Letter to the Editor

Hypothermia Secondary to Ziprasidone Use in a Man With Schizophrenia

To the Editor: Various case reports have been published showing atypical antipsychotics as causing hypothermia, but there are very few cases of hypothermia with ziprasidone. Hypothermia is caused by an imbalance of dopamine and 5-HT₂ receptors.¹ We present a case of a schizophrenic unmarried white man who developed profound hypothermia on ziprasidone treatment.

Case report. Mr A, a 59-year-old patient with DSM-IV-TR schizophrenia who was receiving ziprasidone 80 mg twice daily, presented to the emergency department from his assisted living facility as poorly responsive and lethargic. In the emergency department, he was determined to have an oral temperature of 87°F. At admission, Mr A was listless but could respond to commands. On physical examination, he was able to follow commands, but his pupils were sluggishly reactive. His electrocardiogram showed sinus bradycardia and nonspecific ST segment changes. His vital signs included blood pressure of 100/65 mm Hg, pulse of 60 bpm, respirations of 19/min, oral temperature of 87°F, and rectal temperature of 85°F. His medical history was significant only for schizophrenia for the past 15 years and cataracts, and he received only ziprasidone 80 mg twice daily for the last 3 years. He did not have history of hypothyroidism, stroke, diabetes mellitus, ischemic heart disease, adrenal insufficiency, or arthritis, which could predispose him to hypothermia. Complete blood cell counts and comprehensive metabolic panel were normal. Urine drug screens performed were negative. Cardiac enzymes and thyroid panel findings were within the normal range. His blood gas measurements included a pH of 7.31, Pco2 of 49, Po2 of 121 on 1 L of O2, and Hco₂ of 28. Computed tomography scan of the head revealed no abnormalities, and chest x-ray showed no masses or pneumonias. The patient was admitted to the intensive care unit with warmed saline infusion, humidified oxygen, and other conservative measures such as warming blankets. The psychiatry department was consulted, and Mr A's ziprasidone was discontinued as it was suspected to have caused the hypothermia as no other offending agent was recognized. He was normothermic by day 5 and was discharged to the assisted living facility thereafter. He was followed up later in the outpatient clinic and subsequently never developed hypothermia.

Dopamine acts to lower the body temperature, and 5-HT₂ receptors tend to increase the body temperature. Atypical antipsychotics are more potent inhibitors of 5-HT₂ than the dopamine receptor,^{2,3} so they tend to lower the body temperature more than they increase it.⁴ However, according to a World Health Organization database,⁵ ziprasidone should cause fewer cases of hypothermia in patients as compared to other atypical antipsychotics because of its 5-HT_{1A} receptor agonism. A total of 51% of all cases of antipsychotic-induced hypothermia were found in patients with schizophrenia. Only 11% each were observed in patients with bipolar disorder, dementia, and mental retardation.⁵ Löffler et al⁶ discuss use of high-dose ziprasidone and lorazepam in patients who developed hypothermia on treatment with other atypical antipsychotics. As of January 2007, only 8 cases of ziprasidoneinduced hypothermia were noted, whereas there were more for risperidone (129 cases), clozapine (68 cases), olanzapine (44 cases), quetiapine (21 cases), and aripiprazole (11 cases).⁶ Hypothermia in schizophrenic patients is considered to be a possible link between antipsychotics and unexplained death.^{7,8} Other conditions in psychiatric patients that can increase the risk of hypothermia include nocturnal enuresis, seizure disorder, debilitating physical illness, and mental retardation.8

Second-generation antipsychotic-induced hypothermia has been reported. Although ziprasidone is known to cause

lesser hypothermia because of its 5-HT₁ agonism, and milder dopamine antagonism, it should still be used cautiously in patients with schizophrenia. Development of hypothermia in a patient maintained on predisposing drugs warrants its discontinuation and consideration of alternative drugs. Combination drugs should also be suspected if a patient is taking ziprasidone in conjunction with other medications.⁹

REFERENCES

- Yamawaki S, Lai H, Horita A. Dopaminergic and serotonergic mechanisms of thermoregulation: mediation of thermal effects of apomorphine and dopamine. *J Pharmacol Exp Ther*. 1983;227(2):383–388.
- Razaq M, Samma M. A case of risperidone-induced hypothermia. Am J Ther. 2004;11(3):229–230.
- Löffler S, Danos P, Schillen TB, et al. [Recurrent dysregulation of body temperature during antipsychotic pharmacotherapy]. *Psychiatr Prax.* 2008;35(2):91–93.
- Gibbons GM, Wein DA, Paula R. Profound hypothermia secondary to normal ziprasidone use. Am J Emerg Med. 2008; 26(6):737.e1–737.e2
- van Marum RJ, Wegewijs MA, Loonen AJ, et al. Hypothermia following antipsychotic drug use. Eur J Clin Pharmacol. 2007;63(6):627–631.
- Löffler S, Cordes J, Danos P, et al. Ziprasidone might prevent lifethreatening hypo- and hyperthermia induced by antipsychotics. *Ger J Psychiatry*. 2008;1:126–127.
- Kudoh A, Takase H, Takazawa T. Chronic treatment with antipsychotics enhances intraoperative core hypothermia. *Anesth Analg.* 2004;98(1):111–115.
- Young DM. Risk factors for hypothermia in psychiatric patients. Ann Clin Psychiatry. 1996;8(2):93–97.
- Noto T, Hashimoto H, Sugae S, et al. Hypothermia caused by antipsychotic drugs in a schizophrenic patient. *J Clin Psychiatry*. 1987;48(2):77–78.

Roopa Sethi, MD supa_roopa78@hotmail.com Bush Kavuru, MD

Author affiliations: Department of Psychiatry, Carilion Clinic, Virginia Tech Carilion School of Medicine, Roanoke. Potential conflicts of interest: None reported. Funding/support: None reported. Published online: August 16, 2012. Prim Care Companion CNS Disord 2012;14(4):doi:10.4088/PCC.11/01338 © Copyright 2012 Physicians Postgraduate Press, Inc.