Medical management of primary aldosteronism

Traitement médical de l’hyperaldostéronisme primaire

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Primary aldosteronism is the commonest cause of secondary hypertension. It is identified by screening patients using the aldosterone: renin ratio (ARR) [1]. It is important to recognise, however, that a raised ARR is not a diagnostic of primary aldosteronism [2]. In particular, the ARR is influenced by drug therapy, and varies widely in the normal population [3]. Our own studies and those of other groups have shown that the ARR is a highly heritable phenomenon [4], and that the distribution of the ARR is not different in hypertensive and normotensive patients. Thus, primary aldosteronism, as defined by autonomous aldosterone production that does not suppress during sodium loading, and where aldosterone is independent of normal regulation by the renin/angiotensin system, requires more detailed evaluation. Optimal screening and diagnostic approaches have been described in recent guidelines [5].

A large study in Italy identified that around 11% of hypertensive patients had biochemical evidence of primary aldosteronism, but less than half of these harboured an aldosterone producing adenoma [6]. It is also important to note that surgical removal of aldosterone producing adenomas results in cure of hypertension in less than 50% of patients, although the biochemical abnormalities can be fully corrected. Thus, it is important that medical approaches to the treatment of primary aldosteronism are optimised.

Studies carried out many years ago showed that high dose amiloride or spironolactone produced equivalent reduction in the expanded exchangeable body sodium content in patients with primary aldosteronism when compared with surgical removal of an aldosterone producing adenoma. In this circumstance, effective blood pressure lowering was observed. In order to achieve these results, doses of amiloride (that blocks the epithelial sodium channel in the distal renal tubule) may need to be as high as 40 mg per day. The alternative approach is to use a specific mineralocorticoid receptor antagonist, using either spironolactone or eplerenone. The use of spironolactone is limited by side effects that include gynaecomastia and decreased libido. Eplerenone, which binds with much lower affinity to the androgen receptor, is free of these side effects. However, the recent analysis suggests that, in patients with primary aldosteronism, eplerenone is less effective at lowering blood pressure than spironolactone (in press).

The underlying aetiology of non-tumourous primary aldosteronism remains uncertain; our own studies have suggested that there may be a genetic contribution to the development of primary aldosteronism that is exerted over many years and is associated with polymorphic variation in the genes encoding aldosterone synthase and 11-hydroxylase [7,8]. This may suggest that effective detection at an early stage of subjects liable to develop hypertension with relative aldosterone excess may provide an option for influencing the long-term development of cardiovascular disease.

References


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