Endothelial Dysfunction and Hypertension
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Abstract
The endothelium the largest organ in the human body is no longer considered a dormant organ but is actively involved in the pathogenesis of hypertension. Its dysfunction brought about by various factors causes alteration in the vascular tone primarily and changes in the synthesis of various vasoactive substances which in turn contribute to the development of hypertension. Certain non pharmacological and pharmacological interventions aid in the improvement of the endothelial dysfunction.

Key words: Endothelial dysfunction, micro and macrovascular effects, vasoactive substances, hypertension

Introduction
Endothelium for long considered to be just an inert inner lining of the vessel wall and a mechanical barrier has now its role well established in vascular health and homeostasis. It is one of the largest organs of the body comprising of one trillion cells, weighing over 1 kg and three square meters in a 70 kg male.[1] It is intricately involved in the pathophysiology of hypertension.

This review focuses on the complex interplay between hypertension and endothelial dysfunction and their impact on outcomes in cardiovascular disease. Endothelial dysfunction has been defined as the alteration of the properties of the endothelium leading to impaired vasodilatation of blood vessels, creation of a proinflammatory and prothrombotic milieu, and in the long term, to the development of atherosclerosis.

Pathogenesis
The vascular endothelium that forms the inner lining of blood vessels consists of a single layer of flat cells having a central nucleus with overlapping edges that maintain the integrity of the vessel. The endothelium and its function are impaired in conditions that constitute the risk factors for atherosclerosis including smoking, hypertension, diabetes, dyslipidemia, and chronic kidney disease.[2] Adhesion molecules are expressed by the dysfunctional endothelium. The endothelium regulates vascular tone, its interactions with leukocytes and platelets, and cell growth. It synthesizes and secretes in paracrine manner growth factors and thromboregulatory and vasoregulatory molecules and responds to both physical and chemical signals.

The term “endothelial dysfunction” not only is generally used to denote the deterioration of endothelium-dependent vasodilatation but also implies abnormal regulation of interactions between the endothelium and leukocytes, thrombocytes, other regulatory molecules, and inflammation.[3]

The endothelium secretes both endothelium-derived relaxing factors (EDRFs) and endothelium-derived constricting factors (EDCFs) and, with their action on vascular smooth muscle cells, regulates vascular tone. One major EDRF is nitric oxide (NO), but others such as endothelium-derived hyperpolarizing factor and prostaglandins also contribute to endothelium-derived vasodilation. EDCFs include angiotensin II and endothelins. NO acts as a vasodilator, inhibits inflammation, and has an antiaggregatory effect on platelets. In cardiovascular disease states, increased levels of superoxide anion and reactive oxygen species reduce the bioavailability of NO, resulting in vasoconstriction and platelet aggregation.

The endothelium, thus, plays a critical role in the pathogenesis of cardiovascular diseases such as atherosclerosis, systemic and pulmonary hypertension, cardiomyopathies, and vasculitides.[4] It is often referred to as a “barometer of cardiovascular health.”

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Received 06-07-2018; Accepted 11-08-2018
Hypertension, NO, Microvascular Dysfunction, and Macrovascular Events

Whether microvascular dysfunction is a culprit or a victim in hypertension remains a contentious issue. Atherosclerotic cardiovascular disease risk factors such as aging, smoking, lack of physical exercise, hypertension, diabetes, and atherogenic dyslipidemia are known to reduce NO bioactivity, leading to endothelial dysfunction. In hypertension, the exposure of the microvasculature to sustained high pressures results in unfavorable changes in the endothelium with increased production of reactive oxygen species leading to reduced bioavailability of NO. This endothelial dysfunction results in microvascular dysfunction, which, in turn, appears to be predictive of macrovascular events.

Endothelial dysfunction may be preceded the development of hypertension as it has been noted in subjects with normal blood pressure (BP) with a strong family history of hypertension. This allows one to speculate whether endothelial dysfunction is an early stage of hypertension and whether it is possible to intervene at this stage.

Hypertension induces two types of changes in the microvasculature - vascular remodeling and vascular rarefaction. In vascular remodeling, there is a rearrangement of vessel wall components leading to luminal narrowing and an increase in vascular resistance. This remodeling effect is hypertension dependent as well as pressure independent, where angiotensin II has been implicated. Vascular rarefaction is a reduction in the number of small vessels in a given volume of tissue and could be either structural or functional. Available evidence indicates that the microvascular alterations occur as a result of sustained elevations in BP in hypertension. However, it is possible that microvascular dysfunction in some individuals may predispose them to the development of worsening in hypertension. Some even suggest that there may exist a cyclical process of microvascular damage and hypertension [9,10] [Figure 1]. One condition where endothelial dysfunction plays a pathogenic role is preeclampsia, a hypertensive condition affecting about 15% of pregnant women.

Interventions for Endothelial Dysfunction

Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and newer beta-blockers appear to improve endothelial dysfunction along with their BP reducing effect, whereas first-generation beta blockers and diuretics have no effect. Statins have actions beyond cholesterol lowering, one of them being an improvement of endothelial dysfunction. Lifestyle interventions including a diet rich in fruit and vegetables and regular physical activity also improve endothelial dysfunction.

Conclusion

Endothelial dysfunction pathophysiologically has intricate interactions with hypertension. There is a large body of evidence to suggest that hypertension results in endothelial dysfunction, which in turn leads to microvascular dysfunction. This microvascular dysfunction is highly predictive of future cardiovascular events and is a potential target for intervention. In some instances, however, endothelial dysfunction is clearly involved in the pathogenesis of hypertension.

References

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How to cite this article: Rao S, Manohar KN. Endothelial Dysfunction and Hypertension. Hypertens 2018;4(3): 132-134.

Source of support: Nil, Conflict of interest: None