



Olanzapine-induced hypothermia: A rare case report

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ABSTRACT

We report a case of 40-year-old man who had a diagnose case of schizophrenia on olanzapine had develop symptomatic hypothermia. The majority of documented cases involve short duration of hypothermia often <24 h. Antipsychotics that are a more potent antagonists at 5-hydroxytryptamine 2 (5HT₂) than at dopamine 2 receptors appear more likely to cause hypothermia. Hypothermia is an adverse drug reaction of antipsychotic drug use. It is strong 5HT₂ antagonistic characteristics which induced hypothermia has been proposed. 55% of hypothermia reports are for atypical antipsychotics. A 40-year-old man with schizophrenia who was being treated with a therapeutic dose of olanzapine presented with shivering, slurred speech, and confusion. He had a core temperature of 31.5°C. Electrocardiogram showed sinus bradycardia with Osborn waves or J waves. He did not have any risk factors for developing hypothermia except the use of olanzapine. There was an improvement in his clinical condition with reversal of electrocardiogram changes following gradual re-warming and withhold of olanzapine. Olanzapine-induced hypothermia is rare and has been reported during initiation and increasing the dose or even in stable dose, but this case report raises the possibility of hypothermia even in the patients who are on stable doses of olanzapine for a long period of time. Clinicians should consider the possibility of drug-induced illness in hypothermic patients who are taking antipsychotics.

KEY WORDS: Camel hump sign, hypothermia, J waves, Osborn waves, temperature-dysregulation

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INTRODUCTION

Hypothermia is a traditionally defined as a drop in core body temperature below 35°C (95°F). It is infrequent and rare adverse effect of antipsychotics and associated with electrocardiographic changes of diagnostic and prognostic importance, called Osborn waves, J waves and camel hump sign, i.e., sinus bradycardia and extra deflection at the end of QRS complex, are best seen in the inferior and lateral precordial leads. They become more prominent as the body temperature drops and regress gradually with warming and disappear after 24 h [1,2]. Osborn wave in the hypothermic patients is a warning sign of life-threatening arrhythmias [1,2].

Olanzapine antagonizing predominantly on serotonin ((5-hydroxytryptamine 2) [3], dopamine (D₂) [4], and neurotensin (NT) [5] have recognize as a mediator of hypothermia, especially in patient with schizophrenia. In clinical practice, the most common causes of hypothermia are exposure to cold temperature, malnutrition, medical conditions such as hypothyroidism, sepsis, diabetes mellitus, stroke, adrenal insufficiency, shock, burn, ethanol abuse, and medications such as oral hypoglycemic, sedative-hypnotics, antipsychotics, barbiturates, and alcohol [6].

In schizophrenia, there is a decrease in core temperature after administration of antipsychotics due to thermal dysregulation

and it may be explained by changes in NT level [7]. The symptoms and sign of olanzapine-induced hypothermia are shivering, delirium, slurred speech, fatigue, incoordination, and bradycardia. Depending on the severity of the hypothermia, the patient may show various clinical symptoms from shivering to deep coma.

Olanzapine is an antipsychotics acts on both dopamine and serotonin receptors. Olanzapine also has a lower affinity for histaminergic, cholinergic, muscarinic, and alpha-adrenergic receptors. Blocking of alpha 2 adrenergic receptors may also increase the hypothermic effect. NT has also been in addition to this mechanisms has been recognize as a mediator of hypothermia. NT is one of the thermoregulatory peptides that also play a role in the actions of antipsychotics medications.

According to published data in the world health organization database. PubMed, EMBASE only a few cases of hypothermia associated with olanzapine have been reported since its introduction into clinical use [8]. The most common psychiatric disorder associated with hypothermia is schizophrenia [9]. Studies in schizophrenic patients show that core temperature decreases following the administration of antipsychotics [10,11]. In this report, a case of hypothermia, possibly associated with olanzapine, is described.

CASE REPORT

A 40-year-old, good body built, ex. soldier, unemployed, suspended from the job due to psychiatric illness, he is belonging to low socio-economic status. The patient was admitted to Mental Health Hospital, Taif for his disturbed behavior and non-compliance with medications since 3 months. He was diagnose a case of schizophrenia for the past 3 years was stable on olanzapine 10 mg daily since long no other drugs were administered, on readmission increased dose 10 mg twice a day. He did not have any history of diabetes, hypothyroidism, stroke, ischemic heart disease, and hypopituitarism predisposing him to hypothermia and no history of drug abuse or overdose. There was no positive family history of psychiatric illness or drug abuse. He was asymptomatic in the previous night and suddenly in morning present with shivering, slurred speech, confusion, unable to walk. His Glasgow Coma Scale score was 8/15, pulse rate 60 beats/min and core temperature was 31.5°C. Electrocardiogram showed sinus bradycardia with Osborn waves which are seen in hypothermia [12], and no any other side effect except hypothermia. Blood investigation and computerized tomography scan were unremarkable. On the basis of the clinical findings, the patient's body temperature and electrocardiogram findings, the diagnosis of hypothermia was made. The patient did not have any risk factors for developing hypothermia except for the use of olanzapine. Figure 1 A 12-lead Electrocardiogram obtained, at the times of hypothermia showing sinus bradycardia and Osborn wave, an extra deflection at the end of QRS complex indicated by arrow. Figure 2 A 12-lead Electrocardiogram obtained, after clinical improvement showing reversal of previous changes. Osborn wave seen in Figure 1 have resolved.

He was warmed gradually with blankets and olanzapine was discontinued, his level of consciousness and vital signs were closely monitored. The patient gradually regained consciousness, and all the previous sign and symptoms were reduced. Then, restarted low dosage of olanzapine 5 mg once daily with caution and increased it on follow-up after 2 weeks 5 mg twice a day, again called patient for next follow-up after 2 weeks and he was maintaining well with no recurrence of hypothermia.

DISCUSSION

In our patient, the general medical conditions predisposing them to the development of hypothermia such as hypothyroidism, malnutrition, sepsis, diabetes mellitus, stroke, and adrenal insufficiency were not found. However, it is shown in literature that schizophrenia *per se* is a risk factor for hypothermia [4]. Furthermore, there was no history of an overdose in our patient or any history of substance abuse; therefore in this case, there were no risk factors for the development of hypothermia in the history, examination or in investigations, other than the use of olanzapine and being patient with schizophrenia.

On the basis of the clinical findings sudden onset of shivering, slurred speech, confusion, unable to walk and electrocardiogram shows a sinus bradycardia with Osborn waves, it usually occurs

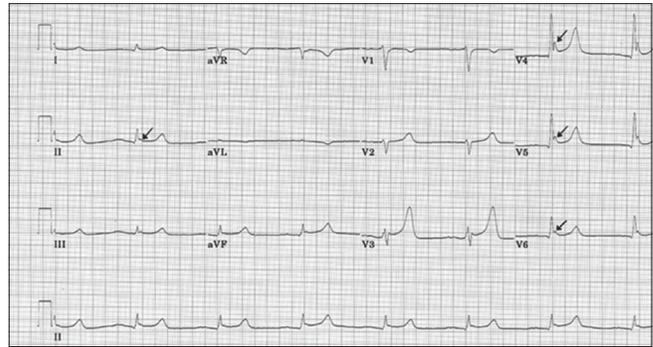


Figure 1: Electrocardiogram at a body temperature 31.5°C, showing Osborn wave or J wave

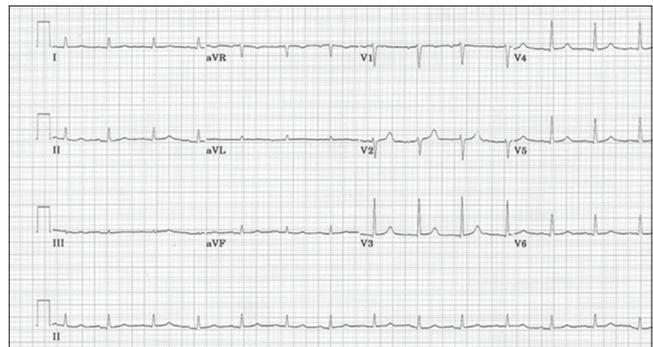


Figure 2: Electrocardiogram after rewarming patient, with disappearance of Osborn wave or J wave

below 32°C, we diagnose him a case of olanzapine-induced hypothermia.

Hypothermia is usually caused by prolonged exposure to cold temperature and other causes, but in this case, report patient did not have any risk factor for developing hypothermia except for the use of olanzapine. Hypothermia in a schizophrenic patient with atypical antipsychotics drug like olanzapine is a serious unpredictable adverse drug reaction and idiosyncratic reaction that needs hospitalization to intensive care unit and if not treated promptly leads to life-threatening complications and death.

CONCLUSION

This case report raises the possibility of hypothermia even in patients who are on stable doses of olanzapine for a long period of time and should alert physicians of the risk of hypothermia in psychiatric patients using antipsychotics. There seems to be no direct relation between stable drug dose and the adverse drug reaction; the period shortly after starting the antipsychotics or dose increase seems to be high-risk period. Furthermore, every change in behavior or co-morbidity, e.g., infection, should be a warning sign to look for hypothermia. In such a context, it is necessary to monitor body temperature very carefully along with the correct dosage of the drug and the time interval of increase in dose.

Drug-induced hypothermia is unnoticed in patients, and in extreme cases can be life-threatening, so clinicians should be aware and alert, the risk of hypothermia is highest after initiation of the drug or often increase in dosage.

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