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Symptomatic remission and patient quality of life in an observational study of schizophrenia: Is there a relationship?

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ABSTRACT

This analysis aimed to examine the association between remission and quality of life (QOL) in schizophrenia. In *post-hoc* analyses of the 3-year, prospective, observational Schizophrenia Outpatients Health Outcomes (SOHO) study, we compared the QOL of patients who achieved symptomatic and clinical remission with those who did not, and the factors associated. Symptomatic remission was defined as achieving a score of ≤ 3 on the Clinical Global Impression-Schizophrenia (CGI-SCH) scale, maintained for 6 months and without hospitalization. QOL was patient self-rated using the European-QOL. Of the 6516 patients analyzed, 38% were in symptomatic remission 12 months post-baseline and 52% at 36 months. Functional remission remained fairly constant from 12 months to 36 months (22.4% at both time points). At all visits from 12 to 36 months, patient QOL and social functioning were significantly higher for patients in symptomatic remission. QOL was higher in patients in functional remission. Patients with maintained symptomatic remission over the 3-year follow-up had a much greater improvement in QOL than patients with no symptomatic remission or symptomatic remission for part of the period. Factors associated with a better QOL also included paid employment, socially active, a higher CGI-SCH cognitive score, good compliance, and a better baseline QOL.

1. Introduction

A few years ago, the Remission in Schizophrenia Working Group (Andreasen et al., 2005) proposed that treatment effects should be assessed using measures that have a significant meaning for the patient. Most clinical trials have used a clinical severity scale, such as the Positive and Negative Syndrome Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS), as the main outcome measure. However, a decrease in such scale scores cannot easily be translated into patient clinical status. The Working Group proposed 'remission' as a construct that has a clear meaning for patients and, thus, has direct implications for their well-being. Remission has been defined as having none or a minimal level of symptoms in key areas of schizophrenia for a period of 6 months or more (Andreasen et al., 2005).

Since then, this definition of symptomatic remission has been applied in a number of studies with different samples of patients with schizophrenia in an attempt to validate it (Lasser et al., 2007; Bodén et al., 2009; Ciudad et al., 2009). These validation studies applied an external validity criterion by comparing the key functioning and quality of life aspects of patients who were in symptomatic remission with those who were not in symptomatic remission. The findings of better social functioning for patients in symptomatic remission were highly consistent (Lasser et al., 2007), whereas the quality of life results were discordant (van Os et al., 2006; Emsley et al., 2007; Wunderink et al., 2007; Bodén et al., 2009). Some studies found that patients in symptomatic remission did not have a better quality of life than patients not in symptomatic remission (van Os et al., 2006; Wunderink et al., 2007), while others found a difference in quality of life between remitters and non-remitters (Emsley et al., 2007; Bodén et al., 2009). The differences may be explained by the use of different measures of quality of life, and because some studies had small sample sizes.

Quality of life is complex and influenced by many social, psychological and clinical factors, including the patient's age and sex, insight into illness, severity of current symptoms, and side effects of medications (Hofer et al., 2004). Katschnig (2000)

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proposed that quality of life encompassed three areas; subjective wellbeing/satisfaction, and two objective aspects related to functioning and external resources. Among psychiatric patients, the relationship between these areas is complex, and the different areas have more or less influence on overall quality of life depending on the impact of disease at that point in time; when disease has a large impact on functioning, quality of life is reduced (Becker et al., 2005). A variety of measures are used to assess quality of life, including patient self-report measures (e.g., a summary measure on a visual analog scale, VAS) and clinician-rated scales (e.g., the Heinrich's QOL). There is, however, a discrepancy between self-reported and clinician-rated quality of life, as many of the clinician-rated scales measure functioning rather than subjective well-being (Lasalvia et al., 2002; Jung et al., 2010). In this analysis, we were interested in self-reported quality of life as the impact of multiple relevant factors in a single, global, subjective judgement as a summary rating on a VAS. The setting of studies of quality of life is also important; quality of life measures have been applied in naturalistic settings and in clinical trials, but only the former setting characterizes the broader range of patients seen in everyday clinical practice. As quality of life profiles are reported by patients, not their clinicians, they are of interest to purchasers and providers of psychiatric services.

Some of the studies that found an association between quality of life and symptomatic remission did not take into account the presence of confounders (Bodén et al., 2009): factors such as gender, age, or medication are known to be associated with both quality of life and symptomatic remission frequency, and may confound the relationship. van Os et al. (2006) did take confounding factors into account, but did not find an association between quality of life and symptomatic remission. In addition to these clinical factors, there are many other social factors that influence quality of life and may also confound the results.

The Schizophrenia Outpatients Health Outcomes (SOHO) study, a 3-year prospective, observational study on the course of schizophrenia in the outpatient setting (conducted from September 2000 to January 2005), provides an excellent opportunity to address the issue of whether remission and quality of life are related. The objectives of these *post-hoc* analyses are to compare the quality of life of patients who achieve symptomatic remission of schizophrenia with those who do not achieve symptomatic remission. We also analyze whether the association between symptomatic remission and quality of life, if present, can be explained by the presence of confounding factors. For this, the regression model can be adjusted for other factors known to impact on quality of life and to be associated with remission (e.g., age, gender and medication) (Haro et al., 2006; Yen et al., 2008; Potkin et al., 2009). Finally, we have described the relationship between functional remission and quality of life.

2. Methods

The SOHO study was a prospective, observational study conducted in 10 European countries. The rationale, design and methods of the study have been described in detail elsewhere (Haro et al., 2003b). Full ethical approval (including patient consent) was obtained in all countries, either at the site, region or national level, depending on country regulations. The study was carried out in accordance with the Declaration of Helsinki. A total of 1096 psychiatrists offered enrollment to patients who were: initiating or changing antipsychotic medication for the treatment of schizophrenia (diagnosed using ICD-10 or DSM-IV criteria); presenting within the normal course of care in the outpatient setting or in the hospital when admission was planned for the initiation or change of antipsychotic medication and discharge planned within 2 weeks; at least 18 years of age; and not participating in an intervention study. Patients were included irrespective of the reason for treatment change (e.g., lack of response, side effects, etc.), and regardless of whether an antipsychotic drug was being initiated as a replacement for a previous medication, was an addition to existing treatment, or was being initiated for the first time or after a period of no treatment.

Since the initial objective of the SOHO study was to compare treatment with olanzapine versus treatment with other antipsychotics, the study was designed to provide two patient cohorts of approximately equal size: patients who initiated therapy with or changed to olanzapine; and patients who initiated therapy with or changed to a non-olanzapine antipsychotic. To achieve approximately equal numbers in the olanzapine and non-olanzapine groups, different sample fractions entered each cohort. This resulted in a stratified sample, with the olanzapine group as the 'over-sampled' stratum. In the present analyses, however, the non-olanzapine group was divided into groups according to the specific antipsychotic medication prescribed.

Effort was made to avoid interference with clinical practice. Investigators were instructed to make treatment decisions independently of the study and then evaluate whether patients were eligible for inclusion based on the entry criteria and the alternating structure of enrollment. The recruitment period was intentionally long and no minimum number of cases was required by each investigator.

Patients were evaluated during visits occurring within the normal course of health care, which were planned at approximately 3, 6, 12, 18, 24, 30 and 36 months after baseline. The routine outpatient visit at which patients were enrolled served as the time for baseline data collection.

Clinical severity was assessed using the Clinical Global Impression-Schizophrenia scale (CGI-SCH) (Haro et al., 2003c), which evaluated positive, negative, cognitive, depressive and overall symptoms in the week before the day of assessment. This physician-rated scale ranges from 1 (not ill) to 7 (among the most severely ill).

Health-related quality of life (HRQL) was assessed using the European Quality of Life Questionnaire (EQ-5D, formerly EuroQol) (Brooks et al., 2003). This is a patient self-rated, generic, HRQL instrument that includes a visual analog scale (EQ-VAS) which patients use to assess their perceived current level of health on the day of scoring from 0 (worst imaginable health state) to 100 (best imaginable health state).

Other data collected included socio-demographics, psychiatric history, patient functioning, medication use and adverse events. Data on baseline variables such as employment and social activities were collected using single-item questions completed by the participating investigators to the best of their knowledge including information from the patient and other sources and assessing the status during the previous four weeks.

Further details about the design of the SOHO study and the results at 6 months and 3 years have been provided elsewhere (Haro et al., 2003a, 2003b, 2003c, 2005, 2006).

2.1. Definition of remission

In this analysis, remission was described in two ways; symptomatic remission (based on the CGI-SCH) and functional remission (based on social functioning).

Symptomatic remission was defined as achieving a score of 3 (mild severity) or less on the 1–7 scale for each of the CGI-SCH items of overall severity, positive, negative and cognitive symptoms, and maintained for a period of 6 months or more. In addition, the patient must not have been hospitalized for their schizophrenia during this period. This definition has been shown to have an excellent agreement (Cohen's kappa value of 0.80) with the Remission in Schizophrenia Working Group definition (Haro et al., 2007a). In order to avoid a bias in favor of patients who entered the study with a good clinical status, symptomatic remission was defined starting at the 6-month visit.

Functional remission was based on good social functioning and was defined at each visit. To achieve functional remission required the patient to fulfill three criteria: (i) positive occupational/vocational status (i.e., paid or unpaid full- or part-time employment, being an active student in university, or housewife); (ii) living independently; and (iii) socially active (i.e., having more than one social contact during the last 4 weeks or having a spouse or partner).

2.2. Statistical analysis

Only patients assessed at all visits or having at most one missing visit were included in the analysis. For patients with one missing visit, values from the previous visit were imputed for that visit ($n=6752$). Of these, 236 (3.5%) had missing information on CGI-SCH ratings and were not included in the analysis. Thus, a total of 6516 patients were included in the analysis.

Baseline characteristics of the study sample were summarized using descriptive statistics. Quality of life (EQ-VAS) and functional remission (percentage of patients in a relationship, living independently, in paid employment, and socially active) at each visit from 12 months onwards were compared with patients in functional remission and not in remission at that visit using Student's t-tests and χ^2 tests.

Based on the above definition of symptomatic remission, patients were also classified into one of three symptomatic remission groups based on their symptomatic remission status over the whole 3-year follow-up period:

i) Those not achieving symptomatic remission at any time during follow-up (no symptomatic remission);
ii) those starting symptomatic remission at 6 months and maintaining symptomatic remission during the 3 years (always symptomatic remission); and