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Case Report

Profound hypothermia secondary to normal ziprasidone use

Abstract

Clinically significant hypothermia is a commonly evaluated condition in emergency medicine. Most cases are related to prolonged exposure to the environment, infection, or endocrinopathies.

Presented here is a case of hypothermia likely induced by an atypical antipsychotic medication.

A 69-year-old incarcerated man presented to our emergency department with an oral temperature of 85°F (29.4°C). The patient was taking ziprasidone (Geodon, Pfizer, New York, NY) 80 mg twice daily.

Atypical antipsychotic medications have been implicated in numerous cases of clinically significant hypothermia. The mechanism of action for antipsychotics has not been fully elucidated, but the hypothermia induced by this class of medications is believed to be driven through the antagonism of the dopamine ($D_{1\text{-}4}$) and 5-hydroxytryptamine-2 (5-HT2) receptors. It has been theorized that under normal conditions, there is a balance between dopamine acting to reduce the body temperature and 5-HT2 acting to elevate body temperature. Atypical antipsychotics, particularly ziprasidone, appear to have a higher affinity to antagonize the 5-HT2 receptor and less at the D_2 receptor, therefore creating an imbalance favoring the lowering of core body temperature. Other theories include the antagonism of α_1 receptors by these medications causing vasodilatation and shunting of blood to the skin causing profound heat loss.

An antipsychotic medication can be the sole cause of hypothermia or it can be one of a number of possible causes coexisting in the individual with hypothermia.

Clinically significant hypothermia is a commonly evaluated condition in emergency medicine. Most cases are related to prolonged exposure to the environment, infection, or endocrinopathies. Presented here is a case of hypothermia likely induced by an atypical antipsychotic medication.

A 69-year-old incarcerated man presented to our emergency department after being found poorly responsive by guards in an air-conditioned jail cell. The patient was seen by the nurse at the infirmary and was determined to have an oral temperature of 85°F (29.4°C). The patient was sent to our facility for evaluation. Upon arrival, the patient was listless but oriented, able to follow commands, and able to move all extremities. Medical history was significant for schizophrenia and peptic ulcer disease. Current medications included ziprasidone (Geodon, Pfizer, New York, NY) 80 mg twice daily and ranitidine (Zantac, GlaxoSmithKline, Philadelphia, PA) 150 mg twice daily. Initial vital signs were blood pressure of 101/63, pulse of 50, respirations of 18, and rectal temperature of 84.9°F (29.4°C). Physical examination was significant for sluggish but equal, round, reactive pupils. Cardiopulmonary examination finding was normal. He was neurologically intact, with no external signs of injury or infection. The remainder of the physical examination was without significant findings. Electrocardiogram demonstrated sinus bradycardia with nonspecific ST-segment changes. Chest x-ray showed no active disease. Computed tomographic scan of the head confirmed no acute processes. Complete blood count and complete metabolic profile were within normal limits. Cardiac enzymes were negative, thyroid-stimulating hormone was normal, and random cortisol was slightly elevated at 28.8. Urine drug screen and toxicology screens were negative. Arterial blood gases were as follows: pH 7.32, pCO_2 47, pO_2 151 on 2 L via nasal cannula, HCO_2 25.The patient was gently warmed using an air-circulating blanket, humidified oxygen, and warmed intravenous normal saline. He was admitted to the intensive care unit for further evaluation and stabilization. The patient was evaluated by neurology for the alerted mental status and the ziprasidone was discontinued. By hospital day 3, the patient became consistently euthermic with normalization of his electrocardiogram. Electroencephalogram demonstrated mild background slowing. Echocardiogram showed mild left ventricular hypertrophy, mild pulmonary hypertension, and an ejection fraction of 50% to 55%. He had no further episodes of hypothermia, hypotension, or arrhythmias. The remainder of the hospitalization was unremarkable. The patient was discharged back to jail on hospital day 8 after return to baseline function.

Although the mechanism of action for antipsychotics has not been fully elucidated, it is hypothesized that it is driven through the antagonism of the dopamine ($D_{1\text{-}4}$) and 5-hydroxytryptamine-2 ($5\text{-}HT_2$) receptors [1]. Yamawaki et al [2] postulates that under normal conditions, there is a balance between dopamine acting to reduce the body

temperature and 5-HT acting to elevate body temperature. Atypical antipsychotics, particularly ziprasidone, appear to have a higher affinity to antagonize the 5-HT_2 receptor and less at the D_2 receptor [3], therefore creating an imbalance favoring the lowering of core body temperature. Neuroleptic malignant syndrome is theorized to be caused by the opposite imbalance of increased D_2 antagonism causing dramatic increase in body temperature [4], further supporting this hypothesis.

Atypical antipsychotics are also known to antagonize α_1 receptors. These receptors are responsible for vasoconstriction and shunting of blood away from the skin to maintain core body temperature. Antagonism of these receptors could also contribute to profound heat loss, particularly in a cooler environment. Risk factors for developing hypothermia with antipsychotic therapy are difficult to identify. In 2007, van Marum et al noted that 51% of all cases of antipsychotic-induced hypothermia were observed in patients with a diagnosis of schizophrenia. Bipolar disorder, dementia, and mental retardation were responsible for 11% each. Eighty percent of the cases of hypothermia were noted to occur at the start of therapy or after a recent increase in the dose of the medication [5]. As of January 2007, the World Health Organization International Database for Adverse Drug Reaction reported 8 cases of hypothermia in patients taking ziprasidone. The occurrence was much higher in risperidone (Risperdal, Janssen, Titusville, NJ) at 129 reported cases, likely secondary to increased prescribing habits of that medication [5]. In conclusion, atypical antipsychotic medications have been implicated in numerous cases of clinically significant hypothermia. An antipsychotic medication can be the sole cause of hypothermia or it can be one of a number of possible causes coexisting in the individual with hypothermia. Medication-related hypothermia is quite rare; therefore, all other causes should be adequately investigated. Fortunately, our patient did not develop significant cardiac, respiratory, or central nervous system complications. The importance of this article is to provide emergency physicians with information regarding a potentially devastating complication of antipsychotic therapy.

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