A Case of Severe, Refractory Antipsychotic-Induced Orthostatic Hypotension

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Introduction: *Antipsychotics have many adverse effects including orthostatic hypotension. Orthostatic hypotension is ideally treated with non-pharmacological strategies; however, these often fail leading to utilization of pharmacological methods. Currently, there is no agreed upon management or protocol for addressing antipsychotic-induced orthostatic hypotension and research in this area is limited.*

Patient profile: *A 60-year-old man with a long history of schizophrenia who was receiving Haldol® Deconoate 200 mg injections every 4 weeks due to previous non-compliance. He was admitted to the inpatient psychiatric service due to worsening psychosis and suicidal behavior.*

Intervention: *Despite use of medications, the patient was switched to risperidone with a goal of transition to an atypical long-acting injectable. The psychosis improved, but the patient developed orthostatic hypotension. After his medications were held, his blood pressure continued to be grossly abnormal. A number of different tests were completed followed by standard non-pharmacological treatment, which proved unsuccessful. Despite receiving intravenous fluid boluses to maintain his blood pressure, the patient required pharmacological treatment. This included midodrine and fludrocortisones, and concluded with Adderall® as his blood pressure stabilized.*

Conclusion: *This case of a 60-year-old man with antipsychotic-induced orthostatic hypotension elucidates the frustration healthcare professionals and patients face with this common treatment-resistant condition. A treatment algorithm for managing drug-induced orthostatic hypotension is proposed and is a nidus for development of future protocols.*

Keywords: *orthostatic hypotension; antipsychotics; refractory; side effects; schizophrenia; management guidelines*

INTRODUCTION AND PATIENT PROFILE

Compliance with antipsychotic medications is poor given the high degree of intolerability of the adverse effects. Mackin indicates that the most common adverse autonomic side effect of antipsychotics is orthostatic hypotension.[1] Alpha-1 adrenergic receptor antagonism has been shown to play a key role in this mechanism.[2–4] Dosages are often limited and medications switched to avoid continued hypotensive episodes. Orthostatic hypotension is ideally treated with non-pharmacological strategies; however, these often fail and use of alpha agonists has become a first-line treatment for resistant orthostatic hypotension.[4] Although the use of midodrine and other medications is not new, little is known about their effectiveness with antipsychotic-induced orthostatic hypotension.[3] One study in rabbits showed midodrine's effectiveness in chlorpromazine-induced orthostatic hypotension.[3] The case of a 60-year-old man with antipsychotic-induced orthostatic hypotension, recently managed on the inpatient psychiatry service, illustrates the frustration providers and patients encounter with this occasionally treatment-resistant condition. A treatment algorithm for managing drug-induced orthostatic hypotension is presented.

The patient is a 60-year-old single, never married, Caucasian male with a history of schizophrenia dating back to his early twenties. The local community mental health team was managing his care, and he required a long-acting injectable because of his history of medication non-compliance. His regimen consisted of Haldol® Deconoate 200 mg injections every 4 weeks and Prozac® 10 mg daily. Despite his medication compliance, he experienced an exacerbation evidenced by increased preoccupation with bothersome, tormenting comments of his former landlord. His speech was rambling and disorganized. He exhibited blunted affect, social isolation, and decreased motivation. His hallucinatory experiences resulted in increased depressive symptoms with suicidal ideations and one attempt

of slitting his wrists. He had also begun to experience involuntary finger twitching and orobuccolingual dyskinesias. Because of his worsening psychosis, suicidal behavior, and need to adjust his medication regimen, he was admitted to the inpatient service.

INTERVENTIONS AND OUTCOMES

Given his recent relapse despite continued use of the medications, he was switched to oral risperidone with a goal of transition to an atypical long-acting injectable. His dosage was titrated up to 4 mg nightly. As his auditory hallucinations became less frequent and thoughts became more organized, he began to complain of intensifying dizziness and his blood pressure recordings were exceedingly low (i.e., 60s/30s). Given the likelihood fluoxetine was inhibiting the metabolism of the risperidone, thus, dramatically increasing his dosage, the risperidone and fluoxetine were both held. His orthostatic blood pressures were checked and noted to be grossly abnormal. Basic laboratory testing illustrated a mild anemia, which was present on admission. Thyroid studies and morning cortisol levels were within stated limits. ECGs and an echocardiogram were normal. Cardiac markers were not elevated. There was no other medical condition or neurological complaint that could account for his orthostatic hypotension.

Standard non-pharmacological treatment methods, including compression stockings, increased fluid and salt intake, and supine positional exercises, were utilized.[4–7] Despite this, the patient required frequent intravenous fluid boluses to maintain his blood pressure and improve his dizziness. As his blood pressure stabilized, it was determined safe to reintroduce an antipsychotic.[4–7] Paliperidone was substituted for risperidone in hope of transitioning to an atypical long-acting injectable that has less inclination for orthostatic hypotension. Fluoxetine was replaced by desvenlafaxine in hopes of utilizing the medication-induced increases in blood pressure. Despite the low dosage of paliperidone used, his orthostatic hypotension persisted. Therefore, it was felt at that point he would require adjuvant treatment with a first-line medication such as midodrine. Ten milligrams three times daily was initiated. Despite initial benefit, his orthostatic hypotension persisted and required addition of fludrocortisone 0.2 mg daily. The combination of these medications had little effect on his blood pressure and addition of 15 mg Adderall XR® was necessary. Interestingly, throughout his continued struggle with orthostatic hypotension and dizziness, his psychotic symptoms remained stable. His dizziness and orthostatic hypotension did improve with the altered pharmacological regimen, and he was stabilized for discharge with hopes of slow titration off the supplementary medications.

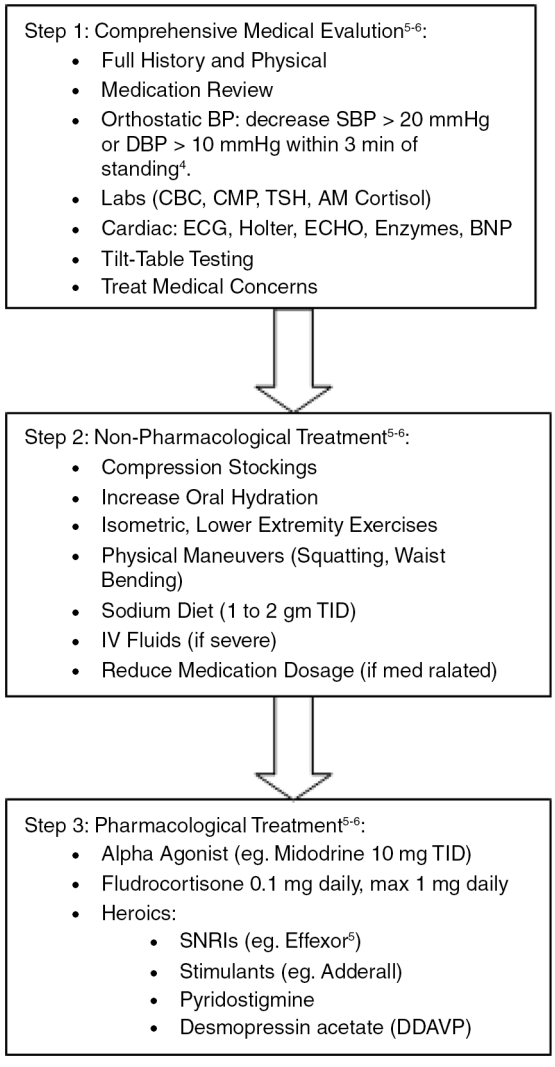

Figure 1. Proposed treatment plan for drug-induced hypotension with special consideration for antipsychotics. This protocol is an illustration of a step-by-step procedure if orthostatic hypotension remains refractory. The first step highlights the importance of confirming the diagnosis and ruling out other medical concerns. If orthostatic hypotension persists, the next step is use of non-pharmacological treatment. If the orthostatic hypotension remains, our protocol advises to rely on pharmacological treatment. Midodrine and fludrocortisone are commonly used first-line agents. Second- and third-line agents are also available if needed. From Refs. (2,5,6).

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DISCUSSION

This case shows the frustration a highly resistant iatrogenic orthostatic hypotensive episode can create. Additionally, untreated orthostatic hypotension can lead to complications such as falls, myocardial infarction, stroke, and death. Both non-pharmacological and pharmacological methods were utilized and despite best efforts to manage the condition, eventual addition of three medications was necessary to prevent dramatic decreases in his blood pressures upon standing. Currently, there is no agreed upon management of antipsychotic-induced orthostatic hypotension and research in this area is limited. For example, Gugger proposed the use of midodrine and fludrocortisone for management, but also emphasized the lack of existing evidence.[4] Therefore, these agents are used, but there is no consensus and strict protocol to follow. Figure 1 is a treatment regimen for drug-induced hypotension giving special attention to antipsychotic medications and the subject of this case report. This treatment development of a step-by-step protocol for refractory antipsychotic-induced hypotension. Furthermore, many studies propose the use of non-pharmacological treatment followed by midodrine and fludrocortisones as first-line treatments.[3,4] However, similar to our case, these medications can prove futile and thus other agents, including desmopressin and pyridostigmine, are suggested in our protocol. Furthermore, our case and treatment protocol highlights the use of Adderall, which is an uncommon agent used to combat orthostatic hypotension and research into its effectiveness is limited. The proposed treatment regimen is the amalgamation of agents used in the literature but advocates for a unified standard protocol for all patients. In all, this case begs for alternative management of orthostatic hypotension created by antipsychotic medications to allow patients the opportunity to receive all the benefits these medications have to offer.

LEARNING POINTS

- Resistant anti-psychotic induced orthostatic hypotension is a common frustration shared among healthcare professionals.
- Although non-pharmacological and pharmacological treatments are used commonly to eradicate this side effect, there is no consensus or standard protocol and there is limited research in this area.
- A standard treatment algorithm for managing drug-induced orthostatic hypotension is proposed in parallel with our case.
- Our protocol includes the amalgamation of current pharmacological treatments used but also highlights possible second-line and third-line agents.

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