

# A Case of Clozapine-Induced Hypothermia

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## Introduction

The antipsychotic drug adverse reaction of hyperthermia from neuromalignant syndrome is more well known and investigated than hypothermia. The first antipsychotic drug produced in the 1950s, chlorpromazine, was used in anesthesia to cause artificial hibernation by lowering the patient's body temperature before its antipsychotic efficacy was known [1]. The preoptic anterior hypothalamus is the control center that compares actual body temperature to target values to signal compensatory mechanisms such as vasomotor and behavioral reactions when mismatched. In experimental research, rats with hypothalamic lesions given haloperidol caused a significant decrease in body temperature than rats with an intact hypothalamus [1]. Body temperature is regulated in tight parameters by not fully understood mechanisms, nor is it entirely understood how antipsychotics alter thermoregulation. Hypothermia is a body temperature characterized as lower than 35 °C (95 °F). The importance of this adverse drug reaction is highlighted in the data from the FDA Adverse Event Reporting System in the years 1990 to 2019. This data exhibited 109 patients on a clozapine regimen suffering from hypothermia. In 83 of these cases, clozapine was the top differential. Most of the cases were considered severe, with 21 of them resulting in death [2]. Some risk factors that make those taking antipsychotics susceptible to hypothermia include the adjuvant use of benzodiazepines, exposure to cold, advanced age, and subclinical hypothyroidism [3]. In this case report, we discuss a patient suffering from antipsychotic drug-induced hypothermia.

## Case Presentation

A 54-year-old African American female with a past medical history of type 2 diabetes, hypertension, schizophrenia, and seizure disorder admitted to a psychiatric hospital developed generalized weakness, garbled speech, urinary incontinence, and altered mental status. She was transferred to an emergency department as a stroke code and was admitted for further workup. For the patient's acute encephalopathy, a head CT scan showed no acute intracranial pathology ruling out a stroke, the blood cultures were negative ruling out an infection, and the patient neurologically returned to baseline within a day ruling out an ongoing neurological cause of encephalopathy. The patient was hypothermic at 27.1 °C (80.78 °F) on admission but otherwise hemodynamically stable. Medical workup for hypothermia resulted in negative blood cultures ruling out infection and TSH/T4 levels within normal limits ruling out hypothermia or myxedema coma. The patient's core body temperature stabilized with external warming by using a Bair Hugger. The patient was already on clozapine 250 mg before admission to the inpatient psychiatric facility and was known to be on this current regimen for longer than three months. She was also currently taking topiramate 100 mg at bedtime for her seizure disorder. She had had recent medication changes a week prior to the onset of these symptoms with discontinuation of bupropion and initiation of clonazepam 1 mg twice daily. Due to persistent somnolence and dysarthric speech, her clonazepam was decreased to 0.5 mg twice daily. In suspicion of clozapine-induced hypothermia, her clozapine was discontinued, and quetiapine 50 mg at bedtime was initiated to treat her chronic schizophrenia. The patient's body temperature stabilized within a few days.

## Discussion

This case highlights hypothermia as a possible adverse reaction to clozapine and illustrates the importance of monitoring patients' body temperature, especially when initiating treatment or increasing the dosage. Hypothermia induced by antipsychotic drugs is an unpredictable and severe reaction that often causes patients to be admitted to the ICU and, at times, cause death. Common medical causes of hypothermia include hypoglycemia, sepsis, hypothyroidism, and stroke, which were all ruled out in this case. This patient's Naranjo Scale scored 4 points for the probability of an adverse drug reaction, which is in the possible range. Despite not having a temporal relationship between the initiation or titration of clozapine and hypothermia, the resolution of hypothermia after the cessation of clozapine supports a causal relationship. It is also important to acknowledge this patient's risk factor of taking a benzodiazepine, which was added to her regimen a week before developing hypothermia. Antipsychotics containing strong 5-HT<sub>2A</sub> antagonism are more frequently associated with hypothermia. Also, the blocking of alpha<sub>2</sub>-adrenergic receptors by antipsychotic drugs such as clozapine, chlorpromazine, risperidone, and thioridazine, have a proposed hypothermic effect by inhibiting peripheral responses to cold temperatures, which does not allow for vasoconstriction or shivering responses [4]. However, both typical and atypical antipsychotics have been reported to cause hypothermia. In the literature, there are more case reports of antipsychotic-induced hypothermia in schizophrenic patients than any other antipsychotic users such as the elderly with dementia or delirium. This is speculated to be from neurotensin, a thermoregulatory peptide, which is low in the CSF of schizophrenic patients [4]. Research is needed to increase the understanding of how antipsychotic drugs alter the thermoregulatory system.

## Conclusion

Hypothermia is a significant adverse reaction to consider when taking care of patients on antipsychotics. Careful monitoring of the patient's body temperature should be implemented, especially when initiating treatment or increasing the dosage.

## References

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