Real-World Outcomes of Once-Daily Risperidone Dosing

Sanjay Gupta, M.D.; Sadiq Al-Samarrai, M.D.; Prakash S. Masand, M.D.; Barbara J. Lentz, R.N.; Peggy J. Keller, R.N.,C., M.S.; and Thomas M. Droney, R.N.

Background: Recent reports have shown that risperidone, which has established antipsychotic efficacy, is effective and safe in a once-daily dosing regimen.

Method: The efficacy and safety of once-daily risperidone were assessed in a retrospective study of 27 patients with a variety of psychiatric disorders who were attending a community day treatment program. Their DSM-IV diagnoses included schizophrenia, schizoaffective disorder, bipolar disorder, major depression with psychosis, and posttraumatic stress disorder. They had received once-daily risperidone for a mean of more than 18 months.

Results: Disorders of most patients were controlled with once-daily dosages of 1 to 6 mg/day of risperidone. The nighttime once-daily risperidone dosage was well tolerated by patients. In addition, there was no increase in antipsychotic-related side effects, and compliance was enhanced.

Conclusion: Risperidone was well tolerated, and no patient needed antiparkinsonian medications even at high dosages of risperidone once daily.

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Received Jan. 4, 2000; accepted Feb. 28, 2000. From the Department of Psychiatry, Olean General Hospital, Olean (Drs. Gupta and Al-Samarrai); the Department of Psychiatry, SUNY Upstate Medical University at Syracuse, Syracuse (Drs. Gupta and Masand); the Department of Psychiatry, University of Buffalo, Buffalo (Dr. Gupta); and Cattaraugus County Continuing Day Treatment Program, Olean, N.Y. (Mss. Lentz and Keller and Mr. Droney).

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Reprint requests to: Sanjay Gupta, M.D., Research and Education Division of Psychiatric Network, 2221 W. State St., Olean, NY 14760.

Risperidone is a safe and effective new antipsychotic that has a high binding affinity for both serotonin and dopamine receptors.[1] Several well-designed controlled clinical trials have been conducted to establish the antipsychotic efficacy of risperidone.[2,3] In a previously published report,[4] we had mentioned the rationale for using a once-a-day dosage schedule for risperidone based on the elimination half-life of risperidone and its active metabolite, 9-hydroxyrisperidone, to enhance compliance. Since that time, the use of risperidone once daily has been studied and recommended. In the setting of a community day treatment program, we had switched patients from a twice-a-day risperidone dosage schedule to a once-daily dosage and found it to be effective. In a retrospective chart review published earlier, we found no increase in side effects such as neuroleptic-induced extrapyramidal symptoms or sedation in patients taking once-daily risperidone.[5] We found the once-daily dosage to be safe, and patient compliance was enhanced.

We now report a retrospective chart review of patients who had been on once-daily risperidone treatment for an extended period of time. The aim of this study was to assess the efficacy, extrapyramidal side effects, and tolerability of risperidone in these patients over an extended period of time.

METHOD

The medical records of 27 patients who had been on once-daily risperidone treatment for more than 6 months were reviewed. The majority of these patients were registered at a local continuing day treatment program. Rating scales are used in the program as part of the clinical evaluation and follow-up process to monitor efficacy and antipsychotic-induced side effects. All ratings reported in this study were done by the treating psychiatrist (S.G.) to maintain rater reliability.

The data collected from the charts pertained to neuroleptic-induced extrapyramidal symptoms, diagnosis, and substance abuse. The total duration of treatment with risperidone and the duration on once-daily dosage was also obtained. The rating scales used included the Scale for the Assessment of Negative Symptoms (SANS),[6] the Brief Psychiatric Rating Scale (BPRS),[7] the Simpson-Angus Scale,[8] and the Abnormal Involuntary Movement Scale (AIMS).[9] The ratings presented are from the last psychiatric visit in the chart at the time of medical record review. Because the use of rating scales was instituted recently, no rating scale data were available at the time risperidone treatment was switched to a once-daily dosage. Medication compliance was monitored by the therapists working with the patients and also during medication education groups conducted in the continuing day treatment program.

Table 1. Demographic, Treatment, and Outcome Characteristics of 27 Patients Treated With Once-Daily Risperidone[a]

Patient	Age (y)	Substance Abuse	Diagnosis	Rating Scale Score				Risperidone Dose (mg hs)	Duration of Risperidone Treatment (mo)		
				BPRS	Simpson-Angus Scale	SANS	AIMS		Duration	Nighttime Dosing	Improvement (patient perception)
1	37	Alcohol	Schizophrenia	33	1	36	8	12	28	24	Moderate
2	23	Drugs	Bipolar affective disorder	22	NA	NA	NA	2	10	8	Mild
3	41	None	Schizoaffective disorder	27	1	20	0	4	38	24	Moderate
4	33	Drugs	Schizophrenia	25	0	15	0	5	28	24	Moderate
5	24	Drugs + alcohol	Bipolar affective disorder	NA	NA	NA	NA	1	16	13	Moderate
6	41	None	Schizophrenia	33	3	36	0	10	40	18	Mild
7	71	None	Bipolar affective disorder	NA	NA	NA	0	2	36	36	Moderate
8	56	None	Schizophrenia	26	NA	25	7	4	44	22	Marked
9	54	Alcohol	Schizoaffective disorder	26	NA	NA	0	6	9	9	Mild
10	77	None	Schizophrenia	20	2	27	2	3	33	24	Moderate
11	45	None	Schizophrenia	28	1	47	0	12	22	22	Mild
12	66	None	Major depressive disorder with psychosis	21	NA	NA	5	3	46	25	Moderate
13	50	None	Schizoaffective disorder	27	0	24	6	8	47	11	Mild
14	42	Alcohol + drugs	Schizophrenia	24	0	23	0	7.5	30	9	Moderate
15	38	None	Schizophrenia	27	0	NA	NA	2	9	9	Mild
16	45	None	Posttraumatic stress disorder	NA	NA	NA	NA	1.5	21	21	None
17	61	None	Bipolar affective disorder	NA	NA	NA	NA	2	14	14	Moderate
18	41	Alcohol	Schizophrenia	32	1	35	0	10	28	28	Moderate
19	29	None	Schizophrenia	33	2	38	0	14	43	12	Mild
20	60	None	Bipolar affective disorder	NA	NA	NA	0	2	16	16	Moderate
21	51	None	Schizophrenia	23	0	NA	1	10	41	19	Moderate
22	71	None	Major depressive disorder with psychosis	NA	0	NA	1	1	22	22	Moderate
23	42	None	Major depressive disorder with psychosis	NA	0	NA	0	10	28	28	Moderate
24	41	None	Schizophrenia	19	0	13	0	6	12	12	Marked
25	30	None	Schizophrenia	NA	NA	NA	0	8	34	20	Moderate
26	38	None	Schizoaffective disorder	36	2	23	0	16	28	12	Moderate
27	40	Alcohol + drugs	Schizophrenia	38	NA	NA	0	4	22	18	Mild

[a]Abbreviations: AIMS = Abnormal Involuntary Movement Scale, BPRS = Brief Psychiatric Rating Scale, NA = not available, SANS = Scale for the Assessment of Negative Symptoms.

RESULTS

The sample consisted of 27 patients with varying DSM-IV diagnoses who had been switched in an uncontrolled fashion to once-daily dosage of risperidone and had periodic follow-up over several months. The sample consisted of 15 women and 12 men. The age range was 23 to 77 years (mean = 47.7 years). The diagnoses included schizophrenia (N = 14), bipolar affective disorder (N = 5), schizoaffective disorder (N = 4), major depressive disorder with psychotic features (N = 3), and posttraumatic stress disorder (N = 1) (Table 1). Three patients had alcohol abuse, 2 had drug abuse, and 3 had a combination of alcohol and drug abuse.

The mean duration of treatment with risperidone was 27.6 months (range, 9–47 months) and the mean duration of once-daily (nighttime) treatment was 18.5 months (range, 8–36 months). The mean bedtime dosage of risperidone was 6.1 mg (range, 1–16 mg) (see Table 1). Patient report of treatment outcome at the time of chart review indicated marked improvement in 2 patients, moderate improvement in 16, mild improvement in 8, and no improvement in 1 (see Table 1) based on Clinical Global Impressions Scale rating.[10] BPRS data were available for 19

patients, with a mean score of 27.4. SANS scores were available for 13 patients, with a mean score of 27.8. The rating scale scores reflect a low level of symptomatology and minimal medication-related side effects. None of the patients had neuroleptic-induced parkinsonism on the basis of review of the psychiatrist's progress notes and Simpson-Angus Scale scores, available for 16 patients (mean = .08; see Table 1). One patient had good symptomatic relief on 16 mg of risperidone at bedtime and did not manifest any side effects. The patients had improved compliance with the medication being given once daily, as noted by the individual therapists and the medication education groups.

DISCUSSION

In a fixed-dose study (N = 211), Nair et al.[11] randomly assigned subjects to receive 8 mg of risperidone once daily or 4 mg twice daily for 6 weeks.[11] They report both dosage schedules to be similar in clinical efficacy and latency of response to risperidone. No differences were found in side effects between the 2 groups.

Our study has limitations, which include the retrospective design and lack of prechange and postchange data so that a comparison cannot be made of the various measures with regard to twice-daily versus once-daily dosage schedule. Rating scale data were partially or completely missing for some of the patients. Another limiting factor is the lack of availability of rating scale information at the time of the switch to once-daily risperidone.

A strength of this study is the use of standardized rating scales in the clinic on a regular basis, which provided us with objective measures for assessing symptoms and side effects. These rating scales are used in most clinical trials for assessing medication efficacy and side effects. The BPRS is an 18-item scale that is the gold standard for assessing the level of psychosis in clinical trials and is accepted worldwide. It measures symptoms such as auditory hallucinations, delusions, disturbance of thought, agitation, hostility, and affect. The Simpson-Angus Scale assesses the motor side effects of antipsychotics, which include drug-induced parkinsonism. The SANS quantifies negative symptoms of schizophrenia such as anhedonia, avolition, poverty of speech, affective flattening, and disturbance of attention. The AIMS is used to monitor neurologic side effects of antipsychotic agents, such as tardive dyskinesia, a disorder characterized by abnormal involuntary choreiform movements.

Primary care physicians treat more complex patients today, including those with major mental illnesses such as schizophrenia or depression with psychotic symptoms, especially after stabilization. In other instances, they may treat such patients jointly with a psychiatrist. This study provides information for primary care physicians on safety, tolerability, and efficacy when risperidone is used over an extended period of time (mean = 27.6 months; range, 9–47 months). Information at this time about the long-term use of risperidone is limited. Most patients who need antipsychotics require maintenance on them over their lifetime as is done for diabetes or hypertension. The new-generation antidepressants and antipsychotics have a much improved side effect profile and are more patient friendly. It is important for primary care physicians to be familiar with them with regard to dosage schedules and side effects.

Our study found risperidone to be safe, effective, and well tolerated even at high dosages in a once-daily dosing schedule over a prolonged period of treatment. The once-daily risperidone dosing was found to enhance treatment compliance in this community setting as noted by the therapists and the medication education groups. In this community, we are currently using risperidone in a once-daily dosage schedule. Future controlled studies are recommended to replicate these findings in different populations of patients.

Drug name: risperidone (Risperdal).

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