

Letters to the Editor

Rectal Antidepressant Medication in the Treatment of Depression

Sir: In recent years, advances in gastrointestinal surgery and the ability to support patients on total parenteral nutrition have led to the withdrawal of oral medications for extended periods of time in more and more patients. Depression can be a significant issue in some of these patients. As most of the antidepressants are available only as oral preparations, alternate routes of administration must be used if an antidepressant is to be continued or initiated.

The rectal route of administration is considered infrequently in adults. However, it provides an effective access route when other routes are unavailable or impractical.¹ Absorption from the rectal mucosa is rapid and reliable.² Although few medications are available in suppository form, skilled pharmacists are readily able to make suppositories from many oral medications.³ For the depressed patient who cannot use oral medication, needs an antidepressant, and cannot tolerate the two available injectable antidepressants (imipramine and amitriptyline) because of side effects or excess volume of injection, the rectal route can be helpful. The following case demonstrates the use of rectal antidepressant medication.

Case report. Mr. A, a 42-year-old man, was admitted with bowel obstruction related to a history of excision of pancreatic pseudocyst and distal pancreatectomy. He had a pylorojejunoplasty for hypertrophic pyloric stenosis that required 7 days of bowel rest. Prior to surgery, he had been on trazodone 200 mg orally at bedtime for major depression, recurrent type. In the past, he had noted increased depression when off trazodone for a period of a week. On the third postoperative day, he requested to see psychiatry because of his concern that his depression would return. He was found to have depressed mood and affect and wished to resume trazodone therapy. He agreed to the use of a suppository to deliver the trazodone dose. This was begun on the fourth postoperative day. By the sixth postoperative day, he reported improved mood and better sleep. He was able to resume oral medication by his eighth postoperative day.

While this was a fairly rapid response to trazodone and may represent a response to the hypnotic rather than the antidepressant effect of trazodone, the usefulness of the rectal route is demonstrated. Other antidepressants could be administered by the same route.³⁻⁵ Initiation of antidepressant medication by the rectal route should also be considered when symptoms or diagnosis indicates need in the patient without oral intake.

Various pitfalls may be encountered in the use of rectal medications. Some patients may not wish to use rectal medications for psychological reasons and may misinterpret the administration of rectal medication. Some medications may be irritating and difficult to retain. Positioning of the suppository may alter absorption.^{1,2}

Rectal administration of antidepressant medications has been little studied physiologically or psychologically.³⁻⁵ As we are able to sustain patients for long periods of time without oral intake and are more sensitive to the need for antidepressants, a better understanding of the rectal route is warranted.

REFERENCES

1. Warren DE. Practical use of rectal medications in palliative care. *J Pain Symptom Manage* 1996;11:378-387
2. van Hoogdalem EJ, de Boer AG, Breimer DD. Pharmacokinetics of rectal drug administration, I: general considerations and clinical applications of centrally acting drugs. *Clin Pharmacokinet* 1991;21:11-21
3. Holmes TF, Sabaawi M, Fragala MR. Psychostimulant suppository treatment for depression in the gravely ill [letter]. *J Clin Psychiatry* 1994;55:265-266
4. Storey P, Trumble M. Rectal doxepin and carbamazepine therapy in patients with cancer. *N Engl J Med* 1992; 327:1318-1319
5. Adams F. Amitriptyline suppositories [letter]. *N Engl J Med* 1982;306:996

Marlene M. Mirassou, M.D.
Sacramento, California

Risperidone-Induced Tardive Dyskinesia

Sir: I present a case of risperidone-induced tardive dyskinesia that is unusual because the patient had never been treated with the typical antipsychotics and the dose of risperidone was only 1 mg/day. During his withdrawal, symptoms fluctuated in an inverse relationship with the increase and decrease of risperidone dose.

Case report. Mr. A, a 50-year-old divorced white man, has been receiving psychiatric treatment for 16 years. He suffers from recurrent major depression and was hospitalized twice in the past 5 years with suicidal ideation. In addition to various antidepressants, he was tried for short periods of time on lithium, carbamazepine, and divalproex sodium with no discernible benefit. In the spring of 1996, after unsuccessful trials of paroxetine and nefazodone, he was started on fluvoxamine 50 mg/day and risperidone 0.5 mg h.s. A month later, risperidone was increased to 1 mg h.s., and fluvoxamine was slowly increased to 200 mg/day.

In the fall of 1996, because Mr. A was no better, fluvoxamine was tapered off, and he was given fluoxetine 40 mg/day with which he was treated successfully a few years earlier. Risperidone 1 mg/day was continued. In late November 1996, he showed blinking of the eyes, parkinsonian tremor of the hands, and some tongue-rolling movements. Risperidone was stopped and fluoxetine reduced to 20 mg/day. Gradually, the abnormal movements worsened, and a month later the blinking was so frequent and constant that he was not able to read, watch television, or drive his car. His respiration became labored and deep with occasional high-pitched vocal sounds during expiration. He was restarted on risperidone 0.5 mg h.s., and a month later clorazepate 15 mg/day in divided dosage was added.

His symptoms improved minimally, but he developed suicidal impulses and was rehospitalized for 8 days in January 1997. His symptoms were suppressed with increased dosage of risperidone 2 mg/day and fluoxetine 40 mg/day. Another attempt was then made to withdraw risperidone. Blepharospasm and labored breathing returned. He also started to make cluck-

ing sounds with his tongue. The clucking sounds occurred about every 10 seconds and were suppressed when he was either talking or singing. A few weeks later, the vertical movements of the tongue changed to rapid transverse movements, at the rate of about 3 or 4 per second, one centimeter in each direction from the midline.

In mid-March 1997, at Mr. A's request, in spite of the persistent side effects, risperidone treatment was stopped. He was continued on fluoxetine 40 mg/day, the dose of clorazepate was increased to 30 mg/day, and perphenazine 4 mg t.i.d. was added. This regimen slowed the horizontal tongue movements to about 1 per second, and the blinking of the eyes became intermittent. One month later, reserpine 0.25 mg b.i.d. was added to the above medications with marked relief in symptoms. The tongue movements changed to the classical tongue rolling of tardive dyskinesia. The blinking of the eyes almost disappeared, and there was only occasional deep and labored breathing. Perphenazine was tapered off over the next month. At the end of May, he complained of worsening depression with crying spells lasting 1–2 hours at a time. Reserpine was tapered off and dyskinetic movements became worse. Perphenazine had to be restarted. Three months later, he was receiving perphenazine 4 mg q.i.d., fluoxetine 20 mg b.i.d., and clorazepate 7.5 mg q.i.d. He still had tongue rolling movements with pushing of the left cheek, some puckering of the lips, and occasional deep sighing respirations. Mr. A denied being depressed and had enrolled in two college courses.

The severity of dyskinetic movements generally correlated with the depth of depression, except when he was taking reserpine. While he was taking reserpine 0.25 mg b.i.d., the dyskinesia was in reasonable control, but the depression was worse.

Risperidone, a newer antipsychotic agent, is classified as an atypical agent because it has a low $D_2/5\text{-HT}_2$ binding ratio and a lower incidence of extrapyramidal side effects compared with typical antipsychotics. It is too early to judge its potential for causing tardive dyskinesia. There have been isolated case reports of patients who were treated with typical antipsychotics in the past who developed tardive dyskinesia when they were treated with a dosage of risperidone 6 mg or higher.^{1–4} Mr. A had never before taken antipsychotics, and he only took risperidone 1 mg/day for 6 months. An unusual presentation was the variety of tongue movements. The progression from slight tongue rolling to slow, large amplitude vertical movements to rapid small amplitude horizontal movements and finally to tongue rolling suggests that, in an acute phase, the tongue-rolling dystonic movements can split into two components of vertical and horizontal movements. The three predisposing factors in this case were age, diagnosis of depression, and concomitant use of fluoxetine. Fluoxetine would have increased the blood levels of risperidone and could also have enhanced extrapyramidal symptoms by altering the central dopamine/serotonin ratio in the nigrostriatal system. Fluoxetine itself has been implicated in the causation of tardive dyskinesia.⁵

On the basis of its data, the Janssen Pharmaceutical Research Foundation estimates that the risk of tardive dyskinesia in patients receiving risperidone is 0.0034 per treatment year.⁶ Compared with typical antipsychotics, risperidone is less likely to cause tardive dyskinesia, but the risk does exist.

REFERENCES

1. Addington DE, Toews JA, Addington JM. Risperidone and tardive dyskinesia: a case report [letter]. *J Clin Psychiatry* 1995;56:484–485
2. Buzan RD. Risperidone-induced tardive dyskinesia [letter]. *Am J Psychiatry* 1996;153:734–735

3. Anand VS, Dewan MJ. Withdrawal-emergent dyskinesia in a patient on risperidone undergoing dosage reduction. *Ann Clin Psychiatry* 1996;8:179–181
4. Woerner MG, Sheitman BB, Lieberman JA, et al. Tardive dyskinesia induced by risperidone? [letter] *Am J Psychiatry* 1996;153:843
5. Dubovsky SL, Thomas M. Tardive dyskinesia associated with fluoxetine. *Psychiatr Serv* 1996;47:991–993
6. Ayd FJ Jr, Pies RW. A specific comparison of the atypical antipsychotics. *Advances in Psychopharmacology* 1997;61–62

Brij M. Saran, M.D., Ph.D.
Gloversville, New York

Naltrexone-Induced Reduction of Tobacco Intake

Sir: Naltrexone is an opioid blocker that may alter taste perception. We present the cases of two patients, both of whom smoked heavily and were opiate dependent, who spontaneously and rapidly reduced their daily tobacco intake when undergoing naltrexone treatment.

Case 1. Mr. A, a 28-year-old man, had smoked approximately 50 cigarettes per day for 14 years and had never tried to quit. He started smoking at the age of 14 and abusing heroin at the age of 23. Ten days after completing opiate detoxification, he started naltrexone 50 mg/day. From the third day of naltrexone treatment, he reported less desire to smoke and a slight reduction in food intake. After 1 week, Mr. A reported an abrupt reduction in cigarette smoking (to around 5 per day), which was attributed to an inability to taste tobacco. He did not report nicotine withdrawal. Two months later, naltrexone was suspended for 1 week, during which the ability to taste tobacco and the desire to smoke returned. After 3 months, naltrexone was discontinued, which led to an increase in tobacco intake. The intake, however, did not reach its previous amount. At the time of this report, Mr. A has maintained his opiate-free status, continues to attend the outpatient facility, and is engaged in a smoking cessation program.

Case 2. Mr. B, a 31-year-old man, had smoked up to 40 cigarettes per day for 16 years and had made several attempts to quit, which were unsuccessful due to nicotine craving. He started smoking at the age of 15 and abusing codeine at the age of 29. Two weeks after completing detoxification, he was administered naltrexone (100 mg on Monday, 100 mg on Wednesday, and 150 mg on Friday each week). After 1 week, he reported smoking cessation, which was explained by an inability to taste tobacco. He developed a slight nicotine withdrawal syndrome that consisted of insomnia and irritability and reported a reduction in food intake. Two months later, naltrexone was suspended for 1 week, during which the previous ability to taste tobacco returned. After 6 months, naltrexone was stopped, and Mr. B started to smoke again. He was opiate-free, continued attending the outpatient facility, and was referred to a smoking cessation program.

There is some evidence of the efficacy of naltrexone for smoking cessation.¹ Naltrexone may alter taste perception and nutrient intake in humans, perhaps through endogenous opioid release.² Our patients reduced smoking and food intake due to an inability to taste nicotine and food. We think that naltrexone may affect the ability to taste nicotine and thus may be useful in some cases of nicotine dependence in diminishing smoking reinforcement and in facilitating smoking cessation programs. However, the results we observed suggest the need for con-