The effectiveness and safety of amisulpride in Chinese patients with schizophrenia: An 8-week, prospective, open-label, multicenter, single-arm study

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Keywords
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Abstract
Introduction: This study evaluated the effectiveness and safety of amisulpride in Chinese schizophrenia patients.
Methods: A multicenter, single-arm Phase IV study (NCT01795183). Chinese patients with schizophrenia received amisulpride for 8 weeks. The primary endpoint was ≥50% decrease in Positive and Negative Syndrome Scale total score from Baseline to Week 8.
Results: A total of 316 patients were enrolled; 295 were included in the effectiveness analysis; 66.8% (197/295) achieved ≥50% decrease in Positive and Negative Syndrome Scale total score from Baseline to Week 8. Nine patients discontinued treatment because of adverse events.
Discussion: Amisulpride had clinical effectiveness and was relatively well tolerated in Chinese patients with schizophrenia.
designed in order to assess the effectiveness and safety of amisulpride in Chinese patients with schizophrenia.

Methods

Study design and patients

This 8-week, prospective, multicenter, single-arm Phase IV study was conducted at 13 psychiatric-specialist Tier 1 hospitals in China between 30 October 2012 and 3 December 2013. Adults (18–65 years) who met the ICD-10 criteria for schizophrenia, and had a Positive and Negative Syndrome Scale (PANSS) total score ≥60, were eligible for inclusion. Enrollment included patients treated as inpatients and outpatients. The study was conducted in accordance with the principles of the declaration of Helsinki and received ethical approval from local institutional ethics review boards at all participating centers. Written informed consent was obtained from all study subjects. The study was registered at ClinicalTrials.gov (NCT01795183).

Treatment

After a screening phase, amisulpride tablets (50 mg/tablet) were administered orally for 8 weeks; dosing and titration were in accordance with the approved Chinese labeling (http://drugs.medlive.cn/drugref/html/15330.shtml. Accessed October 2015). In patients switching from other antipsychotics (because of suboptimal treatment response or unacceptable adverse events [AEs]), the dose of the previous medication was gradually reduced upon initiation of amisulpride, with the aim of complete discontinuation within 1 week.

Measurements

The primary effectiveness endpoint was a ≥50% decrease in PANSS total score from Baseline to Week 8. Two subgroup analyses were conducted: in treatment-naive patients versus patients who were switched to amisulpride, and in patients with predominantly positive versus predominantly negative symptoms. Safety data were continuously monitored from Baseline to the end of the study. Blood samples for prolactin level testing were taken from patients in the morning before breakfast.

Statistics

Using an estimate that 60% of patients would achieve a ≥50% improvement in PANSS total score after 8 weeks, enrollment of 300 patients would provide a 95% confidence interval of 53.64% to 66.12%, accounting for a 16% dropout rate. (Kuang et al., 2009)

All statistical analyses and treatment effects were tested at a two-sided significance level of 0.05. Statistical Analytic System software version 9.2 (SAS Institute, Cary, North Carolina, USA) was used to perform all statistical analyses.

Results

In total, 316 patients were enrolled, and 251 completed the 8-week study. Among patients in the effectiveness analysis, 66.8% (197/295) achieved the primary endpoint (Table 1). An early clinical response (≥20% improvement in PANSS total score after 2 weeks of treatment) was achieved by 56.6% of patients.

A similar proportion of the treatment-naive and previously treated patients achieved a ≥50% decrease in PANSS total score from Baseline to Week 8 (68.6% versus 66.2%) (Table 1). Among the 266 patients with predominantly positive symptoms, 68.4% achieved a ≥50% decrease in PANSS total score by Week 8. Of the 26 patients with predominantly negative symptoms, 50.0% achieved a ≥50% decrease in PANSS total score at Week 8.

A total of nine (3.1%) patients withdrew from the study because of an adverse reaction, and one patient experienced a serious AE (suicide attempt), which the investigator judged was not related to the study treatment. The incidence of drug-related, treatment-emergent AEs was 58.9% (186/316) (Table 1).

Discussion

The results of this single-arm study show that 8-week treatment with amisulpride effectively improved the clinical symptoms of Chinese patients with schizophrenia; approximately two thirds (66.8%) of patients achieved a ≥50% decrease in PANSS total score from Baseline to Week 8. In addition, a rapid response to amisulpride treatment was observed in the majority of patients; 56.6% of study subjects achieved a ≥20% improvement in PANSS total score from Baseline to Week 2. Interestingly, results of a subgroup analysis suggested that amisulpride is equally effective for treatment-naive schizophrenia patients and those who switch to amisulpride from other antipsychotics.

Although a direct comparison of this study with previous research is difficult, because of variability in study duration, enrolment criteria, and assessment variables, the effectiveness results broadly support several prior studies conducted in other countries. (Carriere et al., 2000; Sechter et al., 2002; Mortimer et al., 2004) The incidence of extrapyramidal side effects reported in the present study (25.9%) is comparable with two...
previous reports (23% and 13%) (Carriere et al., 2000; Colonna et al., 2000).

The primary limitation of this study was that patients with predominantly positive symptoms accounted for the majority of the patients included, which may limit the generalizability of the results.

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### Contributorship statements

All authors drafted or revised the work for intellectual content and approved the final version. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately
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