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Adverse effects of antipsychotics and quality of life

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Introduction. New antipsychotics are associated with fewer adverse effects than classical ones. However, an increase in the patient's quality of life is not clear, given the complex relationship between quality of life and schizophrenia.

Objetive. To show there are no real differences in adverse effects and quality of life of schizophrenic patients treated with atypical and typical neuroleptics.

Methods. Cross-sectional study. The sample (78 male and female patients between 18 and 80 years old) was divided into three treatment groups: atypical, typical and both kinds of neuroleptics. Measurement instruments used were Udvalg Für Kliniske Undersogesler (UKU) for adverse effects and Quality of Life Scale (QLS) for quality of life.

Results and conclusions. Treatment with atypical antipsychotic is significantly associated with fewer extrapyramidal adverse effects but not with a better quality of life in the scales applied. Probably quality of life does not only depend on treatment. It may also be affected by other several factors such as negative sympthomatology and a long-term evolution of schizophrenia, which are not included in the quality of life scales used. However, this is a pilot study, in which we have used only a quality of life scale and a small sample chosen without previous sample calculus. Taking this into account, general conclusions on efficacy and global acceptance of antipsychotics cannot be deduced.

Key words:
Schizophrenia. Quality of life. Adverse effects. Neuroleptics. Antipsychotics.

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Efectos adversos de los antipsicóticos y calidad de vida

Introducción. Los nuevos antipsicóticos se asocian con menores efectos secundarios que los clásicos, pero no está claro que proporcionen una mayor calidad de vida (CV) dada la compleja interrelación entre CV y esquizofrenia.

Objetivo. Demostrar la que no existen diferencias reales en los efectos adversos y en la CV de pacientes esquizofrénicos tratados con neurolépticos atípicos y típicos.

Métodos. Estudio transversal en que la población (78 pacientes de ambos sexos entre los 18 y los 80 años) se dividió en tres grupos en función del tratamiento (neurolépticos atípicos, típicos y ambos). Los instrumentos de medida utilizados fueron la *Udvalg Für Kliniske Undersogesler* (UKU) para los efectos secundarios y la *Quality of Life Scale* (QLS) para la CV.

Resultados y conclusiones. El tratamiento con antipsicóticos atípicos se asocia significativamente con menores efectos extrapiramidales, pero no con una mayor CV en las escalas aplicadas. Ello puede deberse a que la CV no sólo depende del tratamiento, sino también de otros factores como la sintomatología negativa o una larga evolución de la enfermedad que no se recogen en las escalas de calidad de vida utilizadas. No obstante, estamos tan sólo ante un estudio preliminar en que sólo hemos utilizado una escala de CV y una muestra pequeña tomada sin cálculo muestral previo, por lo que no pueden extraerse conclusiones generales sobre la eficacia y aceptación global de los antipsicóticos.

Palabras clave:
Esquizofrenia. Calidad de vida. Efectos secundarios. Neurolépticos. Antipsicóticos.

INTRODUCTION

Quality of life (QL) in schizophrenia is now a subject that everyone is talking about and it has clear interest, in spite of the difficulties that its evaluation has in this type of patients[1]. The schizophrenic patient has the problem of the validity of self-evaluations, a characteristic element in the measurement of QL[2]. In this sense, there are apparently opposite opinions which, in the last case, are probably not so different. For example, in 1990, Skantze et al.[3] demonstrated that schizophrenic patients are capable of feeling and communicating

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Table 1 Quality of live assessment instruments in schizophrenia

	QLS	QOLI	SQQL
Conceptual model	Assessment of schizophrenic defect by the clinican	Feeling of personal well being influenced by personal characteristics and QL objective and subjective indicators	Subjective assessment of the disease, its impact and treatment impact
Dimensions	4: intrapsychic function, interpersonal relationships, instrument role (use of common objects) and daily activities	Global satisfaction and others 8: place of residence, daily activities, family, social relationships, economy, work/study, legal situation and health	2: favorable (life satisfaction, harmony and self-esteem) and unfavorable (lack of cognitive understanding, loss of energy, lack of internal control, difficulty of emotional and cognitive expression, alienation, fear of loss of control, contained hostility and automatism)
Type and administration	Specific Heteroadministered	Specific Heteroadministered (self-evaluated)	Specific Self-administered
No. of type	21	143	59
Score	Score of 0 (worse functioning level) to 120 (best functioning)	From 1 (totally unsatisfied) to 7 (totally satisfied)	From 1 (totally in disagreement) to 5 (totally in agreement)
Version in Spanish	Yes	No	Yes

QLS: Quality of Life Scale (Heinrichs et al., 1984); QOLI: Quality of Life Interview (Lehman, 1988); SQQL: Seville Questionnaire on Quality of Life.

their own social deficits. In 1983, Lehman[4] had already demonstrated that, from a methodological point of view, schizophrenic patients may provide statistically reliable data on their QL. Both findings would reinforce the hypothesis that QL may be evaluated subjectively by schizophrenia patients themselves. However, Lehman recommends caution about the validity of the QL evaluations made by serious mental patients, in spite of having demonstrated convergent validity between the QL assessments between the symptoms and the patients[5]. Along this line, Browne et al.[6] comment the need to perform a clinical evaluation of QL along with that made by the patient, since the self-evaluations may be influenced by several factors such as persistent psychotic symptoms, adaptation to adverse circumstances and idiosyncratic factors. In fact, discrepancies in the assessment of QL between the symptoms and the patients have already been reported[7].

Thus, the problem is found in if the judgment made by a serious mental patient (with dementia, or, above, all, delusional in the case in question) may really be considered valid based on the symptoms and, in case of discrepancies, what should be done[4].

In spite of the difficulties, we have several valid and reliable measurement instruments, among which the following may be mentioned as the most important and known (table 1):

- QLS (Quality of Life Scale) of Heinrichs et al.[8]: specific scale, heteroapplied, with international validity and adaptation to Spanish.
- QOLI (Quality of Life Interview): developed by Lehman[9] in 1988. He performs a subjective and objective evaluation of QL, there also being a version in Spanish of Bobes, González and Wallace[10].
- SQQL (Seville Questionnaire on Quality of Life): it performs a subjective evaluation of the altered functions, of the impact of psychopathology and of the treatment side effects[11].

On the other hand, it is clear that schizophrenia causes important limitations in mental, physical and social functioning. It is also clear, practically until now, that the objective of psychiatric treatment has focused on the control of the psychotic symptoms. From the medical and also family point of view, their improvement has been interpreted as an improvement in the patient's condition. In fact, there are data in the literature that support that both the psychotic (especially the negative ones)[12,13] as well as the affective symptoms[14] could be considered predictive of QL. However, it is not clear that the semiological aspect is the most relevant from the patient's perspective and other factors could very well play an important role in the QL of schizophrenic patients[15].

In relationship to the QL and schizophrenia binomial, the results of the studies published supply the following information:

- QL of the schizophrenics is worse than that of the general population and that of patients suffering physical diseases[10].
- Young patients, women, married patients and those who have a low education level have better QL[16,17].
- The greater the disease course time, the worse the QL[18].
- Psychopathology, above all the negative symptoms, is inversely correlated with QL[17,19,20]. On the contrary, other studies demonstrate a scarce correlation between psychopathology and QL[10].
- The patients integrated into the community report better QL than those in an institution[21-27].
- The combination of psychopharmacological and psychotherapeutical treatment improves QL. In this sense, Cohi[28] compares the quality of life of the schizophrenic patients according to three treatment modalities: pharmacological treatment, pharmacological treatment and protected workshop, and pharmacological treatment and rehabilitation center. Performing the evaluation with the QLS scale (Heinrichs et al., 1984), the pharmacological treatment group and protected workshop showed the greatest quality of life level.
- Finally, it seems that the use of neuroleptics with limited side effects such as those of the new generation would also improve QL[29,30].

Specifically referring to antipsychotic treatment, the appearance of atypical neuroleptics has promoted the development of studies on quality of life (QL) of schizophrenic patients under different treatments[2]. Given that they are associated with fewer side effects than the classical ones, it is supposed that they would provide better QL. However, the evidence in this point is limited, since, in fact, QL and schizophrenia maintain a very complex interrelationship in which, as has been seen, different factors participate.

The null hypothesis in the evaluation of QL of schizophrenic patients under treatment with the new atypical antipsychotics would be that, given their better tolerability profile and fewer side effects, they would increase their QL more regarding those patients under treatment with classical antipsychotics. In fact, the Franz et al. studies[31] with clozapine, zotepine and risperidone versus haloperidol and flufenazine, Rosenheck et al.[32] with clozapine versus haloperidol, Revicki et al.[33] with olanzapine versus haloperidol and Hamilton et al.[34] with olanzapine versus placebo and haloperidol, seem to confirm it. However, in the same study of Franz[31], zotepine was not shown to be superior versus haloperidol or flufenazine. Thus, in spite of the indexes on the greater positive effect on QL of atypical antipsychotics, it must be considered that the quality of the evidence varies greatly and is even very limited in some studies. This has led Bobes et al.[2] to recommend caution when basing clinical decisions on these results.

OBJECTIVE

To demonstrate the null hypothesis consisting in the fact that there are no real differences in the adverse effects and in the QL of schizophrenic patients treated with atypical neuroleptics and typical neuroleptics.

METHODOLOGY

Population

88 patients of both genders (n = 88) diagnosed of schizophrenia according to ICD 10 criteria, seen in the Complejo Hospitalario San Luis. The patients came from different health care services: eight patients from Out-patient clinics, 22 from the Acute Unit, 26 from the Mean and Long Stay Units and 31 from intermediate resources (residences and assisted apartments). Of the 88 participants, 10 (from the middle and long stay units and intermediate resources) were excluded due to suffering chronic concomitant somatic diseases. Of the remaining number (78 patients), age ranged from 18 to 80 years, with a mean age of 50.86 years and standard deviation of 15.51. Regarding gender, 23 patients (29.1%) were men and 55 (70.9%) women.

Material

The known and widely used Udvalg Für Kliniske Undersogesler (UKU) scale was used as a measurement instrument of the prevalence of the side effects in our sample. This instrument classifies the possible adverse effects of the medication into three subgroups: neurological, autonomic and other effects.

Choosing the questionnaire to measure QL has major problems since several patients (27) came from middle-long stay hospital units, their chronicity and serious psychopathology, which makes the use of a self-applied scale difficult, standing out. Thus, we decided to use the QLS (Heinrichs et al., 1984): specific scale, heteroapplied, with international validity and adaptation to Spanish. It is based on the evaluation by the clinician of four dimensions: intrapsychic functions, interpersonal relationships, instrumental role (use of common objects) and daily activities. It provides a score for each dimension and a total score that varies in a range of 0 (worse functioning level) to 120 (best functioning level).

Method

It is a cut-off study (cross-sectional) in which the population (n = 78) was divided into three groups based on treatment:

– Group with atypical neuroleptic (including risperidone, clozapine and olanzapine): 35 patients.
– Group with typical neuroleptics (rest of neuroleptics): 31 patients.
– Group with both: 12 patients.

Thus, three variables were defined, one independent and two dependent on the anterior:

– *Independent variable.* Corresponding to the treatment group. The treatment of the patients when the study was performed was that which they had been taking by indication of their psychiatrist and based on their clinical symptoms.
– *Dependent variables.* QL and side effects of each one of the treatment groups.

In order to complete both scales, one or two individual interviews per patients were held. The scales were performed by the psychiatrist or psychologist responsible for each patient.

RESULTS

In order to obtain the intergroup statistical significance, the data analysis was performed with parametric tests (analysis of the variance: ANOVA) based on the arithmetic means obtained for each one of the three patient subgroups in the different dimensions of both scales (UKU and QL of Heinrichs et al.).

In the case of the UKU scale (table 2), the mean scores obtained for each study group (atypical antipsychotics, typical antipsychotics and taking both) are reflected in each subscale (neurological effects, autonomic effects and other effects) with the corresponding standard deviations between parentheses. It is seen that the neurological side effects in the treatment group with atypical neuroleptics (mean: 1.04) are significantly less (p = 0.012) than in the treatment group with typical neuroleptics (mean: 2.56). The sections of autonomic side effects and other effects lack intergroup statistical significance.

Analyzing the results obtained in the QLS scale (table 3), we observe that the treatment group with atypical neuroleptics obtain a mean score in total QL (71.86) and in intrapsychic function (30.97) superior to that of the treatment group with classical neuroleptics (70.87 and 27.90, respectively) and of both neuroleptics (69.42 and 27.67, respectively). However, the differences are far from being statistically significant (p = 0.949 and p = 0.399, respectively). The differences of the scores found in the three treatment groups in the interpersonal relationships and instrumental role subscales also did not show statistical significance.

CONCLUSIONS AND DISCUSSION

As limitations of the study, it should be mentioned that we only have made a preliminary study in which a QL scale is used in a small sample and taken without previous sampling calculation, from diverse origin and with a high number of chronic, institutionalized patients. Thus, the global conclusion obtained that there are no relevant differences in the QL is invalid and this result could not be extrapolated to the schizophrenic population in general.

In any case, according to the data obtained in our study, treatment of schizophrenia with new generation antipsychotics is significantly associated with fewer extrapyramidal adverse effects than treatment with traditional antipsychotics. That is, we could not demonstrate the null hypothesis consisting in that the differences in the adverse effects of the schizophrenic patients under treatment with atypical and typical neuroleptics were due to chance. This result agrees with the data offered repeatedly by the literature.

However, on the contrary to what could be expected, the therapy with these new generation antipsychotics is not as-

Table 2 UKU scale

	Neurological effects	Autonomic effects	Other effects
Atypical neuroleptics group	1.04 (1.33)	0.58 (0.8)	0.87 (0.85)
Typical neuroleptics group	2.56 (2.02)	1.20 (1.32)	0.88 (1.09)
Group of both neuroleptics	2 (1.69)	0.37 (0.51)	0.75 (1.16)
Intergroup statistical significance (ANOVA)	p = 0.012	p = 0.06	p = 0.94

Table 3 QLS scale

	Interpersonal relationships	Instrumental role	Intrapsychic function	Total score
Atypical neuroleptics group	26.57 (9.97)	14.37 (5.34)	30.97 (8.79)	71.86 (20.56)
Typical neuroleptics group	26.03 (10.58)	16.94 (5.47)	27.90 (9.37)	70.87 (22.78)
Group of both neuroleptics	28.08 (11.03)	13.67 (8.12)	27.67 (13.86)	69.42 (30.50)
Intergroup statistical significance (ANOVA)	p = 0.845	p = 0.130	p = 0.399	p = 0.949

sociated with a greater QL (the treatment group with atypical neuroleptics obtained a mean score of total QL and intrapsychic function superior to that of the treatment group with classical neuroleptics, but the differences are not at all statistically significant). In brief, our study would demonstrate the null hypothesis, according to which the differences observed in the QL of schizophrenic patients treated with atypical neuroleptics and typical neuroleptics are due to chance, no real differences thus existing. However, given the preliminary character of the study and the methodological deficiencies previously mentioned, general conclusions cannot be drawn on the efficacy and global acceptation of the antipsychotics.

We believe that the QL constitutes a wide concept that depends on many factors such as the long course of the disease and the negative symptoms, characteristics standing out in our study's population. These and other factors may be as evaluated by the patients as the side effects themselves of the treatment. This is in consequence with the complex interrelationship maintained by QL and schizophrenia, in which, according to the literature[35], several factors participate:

— Common factors with other diseases: chronicity, lack of a totally effective treatment and the adverse effects of the medications.

— Factors characteristic of the disorder: the important incapacity, social stigma that still exists and psychopathology. Regarding the latter, it has been mentioned that the negative syndrome correlates inversely with the quality of life[10].

That is, at least in certain populations, it is possible that there is no direct cause-effect relationship between QL and the side effects of the antipsychotics. Our results would be along the line of those obtained by Franz[31] in regards to zotepine, an atypical neuroleptic that was not shown to be superior to haloperidol or flufenazine. Thus, we totally agree with some authors[2] when they recommend caution when basing clinical decisions on the results provided by the different studies carried out up to now on QL and type of antipsychotic treatment used.

We are presently analyzing other variables that could influence the QL of our patient population, variables such as disease course time, type of residence (family home, intermediate resources or long stay units), possible consumption of toxics or not, seriousness of the psychopathology or cognitive deterioration, among others. In any case, we consider the performance of new studies in larger populations to be of interest.

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