations with age, gender, duration of illness, or years of education ($P > .05$). The SWN score had a significant negative

Table 1
Demographic and clinical characteristics of the subjects (n = 40).

Variables	Mean ± SD/Number (percentage)
Age (y)	33.0 ± 8.1
Gender	
Male	23 (58.0%)
Female	17 (42.0%)
Duration of illness (y)	10.0 ± 7.2
Education (y)	13.9 ± 2.1
Marital status	
Single	33 (82.5%)
Married	7 (17.5%)
PANSS factor score	
Positive	31.7 ± 7.0
Negative	22.1 ± 7.9
Cognitive/disorganized	15.4 ± 5.8
Depression/anxiety	15.1 ± 4.5
Excitement	10.7 ± 3.9
Total score	94.0 ± 19.8

SD indicates standard deviation; PANSS, Positive and Negative Syndrome Scale.