Effect of Risperidone on Behavioral and Psychological Symptoms and Cognitive Function in Dementia

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Aims: This open-label study examined the efficacy and tolerability of risperidone in the treatment of aggression, agitation, and psychotic symptoms in dementia. The influence of risperidone on cognitive function was also assessed under conditions reflecting normal, daily clinical care.

Method: A total of 34 hospital inpatients and outpatients (mean age = 76 years) with DSM-IV dementia disorders were treated with flexible doses of risperidone (0.5–2 mg/day) for 8 weeks. Assessments, conducted at baseline and after weeks 4 and 8, included the Clinical Global Impressions scale (CGI) and Neuropsychiatric Inventory (NPI) ratings. Cognitive function assessments included the Mini-Mental State Examination (MMSE) and specific measures of cognition (Age Concentration Test [AKT] and Brief Syndrome Test [SKT]). Frequency of extrapyramidal symptoms (EPS) was measured according to the Extrapyramidal Symptom Rating Scale (ESRS).

Results: At the end of the study, 50% of patients (N = 17) were receiving risperidone, 1 mg/day, 18% (N = 6) were receiving 0.5 mg/day, and 32% (N = 11) received > 1 mg/day (mean dose at endpoint = 1.1 mg/day). An improvement in symptoms, as measured by the CGI-Global Impression of Change scale, was reported for 82% of patients (N = 28) (59% [N = 20] much or very much improved). The frequency and severity of delusions, hallucinations, agitation/aggression, and irritability decreased as measured by the NPI. Multiplication of frequency and severity scores revealed a significant decline during the course of treatment ($p < .001$, end of study vs. baseline). Caregiver responses on the NPI also showed an improvement, with the mean ± SD total score decreasing from 24.2 ± 7.3 at baseline to 21.2 ± 6.3 at study end ($p = .002$). MMSE, AKT, and SKT results indicated that there was no decrease in cognitive function during the study. Risperidone treatment was well tolerated, and no clinically relevant changes in EPS, vital signs, or weight were detected.

Conclusion: During treatment with low-dose risperidone, behavioral and psychological symptoms improved overall in 34 patients with dementia, and cognitive function was maintained throughout the treatment period.

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Increasing life expectancy in most Western industrialized societies has led to a rapidly growing number of elderly people. The prevalence of dementia has, therefore, also increased dramatically, since dementia affects approximately 10% of individuals aged 70 to 80 years and 20% to 30% of those aged over 80 years.[1,2] Dementia of the Alzheimer's type accounts for the majority (approximately 70%) of all dementias, with vascular and mixed type accounting for the rest.[3] The onset of dementia is defined by loss of short- and long-term memory and by the presence of other cognitive deficits that worsen progressively. Moreover, dementias are associated with noncognitive symptoms, which include delusions, hallucinations, aggression, and agitation.[4–10]

The noncognitive symptoms can be clustered into alterations of behavior and psychological disturbances. In view of this, in 1996, the International Psychogeriatric Association (IPA) put forward the term *behavioral and psychological symptoms of dementia* (BPSD) to describe these symptoms.[5] Behavioral disorders, particularly aggression and agitation, are frequently cited by caregivers as major reasons for placing patients with dementia in an institution.[11–13] This finding is not unexpected, since behavioral symptoms produce high levels of burden and stress in the caregiver as well as negative feelings by caregivers toward their patients.[14–16]

Pharmacologic interventions are an important component of care programs for patients with BPSD. However, drug-related adverse events can be particularly problematic in older patients. For example, conventional neuroleptics have the drawback of being associated with extrapyramidal and anticholinergic effects in elderly populations.[17] Novel antipsychotic agents offer an advantage over conventional neuroleptics because of their lower potential for causing adverse effects. Indeed, the novel antipsychotic risperidone has shown promising results in elderly patients with dementia,[18–26] whereas conflicting results have been reported with olanzapine.[27,28] In 2 large, randomized, double-blind studies conducted in this pa-

tient population,[18,23] treatment with risperidone reduced the severity and frequency of behavioral symptoms, particularly aggression, over a 3-month period. Risperidone (average dose ≈ 1 mg/day) was well tolerated in these studies, and the frequency of extrapyramidal symptoms (EPS) in risperidone-treated patients was similar to that seen in placebo-treated patients[18,23] and less than that in patients treated with the conventional neuroleptic haloperidol.[18] There was also evidence in the clinical trials that risperidone does not cause a decline in cognition.[18,23,24] Additionally, in a 9-month comparative study of risperidone and haloperidol, Jeste et al.[22] observed that risperidone was significantly less likely to produce tardive dyskinesia than haloperidol in older patients.

As in most clinical studies, patients in the majority of risperidone trials were subject to strict inclusion and exclusion criteria based on neuropsychiatric assessments that confine cognitive and behavioral impairment of the patient population to a relatively narrow range. Typically, only patients with a Mini-Mental State Examination (MMSE) score of 23 or lower, a global rating of higher than 1 on the Behavior Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) combined with a total score of 8 or higher on the BEHAVE-AD, and a score of 4 or higher on the Functional Assessment Staging (FAST) scale were enrolled.[18,23] In normal clinical practice, it is usually impractical to apply such conditions on a daily basis. The primary objective of the present trial was to assess the efficacy of risperidone in the treatment of BPSD under conditions reflecting normal clinical situations. Therefore, our inclusion and exclusion criteria were less restrictive. Moreover, the influence of risperidone treatment on cognitive function was assessed using specific tests of cognition.

METHOD

Patients

All the subjects (N = 34) were inpatients (N = 6) or outpatients (N = 28) of the psychiatric ward of the Sozialmedizinisches Zentrum-Ost (SMZ-Ost), Vienna, Austria. They were required to be 50 years or older and to have DSM-IV diagnoses[29] of dementia of the Alzheimer's type, vascular dementia, mixed dementia, or dementia with Lewy bodies. Standardized assessments were used, based on the Structured Interview for the Diagnosis of Dementia of the Alzheimer Type and Multi-Infarct Dementia (SIDAM)[30] and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable Alzheimer's disease.[31] All patients were required to have been suffering from mild-to-moderate illness for at least 6 months, with scores between 8 and 26 (inclusive) on the MMSE both at screening and at baseline. In addition, they were required to exhibit 1 or more of the following behavioral or psychological symptoms of dementia from the Neuropsychiatric Inventory (NPI)[32] that call for the administration of antipsychotic drugs: delusions, hallucinations, agitation/aggression, irritability, and disinhibition. The patients also needed to have sufficient knowledge of the German language to understand and respond to all interview questions and to undergo neuropsychological testing without the assistance of an interpreter. Finally, every patient was required to have a caregiver or close relative who would have regular personal contact with the patient on several days of the week and would participate actively in caring for the patient. The caregivers needed to be willing to ensure that the patient complied with all aspects of the protocol, including regular drug intake, reporting adverse events, accompanying the patient to the clinical visits, and rating activities of daily living.

Patients were excluded from the study if they were known or suspected to have other current neurodegenerative diseases (e.g., Huntington's disease, Creutzfeld-Jakob disease) or neurologic conditions (e.g., stroke, infectious central nervous system disease, brain tumor) or had been diagnosed with a psychiatric disorder (DSM-IV criteria) within 1 year of enrollment. Patients with current major depression, moderate or severe depressive symptoms (total HAM-D score of 15 or more), or HAM-D item 1 (depressed mood) score of more than 2 were also excluded, as were those with a history of substance abuse or addiction in the previous 5 years. Severe or insufficiently controlled physical illness was also a reason for exclusion (e.g., cardiovascular, renal, or hepatic dysfunction; diabetes mellitus; vitamin B_{12} or folic acid deficiency; active malignancies), as were any disabilities that could prevent the patient from cooperating adequately or could interfere with performance in neuropsychological tests (e.g., problems with vision, hearing, or language). Patients were not allowed to have been involved in other experimental drug trials in the previous 4 weeks before baseline. Those with gastrointestinal diseases that could impair the absorption of orally applied drugs (e.g., peptic ulcer disease) were also excluded, as were those with known hypersensitivity to risperidone.

At screening, each patient's medical history was reviewed, including the duration of dementia, concomitant diseases and treatment, vital signs, and body weight.

Study Design

The trial was an open-label, 8-week, single-center study. Patients discontinued all previous antipsychotic medication; discontinuation was followed by a 14-day washout period before the start of treatment with risperidone. Treatment of patients with Alzheimer's disease (comprising 59% of our population [N = 20]) with cholinesterase inhibitors was continued at the established doses; of these patients, 60% (N = 12) were treated with donep-

ezil, and 20% (N = 4) each with galantamine or rivastigmine. Use of low-potency neuroleptic medication (prothipendyl, continued at stable doses of 40–80 mg/day for those patients who had been put on this regimen prior to initiation of risperidone; less than 10% of the study population) and of zolpidem as hypnotics was allowed during the washout phase and the subsequent study, as was oxazepam (up to 30 mg/day for up to 4 days within the first 4 weeks of risperidone treatment).

Risperidone was given in a once-daily oral dose, and the investigator was allowed flexibility regarding the dose administered according to the behavioral symptoms observed. (See Results for the distribution of doses administered and their change over time.) Evaluations were performed at baseline and during weeks 4 and 8. Efficacy was assessed by the Clinical Global Impressions scale (CGI)[33] and the NPI.[32]

The CGI-Severity scale (CGI-S) rating made by the investigator quantified behavioral symptoms on a 4-point scale of increasing severity (mild, moderate, severe, or very severe). The CGI-Global Impression of Change scale (CGI-Change) was used to detect improvements in the patients' conditions, measured on a 7-point scale ranging from "very much improved" to "very much worse."

The frequency and severity of behavioral disturbances were assessed according to the NPI[32] together with an additional rating for wandering. At each assessment, the patient's family and/or caregivers were questioned about the presence or absence of each behavior and were asked to rate the frequency (1 = "seldom," 2 = "sometimes," 3 = "often," 4 = "very often") and the severity of each behavior (1 = "mild," 2 = "moderate," 3 = "severe"). For each of the symptom categories, a subscale score was calculated (frequency multiplied by severity), and the total NPI score for each patient was calculated as the sum of the subscale scores.

The caregivers were also asked to complete a questionnaire (Appendix 1) designed to rate their attitude toward the patient's condition and the level of distress that the caregivers experienced as a result of coping with the patient's condition. At each assessment, the answers to the questionnaire were based on the patient's behavior over the previous 2 weeks.

The cognitive status of the patients was evaluated using the MMSE[34] and 2 specific cognitive tests: the Age Concentration Test (Alters-Konzentrations-Test, AKT)[35] and the Brief Syndrome Test (Syndrom-Kurz Test, SKT).[36] The AKT was developed to assess the course of cognitive decline (concentration and attention/vigilance) and has been validated for use in patients aged 55 to 95 years. Patients are presented with a number of simple geometrical symbols in various orientations and are required to match these to a reference symbol. Test performance is reflected by the number of correct and incorrect responses and the time taken to complete the test.[35] The SKT has also been used to examine cognitive function in elderly patients with dementia, in particular attention and memory. It consists of 9 subtests involving the identification of objects presented as simple drawings and the understanding and ordering of numbers and symbols. On this scale, a score of 9 through 13 points indicates mild dementia, whereas the ranges of 14 through 18 and 19 through 23 points are indicative of moderate and severe dementia, respectively.[36]

Assessments of tolerability included the Extrapyramidal Symptom Rating Scale (ESRS)[37] to examine the severity of EPS at each visit and reports of adverse events, as well as measurements of vital signs and body weight.

Table 1. Patient Characteristics at Baseline[a]

Characteristic	Value
Sex, M/F	14/20
Age, y, mean ± SD (range)	76.4 ± 10.3 (53.2–89.4)
Weight, mean ± SD (range)	
kg	65.3 ± 9.6 (40.0–86.0)
lb	145.1 ± 21.3 (88.9–119.1)
Cause of dementia	
Alzheimer's dementia	20 (59)
Vascular dementia	2 (6)
Mixed dementia	6 (18)
Other	6 (18)
Patients with previous hospital admissions	4 (12)
Patients who had previously received psychotropic treatment	7 (21)
Disease severity (per CGI scale)	
Mild/moderate	10 (29)
Moderately severe/severe	24 (71)

[a]Values shown as N (%) unless specified otherwise.
Abbreviation: CGI-S = Clinical Global Impressions Severity scale.

Statistical Analyses

All patients recruited were included in the efficacy and tolerability analyses. Data from the baseline, week 4, and week 8 assessments were analyzed using an analysis of variance (ANOVA). For data that were not normally distributed, or when the variances were not homogenous, the Friedmann test was used. For all analyses, $p \leq .05$ was considered to be statistically significant. Individual comparisons between groups were made using the method of Wilcoxon and Wilcox. The majority of results are expressed as mean value ± standard deviation (SD).

RESULTS

All 34 patients who entered the study completed the trial period of 8 weeks, which began in May 1998. The ages of the patients ranged from 53 through 89 years (Table 1), with the majority aged between 70 and 89 years (35.3% [N = 12], 70–79 years; 44.1% [N = 15], 80–89 years). The primary diagnosis was Alzheimer's type dementia (59% of patients [N = 20]). Patients with vascular or mixed dementia were also included. At baseline, most patients (N = 24; 71%) had illness categorized as "severe" or "very severe" according to the CGI-S. The most common symptoms at

Figure 1. Number of Patients Exhibiting Specific Behavioral and Psychological Symptoms of Dementia at Baseline and at the End of the Study (week 8) as Categorized in the Neuropsychiatric Inventory

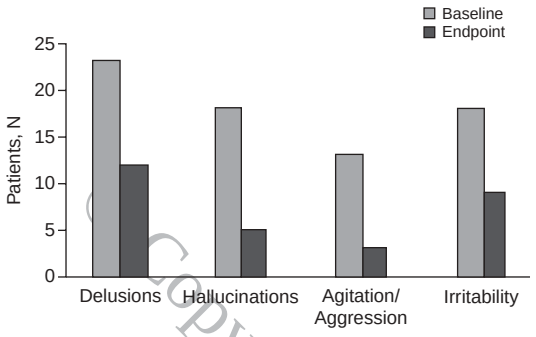
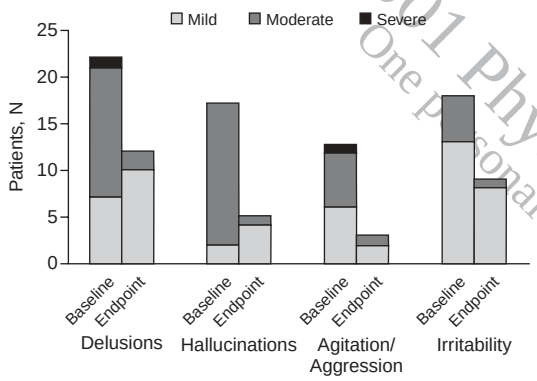


Figure 2. Severity of the Most Common Symptoms (Neuropsychiatric Inventory ratings) at Baseline and at the End of the Study (week 8)



baseline were delusions (including parnoid ideation and suspiciousness, affecting 68% [N = 23]), hallucinations (N = 18; 53%), irritability (N = 18; 53%), dysphoria (N = 19; 56%); apathy (N = 18; 53%), and agitation/aggression (N = 13; 38%).

At the beginning of the study, 18 patients (53%) received risperidone, 1 mg/day; 11 (32%) received 0.5 mg/day; and 5 (15%) received 2 mg/day. At the end of the trial, a similar number of patients (N = 17, 50%) received 1 mg/day, with 6 (18%) receiving 0.5 mg/day and 11 (32%) receiving more than 1 mg/day (8 patients received 2 mg/day). At endpoint, the mean dose of risperidone administered was 1.1 mg/day.

Treatment Efficacy

Symptoms of psychopathology, as assessed by the NPI, were improved after 8 weeks of risperidone treatment. Specifically, fewer caregivers reported the presence of delusions, hallucinations, agitation/aggression, and irritability/lability at week 8 than at baseline (Figure 1). The number of patients who were reported to exhibit dysphoria, anxiety, and apathy did not change during the study. There were few reports of euphoria, disinhibition, and aberrant motor behavior, and wandering was also reported relatively rarely (in 6 patients at baseline and 3 patients at week 8).

Table 2. Neuropsychiatric Inventory: Product of Frequency and Severity Scores at Each Timepoint[a]

Symptom	Baseline (N = 34)	Week 4 (N = 34)	Week 8 (N = 34)	p Value[b]
Delusions	4.7 ± 2.7	2.7 ± 2.2*	2.4 ± 2.0*	.0002
Hallucinations	4.0 ± 3.0	2.3 ± 2.1*	1.6 ± 1.6*	.0033
Agitation/ aggression	2.9 ± 2.5	1.7 ± 1.8	1.4 ± 1.3	NS
Depression/ dysphoria	3.9 ± 2.7	3.5 ± 2.5	3.8 ± 2.6	NS
Anxiety	2.3 ± 2.3	2.2 ± 2.3	2.1 ± 1.9	NS
Euphoria	1.1 ± 0.7	1.0 ± 0.0	1.0 ± 0.0	NS
Apathy	3.9 ± 2.9	3.6 ± 2.8	3.7 ± 2.7	NS
Disinhibition	1.8 ± 1.9	1.7 ± 1.6	1.5 ± 1.4	NS
Irritability/ lability	3.3 ± 2.3	2.7 ± 2.2	2.0 ± 1.8*	.0452
Aberrant motor behavior	1.2 ± 0.9	1.0 ± 0.0	1.1 ± 0.7	NS
Wandering	1.8 ± 1.8	1.8 ± 1.8	1.4 ± 1.3	NS
Total[c]	30.9 ± 7.8	24.0 ± 9.1*	22.0 ± 8.4*	< .0001

[a]Data shown as mean ± SD.
[b]Friedmann test; NS = not significant.
[c]Includes a rating for wandering.
*p < .05 vs. baseline, Wilcoxon and Wilcox.

In those patients who exhibited symptoms, the frequency at which symptoms were observed (seldom, sometimes, often, or very often) decreased from baseline to week 8, in accord with the trend in the number of patients in whom symptoms were reported. The severity of symptoms was also substantially reduced between baseline and week 8 (Figure 2). Table 2 shows the total and subscale scores on the NPI (frequency multiplied by severity). Compared with baseline values, total NPI scores were significantly reduced at weeks 4 and 8 ($p < .05$, Wilcoxon and Wilcox). Moreover, there were significant reductions during the study in subscale scores for delusions, hallucinations, and irritability/lability. The change in agitation/aggression score was of borderline statistical significance ($p = .06$).

Responses to the Caregiver Distress Questionnaire (see Appendix 1) also showed an improvement during the study. The questions were scored 1 to 5, with a score of 1 corresponding to "never" and 5 to "all of the time." A total score was calculated as the sum of all scores for individual questions. The total score for the questionnaire decreased from 24.2 ± 7.3 at baseline to 21.5 ± 6.5 at week 4 and 21.4 ± 6.3 at week 8 ($p < .05$ vs. baseline, Wilcoxon and Wilcox). With regard to the individual questions, significant reductions in scores were observed for questions 4, 6, and 9 ($p < .05$ vs. baseline) at week 8.

CGI-Change scores demonstrated that 82% of patients (N = 28), exhibited improvements in symptoms at the end of the study; 59% of patients (N = 20) were rated as "much" or "very much improved" (Figure 3).

Figure 3. Improvement of Patients' Symptoms at Week 8 Evaluated Using the Clinical Global Impressions of Change Scale

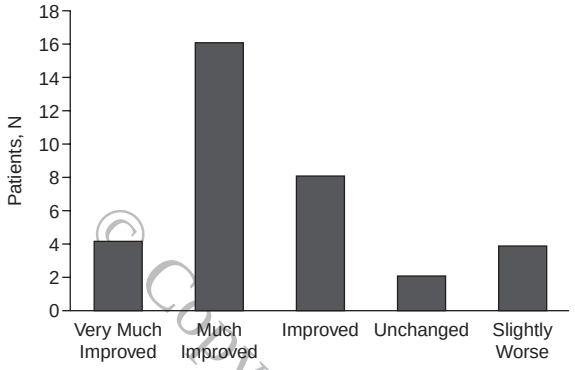


Table 3. Results on the Age Concentration Test[a]

Variable	Baseline (N = 26)	Week 4 (N = 25)	Week 8 (N = 25)
Time required to complete test, min:sec	3:10 ± 1:31 (3:22)	3:05 ± 1:28 (3:28)	2.56 ± 1:23 (2:50)
No. of correct answers	15.2 ± 5.0 (17.0)	16.52 ± 3.0 (17.0)	16.2 ± 4.0 (18.0)
No. of wrong answers	5.3 ± 5.9 (3.0)	4.2 ± 3.4 (4.0)	6.2 ± 7.2 (5.0)
Overall score	45.0 ± 8.6 (47.0)	47.3 ± 5.0 (47.0)	45.1 ± 8.5 (47.0)

[a]Data shown as mean ± SD (median). Overall scores of 42 to 47 points correspond to mild dementia; 34 to 41 points, to moderately severe dementia; < 34 points, to severe dementia.

Cognition

MMSE scores did not change significantly during the study (baseline, mean = 19.0; week 8, mean = 19.2). The results of the AKT are shown in Table 3. Although the number of symbols identified correctly was comparable at each assessment, the median (but not the mean) time needed to complete the test (a surrogate measure of alertness, which is a secondary measure by the AKT definition) was substantially reduced between week 4 and week 8 (not statistically significant). Similarly, the results of the SKT demonstrated that patients' attention and memory were maintained during the study (mean score = 22.3 ± 4.1 at baseline and 22.0 ± 5.3 at week 8).

Extrapyramidal Symptoms and Other Adverse Events

Treatment was well tolerated, and no clinically significant adverse events were observed that could be attributed to the use of risperidone. The mean ESRS score increased from 2.4 ± 3.9 at baseline to 3.2 ± 4.4 at week 8 ($p < .01$). However, none of the patients experienced problems due to EPS, and no patients withdrew from the trial due to the presence of EPS or other side effects. Some nonspecific adverse events were observed (orthostatic dysregulation in 3 patients, sedation in 3 patients, and vertigo in 2 patients). The patients' weight remained stable throughout the study (mean = 65 kg [144.4 lb]), as did systolic and diastolic blood pressure.

DISCUSSION

Risperidone has previously been shown in large, controlled studies to be efficacious and well tolerated in the treatment of behavior pathology in Alzheimer's disease.[18,23] These findings are confirmed and extended in the present trial, in a setting reflecting usual clinical care conditions. Patients with dementia were treated with flexible doses of risperidone and were not subject to restrictive inclusion and exclusion criteria.

Behavioral symptoms have a major impact on the quality of life of both patients and caregivers.[38] Aggressive behavior is often particularly distressing to caregivers, and violence is a constant problem in nursing homes. Moreover, behavioral symptoms are a primary motivation for institutional care,[11–13] which increases associated costs dramatically. Since no cure or effective prophylactic treatment exists for dementia, means of alleviating BPSD are necessary.

Most patients in the current trial were rated as impaired or severely impaired on the CGI-S, indicating cognitive and functional deficits severe enough to impair activities of daily living, such as dressing and bathing. At this advanced stage, behavioral symptoms are frequent,[39] and, in the current study, the most common symptoms at baseline were delusions (including paranoid ideation and suspiciousness, affecting 68% of patients [N = 23]), hallucinations (N = 18; 53%), irritability (N = 18; 53%), dysphoria (N = 19; 56%), apathy (N = 18; 53%), and agitation/aggression (N = 13; 38%). One of the selection criteria was that the patients were likely to comply with the experimental protocol and cooperate in the cognitive tests, and, as a result, fewer patients with high levels of agitation or disinhibition were included. It must be noted that the symptomatology of the patients in this study is therefore still not fully representative of the broad range of dementia patients encountered in clinical practice. We believe, however, that our population nevertheless represents a better approximation of institutional and community treatment reality than that seen in the highly preselected populations of phase 3 trials, and that our results represent reasonable measures of practical clinical effectiveness of risperidone, as opposed to efficacy data that are primarily collected to support regulatory filings.

Risperidone reduced the severity and frequency of behavioral and psychological symptoms, as assessed using the NPI. Total NPI scores showed a statistically significant decline between baseline and endpoint, as did several of the NPI subscale scores. Furthermore, 82% of patients experienced an improvement in their symptoms as evaluated

by the CGI-Change. This was reflected in the impact on caregivers as measured by the Caregiver Distress Questionnaire, with embarrassment, frustration, and hopelessness among the feelings that were most significantly reduced.

MMSE ratings in previous studies suggested that risperidone does not cause a decline in cognition.[18,23,24] In addition to the MMSE, this trial also used specific tests (the AKT and SKT) to measure the effect of treatment on cognitive function. Risperidone did not impair cognitive performance according to these tests; there were no significant differences between baseline and endpoint on any of the tests of cognition used in the study. Indeed, the time to complete the AKT was reduced substantially by the end of the study, although the number of symbols identified correctly remained the same.

The change in ESRS score (+0.8) observed in the current study was within the range reported in previous placebo-controlled studies of risperidone. For example, Katz et al.[23] reported changes in the parkinsonism and hypokinesia subscales of the ESRS over 12 weeks of –0.22 and 0.17 in placebo-treated patients and 0.84 and 0.95 in patients receiving risperidone (1 mg/day). However, the differences between the risperidone and placebo groups were not statistically significant. This finding is consistent with our conclusion that the increase in ESRS score in the present study was not clinically relevant, although the absence of a placebo group prevented us from examining this question directly.

Few adverse events were observed, and none was clinically significant. None of the reported adverse events led to discontinuation of treatment. Doses of risperidone of 0.5 mg/day and 1 mg/day were very well tolerated. Only 1 patient suffered from sedation with the most widely used dose of risperidone (1 mg/day). Orthostatic dysregulation (3 patients), vertigo (2 patients), and sedation (2 patients) were observed with 2 mg/day of risperidone. Thus, risperidone treatment was very well tolerated overall by the patients in the study.

Flexibility was permitted in the dose of risperidone administered to patients. Thus, the doses actually used should reflect the level of dosing that physicians judged to be both effective and well tolerated. The majority of patients in the current study (68%) received risperidone at 1 mg/day or less, confirming that low doses are appropriate for patients with dementia. This level of dosing is in accord with that reported by De Deyn et al.[18] in their 12-week, flexible-dose risperidone trial.

This open-label study of patients with dementia demonstrated that risperidone was well tolerated and effective in improving behavioral and psychological symptoms. Moreover, cognitive function was maintained during treatment with risperidone; this characteristic of risperidone is of great benefit in relation to treatment of patients with dementia. These results, obtained in a setting reflecting normal, daily clinical practice, further suggest that low-dose risperidone can improve the care of patients with BPSD and alleviate the burden of caregivers.

Drug names: donepezil (Aricept), galantamine (Reminyl), haloperidol (Haldol and others), olanzapine (Zyprexa), risperidone (Risperdal), rivastigmine (Exelon), zolpidem (Ambien).

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Appendix 1. Caregiver Distress Questionnaire

1. Did you think that you could no longer cope with the situation?
2. Did you think that you needed a break?
3. Were you depressed because of your situation?
4. Did you think that the problem would never end?
5. Were you concerned that your partner could have accidents?
6. Did your partner ever embarrass you?
7. Can you have visitors?
8. Were you angry or cross with the patient?
9. Were you sometimes frustrated because of your partner?
10. Did your own health suffer in any respect?

Options for responses:
1 = Never
2 = Rarely
3 = Sometimes
4 = Most of the time
5 = All of the time