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A LONG-TERM, MULTICENTER, OPEN-LABEL STUDY OF RISPERIDONE IN ELDERLY PATIENTS WITH PSYCHOSIS

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ABSTRACT

Rationale. Studies have shown that risperidone is safe and efficacious in young and middle-aged adults with chronic schizophrenia, but considerably fewer data are availabale on the treatment of elderly patients with schizophrenia or other psychotic disorders, particularly long-term outcomes.

Objective. A 12-month, open-label study was conducted to assess the effects of risperidone in elderly, chronically ill, psychotic patients.

Methods. This study enrolled 180 elderly, chronically ill, psychotic patients (median age, 72 years [range 54–89]), 97 of whom completed the 12-month study. At endpoint, the mean dose of risperidone was 3.7 mg/day.

Results. Clinical improvement ($\geqslant 20\%$ reduction in Positive and Negative Syndrome Score [PANSS] total score) was achieved by 54% of patients at endpoint. There were significant reductions in PANSS total, subscale (positive, negative, and general psychopathology), and cognition cluster scores at endpoint ($p < 0.001$). Clinical Global Impressions severity of illness scores showed continued improvement through month 12 ($p < 0.001$). In contrast, PANSS data from a historical comparable control group of patients receiving conventional antipsychotic agents showed no symptom improvement over a 12-month treatment period. The severity of preexisting extrapyramidal symptoms (EPS) in patients treated with risperidone decreased significantly from baseline to endpoint ($p < 0.001$), and the use of antiparkinsonian medication decreased from 41.1% of patients before the trial to 25.6% during the trial. There were no spontaneous reports of tardive dyskinesia (TD) and the incidence of assessed TD was 4.3% in contrast to the expected 26% reported in middle-aged and elderly patients receiving conventional antipsychotic agents for 1 year.

Conclusions. Long-term treatment with risperidone was associated with continued symptom improvement, a decrease in the severity of preexising EPS, and a low incidence of TD in elderly psychotic patients.

KEY WORDS—risperidone; elderly; psychosis; schizophrenia; efficacy; safety

INTRODUCTION

Previous studies have shown that risperidone is safe and efficacious in young and middle-aged adults with chronic schizophrenia (Chouinard *et al*., 1993; Marder and Meibach, 1994; Peuskens *et al*., 1995). Clinically effective doses (2–6 mg/day) are associated with a relatively low risk of extrapyramidal symptoms (EPS), and data suggest that risperidone may even reduce preexisting EPS and have an antidyskinetic effect (Chouinard *et al*., 1993; Khan and Glazer, 1996). It is important to note that these studies, as well as most clinical trials of other

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conventional or novel antipsychotic agents, involve young and middle-aged patients with schizophrenia. Unfortunately, considerably fewer data are available to evaluate the risk/benefit ratio of antipsychotic treatment in elderly patients with schizophrenia or other psychotic disorders, particularly long-term (i.e. 1-year) outcomes. Changes in drug absorption, distribution, metabolism, and elimination, as well as neuronal function, occur with aging and can influence a patient's response to treatment (Pollock, 1998; Williams, 1989; Zaleon and Guthrie, 1994). Also, there is considerably greater inter-individual variation in these factors in the elderly than in younger persons, rendering the effects of these drugs less predictable in the elderly patient (Benet *et al*., 1990; Nies, 1990). Hence, the information obtained in clinical trials of young and middle-aged individuals may not be applicable to the elderly patient.

Certain side-effects are of particular concern in the treatment of elderly patients. EPS are the most frequent and bothersome adverse effects of antipsychotic agents, and the risk of EPS (particularly parkinsonism) and tardive dyskinesia (TD) increases with age. The cumulative annual incidence of TD in the elderly is approximately five to six times higher than that in younger patients, affecting up to 60% of older patients after 3 years of treatment with conventional antipsychotics (Kane, 1995; Jeste *et al*., 1995). Anticholinergic (antimuscarinic) side-effects common to many psychotropic drugs may also be problematic in the elderly (i.e. drowsiness, blurred vision, cardiovascular dysfunction, constipation, urinary dysfunction, and cognitive impairment). The reduced risk for EPS associated with clinically effective doses of risperidone, and its lack of *in vitro* binding affinity for muscarinic receptors, are potential advantages for use in elderly patients (Chouinard *et al*., 1993; Marder and Meibach, 1994; Peuskens *et al*., 1995; Schotte *et al*., 1996).

As the proportion of elderly persons in the population continues to grow (Brookmeyer *et al*., 1998), data addressing the risk/benefit ratio of treating the elderly psychotic patient with antipsychotic agents become essential for daily clinical practice. One open-label, 12-week study of 103 elderly patients and a few small case series (Madhusoodanan *et al*., 1995, 1999; Berman *et al*., 1996; Lacro *et al*., 1996; Sajatovic *et al*., 1996) suggest that risperidone is a useful therapeutic option in elderly psychotic patients. The present multicenter, open-label study assessed the long-term efficacy and tolerability of risperidone in chronically ill elderly psychotic patients. Comparisons of efficacy were made with a comparable group of patients from a previous study who received long-term treatment with conventional antipsychotic agents and were studied for a similar follow-up period.

MATERIALS AND METHODS

Inclusion criteria for study participation included an age of at least 65 years, a DSM-III-R diagnosis of schizophrenia, schizophreniform disorder, or delusional disorder (American Psychiatric Association, 1987), and a Positive and Negative Syndrome Scale (PANSS; Kay *et al*., 1987) total score of 60–120. Exclusion criteria included clinically relevant organic or neurological disease, history or presence of TD, and treatment with antidepressants that could not be discontinued at selection. To participate in the study, which received institutional review board approval at each site, subjects gave written informed consent before enrollment.

Previous antipsychotic treatment was discontinued on day 0, and risperidone treatment began on day 1. When medically appropriate, gradual discontinuation of previous psychoactive agents began while risperidone was initiated. For patients switched from depot antipsychotic agents ($n = 46$), risperidone was initiated in place of the next scheduled injection.

Treatment began with 0.5 mg b.i.d. of an oral risperidone solution (1.0 mg/ml). The dose could be increased to 1.5 mg b.i.d. by day 3 and maintained until the end of week 1. The following 3 weeks comprised a dose-adaptation period. During this period, the dose was adjusted at weekly intervals based on the Clinical Global Impressions (CGI; Guy, 1976) change score. A CGI change score of 'improved' on day 7, 14, or 21 dictated no change in dose; a score of 'unchanged' or 'worsened' permitted a dose increase. The dose could be increased by 2 mg/day to a maximum dose of not greater than 8 mg/day (4 mg b.i.d.). Thereafter, the dose was adjusted if clinically indicated according to the clinician's judgment.

With the exception of the study drug, all psychoactive mediations were disallowed during the study. All antiparkinsonian medication was discontinued at trial entry but allowed during the trial to treat EPS. Short-acting sedative/hypnotic

medication was allowed when needed but limited to the lowest extent possible.

Primary efficacy measures were defined *a priori* as (1) the mean change in total score for PANSS (Kay *et al.*, 1987) from baseline to endpoint, and (2) the percentage of patients with clinical improvement (defined as $\geqslant 20\%$ reduction in PANSS total score from baseline to endpoint). Secondary efficacy assessments included changes in PANSS subscale scores (positive, negative, and general psychopathology) and cognition cluster score (the sum of item scores for conceptual disorganization [P2], deficits in abstract thinking [N5], disorientation [G10], attentional impairment [G11], and preoccupation [G15]).

EPS assessments included the Extrapyramidal Symptom Rating Scale (ESRS), a 55-item scale divided into six sets ([I] questionnaire to evaluate the subjective effects of EPS; [II] a detailed objective clinical evaluation of parkinsonism, [III] dystonia, and [IV] dyskinesia; and [V] CGI scales to assess the severity of dyskinesia and [VI] parkinsonism) (Chouinard *et al.*, 1980). EPS severity measures were the mean shift from baseline. PANSS, CGI and ESRS scores were assessed at baseline and months 1, 2, 3, 6, 9, and 12 or last visit.

The five dyskinesia items of the ESRS were used to assess TD (dyskinesia, hyperkinesia, buccolinguomasticatory factor, choreoathetoid limb movement, CGI severity of dyskinesia). Dyskinesia at baseline was defined as $\geqslant 2$ points on any two of the dyskinesia items of the ESRS or $\geqslant 3$ points on any one item. Persistent TD was defined as an increase of $\geqslant 3$ points from baseline on a single item or an increase of $\geqslant 2$ points on two or more items seen on two or more consecutive visits (Schooler and Kane, 1982). These data were assessed by the Kaplan–Meier survival analysis (Kaplan and Meier, 1958).

Adverse events were recorded at every visit. TD observed and recorded as an adverse event was referred to as a spontaneous report of TD. Adverse events classified as 'EPS-like' included retarded motor activity, akathisia, dyskinesia, extrapyramidal disorder, gait disturbance, unsteady gait, hypertonus, hypokinesia, muscle rigidity, parkinsonism, psychomotor hyperactivity, psychomotor restlessness, marked restlessness, sluggishness, spastic involuntary tongue protrusion, tremor, limb tremor, and walking difficulty. All other adverse events were classified as 'not EPS-like'.

PANSS change scores were analyzed by the Friedman test and the Wilcoxon matched-pairs signed-rank (MPSR) test (Siegel and Castellan, 1988). CGI ratings were analyzed using the Friedman test, the Page test, and the Wilcoxon MPSR test.

A subgroup analysis compared patients who received a modal dose of <3, 3–4, or >4 mg/day. Patients were assessed as described above.

Historical comparison group

To improve the validity of the interpretation of results from this open-label trial, comparison data were available on a demographically comparable group of patients with chronic schizophrenia who were treated with conventional antipsychotic agents for 1 year (Table 1) (Davidson *et al.*, 1995). These patients were enrolled in a large-scale longitudinal study of late-life schizophrenia and assessed with the PANSS at selection and at a 12-month follow-up period. These data served as comparative data on the relative stability of psychotic symptoms in patients receiving conventional antipsychotic agents. Patients were not rated by the ESRS or examined at intervening intervals. As part of their normal clinical care, patients received an annual physical examination and changes in their medication status were monitored annually. These patients' diagnoses and recruitment have been described previously (Davidson *et al.*, 1995).

RESULTS

This trial enrolled 180 patients. Demographic data are shown in Table 1. The historical comparison group consisted of 310 patients who received conventional antipsychotic agents.

Of the 180 patients enrolled in the risperidone trial, 160 patients were treated for at least 1 month, 136 patients for at least 3 months, 125 for at least 6 months, and 97 for 12 months. The most common reason for discontinuing treatment was adverse experience ($n = 30$) or insufficient response ($n = 26$).

The mean dose of risperidone at endpoint was 3.7 mg/day (mean minimum 2.6 mg/day and mean maximum 4.5 mg/day). The PANSS total score showed continual symptom improvement throughout the 12-month study (Fig. 1). Mean PANSS total, subscale (positive, negative, and general psychopathology), and cognition cluster scores all improved significantly from baseline to

Table 1. Characteristics of patients in the present risperidone trial and the previous trial of conventional antipsychotics

	Risperidone trial $n = 180$	Conventional antipsychotics $n = 310$
Male/female (%)	38/62	48/52
Mean age (range) (years)	73 (54–89)	75 (58–98)
54–70 (%)	34	29
71–80 (%)	53	46
> 80 (%)	13	25
Mean (SD) age at onset of psychosis (years)	37 (18.3)	28 (0.6)
Hospitalized, *n* (%)	L66 (92)	310 (100)
Mean (SD) duration of current hospitalization (years)	17 (17.3)	NA
Receiving antipsychotic agents before study *n* (%)		
Oral	149 (83)	310 (100)
Depot	46 (26)	0 (0)
Diagnosis, *n* (%)		
Schizophrenia	170 (94)	310 (100)
Schizophreniform	10 (6)	0 (0)

NA = not assessed.

endpoint (Table 2). The mean PANSS total score decreased 26.7% from baseline to endpoint ($p < 0.001$, Wilcoxon MPSR test) and 43.1% from baseline to month 12. Clinical improvement (defined as $\geqslant 20\%$ reduction in PANSS total score from baseline) was achieved by 41% of patients after 4 weeks of treatment and by 54% at endpoint. The rate of clinical improvement remained above 41% throughout the 12-month study.

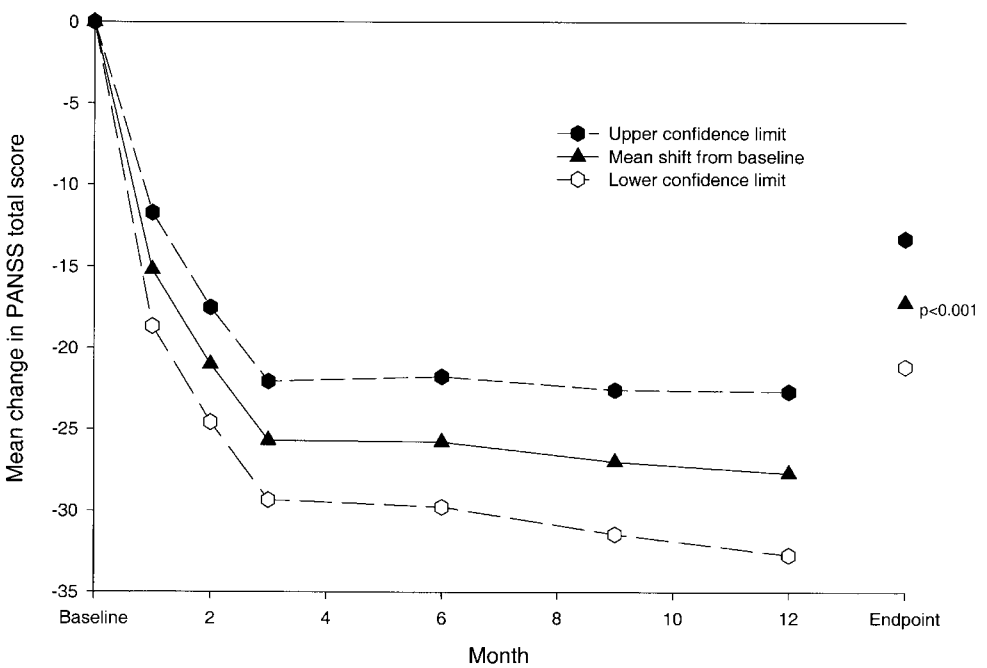

Fig. 1. Mean change in PANSS total score over time in patients receiving risperidone

Table 2. Mean (95% CI) PANSS scores at baseline and change scores at month 12 and endpoint

PANSS	Risperidone			Conventional antipsychotics	
	Baseline $n = 179$	Change at month 12 $n = 97$	Change at endpoint $n = 179$	Baseline $n = 310$	Change at month 12 $n = 310$
Total	94.3 (92.1; 96.6)	−27.7 (−32.7; −22.7)	−17.2 (−21.2; −13.3)*	90.4 (88.2; 92.7)	5.8 (3.4; 8.2)
Positive	20.3 (19.4; 21.2)	−6.5 (−8.2; −4.9)	−4.2 (−5.5; −2.9)*	18.8 (18.1; 19.5)	0.4 (−0.41; 1.2)
Negative	27.8 (26.7; 29.0)	−7.8 (−9.3; −6.2)	−5.0 (−6.2; −3.8)*	28.9 (27.9; 29.9)	1.7 (0.9; 2.6)
General psychopathology	46.3 (45.0; 47.5)	−13.4 (−16.0; −10.8)	−8.0 (−10.0; −6.0)*	42.7 (45.6; 43.9)	3.6 (2.3; 4.9)
Cognition cluster	16.7 (16.0; 17.3)	−4.2 (−8.6; −3.5)	−2.9 (−3.6; −2.1)*	20.3 (19.5; 21.0)	2.5 (1.8; 3.3)

*$p < 0.001$ vs baseline, Wilcoxon matched-pairs signed-rank test.

In contrast to the risperidone-treated patients, there was no change (improvement) in mean PANSS total, subscale, or cluster scores at month 12 in the comparison group of patients treated with conventional antipsychotic agents (Table 2).

CGI severity of illness ratings indicated that 174 of the 180 patients treated with risperidone were at least moderately ill (mean CGI score, 4.9) or markedly ill at baseline. The CGI severity of illness score improved throughout the 12-month treatment period ($p < 0.001$, Page test); the mean scores at month 12 and endpoint were 3.7 and 4.1, respectively. At month 12, 79.4% of the patients were improved according to the CGI change score. At endpoint, 58.9% of the patients were at least minimally improved and 37.7% of the patients were rated as much or very much improved.

According to ESRS scores, most EPS present at baseline were parkinsonian symptoms (Table 3). At endpoint, there was a significant decline in the scores for questionnaire, parkinsonism, total (parkinsonism + dystonia + dyskinesia), and CGI parkinsonism scores (Table 3). At trial entry, 41.1% of patients regularly received antiparkinsonian medications, compared with only 25.6% of patients who received these medications during the course of the trial.

A subanalysis of patients receiving a modal dose of <3, 3–4, or >4 mg/day risperidone showed improvements in PANSS scores in patients receiving a modal dose of $\leqslant 4$ mg/day risperidone. At endpoint, there were significant decreases on all PANSS measures (Table 4) and a decrease in ESRS scores for these patients. Patients receiving >4 mg/day risperidone did not show significant improvements in symptom scores.

There were no spontaneous reports of TD. Among the 179 patients for whom ESRS data were available, there were only eight cases of

Table 3. Mean (95% CI) ESRS scores at baseline and change scores at endpoint in patients receiving risperidone

ESRS	Baseline $n = 179$	Change at endpoint $n = 165$
I Questionnaire	4.5 (4.0; 5.0)	−0.7 (−1.3; −0.1)*
II Parkinsonism	9.4 (8.5; 10.4)	−1.5 (−2.5; −0.6)†
III Dystonia	0.6 (0.4; 0.8)	−0.1 (−0.3; 0.0)
IV Dyskinesia	2.8 (2.1; 3.5)	−0.4 (−1.0; 0.3)
Total (II + III + IV)	12.8 (11.4; 14.3)	−2.0 (−3.5; −0.6)†
CGI dyskinesia	1.2 (0.1; 1.5)	−0.2 (−0.4; 0.0)
CGI parkinsonism	2.1 (1.9; 2.4)	−0.5 (−0.8; −0.3)†

*$p < 0.01$; $n = 164$. †$p < 0.001$ vs baseline, Wilcoxon matched-pairs signed-rank test.

Table 4. Mean PANSS and ESRS scores at baseline and change scores (95% CI) at endpoint in patients receiving a modal dose of 3–4 mg/day of risperidone

PANSS	Baseline $n = 100$	Change at endpoint $n = 100$
Total	95.2	−22.0 (−27.3; −16.6)†
Positive	20.7	−5.5 (−7.3; −3.6)†
Negative	28.2	−6.4 (−7.9; −4.9)†
General psychopathology	46.3	−10.1 (−12.9; −7.4)†
ESRS	$n = 100$	$n = 92$
I Questionnaire	4.8	−1.1 (−1.9; −0.3)*
II Parkinsonism	9.7	−2.1 (−3.3; −0.9)†
III Dystonia	0.7	−0.2 (−0.4; 0.0)
IV Dyskinesia	2.9	−0.7 (−1.5; 0.1)
Total (II + III + IV)	13.3	−3.0 (−4.9; −1.1)†
CGI dyskinesia	1.4	−0.5 (−0.8; −0.2)*
CGI parkinsonism	2.2	−0.7 (−1.0; −0.3)†

*$p < 0.01$. †$p < 0.001$ vs baseline, Wilcoxon matched-pairs signed-rank test.

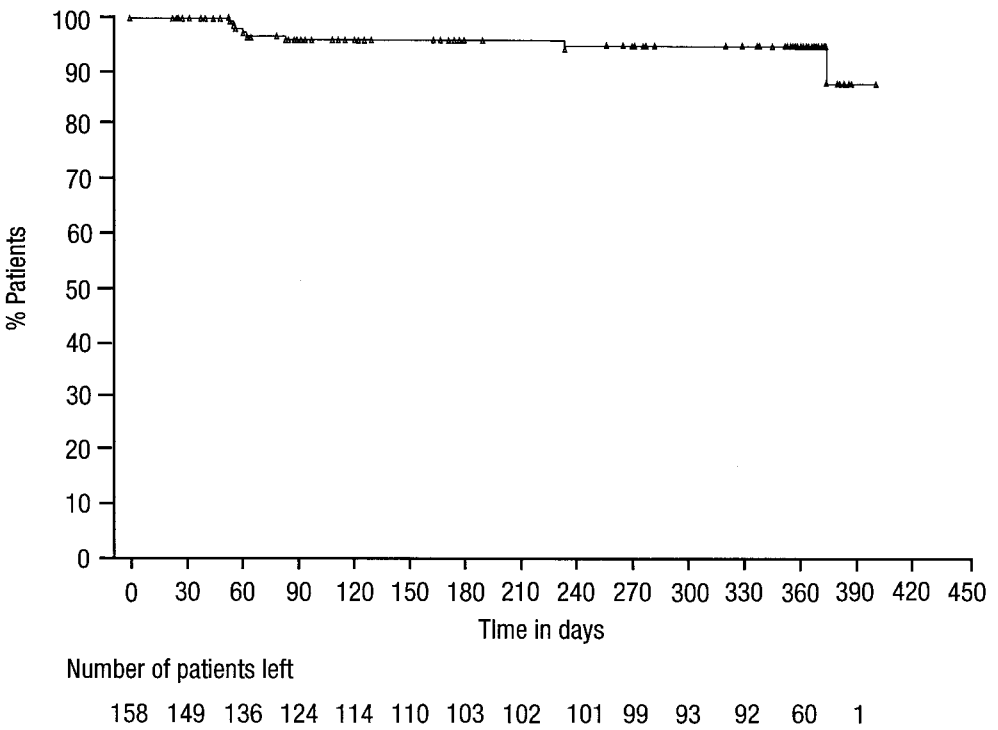

Fig. 2. Kaplan–Meier survival curve for time to occurrence of persistent TD in patients receiving risperidone

persistent TD (defined as an increase of $\geqslant 3$ points from baseline on a single dyskinesia ESRS item or an increase of $\geqslant 2$ points on two or more items for two or more consecutive visits) throughout the 12-month study (4.5%). Survival analysis shows a 1-year survival rate of no TD of 86.9% for all patients (Fig. 2) and 86.6% for patients without symptoms of TD at baseline. Of the 139 patients without symptoms of dyskinesia at baseline, only six cases of persistent TD emerged during the 12-month study period (4.3%). The five dyskinesia factor scores of the ESRS were assessed for the 40 patients with dyskinesia at baseline (defined as $\geqslant 2$ points on any two of the dyskinesia items of the ESRS or $\geqslant 3$ points on any one item). There were significant improvements at endpoint on the mean score for all five dyskinesia factors in these patients ($p < 0.001$; Table 5).

Fifty-four EPS-like adverse events were reported by 40 patients (22.2% of patients); the most common were marked restlessness ($n = 13$), tremor ($n = 8$), and muscle rigidity ($n = 5$). Not EPS-like adverse events reported in at least 10% of patients were insomnia ($n = 32$), agitation ($n = 28$), urinary tract infection ($n = 21$), constipation ($n = 19$), and dizziness ($n = 18$). Adverse events reported by at least five patients and deemed by the local clinical investigator as possibly related to the study medication were insomnia ($n = 18$), dizziness ($n = 13$), agitation ($n = 11$), tremor ($n = 10$), somnolence ($n = 10$), extrapyramidal disorder ($n = 7$), constipation ($n = 7$), dyskinesia ($n = 6$), fatigue ($n = 5$), hypertonia ($n = 5$), increased saliva ($n = 5$), and urinary incontinence ($n = 5$).

Table 5. Mean ESRS at baseline and change scores (95% CI) in patients with symptoms of dyskinesia at baseline in patients receiving risperidone

ESRS	Baseline $n = 40$	Change at endpoint $n = 38$
Dyskinesia	9.8	−4.0 (−5.6; −2.4)†
Hyperkinesia	4.2	−1.6 (−2.3; −0.8)†
Buccolinguomasticatory factor	6.1	−2.2 (−3.1; −1.3)†
Choreoathetoid limb movement	1.3	−0.9 (−1.5; −0.4)†
CGI severity of dyskinesia	3.4	−1.3 (−1.8; −0.7)†

†$p < 0.001$ vs baseline, Wilcoxon matched-pairs signed-rank test.

There were no clinically relevant changes (in the opinion of the local clinical investigator) in laboratory tests, vital signs, or electrocardiograms. There was a nonsignificant mean weight change of +0.1 kg at endpoint ($p > 0.1$, Wilcoxon MPSR test).

DISCUSSION

The results of this 12-month, open-label trial confirm the safety and efficacy of risperidone for elderly patients requiring treatment with an antipsychotic agent. More than 50% of these chronically ill elderly patients showed clinically significant improvements in psychopathology. Mean PANSS total and subscale scores decreased significantly at endpoint. Furthermore, the severity of EPS decreased at endpoint. These findings are particularly noteworthy when one considers the chronic and severe nature of the illness in these patients. Baseline data show that the mean PANSS total score was 94.3, the mean ESRS total score was 12.8, the mean duration of current hospitalization was 17 years, the mean age at onset of psychosis was 37 years, and 83% of patients received antipsychotics before the present study (Tables 1–3). These long-term data are consistent with data from an earlier open-label, 12-week study of risperidone in 103 elderly patients (mean age, 71 years) with schizophrenia or schizoaffective disorder, in which the severity of EPS (based on ESRS scores) and symptoms of psychopathology (PANSS total and subscale scores) were significantly reduced (Madhusoodanan *et al.*, 1999).

The improvement on the PANSS cognition cluster score in these elderly psychotic patients deserves comment. Although the cognition cluster is not based on formal neuropsychological tests, it measures constructs that are relevant to various cognitive functions. Improved cognitive performance may be attributed to the decreased use of anticholinergic drugs, to discontinuation of a neuroleptic that might have deleterious effects on aspects of cognitive performance, or to a direct effect of risperidone. Nonetheless, the improvement in cognition with risperidone is a clinically important finding that is consistent with several previously published reports in younger patients with schizophrenia (Gallhofer *et al.*, 1996; Stip and Lussier, 1996; Green *et al.*, 1997; Kee *et al.*, 1998) and in one study in the elderly (Berman *et al.*, 1996).

A major limitation of this trial was the lack of a randomized parallel comparison group (i.e. patients treated with placebo or with an active comparator). Thus, it could be argued that the 12-month improvements observed with risperidone were due to either 'symptom burnout' (Bridge *et al.*, 1978) or would have occurred during 1 year of treatment with any antipsychotic drug. However, most data indicate that schizophrenic symptoms do not burn out, at least in a considerable number of elderly patients (Davidson *et al.*, 1995; Kay, 1991; Kay and Sevy, 1990). Furthermore, PANSS scores from elderly patients with chronic schizophrenia treated with conventional antipsychotic agents were examined at a 1-year interval to determine symptom changes in these patients (Davidson *et al.*, 1995). Demographic characteristics of these patients were similar to those of the patients treated with risperidone (Table 1). The mean change in PANSS total and subscale scores at 1 year showed no symptom improvement with conventional antipsychotic agents in contrast to the significant improvement observed with risperidone (Table 2). Likewise, it could be argued that the differences (improvements) showed by the patients treated with risperidone at endpoint or month 12 compared with baseline are the result of symptom aggravation associated with the washout from previous neuroleptic medication. However, this is not the case because risperidone was started the day after the neuroleptic medication was discontinued. Taken together, these data indirectly support the claim that the improvement in psychopathology described in the open-label risperidone trial can be attributed to the study medication.

The results of the present study were favorable when one looks at adverse events of particular concern in elderly patients. An important finding was the fact that long-term risperidone use was accompanied by a decrease in the severity of preexisting EPS and a concomitant decrease in the use of anticholinergic drugs. As expected in this elderly population, the mean ESRS total score (parkinsonism + dystonia + dyskinesia) at baseline was relatively high (12.8) and primarily due to symptoms of parkinsonism (Table 3). All ESRS scores decreased at endpoint, with significant improvements in the questionnaire, parkinsonism, dyskinesia, ESRS total, and CGI severity of parkinsonism scores ($p < 0.001$, Wilcoxon MPSR test) (Table 3).

The present study also suggests a low risk of TD with risperidone in elderly patients. There were no

KEY POINTS

- Risperidone was effective and well tolerated in elderly psychotic patients.
- The incidence of tardive dyskinesia was considerably lower than reported in elderly patients treated with conventional antipsychotics.

spontaneous reports of TD (observed and recorded as an adverse event at follow-up visits). Assessed TD was defined by specific research criteria (increase of $\geqslant 3$ points from baseline on a single item or an increase of $\geqslant 2$ points on two or more items for two or more consecutive visits). These analyses showed only six new reports of TD (4.3%) in a population of patients that is at high risk for EPS and TD. This is much lower than the incidence reported in middle-aged and elderly psychotic patients receiving conventional antipsychotic agents for 1 year (26%; Jeste *et al*., 1995). In a direct comparison of the risk of TD with risperidone and haloperidol, over a 9-month treatment course, low-dose risperidone was less likely to produce TD than was low-dose haloperidol; cumulative 9-month TD incidence was 5.0% and 31.9%, respectively (Jeste *et al*., 1999). Also it is conceivable that in the current study some cases of apparently 'new TD' predated the beginning of the study but were masked at baseline by the protracted effect of the classic neuroleptics from which participants in the study have been withdrawn. Finally the very long prior exposure to classic neuroleptics could have been responsible for some of the emerging TD.

In the present study, there were no clinically significant cardiovascular adverse effects, no abnormal laboratory values attributed to the study medication, and few possible anticholinergic effects attributed to risperidone.

Considering the patients' advanced age, the presence of co-morbid conditions and chronic nature of their illness, and the 12-month duration of the study, the completer rate of 53% suggests that the drug was well tolerated. Although the present study allowed a maximal dose of 8 mg/day, a subanalysis showed that optimal outcome was obtained at 3–4 mg/day. None of the patients treated with classic neuroleptics and only very few of patients treated with risperidone suffered from late-onset psychosis. It is conceivable that even doses as low as 1–2 mg of risperidone would be sufficient for elderly patients suffering from late onset psychosis or psychosis associated with Alzheimer's disease (Katz *et al*., 1999). In summary, these data support a favorable risk/benefit ratio when elderly psychotic patients are treated with low-dose risperidone.

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