P.2.115 Effectiveness and safety of olanzapine versus conventional antipsychotics in the treatment of inpatient with acute schizophrenia: A multivariate analysis

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Objective: The aim of this study was to assess the real benefit provided by olanzapine compared to conventional antipsychotics in the daily clinical treatment of acute exacerbations of schizophrenia at in-patient units.

Methods: This report consists of a reanalysis of the data from a larger, prospective, comparative, non-randomized, open and observational study (EUROPA1), using a multivariate methodology in order to control all the variables affecting final results. The sample population was composed by acutely exacerbated inpatients with schizophrenia (ICD-10) assigned to olanzapine in monotherapy (Olanzapine Group=OG; n=339) or a conventional antipsychotic in monotherapy (Control Group=CG; n=385) following clinical criteria. Clinical status was assessed weekly until discharge through the Clinical Global Impression-Severity (CGI-S) and Brief Psychiatric Rating (BPRS) scales. An abbreviated questionnaire based on the section of extrapyramidal symptoms (EPS) of the UKU scale was used to detect EPS. Treatment-response was defined as a $\geqslant$40% decrease from baseline in BPRS total score plus an endpoint BPRS score<18 or a an endpoint CGI-S score $\leqslant$3.

Results: Patients in the CG were slightly but significantly older than the olanzapine-treated patients (37.4 vs 35.0; t-test, p=0.004) and had significantly higher baseline scores in BPRS total (45.4 vs 42.7; t-test, p=0.004), positive (15.3 vs 14.1; t-test, p<0.001) and agitation items (15.2 vs 13.2; t-test, p<0.001) and CGI-S scale (61.6% vs 38.4% severe; Chi2, p=0.006). Both treatment groups were similar in other relevant baseline variables. Treatment-response was significantly higher in the OG (72.9%) compared to CG (62.8%) after controlling by age, baseline CGI-S and BPRS total scores, presence of agitation and positive symptoms (logistic regression model, Chi2=6.1; p=0.014). Patients in OG presented 51.2% more chance to response than those in CG (RR=1.51 CI95%[1.1; 2.1]). Mean initial dose in OG was 14.1 mg, whereas throughout the study modal mean dose was raised to 16.6 mg. Although no association between a higher dose of olanzapine and response could be established, a higher percentage of patients were taking 20 mg o more at discharge (52.9%) than initially (36.2%). A statistically significant association between response and absence of EPS was detected in the OG (Cochran-Mantel-Haenzsel test controlling by CGI-S, p=0.002), whereas no association could be detected in the CG (Cochran-Mantel-Haenzsel test controlling by CGI-S, p=0.474) [Table 1]

Regarding the incidence of general adverse events, OG showed better tolerance than CG: 23.3% vs 54.6% (weight gain: 1.8% vs 0.3%).

Conclusion: Olanzapine in monotherapy was effective in a non-selected sample of acutely hospitalized schizophrenic inpatients even when controlling by severity variables. Furthermore, olanzapine showed a favorable safety profile with lower incidence of EPS than conventional antipsychotics.

Table 1

Severity	Conventional antipsychotics (n=385)	Olanzapine (n=339)
Mild (CGI-S$\leqslant$3)	51.3%	68.9%
Moderate (CGI-S=4–5)	30.5%	67.5%
Severe (CGI-S$\geqslant$6)	33.6%	64.0%
Total	37.8%	67.2%

Each cell represents the percentage of treatment-responder patients without new EPS.

References

[1] A. Ciudad, JC Gómez, E Alvarez, J. Bobes, F. Cañas, J.L. Carrasco. Effectiveness and Safety of different treatment regimens of Olanzapine in the Treatment of Inpatients with Schizophrenia. Schizophrenia Research Vol. 49 No. 1–2, supplement, 15 April 2001, page S222.

P.2.116 Increased rates of antipsychotic-induced EPS in mood disorders: Myth or reality?

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Objective: Extrapyramidal symptoms (EPS) limit the use of typical antipsychotic agents for treating bipolar disorder. In fact, several studies suggest increased EPS vulnerability in patients with bipolar disorder compared to those with schizophrenia. The purpose of this study was to determine antipsychotic-induced EPS vulnerability in these two patient populations.

Methods: Acute EPS profiles of olanzapine (5–20 mg/d, n=125) and placebo (n=129) were compared in two randomized double-blind trials of patients with bipolar disorder (manic/mixed). The EPS profiles of olanzapine (5–20 mg/d, n=234) and haloperidol (3–15 mg/d, n=219) also were compared in a clinical trial of similarly diagnosed patients. Patients were monitored weekly by three methods of EPS assessment: 1) detection of extrapyramidal adverse events (signs and symptoms) by casual observation, non-probing inquiry, and spontaneous report; 2) objective rating scale scores; and 3) use of concomitant anticholinergic medications.

Results: The placebo and olanzapine groups in the bipolar studies exhibited EPS profiles similar to like-treated patients with schizophrenia whereas, the haloperidol group in the bipolar studies exhibited a greater incidence of parkinsonian events than patients with schizophrenia. These results were supported by analysis of mean baseline to endpoint changes and categorical analysis of the Simpson-Angus scale. Interestingly, the increased susceptibility of patients with bipolar disorder to haloperidol-induced EPS occurs in spite of significantly higher mean modal doses of haloperidol in the schizophrenia studies and olanzapine in the bipolar studies.

Conclusions: These findings support the observation of increased EPS vulnerability in bipolar patients treated with conventional antipsychotics. However, this does not appear to be the case for olanzapine, which had placebo-like rates of EPS across both schizophrenia and bipolar disorder trials.