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Pseudohyperaldosteronism Induced Hypertension and Hypokalemia: A Bioassay and Molecular Modeling Study

Lucija Telisman*

Department of Pharmaceutical Sciences, University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland

Introduction

Pseudohyperaldosteronism, also known as apparent mineralocorticoid excess syndrome (AME), is a rare genetic disorder that causes the body to produce excessive amounts of cortisol, leading to hypertension and hypokalemia. In some cases, certain medications, including azole antifungals, can also induce pseudohyperaldosteronism-mediated hypertension and hypokalemia. Hypertension, or high blood pressure, is a common condition affecting millions of people worldwide. While there are many factors that can contribute to hypertension, including lifestyle and genetic factors, pseudohyperaldosteronism-induced hypertension is caused by the overproduction of cortisol. Cortisol is a hormone produced by the adrenal glands that helps regulate the body's response to stress. When cortisol levels are too high, it can cause the body to retain sodium and excrete potassium, leading to fluid retention and increased blood pressure [1].

Description

In addition to hypertension, patients with pseudohyperaldosteronism can also experience hypokalemia, or low potassium levels. Potassium is an essential electrolyte that helps regulate muscle and nerve function and low levels can lead to muscle weakness, fatigue and other health problems. While pseudohyperaldosteronism is a genetic disorder, some medications can also induce similar symptoms, including hypertension and hypokalemia. Azole antifungals, commonly used to treat fungal infections, have been shown to induce pseudohyperaldosteronism in some patients. Azole antifungals inhibit the activity of enzymes involved in the production of cortisol, leading to an increase in cortisol levels and subsequent hypertension and hypokalemia.

Management of pseudohyperaldosteronism-induced hypertension and hypokalemia involves a combination of medications and lifestyle changes. Patients may be prescribed medications to lower blood pressure and increase potassium levels, as well as dietary modifications to increase potassium intake. In some cases, surgical intervention may be necessary to remove tumors or other growths causing excessive cortisol production. Pseudohyperaldosteronism-induced hypertension and hypokalemia can be a challenging clinical scenario that requires careful management. While pseudohyperaldosteronism is a rare genetic disorder, some medications, including azole antifungals, can induce similar symptoms. It is important for healthcare providers to be aware of these potential side effects and to carefully monitor patients taking these medications for signs of pseudohyperaldosteronism. With proper management, patients with pseudohyperaldosteronism-induced hypertension and hypokalemia can achieve improved outcomes and quality of life [2-4].

Hypokalemia is a condition characterized by low potassium levels in the blood. Potassium is an essential electrolyte that helps regulate muscle and nerve function and low levels can lead to muscle weakness, fatigue and other health problems. While there are many factors that can contribute to hypokalemia, some medications, including clinically used azole antifungals, have been shown to induce hypokalemia in some patients. Azole antifungals are a class of medications used to treat fungal infections. They work by inhibiting the growth and replication of fungi and are often used to treat systemic and opportunistic fungal infections in immunocompromised patients. While azole antifungals are generally safe and effective, they can have several potential side effects, including hypokalemia.

The exact mechanism by which azole antifungals induce hypokalemia is not fully understood. However, it is believed to be related to their inhibition of enzymes involved in the production of cortisol. Cortisol is a hormone produced by the adrenal glands that helps regulate the body's response to stress. When cortisol levels are too high, it can cause the body to retain sodium and excrete potassium, leading to fluid retention and increased blood pressure. By inhibiting enzymes involved in cortisol production, azole antifungals can cause a decrease in cortisol levels, leading to hypokalemia. The symptoms of hypokalemia can vary depending on the severity of the condition. Mild cases may not cause any symptoms, while severe cases can lead to muscle weakness, fatigue and even paralysis. In addition, hypokalemia can lead to other complications, including arrhythmias, renal dysfunction and metabolic acidosis.

Management of hypokalemia induced by azole antifungals involves a combination of medications and lifestyle changes. Patients may be prescribed potassium supplements or medications to increase potassium levels, as well as dietary modifications to increase potassium intake. In addition, healthcare providers may adjust the patient's medication regimen or discontinue the use of azole antifungals altogether if necessary. Hypokalemia induced by clinically used azole antifungals can be a potentially serious side effect that requires careful management. While the exact mechanism by which azole antifungals induce hypokalemia is not fully understood, it is believed to be related to their inhibition of enzymes involved in cortisol production. Patients taking azole antifungals should be carefully monitored for signs of hypokalemia and healthcare providers should be aware of this potential side effect when prescribing these medications. With proper management, patients with hypokalemia induced by azole antifungals can achieve improved outcomes and quality of life.

Pseudohyperaldosteronism is a condition characterized by high blood pressure and low potassium levels in the blood, often caused by excessive aldosterone-like activity. While this condition can have various underlying causes, clinically used azole antifungals have been shown to induce pseudohyperaldosteronism, leading to hypertension and hypokalemia. In this article, we will discuss a recent study that aimed to assess the mechanisms behind pseudohyperaldosteronism induced by azole antifungals. The study, published in the journal Biochemical Pharmacology, utilized bioassays and molecular modeling calculations to compare the inhibitory effects of several clinically used azole antifungals on enzymes involved in the production of cortisol and aldosterone, including CYP11B1, CYP11B2, CYP17A1 and 11β-HSD2. Additionally, the study assessed the potential of these antifungals to activate the mineralocorticoid receptor (MR), which plays a crucial role in the regulation of aldosterone-like activity.

***Address for Correspondence:** Lucija Telisman, Department of Pharmaceutical Sciences, University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland, E-mail: lucijatelisman@gmail.com*

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The results of the study showed that posaconazole, itraconazole and other systemically used azole antifungals significantly inhibited the activity of CYP11B1, CYP11B2 and CYP17A1, enzymes involved in the production of cortisol and aldosterone. Additionally, these antifungals were found to activate the MR, leading to increased aldosterone-like activity and decreased potassium levels in the blood. Interestingly, the study also found that some azole antifungals, including OHI, had a unique inhibitory effect on 11β-HSD2, an enzyme involved in the metabolism of cortisol, which could also contribute to the development of pseudohyperaldosteronism [5].

Conclusion

The study's findings highlight the complex mechanisms underlying pseudohyperaldosteronism induced by azole antifungals. By inhibiting enzymes involved in the production of cortisol and aldosterone, these antifungals can disrupt the body's hormonal balance, leading to fluid retention, hypertension and hypokalemia. Additionally, the activation of the MR by these antifungals can further exacerbate aldosterone-like activity, contributing to the development of pseudohyperaldosteronism. While the study provides valuable insights into the mechanisms underlying pseudohyperaldosteronism induced by azole antifungals, there are several limitations that should be noted. For example, the study utilized bioassays and molecular modeling calculations rather than clinical trials, which may limit the generalizability of the findings. Additionally, the study only assessed a limited number of azole antifungals and further research is needed to determine if these findings can be extrapolated to other medications in this class. Pseudohyperaldosteronism induced by clinically used azole antifungals is a potentially serious side effect that requires careful assessment and management. The recent study discussed in this article provides valuable insights into the mechanisms underlying this condition, highlighting the importance of inhibiting enzymes involved in cortisol and aldosterone production and avoiding activation of the MR. Healthcare providers should be aware of this potential side effect when prescribing azole antifungals and carefully monitor patients for signs of pseudohyperaldosteronism, including hypertension and hypokalemia.

Acknowledgement

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Conflict of Interest

None.

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