Seven years of treatment with quetiapine: a case report

Sette anni di trattamento con quetiapina: a case report

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Summary. Introduction. We present the case of a 34-year old man who was affected at the age of 20 by a "paranoid-type schizophrenia". He was treated for years, unsuccessfully, with conventional neuroleptics. **Method.** At the age of 27 years the patient began treatment with quetiapine, in the context of a research protocol being carried out at the Psychiatric Department of the University of Turin. Given the positive and indeed curative therapeutic effects of the treatment, it was decided to continue the treatment beyond the period of the trial (52 weeks). The quetiapine was first requested from the manufacturer for compassionate use; later the Ministry of Health was asked to authorize the import of this compound from Great Britain, a country in which quetiapine was already registered for use and available on the market. Finally, the drug also became commercially available in Italy (May 2000), so the therapy could be continued and maintained at all times using the same dose regimen. **Result and conclusion.** The treatment had good results and is still going on.

KEY WORDS: schizophrenia, atypical antipsycotics, quetiapine.

RIASSUNTO. Introduzione. Il presente lavoro riporta il caso di un ragazzo 34enne affetto, sin dall'età di 20 anni, da "schizofrenia di tipo paranoide", già trattato per anni, ma senza successo, con neurolettici tipici. **Metodo.** All'età di 27 anni il soggetto è stato sottoposto a trattamento con quetiapina, nell'ambito di un protocollo di ricerca condotto presso la Clinica Psichiatrica dell'Università di Torino. Valutati i positivi e risolutivi effetti terapeutici, si è deciso per la prosecuzione di tale terapia anche oltre i tempi previsti dalla sperimentazione (52 settimane). Dapprima è stato chiesto l'uso compassionevole della quetiapina all'azienda produttrice, successivamente è stata richiesta l'autorizzazione al Ministero della Sanità per l'importazione del farmaco dalla Gran Bretagna, Paese nel quale la quetiapina era già registrata e regolarmente in commercio. Infine, una volta avvenuta l'introduzione del farmaco anche in Italia (maggio 2000), si è provveduto alla continuazione ed al mantenimento, tuttora in corso, della terapia in atto, sempre con la medesima posologia. **Risultato e conclusione.** Il trattamento ha avuto buoni risultati.

PAROLE CHIAVE: schizofrenia, antipsicotici atipici, quetiapina.

INTRODUCTION

Schizophrenia affects about 1% of the population at some time in their life[1,2], with the clinical picture being made up of positive symptoms (such as delusions and hallucinations), negative symptoms (such as social and emotional withdrawal, apathy) and cognitive symptoms (such as deficits of memory, concentration and performing functions). The possible deterioration in personality which occurs in the more severe forms leads, over time, to a progressive loss of the capacity to relate to the external world. This has devastating consequences for the individual and his or her family and creates an onerous financial burden for society[3].

Psychopharmacological treatment of schizophrenia was introduced in the 1950s when the so-called "conventional" or "typical" antipsychotics became available. These drugs were an enormous progress in the treatment of schizophrenia, the management of which had been based, up till then, almost completely or indeed entirely on longterm hospitalization in institutions.

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Although the above-mentioned drugs provide a partial improvement in the 'positive' symptomology of the disease, thus allowing patients to return to the community, they are not equally effective on altering the other psychopathological feactures of the disease (negative symptoms, cognitive deficits, concomitant disorders of mood). Furthermore, the onset of side effects, especially those affecting the extrapyramidal nervous system, leads to a notable decrease in therapeutic compliance, with frequent recurrences, new admissions to hospital and, in any case, a poor overall quality of life. These drawbacks of conventional antipsychotics spurred the search for new drugs which could be used. The second generation of antipsychotics, introduced in the 1990s and inappropriately called "atypical", increased the therapeutic armamentarium for the treatment of schizophrenia. Furthermore, besides being shown, both in daily clinical use and in the majority of controlled clinical trials, to be more effective and have a better clinical safety profile (especially in terms of neuromotor and endocrine tolerability) than the conventional antipsychotics, these second generation drugs have considerable advantages for the rehabilitation aspects of the disease.

Quetiapine is one of the second generation antipsychotics that has most recently become available[4-7]. The following case report describes a patient treated continuously with this drugs for seven years.

CASE REPORT

P.G. is a 34-year old man, an only child with a positive family history of mental disorders on both the maternal and paternal side (his father had a bipolar disorder and lived in an institute for many years until his death, his mother had a psychotic disorder and committed suicide after a long period of disease).

There were no significant psychopathological episodes in the patient's personal history. He had a normal childhood and completed high school education with a good outcome, demonstrating a good level of intelligence and cognitive powers.

His psychopathological disorder first became manifest at the age of 20 years old when he was doing his military service and was characterized by a dissociative-like episode, accompanied by confusion, spatio-temporal disorientation, loss of appetite and a feeling of being of observed.

He was admitted to the local Psychiatry Department (SPDC), where he presented florid symptoms of auditory hallucinations, persecutory delusions, disorganized speech (with frequent changes in train of thought and incoherence), and blunted affect. The discharge diagnosis was 'paranoid-type schizophrenia". He was treated with haloperidol, orfenadrine, promazine and flurazepam, but these had very little effect on his symptoms and indeed he needed to be readmitted to the SPDC after only one month.

From then on the patient was treated with regimes based on conventional antipsychotic drugs, at standard therapeutic doses. He obtained a partial response in that the 'positive' factures of his disorder improved (in particular the hallucinatory component), but the negative symptoms progressively worsened (thought impoverishment, apathy, progressive social withdrawal, flattened affect, difficulty in undertaking any type of initiative). Furthermore, the thought disturbances continued, albeit more sporadically, showing a loosening of associations and persecutory ideation.

Since then the patient has been followed up by the Area Community Psychiatric Service; the partial loss of autonomy and the persistence of the symptoms described above led the patient to withdraw progressively from social and occupational activities, such that he was housed in a protected hostel and, at the same time, a request was made for him to be recognized as having an 80% permanent reduction in working capacity and thus be entitled to an invalidity pension.

At the age of 27 years the patient was admitted to the Psychiatry Department of the University of Turin with symptoms characterized by a tendency to social withdrawal, poverty of ideation and affect, apathy, blunted ideokinesis, difficulty in undertaking any initiatives, and formal disturbances of thought. He was enrolled in a research protocol entitled: "A multicentre, double-blind, randomised, comparison trial of the dose and posology of Seroquel in the treatment of patients with acute exacerbations of chronic or subchronic schizophrenia".

The aims of the study were to compare the efficacy of a total daily dose of 450 mg quetiapine administered in two doses (225 mg bid) vs. in three doses (150 mg tid) and vs. 50 mg/die in two doses (25 mg bid), for a period of six weeks, in subjects with acute exacerbations of chronic or subchronic schizophrenia (BPRS at baseline $\geq$ 27).

The protocol allowed for optional continuation of the quetiapine treatment for 52 weeks (at this point the treatment was no longer double-blind) in those patients who had completed the first phase of the study.

The psychiatric evaluations during the study were made using the BPRS and SANS, while possible neurological side effects were assessed by the AIMS and Simpson Angus Scale. Evaluations were carried out at baseline and 4, 6, 12, 24, 36 and 52 weeks of treatment.

Already by 4 weeks the patient showed a notable improvement in symptoms without, however, reaching complete remission of negative symptoms (he was left with a loosening of associations and, at times, a tendency to blunted affect). The results of the evaluations are reported in **Table 1.**

As far as concerns undesired neurological side effects, both the AIMS scale and the Simpson Angus Scale were negative throughout the trial.

Table 1. Trend in BPRS and SANS at the different evaluations.

Time (weeks)	BPRS	SANS
0	48	15
4	44	13
6	39	12
12	36	10
24	34	8
36	32	7
52	30	6

The patient had a substantial clinical improvement, associated with a marked recovery of socialization, relationships and working capacity. Indeed, it became possible for the patient to be included in a grant-employment scheme run by Turin Commune (as apprentice in the library of the Faculty of Biology of the local University), and to arrange his gradual return to living in his own property, once shared with his parents, in the company of his girlfriend.

This improved clinical situation suggested that the theraphy be continued beyond the limits laid down by the trial protocol. We, therefore, first asked the manufacturing company to provide the drug on the grounds of compassionate use (as it was not then commercially available), and subsequently asked the Ministery of Health to authorize importation of the drug from a European Community country (Great Britain) in which quetiapine, had in the meantime, been introduced onto the market. Since then the drug has become commercially available also in Italy (May 2000) and so the patient has been able to continue his treatment with quetiapine 400 mg/die at all times. He undergoes regular outpatient follow-up evaluations which show that he has maintained the clinical results achieved during the 52 weeks of the trial protocol. His full blood counts, thyroid function and main vital signs are also monitored regularly.

The patient has not required further admission to any public or private neuropsychiatric structure during these years of treatment. He completed the above described employment scheme with success and has continued, albeit with the difficulties inherent in the situation, management of his house and cohabitation with his girlfriend.

The patient is receiving treatment with the same dose of quetiapine.

CONCLUSIONS

Schizophrenia is a serious and disabling disease with high direct and indirect individual and social costs. This picture is aggravated by the fact that most subjects with schizophrenia have a chronic disease which needs long-term management and assistance.

Pharmacological treatment has a particular role in both the acute and long-term management of the disorder; its clinical efficacy is influenced not only by the activity of the drug, but also by its tolerability, the patient's willingness to comply with the treatment schedule, the prevention of recurrences, subjective well-being, the patient's satisfaction, quality of life and maintenance of good social relatioships.

The evaluation of antipsychotic drugs in based on short periods of observation (6-8 weeks) which principally allow the effect of the treatment on the psychotic symptoms to be assessed. Extending studies for periods (e.g. 52 weeks), permits evaluation of whether the effects on symptoms are maintained and evaluation of some of the initial consequences for the patient' life. Indeed, only long periods of observation can offer full information on the overall therapeutic role of a drug. In fact, the most important advantage of treatment is that of a possible social reintegration of the patient with recovery of a quality of life similar to that before the onset of the disorder and in any case compatible with a satisfactory degree of autonomy in the context of functions of daily life.

The interesting point of this case report is that it covers a 7-year period during which the patient has remained on a stable dose of the antipsychotic drug, allowing correlations to be made between the therapy used the patient's clinical history.

In particular, quetiapine has been shown to remain effective and active for long periods, offering good control of psychotic symptoms at the same dose that was effectice in the acute treatment.

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