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REVIEW

The effects of antihypertensive drugs on arterial stiffness☆

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Calcium channel blocker

Abstract Ageing and cardiovascular risk factors, particularly uncontrolled hypertension, adversely impact arterial stiffness and wave reflection leading to increased central systolic blood pressure. Carotid-femoral pulse wave velocity is the "gold standard" method for the assessment of aortic stiffness. Increased pulse wave velocity has been independently associated with adverse cardiovascular outcomes. Thus, current European hypertension guidelines acknowledge the reproducibility, predictive value, and cost-effectiveness of pulse wave velocity.

Augmentation index, a marker of arterial stiffness and wave reflection has been also associated with poor cardiovascular outcome.

Current evidence suggests that increased arterial stiffness and wave reflection contribute to target organ damage. Thus, early intervention is fundamental for cardiovascular prevention. Elevated pulse wave velocity and augmentation index can be reduced by normalizing blood pressure and by using specific treatments for reducing arterial stiffness.

This article will review the available evidence on the effect of the different antihypertensive drug classes on arterial stiffness. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers can reduce pulse wave velocity beyond the blood pressure lowering effect. Although blood pressure normalization is the most effective therapeutic tool for reducing parameters of wave reflections, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and calcium channel blockers have beneficial effects on augmentation index.

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Introduction

Ageing and cardiovascular (CV) risk factors, particularly hypertension, cause functional and structural alterations in the macro- and microcirculation, representing common pathologic mechanism for target organ damage and CV events.[1–3]

Arterial stiffness of the large arteries and increased media/lumen ratio or capillary rarefaction in the microcirculation can occur prematurely in susceptible patients as those with hypertension, characterizing the so called early vascular ageing[2,3]

Aortic stiffness is responsible for most of the pathophysiologic effects of central blood pressure (BP) and arterial stiffness on the left ventricle, brain, and kidney.[1–3] The assessment of carotid to femoral pulse wave velocity (PWV) is considered the " gold standard" for measurement of aortic stiffness, since it is a simple, non-invasive and reproducible method.[1] Furthermore, PWV has a large amount of clinical evidence for the predictive value of aortic stiffness for CV events.[4,5] Therefore, it has been included among the established measures of hypertensive target organ damage by previous and current European guidelines.[6,7]

Functional and structural changes in the microcirculation cause altered wave reflection, which contributes to the increase in central BP associated to arterial stiffness. An index of arterial stiffness and wave reflection, such as central BP augmentation, has been also shown to have independent prognostic relevance.[8,9]

According to their pathophysiological role, arterial stiffness and wave reflections have become a therapeutic target in patients with elevated CV risk. The normalization of elevated BP is one of the key approaches for reducing elevated PWV and wave reflections.[1–3] The earlier intervention takes place, the better, as arterial wall damage can never be fully reversed and pharmacological intervention helps normalize the increased rate at which arterial wall damage occurs.[2,3]

The aim of this article is to review how different antihypertensive drug classes may reduce arterial stiffness.

Strategies for reducing PWV

BP normalisation

Increases in distending BP caused by hypertension lead to changes in the composition (elastin/collagen ratio) and structure of arteries (e.g. increased arterial wall thickness and smooth muscle hypertrophy) that accelerate arterial stiffening.[4]

In the short term, arterial stiffness can be reduced without modifying properties of the arterial wall by BP reduction per se, which shifts wall stress to the elastin component, while with arterial stiffening, the haemodynamic load in arteries increases leading to impairment of the natural repair process and damage of the macro- and the microcirculation.[1–3]

Thus, early pharmacological intervention can make a substantial difference in limiting endothelial and arterial wall damage and long-term treatment with antihypertensive medication may reduce arterial stiffness further via the complementary mechanism of arterial remodelling[2,3] (Fig. 1).

In a 5.3-year study of PWV in routine clinical practice in 97 patients with essential hypertension (63 $\pm$ 11 years), long-term treatment with antihypertensive therapy decreased aortic PWV by 3.17 m/s ($p < 0.0001$) from 14.2 $\pm$ 4.2 m/s at baseline.[10] Nearly two thirds (65%) had BP $<$ 140/90 mm Hg. The rate of change of PWV was -0.64 ± 0.06 m/s per year after adjustment for age, sex, heart rate and mean BP. The reduction in PWV was found to account for most of the decrease in central pulse pressure from 59 $\pm$ 22 mm Hg to 54 $\pm$ 14 mm Hg ($p < 0.001$). Brachial systolic BP also decreased by -0.9 ± 0.3 mm Hg per year ($p < 0.05$), but not enough to explain the reduction in PWV. Indeed the decrease in PWV was only slightly modified (rate

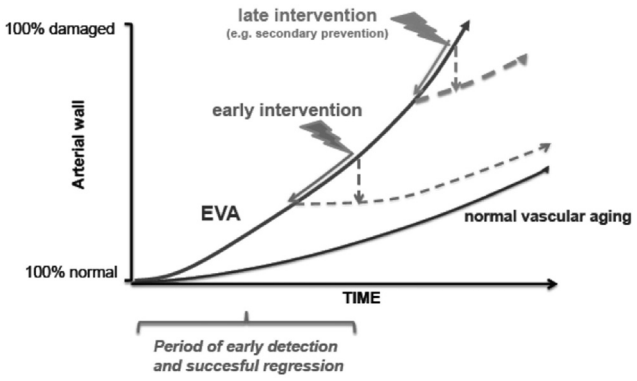

Figure 1 The effect of early and late intervention on preventing arterial wall damage in early vascular ageing (EVA). Modified from Ref [2].