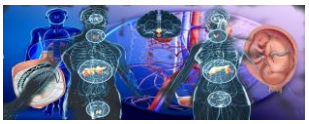
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A Secondary Cause of Hypertension: Primary Aldosteronism Risks and Management

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Abstract

Primary aldosteronism (PA) is a common, but frequently overlooked, cause of arterial hypertension and excess cardiovascular events, particularly atrial fibrillation. As timely diagnosis and treatment can provide a cure of hyperaldosteronism and hypertension, even when the latter is resistant to drug treatment, strategies to screen patients for PA early with a simplified diagnostic algorithm are justified.

Keywords: Primary aldosteronism; refractory hypertension; endothelial dysfunction; angiotensin II

Introduction

PA is defined as inappropriately elevated aldosterone production in the setting of low plasma renin. Once thought to be rare, PA is now known to be the most common cause of secondary hypertension, with a prevalence of 20% among patients with resistant hypertension, 10% in those with severe hypertension (systolic blood pressure [SBP] ≥180, diastolic blood pressure ≥110 mm Hg), and 6% in those with otherwise uncomplicated hypertension.

Detection Rate of PA

PA is currently underdetected for several reasons. First, there is still a quite popular misconception that PA is "a needle in a haystack", notwithstanding unambiguous evidence showing the opposite: the PAPY (Primary Aldosteronism Prevalence in Hypertension) study, the first large prospective survey that used a rigorous methodology to diagnose PA and aldosterone-producing adenoma (APA), reported a rate of 11.2% in consecutive newly diagnosed hypertensive patients.

Evidence from case–control and registry studies suggests that patients with primary aldosteronism experience higher rates of negative health outcomes than patients with essential hypertension. A case–control study conducted in France that involved 124 patients diagnosed with primary aldosteronism during a three-year period, who were matched for age, gender, and systolic and diastolic blood pressure with 465 patients with essential hypertension, found that patients with primary aldosteronism had increased odds of having a stroke, nonfatal myocardial infarction or atrial fibrillation.

Prevalence

Historically considered a niche or rare cause of hypertension, recent studies suggest that primary aldosteronism is a common condition that often goes undiagnosed. The challenges in estimating prevalence are multi-fold. In part, true prevalence should reflect an adequate sampling of the population to provide confidence of generalizability; to date, most studies have been too small to achieve this.

Health Outcomes in Primary Aldosteronism Prior to Targeted Therapy

The relevance of the relatively large prevalence of primary aldosteronism is best contextualized by the clinical consequences attributed to the disease, especially when it is not diagnosed early. A multitude of studies have demonstrated that prior to targeted therapy with MR antagonist medications or surgical adrenalectomy, patients with primary aldosteronism are at a higher risk for a number of adverse health outcomes compared with patients with essential hypertension, independent of blood pressure.

How to Screen for Primary Aldosteronism

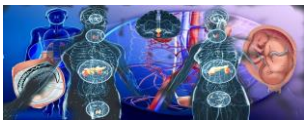
The most often recommended screening test for primary aldosteronism is the aldosterone-to-renin ratio (ARR). ARR testing can easily be performed in the ambulatory setting typically without any additional preparation. The most widely-accepted definition of a positive screen is an ARR > 30 ng/dL per ng/mL/h with a serum aldosterone level > 15 ng/dL. Certainly, the higher the aldosterone level, and the lower the plasma renin activity (PRA), the more obvious the potential diagnosis.

Confirmatory Testing

Confirming the screening results is often necessary. For patients with hypertension, hypokalemia, undetectable renin activity or levels, and serum aldosterone levels that are sufficiently elevated (i.e. 15 or 20 ng/dL or higher), there is no need for further dynamic testing and the diagnosis can be confirmed.

Glucocorticoid Remediable Aldosteronism (GRA)

GRA, also known as Familial Hyperaldosteronism (FH) type I, is a rare form of primary aldosteronism due to BAH that is inherited in autosomal dominant fashion and accounts for < 1% of all cases of primary aldosteronism. These patients carry a mutation which results in a fusion of the promoter sequence of the CYP11B1 (11β-hydroxylase) gene and the coding sequence of the CYP11B2 (aldosterone synthase) gene resulting in ACTH-driven aldosterone secretion.



Genetics and Pathogenesis of Aldosterone Producing Adenomas

Although inheritable forms of primary aldosteronism remain rare, it is now becoming evident that the vast majority of APAs harbor known pathogenic mutations that result in autonomous aldosterone secretion.

Conclusion

Primary aldosteronism is a relatively common, yet often undiagnosed, cause of hypertension that is associated with substantial morbidity and mortality even independent of its effect on blood pressure. In this article, we have discussed the most updated knowledge of this condition and shared our suggested practical diagnostic and treatment approaches based on the most recent available data.

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