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Switching to quetiapine fumarate monotherapy for treatment-resistant schizophrenia: A report of five cases

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We assessed the efficacy and tolerance of switching to monotherapy with quetiapine fumarate (QF) in treatment-resistant schizophrenia with other antipsychotics, including atypical ones. QF treatment was maintained for 8 weeks. The PANSS scores improved at least 40% over this period. QF was well tolerated without the presence of serious adverse effects. Switching to QF in these patients may therefore be considered as optimal in response and tolerance.

Key words:
Schizophrenia, Treatment-resistant, Antipsychotics, Quetiapine fumarate

Actas Esp Psiquiatr 2011;39(5):336-8

Cambio a monoterapia con fumarato de quetiapina en la esquizofrenia resistente al tratamiento: A propósito de cinco casos

Se ha evaluado la eficacia y tolerancia del cambio a monoterapia con fumarato de quetiapina (FQ) en la esquizofrenia resistente al tratamiento previo con otros antipsicóticos, uno de ellos atípico. El tratamiento con FQ se mantuvo durante 8 semanas. Las puntuaciones de la PANSS mejoraron al menos un 40% en este periodo. El FQ fue bien tolerado sin la presencia de efectos adversos relevantes. El cambio a FQ en estos pacientes puede por tanto considerarse como óptimo en respuesta y tolerancia.

Palabras clave:
Esquizofrenia, Resistencia al tratamiento, Antipsicóticos, Fumarato de quetiapina

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INTRODUCTION

It is estimated that approximately 40% of patients with schizophrenia do not respond to conventional antipsychotic treatment.¹ Clozapine, the gold standard for treatment-resistant schizophrenia is effective in only half of these patients.² In addition, it is known that the use of clozapine is limited by its potentially serious side effects, such as agranulocytosis or seizures, that require monitoring. That is why it is very interesting to evaluate efficacy and safety of atypical antipsychotics other than clozapine in treatment-resistant schizophrenia. Recent guidelines for treatment-resistant schizophrenia recommend attempting at least one atypical antipsychotic before initiating treatment with clozapine.^{3, 4, 5}

Quetiapine fumarate (QF), a derivative of the substituted benzamide, is an atypical antipsychotic with high affinity for 5HT_{2A} serotonin receptors and D₁ and D₂ dopamine receptors. The efficacy and tolerability of QF has widely demonstrated in the treatment of schizophrenia.⁶ Therefore, it would be of great interest to also know its efficacy in the treatment of previous treatment resistances, as an alternative to clozapine.

METHODOLOGY

We present a series of 5 cases of male patients who were nonresponders to treatment with two antipsychotics, at least one of which was atypical, at the recommended doses and times.¹ The patients were selected consecutively from a Mental Health Rehabilitation Unit. All the patients gave their consent to participate in the study. At the time of their incorporation into the study, the antipsychotic treatment of the patients included different conventional antipsychotics or atypical antipsychotics in monotherapy or in combination (table 1). Only benzodiazepines were accepted as concomitant medication. The baseline antipsychotic medication was reduced progressively during 11.5 ± 4.1 days. QF was gradually introduced during the

Table 1	Baseline psychopharmacological treatment				
Patient	1	2	3	4	5
Previous antipsychotic and concomitant treatment	Risperidone 9 mg/day + Clonazepam 3 mg/day	Olanzapine 20 mg/day + Zuclopenthixol depot 1 amp i.m. e/21 days	Risperidone 6 mg/day + Clozapine 300 mg/day	Amisulpride 1200 mg/day + Lorazepam 7.5 mg/day	Olanzapine 30 mg/day + Clonazepam 6 mg/day

Tabla 2	Baseline scores and scores at end of the 8 weeks in monotherapy with QF					
Patient		1	2	3	4	5
PANSS-t	BS	135	116	116	111	108
	FS	68	74	74	72	49
PANSS-p	BS	34	40	34	38	32
	FS	17	23	19	20	11
PANSS-n	BS	41	27	31	33	25
	FS	25	16	28	28	13
PANSS-pg	BS	60	49	46	72	51
	FS	35	35	34	50	25

PANSS: Positive and Negative Syndrome Scale; t: total; p: positive; n: negative; pg: general psychopathology. BS: baseline score. FS: final score.

crossed tapering period at doses of 600 mg/day \pm 183.8 mg/day. Treatment with QF in monotherapy was continued for the following 8 weeks.

The clinical status of the patients was evaluated at the baseline visit, before decreasing the previous antipsychotic agent, and at the end of the trial, after 8 weeks of monotherapy with QF. The Positive and Negative Symptoms Scale (PANSS)⁷ and its subscales (positive, negative and general psychopathology) were used. Response criteria were considered to be a decrease of at least 30% in the total score of the PANSS from the baseline visit to the end of the 8 weeks of monotherapy with QF. The Wilcoxon (signed-ranked) test for paired data was used for the statistical analysis.

RESULTS

Mean age of the patients was 35.6 years \pm 8 years, mean duration of disease 11.2 years \pm 7.1 years and mean number of previous hospitalizations 2.9 \pm 2.1. Four of the patients had never received treatment with clozapine and the

remaining patients had received treatment with clozapine for 8 months with doses under 300 mg/day.

A 40% decrease in the total score of the PANSS was seen in four of the patients and 50% in the remaining patients. The subscales of the positive, negative and general psychopathology PANSS decreased by more than 30% in all of the patients (table 2). All of the differences were statistically significant ($p < 0.05$). QF was well tolerated without the presence of relevant adverse effects. In two of the patients, somnolence and sedation having mild to moderate intensity appeared.

DISCUSSION AND CONCLUSION

Given the good results obtained, the hypothesis is suggested that QF could be, as previous treatment to the use of clozapine, a good strategy in monotherapy in patients with resistant schizophrenia. In spite of the clear methodological limitations of a case series, the improvement experienced by the patients, the "wash-out" of the drug on the neurochemical

level and the absence of relevant undesired effects would support, in our opinion, the performance of controlled clinical trials to document the efficacy of QF as an alternative to clozapine and other atypical antipsychotics in treatment-resistant schizophrenia.

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