

The findings of this study suggest that even if a new drug is associated with lower side effects than previous drugs in its class at the patient level, a marked increase in its use can be associated with an apparently paradoxical adverse impact on the population.

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Competing interests: MM has done research in an unrelated content area upon the request of an academic institution whose

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Ethical approval: Sunnybrook and Women's College Health Sciences Centre Ethics Review Board.

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DRUG POINTS

Nose bleeds associated with use of risperidone

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The New Zealand Intensive Medicines Monitoring Programme has received two reports of nose bleeds associated with risperidone. A 57 year old woman began having profuse nose bleeds associated with headaches immediately after starting to take risperidone 1 mg daily. She had no history of hypertension and was taking no other medicines. Risperidone was discontinued four days later and the nose bleeds stopped. A 42 year old man with no history of nose bleeds began having spontaneous nose bleeds while taking risperidone; coagulation tests were reported as normal.

The World Health Organization's international drug monitoring database contained an additional 54 reports of nose bleeds associated with risperidone, of which 37 had sufficient information for causality assessment. In 22 cases, nose bleeds began within three weeks of starting risperidone. In 10 of 12 patients for whom dechallenge data were available the reaction abated on stopping risperidone. Three of the 10 patients underwent rechallenge: two did not have nose bleeds again, but the third, a 15 year old boy, had a recurrence after the rechallenge.

Several pharmacological mechanisms might explain this adverse reaction. Thrombocytopenia is a recognised adverse effect of atypical antipsychotic medicines and has been reported with risperidone.¹ Although one of the New Zealand patients was reported to have a normal blood count, in nine of the 37 WHO cases thrombocytopenia was reported.

Risperidone is also a potent 5-HT_{2A} receptor antagonist. Sarpogrelate, another 5-HT_{2A} antagonist, increases blood flow in the coronary microcirculation by reducing platelet aggregation and vasoconstrictor release from platelets.² Risperidone could plausibly have a similar effect in other parts of the microcirculation.

The New Zealand and UK product information for risperidone does not mention nose bleeds. The US

Physicians Desk Reference states that in premarketing studies nose bleeds occurred in 1 in 100 to 1 in 1000 patients.³ Literature searches did not identify any reports of nose bleeds associated with risperidone, and so we believe these are the first published cases of this adverse drug reaction.

Contributors: MH-W assessed the original New Zealand case reports, performed the literature searches, identified the signal, and wrote the manuscript. DWJC accessed and evaluated the cases from the World Health Organization's database, proposed a possible mechanism, and reviewed the manuscript.

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Competing interests: None declared.

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Endpiece

The end of the party

The closing years of life are like the end of a masquerade party, when the masks are dropped.

Arthur Schopenhauer (1788-1860),
German philosopher

Fred Charatan,
retired geriatric physician, Florida