lead to violence, either directed towards the patient or to others and may result in significant physical, psychological, social and financial consequences. Quetiapine ('Seroquel'), an effective antipsychotic with no greater EPS than placebo across the full dose range, represents an advance in the treatment of psychotic disorders. In a clinical trial comparing five fixed doses of quetiapine with both haloperidol and placebo, aggression and hostility were assessed using the BPRS Factor V score (hostility, excitement, suspiciousness, unco-operativeness) and BPRS hostility item. A specific beneficial effect on the measures of hostility and aggression was evident in all quetiapine treatment groups, reaching statistical significance at 150 mg, 300 mg and 600 mg. This was not the case with haloperidol. In an analyses of responder rates (defined as >40% reduction in BPRS) a significantly greater proportion of patients receiving quetiapine responded over the dose range 150 mg to 750 mg than with placebo. These results provide initial evidence that quetiapine is effective in the treatment of aggression and hostility in patients with acute exacerbations of schizophrenia. With its favourable tolerability profile across the dose range, combined with proven efficacy in the treatment of positive, negative and affective symptoms, quetiapine may present a valuable option for the first-line treatment of schizophrenia and other psychotic disorders.

CHLORPROMAZINE VERSUS PLACEBO FOR THE TREATMENT OF SCHIZOPHRENIA: A SYMSTEMATIC REVIEW

B. Thornley, C.E. Adams, A.G. Awad

Cochrane Schizophrenia Group, Summertown Pavilion, Middle Way, Summertown, Oxford, OX2 7LG, UK

Background: Chlorpromazine, first introduced in 1952 for schizophrenia, is still widely used throughout the world, especially in developing countries. It is also a common benchmark comparison for new treatments in randomised controlled trials. However, if a clinician was asked by somebody with schizophrenia, 'Can you clearly describe my chances of being well, and not suffering side effects such as movement disorders in 6 month's time if I regularly take chlorpromazine?', what would be the answer? Quantitative, systematic and up-to-date reviews of this benchmark treatment are conspicuously absent from the literature.

Methods: Randomised placebo-controlled trials of chlorpromazine for schizophrenia, reporting clinical outcomes, were identified by methodically searching multiple electronic databases. Additional trials were sought by examining references, contacting authors, and writing to pharmaceutical companies. Articles were inspected by two reviewers, and assessed for relevance and quality. Data were extracted, and an intention-to-treat analyses undertaken.

Results: Electronic searches identified over 600 reports of studies. 227 were ordered. 139 were excluded, 72 had data extracted for inclusion in the quantitative analysis and 16 await assessment. Nearly half a century after its introduction as a drug for schizophrenia, this meta-analysis produces clear data on chlorpromazine's efficacy and side effects. Judicious use of this best available evidence will, at last, allow the questions of those with schizophrenia, or their carers, to be answered.

ACUTE AND LONG-TERM EFFICACY AND SAFETY OF ARIPIPRAZOLE: A NEW ATYPICAL ANTIPSYCHOTIC

J.L. Petrie*, A.R. Saha, J.P. McEvoy

**Otsuka America Pharmaceutical, CNS R&D, 2440 Research Blvd., Rockville, MD 20850, USA*

Aripiprazole is a unique atypical antipsychotic, now starting Phase-3 development. A unique feature of aripiprazole is its agonist effect at pre-synaptic dopamine autoreceptors, yet it also has post-synaptic antagonist effect at D_2 and 5-HT_2 receptors. This profile may be responsible for the impressive clinical effectiveness and tolerability seen thus far.

We report the basic efficacy and tolerability results from Phase-2. Two double-blind, 4-week studies enrolled 410 acutely relapsing hospitalized schizophrenic patients. In study 31-93-202, aripiprazole was titrated to 30 mg over 13 days, while in study 31-94-202 patients received a fixed dose of 2, 10, or 30 mg/day from the start. From these two studies, 143 patients participated in the ongoing, follow-on, open-label, outpatient study 31-95-201, in which all patients receive aripiprazole, with a maximum dose of 30 mg/day.

The fixed-dose study showed that 30 mg could be given without titration. The 30-mg dose showed significant effect on all assessments (including PANSS-Negative score) starting at week-1 evaluations. The 10-mg and 2-mg doses showed effect on many assessments, but not on all (and not on PANSS-Negative), starting at week 2 or week 3. All doses were well tolerated, with aripiprazole patients reporting adverse events about the same as 99 placebo patients. Specifically, there was no increased prolactin, weight gain, cardiovascular or neurologic effects, anticholinergic complaints or sedation. Preliminary results from the ongoing open-label study show no additional types of adverse events, and no evidence of delayed-onset cardiovascular or neurologic toxicity, or weight gain.

CHANGES IN PSYCHOPHARMACOLOGICAL TREATMENT STRATEGIES IN SCHIZOPHRENIA—INPATIENT TREATMENT 1989 VS. 1995

M. Kurz*, A. Hausmann, M. Honeder, G. Kemmler, I. Kurzthaler, T. Walch, H. Wechdorn, W.W. Fleischhacker

**Department of Biological Psychiatry, Innsbruck University Clinics, Anichstrasse 35, A-6020 Innsbruck, Austria*

The development of novel antipsychotics and an increasing international consensus about treatment strategies in schizo-

phrenia have been the most progressive steps concerning the pharmacological treatment of schizophrenia in the last few years. We investigated whether there was a measurable effect on in-patient treatment strategies in our hospital by collecting data from patient records of schizophrenic in-patients in the years 1989 and 1995. We present data from 138 in-patients (1989, $n=58$, 1995, $n=80$). The main changes from 1989-1995 concerned preferences for antipsychotics and dose: in 1989 haloperidol was the most common first-choice drug (50%) followed by clozapine (32.8%), while in 1995 risperidone was leading as first-choice antipsychotic (31.3%) followed by haloperidol (25.5%) and clozapine (18.8%). The mean daily dose of haloperidol was about 24 mg/d in 1989 and 15 mg/d in 1995, in the case of clozapine the dose decreased from 285 mg/d in 1989 to 262 mg/d in 1995. The duration of treatment with these first-choice drugs was about 21 days in 1989 vs. 24 days in 1995. There was also a significant reduction of two different antipsychotics during in-patient treatment. The differences in drug use and dose were similar when investigating medication at the time of hospital discharge.

The development of new antipsychotics as well as in the guidelines concerning treatment strategies had specific effects on the in-patient treatment of patients with schizophrenia in our hospital. These were especially evident in terms of drug selection, antipsychotic monotherapy and administration of lower doses.

NEGATIVE SYMPTOMS AND QUALITY OF LIFE IN SCHIZOPHRENIA–RESPONSE TO LOW DOSE NEUROLEPTIC: LESSONS FROM A CLINICAL TRIAL

A.G. Awad, Y.D. Lapierre, C. Angus, A. Rylander, Canadian Remoxipride Study and the Canadian Remoxipride Group

The Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, M5T 1R8, Canada

Several studies reported superiority in response of negative symptoms and quality of life (QOL) with atypical neuroleptics compared to haloperidol. In a previous study, remoxipride (withdrawn due to serious side-effect; aplastic anaemia), was found to be as effective as haloperidol in the treatment of acute psychotic symptoms of schizophrenia, with more improvement in negative symptoms, and lower EPS. This observation led to the design of a long-term (28 weeks) double-blind study to compare the therapeutic effects of the atypical remoxipride with lower doses of haloperidol in the treatment of negative symptoms as well as impact on QOL.

The sample included 205 patients with the diagnosis of schizophrenia and predominant negative symptoms.

Employing a lower dose of haloperidol as the comparator (mean 10.4 mg) than in the previous study, there was no significant difference between both treatment groups in the response of negative symptoms (49.4% versus 47.6% for remoxipride and haloperidol groups). Similarly, there was no significant difference in the number or severity of EPS. QOL data revealed that the distribution of change in QOL showed no statistically significant differences between the two treatment groups, either at the baseline or at the end of the study.

Our data leads to the following conclusions: (1) Small doses of a conventional neuroleptic, haloperidol, can produce improvement in negative symptoms and QOL, comparable to results with the atypical remoxipride. (2) Clinical trials of new atypical neuroleptics have to employ a dose range of the neuroleptic comparator. (3) Our QOL data demonstrates the feasibility of including QOL measures as an outcome in clinical trials of new neuroleptics.

AN AUDIT OF THE USE OF HIGH DOSE NEUROLEPTICS IN TREATING SCHIZOPHRENIA

P.J. Tyson, A. Mortimer, J.A. Wheeler

The University of Hull, Department of Psychiatry, East Riding Campus, Beverley Road, Willerby, Hull HU10 6ED, UK

Neuroleptic medication provides effective remediation from the florid psychotic symptoms observed in schizophrenia. Despite the success of such treatment, concern has arisen that some patients are treated with doses of antipsychotic medication which are above the recommended guidelines for dose schedules in the *British National Formulary* (BNF). There are serious health concerns for such practices: patients experience many more side effects and in some cases risk sudden cardiac death. To minimise these dangers, the Royal College of Psychiatrists produced guidelines which spell out alternatives to high doses, and 11 precautions to be taken if high doses are to be used.

In order to evaluate prescribing practice in light of these guidelines, an audit was undertaken to investigate the use of high dose neuroleptics in treating schizophrenia in Hull and Holderness Community Health NHS Trust. Patients in contact with mental health services with a diagnosis of schizophrenia were ascertained from patient information systems. Neuroleptic medication was recorded from case notes and converted to chlorpromazine equivalents, and percentage of maximum recommended dose. The management of patients on high doses was compared with that recommended by the Royal College of Psychiatrists.

Preliminary results revealed that high doses were prescribed in approximately 3% of cases. However, where high doses were prescribed, few of the management guidelines issued by the Royal College of Psychiatrists were followed. It is concluded that an increase in awareness might help rectify this situation.

DOES PARTICIPATION IN CLINICAL TRIALS PROLONG HOSPITALIZATION?

N.M. Bark, D. Da Silva-Siegel, J. Lewis

Albert Einstein College of Medicine Schizophrenia Research Unit at Bronx Psychiatric Center, 1500 Waters Place, Bronx, New York 10461, USA

Objectives: This study aimed to assess the effect of participation in clinical trials.