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Case Report
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Hypothermia as a Medication Side Effect

Behçet Varışlı

Final International University, Department of Emergency Medicine, Kyrenia, Northern Cyprus

Abstract

In humans, the body temperature stabilizes in the range of 36.5-37.3 °C; below 35 °C is defined as hypothermia. The use of olanzapine, an antipsychotic drug, is one of the least reported drugs in the etiology of hypothermia. A 67-year-old female patient was admitted to the emergency department. Her body temperature was measured 27.8 °C. No cold exposure was found on the first evaluation by the ambulance crew. It was learned that she used olanzapine 10 mg and had taken her first dose 8 h ago. The patient's hypothermia was evaluated because of olanzapine use. Body temperature regulation disorders due to antipsychotic drug use are mostly defined as hyperthermia. It has been reported that antipsychotic drugs may very rarely play a role in the etiology of hypothermia and hyperthermia. Olanzapine is used for treating psychotic diseases by acting via an antagonist mechanism on 5-HT2A/C and dopamine D2 receptors located in the hypothalamic region. The hypothalamus is thought to play a crucial role in central thermoregulation and providing the therapeutic efficacy of antipsychotic drugs. Antipsychotics may also cause hypothermia by blocking peripheral b2 receptors. These common mechanisms explain the cause of hypothermia in this study due to olanzapine use. Olanzapine use should be considered in cases of unexplained hypothermia in the emergency department. Routine body temperature monitoring should be considered in patients who are administered antipsychotic drugs with hypothermia in the side-effect profile, such as olanzapine.

Keywords: Hypothermia, side effect, antipsychotic drug, olanzapine

Introduction

In humans, the body temperature stabilizes in the range of 36.5-37.3 °C, below 35 °C is defined as hypothermia (1). Hypothermia is categorized into three classes: mild (35-33 °C), moderate (33-28 °C) and deep (<28 °C) (1). Depending on the degree of hypothermia, chills and tremors, unconsciousness, deep coma, and even cardiac arrest (CA) may occur (2). Hypothermia may occur as a result of insufficient protection against cold exposure, hypoglycemia, adrenal insufficiency, hypothyroidism, therapeutic applications, and drugs (1). Hypothermia due to antipsychotic drugs has been reported very rarely (3).

Body temperature regulation disorders due to antipsychotic drug use are mostly defined as hyperthermia (4). In this case report, we present a case of hypothermia due to olanzapine use in light of the literature.

Case Report

A 67-year-old female patient was brought to the emergency department by ambulance crews on a day when the air temperature was 17 degrees Celsius, with complaints of immobility in her 4 extremities and impaired speech. No history could be taken from the patient because of speech disorder. She had no history of any other disease, such as diabetes mellitus (DM), hypothyroidism, adrenal insufficiency, cerebrovascular disease (CVD), or ischemic heart disease, apart from known schizophrenia. It was learned that she used olanzapine 10 mg and had taken her first dose 8 h ago. In the emergency department, the body temperature was measured on the skin with a bedside monitor, and it was found to be 27.8 °C (82.04°F), heart rate 33 beats/minute, blood pressure 80/50 mmHg, respiratory rate 14/minute, and oxygen saturation 94% in room air. Deep hypothermia was detected in the patient. No cold exposure was found on the first evaluation by the ambulance

Corresponding Author: Behçet Varışlı MD, Final International University, Department of Emergency Medicine, Kyrenia, Northern Cyprus
Phone: +90 530 820 45 99 **E-mail:** drbehcetvarisli@gmail.com **ORCID ID:** orcid.org/0000-0002-2346-1112

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crew. On physical examination, the patient was confused, her eyes were open spontaneously, she had no verbal response, and she avoided stimuli. The skin and mucous membranes were dry, there was no jugular fullness, and other systemic examinations were within normal limits. In addition, an increase in RR and QT wave intervals, first-degree atrioventricular block, and sinus bradycardia were observed in the first electrocardiogram (ECG) in the emergency department (Figure 1).

In terms of the etiology of hypothermia and impaired consciousness, serum glucose 125 mg/dL, sodium 136 mEq/L, urea 45, creatinine, glomerular filtration rate, cortisol level, thyroid stimulating hormone, free triiodiothyronine, free thyroxine, and complete blood count were within normal limits.

Posteroanterior chest X-ray and brain computed tomography were within normal limits, and no ischemic changes were observed on diffusion magnetic resonance imaging. The patient's hypothermia was evaluated because of olanzapine use.

For the treatment of hypothermia, 1000 mL of intravenous bolus hydration with warmed 0.9% sodium chloride was applied to the patient, and the patient was covered with a thermal blanket. In the first hour of her treatment, her blood pressure was 110/60 mmHg, heart rate was 60 beats/min, and body temperature was 29.7 °C.

The patient, who was admitted to the intensive care unit, continued to be warmed with heated intravenous fluid applications and external active air heater systems. Body temperature was monitored in terms of hypothermia on the skin and recorded hourly (Figure 2).

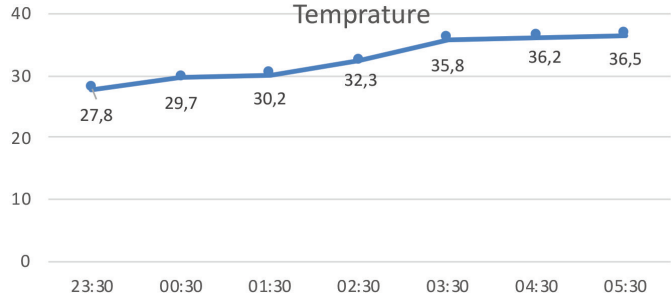

Figure 1. Body temperature chart

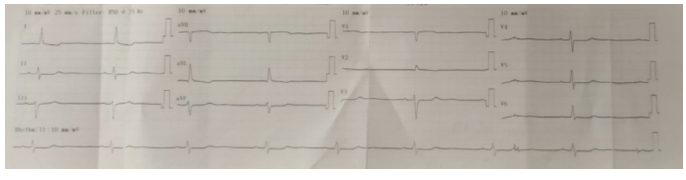

Figure 2. First electrocardiogram in the emergency department

In the body temperature follow-ups, the body temperature reached 36.5 °C at the 6th hour of treatment. In the control evaluation performed at the 24th hour of the patient, it was found that she was conscious, oriented, cooperative, and had full muscle strength in 4 extremities, and motor and sensory examinations were normal. The patient's olanzapine use was terminated, and she was referred to the psychiatric clinic for drug regulation.

Discussion

Body temperature is the basic vital parameter in the evaluation of many diseases and critical patients that require emergency treatment in the emergency department and is measured from the pulmonary artery as the gold standard (5). Besides the pulmonary artery, due to both their invasiveness and the length of the application period, measurements made through the esophagus, bladder, and rectum have left their place to measurements made from the temporal artery, tympanic, or forehead with infrared methods that can be applied more easily in emergency services (5).

In the treatment process of hypothermia, the infusion of heated fluids, delivery of heated fluids to the body cavities, and heated air can be used, while the body temperature of the patients can be monitored with systems that can make hypothermic measurements (6).

In our case, heated fluid infusion and heated air were used for treating hypothermia, and a skin sensor placed on the back of the patient, posterior to the pulmonary region, was used in the follow-up.

Dopamine D1 and D2, alpha-1, 5-hydroxytryptamine 1 and 2 receptors located in the hypothalamus are thought to play a crucial role in central thermoregulation as well as providing the therapeutic efficacy of antipsychotic drugs (7). Antipsychotics may also cause hypothermia by blocking peripheral b2 receptors (8). These common mechanisms explain the etiology of hypothermia in our case due to olanzapine use.

The hypothermic effects of antipsychotic drugs have been tested with animal experiments, and it has been shown that therapeutic hypothermia can be created by administering olanzapine at a daily treatment dose (9). This supports the role of olanzapine in the etiology of hypothermia in our case.

Hypothermia may cause changes in ECG by affecting cardiac electrophysiology (1). Deep hypothermia may cause an increase in the RR interval in wavelengths, an increase in the P wave amplitude, an increase in the PR interval, first- to third-degree atrioventricular blocks, an increase in the QRS width and an

increase in the QT interval, and atrial fibrillation, ventricular fibrillation (VF), and asystole may also be seen as arrhythmia (2). An increase in the RR and QT wave intervals, first-degree atrioventricular block, and sinus bradycardia were associated with hypothermia in the ECG of our case.

When CA develops in a hypothermic patient, while chest compression and ventilation are performed in the same way as a normothermic patient in cardiopulmonary resuscitation (CPR) practices, there are differences in electrical therapy and drug applications in the case of VF (2,10). When VF develops, no shock is applied again until the body temperature rises above 30 °C after three shocks (2). Epinephrine is not recommended to be administered below 30 °C, and when it rises above 30 °C, it is recommended to double the application time interval and apply it every 6-10 minutes (2). Delayed CPR can be applied in CA below 28 °C, and it is recommended to return to normal CPR protocols above 35 °C (2).

In the literature, such predisposing factors as infection, hypothyroidism, DM, and long-term drug use are observed in patients who develop hypothermia (11). The absence of predisposing factors in our case supports the association of olanzapine with the etiology of hypothermia.

Body temperature measurement and monitoring are not routinely performed in patients using antipsychotic medication (12). Therefore, it is unknown how often hypothermia occurs in the side-effect profile (12). Considering the timing of the reported cases of hypothermia, it was reported that 20% of them occurred during the long period of drug use, mostly in the first 7-10 days (8). In our case, hypothermia also occurred on the first day of drug use. It can be concluded that body temperature monitoring in the first 10-day period will be beneficial in patients who started to use antipsychotics, especially olanzapine.

Conclusion

In conclusion, olanzapine use should be considered in cases of unexplained hypothermia in the emergency department. Routine body temperature monitoring should be considered in patients who are administered antipsychotic drugs with hypothermia in the side-effect profile, such as olanzapine.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

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