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THE USE OF RISPERIDONE IN SEVERELY DEMENTED PATIENTS WITH PERSISTENT VOCALIZATIONS

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ABSTRACT

Objective. The hypothesis being tested was that low doses of risperidone would diminish persistent, purposeless vocalizations in two severely demented geriatric women. A secondary hypothesis was that the severe tardive dyskinesia observed in one patient would improve after risperidone treatment.

Design. An intrasubject on–off–on design was employed.

Setting. A chronic care facility in Canada.

Subjects. Two inpatients with DSM-IV (American Psychiatric Association) diagnosis of combined Alzheimer–vascular dementia.

Measures. Nursing assessment of frequency of vocalizations, Extrapyramidal System Rating Scale (ESRS) and Folstein Mini Mental State Examination (MMSE).

Results. With risperidone treatment, the vocalizations diminished to less than 20% of baseline ratings. For the patient with dyskinesia, ESRS dyskinetic movement scores decreased (baseline = 27; after risperidone 8 weeks = 16). No change was observed for the MMSE.

Conclusions. The findings support the main hypothesis. The secondary hypothesis was also supported. Further studies of larger numbers of subjects are required to substantiate these preliminary findings.

KEY WORDS—risperidone; dementia; vocalizations; geriatrics; tardive dyskinesia

Geriatric patients with severe dementia who are behaviourally disturbed with repetitive vocalizations are extremely challenging to care for in residences or hospitals. Screaming or constant noisiness is very distressing for other patients and staff and is described in up to 25% of nursing home residents (Cohen-Mansfield *et al*., 1990). As part of a continuum of aggressive behaviours seen in demented patients, screaming can also be associated with depression, severe cognitive impairment, social isolation and marked inability to perform activities of daily living (Cohen-Mansfield *et al*., 1990). Most studies focusing on the treatment of agitation or aggression in dementia do not distinguish screaming or noisiness from other behaviours. However, diminished screaming is reported after ECT (Carlyle *et al*., 1991; Snowdon *et al*., 1994) and with manipulation of the serotonin system after administering trazadone and l-tryptophan (Greenwald *et al*., 1986; Pasion and Kirby, 1993). Although the precise anatomic localization of perseverative vocalizations is unknown, recent literature implicates right frontal lobe pathology (Brugger *et al*., 1996).

The use of antipsychotic medications often causes undesirable side-effects which include excessive sedation, postural hypotension, confusion and a potential for tardive dyskinesia. Here we describe two patients with computerized tomography evidence for cortical and subcortical ischaemic lesions and disruptive, continuous vocalizations which responded well to treatment with risperidone, a novel antipsychotic medication. The second patient also had severe buccolingual tardive dyskinesia which improved following risperidone treatment.

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CASE REPORTS

Mrs A, a 92-year-old widowed Caucasian woman, was hospitalized as she required total care. She last lived independently 3 years prior to admission. Hospitalization was precipitated by a fractured hip resulting from a fall. While being rehabilitated, she fractured her other hip. It was after the second surgical repair that she had a cerebral vascular accident which resulted in mild left lower limb weakness, confusion and agitation, and perseverative vocalizations. A diagnosis of moderate to severe dementia was made as she was transferred to an extended care facility.

In the 2 years prior to the current assessment, while a resident in the same facility, she received varying amounts of haloperidol, methotrimeprazine and chlorpromazine to diminish agitation and perseverative, loud calling out of a single word. At the time of the current psychiatric assessment, she was receiving loxapine 10 mg per day. Most of the antipsychotic medications she received caused sedation but did not decrease the intermittent agitation or calling out and so were abandoned. The patient ate her food enthusiastically and there had been no recent history of weight change. There was no evidence for depression or any medical conditions such as chronic pain or constipation to which the vocalizations could be attributed. There was no prior history of medical or psychiatric illness.

Laboratory investigation revealed normal complete blood count and differential, liver and renal function, folate, vitamin B12 and thyroid status. Electrocardiogram showed mild ischaemic changes while computerized tomography findings indicated left temporal encephalomalacia, bilateral periventricular ischaemic changes and symmetrical reduction in the size of the parahippocampal gyri. These changes were consistent with a combined Alzheimer–vascular dementia.

On mental status examination, Mrs A was alert and cooperative but noted to be moderately agitated, occasionally striking out purposelessly and constantly calling out a single word. She could be distracted only briefly but would quickly resume this behavior as soon as the individual speaking to her was silent or left her immediate vicinity. Although oriented to person, she did not know her location, date of birth or age. She was able to respond to questions in 3–4 word sentences but demonstrated severe memory impairment. Folstein Mini Mental Status (Folstein *et al*., 1975) score was 9/30.

Initially, the dosage of loxapine was increased to 12.5 mg daily but the patient became oversedated so the loxapine dosage was decreased and then discontinued. The calling out became constant when she was awake and sleep was sporadic. This was extremely disruptive to others and was demanding of nursing interventions. After 3 weeks with no psychotropic medications, the patient received risperidone 0.5 mg twice daily. Over the next week, there was a marked decrease in the frequency of the calling out. The nighttime dose of risperidone was increased to 1 mg. Her sleep improved and she slept for 7 hours uninterrupted. After 3 weeks of risperidone 1.5 mg daily, the calling out decreased to less than 10% of baseline nursing ratings and no striking out occurred. The patient was calm but not oversedated. Nursing care requirements decreased. She remained cognitively impaired with a Folstein Mini Mental Status score of 10/30. Repeat liver and renal function tests remained within normal limits. To determine if indeed the risperidone had been effective in treating the target symptoms, it was discontinued, and within 1 week the vocalizations returned, the patient was agitated and sleep was sporadic. With resumption of risperidone alone, she again improved. There was no change in Parkinsonism as assessed by the Extrapyramidal Symptom Rating Scale (ESRS; Chouinard and Ross-Chouinard, 1980) (Parkinsonism baseline = 4; after risperidone 8 weeks = 4).

Mrs B a 78-year-old Caucasian widow, required hospitalization for total nursing care including being fed. Admission diagnoses were multi-infarct dementia, severe buccolingual tardive dyskinesia and a preexisting tonic-clonic seizure disorder (onset age 14). Two years prior to her initial hospitalization, she had a cerebral vascular accident with resulting mild left hemiparesis. She had been cared for in the same extended care facility for the previous 2 years. Medications at the current assessment included clonazepam 0.5 mg qid, haloperidol 0.5 mg qid chloral hydrate 1000 mg hs, phenytoin 200 mg hs (blood level 28—subtherapeutic by laboratory standards) and lorazepam 2 mg every 4 hours as needed for persistent high-pitched shrieking. The reason for the referral was to review medications, advise about the management of the constant shrieking and to decrease demands on nursing staff.

Laboratory investigations revealed normal hepatic, renal and thyroid function. Complete blood count and differential as well as blood glucose were within normal limits. The electrocardiograph

showed right atrial strain while a chest X-ray and urinalysis were normal. Computerized tomography scan of the head revealed periventricular white matter ischaemic lesions and cortical atrophy.

On mental status examination, Mrs B appeared to be a frail woman in a wheelchair who demonstrated severe buccolingual tardive dyskinesia with pronounced tongue protrusion, lip smacking and drooling. Although accessible and cooperative, she was oriented only to person. She denied experiencing pain, perceptual abnormalities or depressed mood. According to nursing staff, she was able to cooperate with feeding, enjoyed her food and was not constipated. There had been no recent change in weight. She repeated two distinct phrases using a very high-pitched tone of voice. Both statements were made out of context. Folstein Mini Mental Status score at this time was 9/30.

Over the next 2 weeks, all psychotropic medications except the phenytoin were reduced and discontinued. The buccolingual tardive dyskinesia predictably worsened somewhat but her calling out persisted at the same frequency. The latter was determined by nurse raters. Sleep was intermittent with frequent wakenings.

After 3 weeks of treatment only with phenytoin, risperidone 0.5 mg twice daily was initiated. Nursing staff continued to record the frequency of shrieking on a flow sheet. After 1 week, the frequency diminished to 50% of baseline. Interrupted sleep continued to be problematic so the nighttime dose of risperidone was increased to 1 mg. This resulted in 6–7 hours of continuous sleep. Eight weeks after risperidone was initiated, nursing ratings revealed that vocalizations had decreased to less than 20% of baseline ratings and nursing demands decreased. No adverse effects were noted. Phenytoin blood levels remained unchanged. No seizure activity occurred. Hepatic and renal function remained normal. She continued to be severely cognitively impaired with a Folstein Mini Mental Status score of 10/30. However, improvement in lip smacking, tongue protrusion and drooling was most marked and resulted in decreased ESRS dyskinetic movement scores (baseline = 27; after risperidone 8 weeks = 16). The Parkinsonian scores were unchanged (baseline = 5; after risperidone = 5).

DISCUSSION

These cases document the effective use of risperidone in elderly, severely demented patients who present with disturbing, persistent vocalizations. For both patients, these undesirable behaviours were diminished following treatment with low doses of risperidone. No changes in hepatic or renal function occurred for either patient. Both were subdued but not oversedated and had improved sleep duration. Risperidone can cause sedation and postural hypotension (Madhusoodanan *et al*., 1995), especially if the dose is rapidly titrated upwards, but this was avoided by administering low doses and titrating slowly. One showed improvement in buccolingual dyskinesia. No changes in Parkinsonism scores were observed for either woman. For one patient, phenytoin blood levels did not change after addition of risperidone. Regrettably, both remained severely cognitively impaired. Patient care costs decreased as total nursing care requirements were reduced.

In 11 elderly subjects, risperidone was reported to be effective in treating positive and negative symptoms of psychosis (Madhusoodanan *et al*., 1995). Side-effects included orthostatic hypotension. Generally, extrapyramidal symptoms improved relative to baseline. In another case series of five patients with aggression, psychosis and dementia, both agitation and psychotic symptoms improved (Jeanblanc and Davis, 1995). Mild extrapyramidal symptoms (EPS) were treated with amantadine. Risperidone was also reported to be effective in treating two geriatric patients, one with agitation and another with apathy and withdrawal (Raheja *et al*., 1995). Psychosis associated with Parkinson's disease or presumed Lewy body disease had worsening of EPS after treatment with risperidone (Rich *et al*., 1995). However, Lee *et al*. (1994) reported on an individual with Lewy body disease who was successfully treated with risperidone. Most of these patients were psychotic and some were agitated. This is in contrast to the two women presented here, where vocalizations were the target symptom.

In younger patients with schizophrenia, risperidone at lower doses (2–4 mg) does reduce the severity of symptoms forming the 'excited' cluster (excitement, hostility, uncooperativeness, poor impulse control) of the positive and negative syndrome scale (Kay *et al*., 1987; Lindstrom and von Knorring, 1994; Kopala *et al*., 1996). For more chronic patients with schizophrenia, risperidone appears to be at least equal in efficacy to older antipsychotics. The high ratio of serotonin $5HT_2$ to dopamine D_2 antagonism may account for this

along with the lower rate of EPS (Meltzer, 1991; Chouinard *et al*., 1993).

Previously, we and others have reported improvement in symptoms of severe tardive dyskinesia in patients with schizophrenia who were treated with risperidone (Kopala and Honer, 1994; Chouinard *et al*., 1993; Madhusoodanan *et al*., 1995). Manipulation of the serotonin system through the use of atypical antipsychotic medications could modulate abnormal movements *and* repetitive vocalizations. Greenwald *et al*. (1986) reported successfully treating a woman who screamed and head-banged with trazadone and l-tryptophan. Other agents such as buspirone might also be effective as it also modulates serotonergic systems, but the high cost of buspirone could be a consideration (Tejera and Saravay, 1995; Modell, 1995). Lott *et al*. (1995) recently documented improvement in behavioural agitation in elderly patients with dementia who were treated with valproate where the proposed mechanism of action was via alteration of the GABA system, not the serotonergic or dopaminergic systems.

Risperidone may prove to be a safe, effective and fiscally responsible alternative medication for the management of disruptive patients with dementia of vascular and other aetiologies. For one of the patients, risperidone was safely coadministered with phenytoin with no apparent adverse effects and no resultant seizure activity. Similarly, Madhusoodanan *et al*. (1995) safely combined risperidone at doses of 1.5–4 mg daily with lithium or carbamazepine in two elderly patients with senile dementia, noting marked improvement in agitation.

For those patients with cerebral injury who are at higher risk of developing tardive dyskinesia, low doses of risperidone may be more effective with less potential for inducing movement disorders.

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