HIPERTENSÃO ARTERIAL RESISTENTE ASSOCIADA AO HIPERALDOSTERONISMO PRIMÁRIO: UMA REVISÃO INTEGRATIVA DA LITERATURA

RESISTANT ARTERIAL HYPERTENSION ASSOCIATED WITH PRIMARY HYPERALDOSTERONISM: AN INTEGRATIVE LITERATURE REVIEW

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RESUMO

Introdução: A hipertensão arterial resistente (HAR) é uma condição de difícil controle, associada a maior risco cardiovascular e lesões em órgãos-alvo. O hiperaldosteronismo primário é uma importante causa secundária de HAR. **Objetivo:** Analisar a relação entre HAR e hiperaldosteronismo primário, considerando diagnóstico, consequências cardiovasculares e tratamento. **Métodos:** Foi realizada uma revisão integrativa da literatura, baseada no artigo de Resende et al. (2023) e em suas referências, abordando resistência, pseudo-resistência, causas secundárias, diagnóstico e tratamento. **Resultados:** O hiperaldosteronismo primário pode estar presente em até 23% dos pacientes com HAR. O diagnóstico envolve a relação entre aldosterona e renina. O tratamento depende da causa, podendo incluir cirurgia ou antagonistas dos receptores mineralocorticoides. A condição aumenta o risco de AVC, doença coronariana, fibrilação atrial e insuficiência cardíaca. **Conclusão:** A investigação de causas secundárias é essencial em pacientes com HAR. O diagnóstico e tratamento precooces do hiperaldosteronismo podem melhorar o controle da pressão arterial e reduzir complicações cardiovasculares e renais.

Palavras-chave: Hipertensão Arterial Resistente. Hiperaldosteronismo Primário. Hipertensão Secundária. Aldosterona.

ABSTRACT

Introduction: Resistant arterial hypertension (RAH) is a condition that is difficult to control and is associated with increased cardiovascular risk and target-organ damage. Primary hyperaldosteronism is an important secondary cause of RAH. **Objective:** To analyze the relationship between RAH and primary hyperaldosteronism, considering diagnosis, cardiovascular consequences, and treatment. **Methods:** An integrative literature review was conducted based on the article by Resende et al. (2023) and its references, addressing resistance, pseudo-resistance, secondary causes, diagnosis, and treatment. **Results:** Primary hyperaldosteronism may be present in up to 23% of patients with RAH. Diagnosis involves the aldosterone-to-renin ratio. Treatment depends on the underlying cause and may include surgery or mineralocorticoid receptor antagonists. The condition increases the risk of stroke, coronary artery disease, atrial fibrillation, and heart failure. **Conclusion:** Investigation of secondary causes is essential in patients with RAH. Early diagnosis and treatment of primary hyperaldosteronism may improve blood pressure control and reduce cardiovascular and renal complications.

Keywords: Resistant Arterial Hypertension. Primary Hyperaldosteronism. Secondary Hypertension. Aldosterone.

INTRODUCTION

High blood pressure (HBP) is a chronic disease and an important modifiable risk factor for cardiovascular disease, chronic kidney disease, and premature death. It can cause damage to target organs such as the heart, brain, kidneys, and blood vessels, and results from multiple genetic, environmental, behavioral, and social factors.

Resistant arterial hypertension (RAH) occurs when blood pressure remains uncontrolled despite the use of three antihypertensive drugs from different classes and lifestyle changes. Patients requiring four or more medications are also considered resistant.

Before diagnosing RAH, pseudo-resistance must be excluded, including incorrect blood pressure measurement, poor treatment adherence, and white coat hypertension. After confirming true resistance, secondary causes should be investigated, especially primary hyperaldosteronism, which may affect 5%–10% of hypertensive patients and up to 23% of those with resistant hypertension.

Primary hyperaldosteronism is characterized by excessive autonomous aldosterone production and is associated with increased cardiovascular and kidney complications. Therefore, this review focuses on its relationship with resistant hypertension, including physiology, diagnosis, treatment, and cardiovascular effects.

METHODS

This is an integrative literature review, developed based on the article “Resistant Arterial Hypertension Due to Primary Hyperaldosteronism: A Case Report,” published by Resende et al. in 2023 in the Revista de Medicina (São Paulo). The main study presents a clinical case of resistant hypertension associated with bilateral adrenal hyperplasia and discusses aspects related to the pathophysiology, diagnosis, and treatment of the condition.

For the review, we considered the scientific references used in the main article, including Brazilian and international guidelines, observational studies, systematic reviews, and meta-analyses related to resistant arterial hypertension and primary hyperaldosteronism. Among the references, the Brazilian Guidelines for Arterial Hypertension, the Brazilian position statement on resistant hypertension, and the Endocrine Society guideline on primary hyperaldosteronism stand out.

Information related to the definition and identification of resistant hypertension, exclusion of pseudo-resistance, investigation of secondary hypertension, diagnosis of primary hyperaldosteronism, therapeutic options, and risk of cardiovascular and kidney damage was prioritized.

RESULTS

The analyzed studies showed that cardiac rehabilitation improves functional capacity, exercise tolerance, quality of life, and hospitalization outcomes. However, the effects vary according to the intervention and patient characteristics.

RESISTANT HIGH BLOOD PRESSURE AND PSEUDO-RESISTANCE

Resistant hypertension affects approximately 20%–30% of hypertensive patients, with a Brazilian study reporting 11.7%. Factors such as obesity, diabetes, sleep apnea, aging, and high salt intake may contribute to its development.

However, high blood pressure despite multiple medications does not always indicate true resistance. Pseudo-resistance may result from incorrect blood pressure measurement, poor treatment adherence, or the white coat effect. ABPM and HBPM can help confirm the diagnosis.

Treatment adherence should also be evaluated, considering treatment complexity, side effects, access to medications, and the doctor-patient relationship. Some medications and alcohol may also increase blood pressure.

SECONDARY HIGH BLOOD PRESSURE

After confirming true resistant hypertension, secondary causes should be investigated. These include obstructive sleep apnea, primary hyperaldosteronism, renal artery stenosis, and kidney diseases.

Identifying the underlying cause is important because appropriate treatment may improve or even resolve hypertension and reduce cardiovascular and renal damage.

PRIMARY HYPERALDOSTERONISM

Primary hyperaldosteronism is more common than previously thought, affecting approximately 5%–10% of hypertensive patients and up to 23% of those with resistant hypertension.

Telerehabilitation may increase access to cardiac rehabilitation. However, a study with 61 patients with heart failure found no significant differences in physical activity, peak oxygen uptake, or quality of life between groups after two years, despite improvements within the groups.

Overall, cardiac rehabilitation improves functional capacity, exercise tolerance, quality of life, and hospitalization outcomes. However, consistent benefits on mortality have not been demonstrated, highlighting the importance of individualized interventions.

DIAGNOSIS OF PRIMARY HYPERALDOSTERONISM

Screening is recommended in patients with resistant hypertension, mainly through the plasma aldosterone/plasma renin activity ratio (PA/PRA). An elevated ratio with adequate aldosterone levels indicates the need for further investigation.

The absence of hypokalemia does not exclude the diagnosis, since low potassium occurs in only 30%–60% of patients. In the reported case, the PA/PRA ratio was 453, and abdominal CT showed bilateral adrenal hyperplasia.

UNDERDIAGNOSIS OF HYPERALDOSTERONISM

Primary hyperaldosteronism remains underdiagnosed. One study found that only 1.6% of more than 269,000 patients with resistant hypertension underwent screening, while another found a screening rate of only 2.1% among 4,660 patients.

This low screening rate represents an important barrier to identifying a potentially treatable cause of resistant hypertension.

TREATMENT AND CARDIOVASCULAR REPERCUSSIONS

Treatment depends on the cause. Unilateral disease may be treated surgically, while bilateral adrenal disease is generally treated with mineralocorticoid receptor antagonists, such as spironolactone.

Excess aldosterone increases the risk of stroke, coronary artery disease, atrial fibrillation, and heart failure. In the reported case, spironolactone reduced blood pressure and allowed discontinuation of other antihypertensive drugs. After two years, proteinuria and left ventricular wall thickness decreased, indicating improvement in target-organ damage.

CONCLUSION

Resistant arterial hypertension is a condition of high clinical importance because it is harder to control blood pressure and carries a higher risk of organ damage and cardiovascular events. Its investigation should start by confirming true resistance, ruling out factors like low adherence, improper measurement technique, and the white coat effect.

After confirming HAR, investigating secondary causes is crucial, especially given the possibility of potentially treatable conditions. Primary hyperaldosteronism stands out because of its high frequency among patients with resistant hypertension and the fact that it often goes undiagnosed.

The assessment of the aldosterone/plasma renin activity ratio is an important screening tool, and diagnostic follow-up is needed depending on the results found. The absence of hypokalemia should not rule out the diagnostic hypothesis.

The treatment should target the underlying cause. While unilateral forms can be treated surgically, bilateral adrenal disease can be managed with mineralocorticoid receptor antagonists. The evidence shows that proper treatment can significantly improve blood pressure control and reduce cardiovascular and kidney damage. So, early identification of primary hyperaldosteronism in patients with resistant hypertension is key to cutting down complications and improving clinical outcomes.

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