

# Symptomatic Bradycardia: an Adverse Event Following Risperidone Initiation in an Elderly Male

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## Abstract

Risperidone, despite having a relatively safe side effect profile, has been reported to cause serious cardiovascular adverse effects. The authors report a case of risperidone use for an elderly male with long-standing bipolar mood disorder and coronary artery disease, which resulted in the sudden onset of symptomatic bradycardia. Symptom reversal occurred after risperidone was discontinued.

**Key words:** Adverse effects, Cardiovascular effects, Risperidone

## Introduction

Risperidone is a newer, atypical antipsychotic agent with a relatively safe side effect profile compared with typical antipsychotic drugs. Even among atypical antipsychotic agents, risperidone has been shown to have a relatively favourable side effect profile, especially in comparison with clozapine.<sup>1</sup> Risperidone use, however, is associated with adverse cardiovascular effects, including tachycardia,<sup>1</sup> hypotension/symptomatic orthostasis,<sup>2</sup> and electrocardiograph (ECG) changes,<sup>3</sup> sometimes with life-threatening consequences.<sup>2,4,5</sup> We report a patient in whom cardiac complications, specifically symptomatic bradycardia, precluded the continued therapeutic use of risperidone.

## Case Report

An elderly man aged 75 years presented with an illness of 39 years duration, characterised by depressive and manic episodes. To date, excluding the current manic episode, this patient had experienced 6 depressive and 5 manic episodes in total. The depressive episodes were of mild to moderate severity and were responsive to antidepressant therapy, while the hypomanic/manic episodes were effectively managed with neuroleptic drugs. Symptomatic management was undertaken for each episode. Lithium prophylaxis was

utilised for a period of 2 years from the age of 60 years (with no associated episodes) but was discontinued by the patient. Approximately 3 years prior to the current presentation, lithium therapy was re-instituted, during which time the patient had 2 hypomanic episodes. Due to intolerable side effects, a trial of carbamazepine and sodium valproate was prematurely discontinued.

Further medical history of note included non-insulin dependent diabetes mellitus (NIDDM), which was well-controlled with second generation oral hypoglycaemic agents. In addition, coronary artery disease (CAD) had been detected in 1997 and the patient had undergone coronary bypass surgery in that year, and commenced medical therapy of atenolol 50 mg/day and diltiazem 90 mg/day. Despite the bipolar pattern of illness, compliance with treatment was extremely good for both the psychiatric and physical illnesses. During this interim period, about 1 year previously, ECG examination revealed a heart rate of 63 beats per minute and ECG intervals in the normal range. The QT<sub>c</sub> interval (QT/RR interval) was 0.4 seconds.

The current manic episode, of 1 month in duration, was initially managed with clonazepam in doses of 3 mg/day to 4 mg/day. However, worsening of symptomatology necessitated adjuvant therapy. Risperidone was therefore initiated at a dose of 2 mg/day. On day 5 of risperidone therapy, the dose was increased to 3 mg/day. On day 7, there was sudden onset of weakness, lethargy, and a tendency to fall. Physical examination revealed no abnormalities other than sinus bradycardia. There was no postural fall in blood pressure. ECG recording revealed a heart rate of 45 beats per minute and a QT<sub>c</sub> interval of 0.4 seconds; there were no other ECG findings of note. There was no evidence to suggest overdose of any of the prescribed medications.

On day 8, risperidone was reduced to 2 mg/day and subsequently discontinued on day 9. Within 12 hours, symptom reversal was evident. Diltiazem and atenolol were also discontinued, with clonazepam the only continuing drug therapy. A repeat ECG on day 12 recorded a heart rate of 66

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beats per minute, and a  $QT_c$  interval of 0.43 seconds, with no other findings of note. Echocardiography and 24-hour Holter monitoring did not reveal any significant abnormality. Subsequently, the manic episode was managed with high doses of clonazepam and remitted after a further period of 4 weeks.

## Discussion

Antipsychotic agents, in particular typical antipsychotics, have been known to induce ECG abnormalities and adverse cardiac effects. With regard to atypical antipsychotics, animal models have shown risperidone to have more potent effects than others in prolonging the QT interval on ECG. Review of the literature has shown that cardiac arrest can occur with risperidone overdose<sup>5</sup> and at lower doses in the elderly,<sup>2</sup> as well as in adults with no pre-existing cardiac disease.<sup>4</sup>

The patient described in this report showed a temporal relationship between the onset of cardiac symptoms, bradycardia, and ECG changes and the use of risperidone therapy. However, it must also be considered that the patient had pre-existing CAD, and was receiving regular treatment with diltiazem and atenolol. Diltiazem, a calcium channel blocker, can induce symptomatic bradycardia when used in conjunction with  $\beta$ -blockers such as propranolol and metoprolol. This effect has not been reported, however, when used in conjunction with atenolol.<sup>6</sup>

The literature search did not reveal any clinically significant interaction between risperidone and these drugs. Although it is possible that pre-existing cardiac disease and calcium channel blocker and  $\beta$ -blocker interactions were underlying factors inducing the ECG changes and symptomatic bradycardia, a potential role for risperidone as a causative or contributing agent cannot be excluded. It would seem advisable, therefore, that risperidone be used with caution among the elderly, those with pre-existing cardiac disease, or receiving cardiac drug therapy, and that risperidone therapy should not be initiated without a proper evaluation of the patient's cardiac status.

## References

1. Sadock BJ, Sadock V. Comprehensive textbook of psychiatry. 7th ed. Philadelphia: Lippincott, Williams and Wilkins; 2000.
2. Zarate CA Jr, Baldessarini RJ, Siegel AJ, et al. Risperidone in the elderly: a pharmacoepidemiologic study. *J Clin Psychiatry* 1997;58:311-317.
3. Drici MD, Wang WX, Liu XK, Woosley RL, Flockhart DA. Prolongation of QT interval in isolated feline hearts by antipsychotic drugs. *J Clin Psychopharmacol* 1998;18:477-481.
4. Ravin DS, Levenson JW. Fatal cardiac event following initiation of risperidone therapy. *Ann Pharmacother* 1997;31:867-870.
5. Kopala LC, Day C, Dilliman B, Gardner D. A case of risperidone overdose in early schizophrenia: a review of potential complications. *J Psychiatry Neurosci* 1998;23:305-308.
6. Sagie A, Strasberg B, Kushireck J. Symptomatic bradycardia induced by the combination of oral diltiazem and beta blockers. *Clin Cardiology* 1991;14:314-316.