

Can Whole Body Blood Flow Autoregulation Lead to Hypertension? Testing Its Role by Computer Simulations

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Introduction: Volume-loading hypertension is characterized by an initial increase in cardiac output (CO) followed by a secondary blood flow autoregulatory vasoconstriction due to the overperfusion of tissues, leading to chronic hypertension with a relatively normal CO, but a high total peripheral resistance (TPR). This concept of whole body blood flow autoregulation (WBFAR) has often been used to explain the increase in blood pressure (BP) in various models of salt-loading hypertension.

Objective: To test the role of WBFAR in achieving salt balance and BP control during salt-loading since it is not possible to block WBFAR experimentally.

Material and Methods: Using Guyton's large circulatory model, we tested, in the presence or absence of WBFAR, the hemodynamic and fluid volume changes that occur after a 10-fold increase in salt intake in three different situations: (A) normal neurohormonal modulation; (B) fixed circulating angiotensin II at a normal level; (C) full neurohormonal blockade (fixed angiotensin, aldosterone and ANP, and fixed autonomic output). In the presence of WBFAR, BP after salt-loading remained stable in situation A, but increased by ~10 mmHg in situation B, and by ~30 mmHg in situation C. We further tested the role of WBFAR in three classical models of volume-loading hypertension.

Results: Even then, changes in CO and blood volume (BV) were minimal (less than 4% and 2%, respectively). In the absence of WBFAR, the same simulations led to similar changes in BP. However, a nearly two-fold increase in CO and an increase in BV by more than 20% were required to achieve salt-balance in situation C. In the first model, hypertension was induced by reducing renal mass to 30% of normal and increasing salt intake by 6-fold. In the presence of WBFAR, the development of hypertension (+30 mmHg) was characterized by an initial increase in CO by ~30% followed by a secondary increase in TPR (+25%). In the absence of WBFAR, there was a similar long-term increase in BP. However, a nearly 2-fold increase in CO and an increase in extracellular fluid volume by more than 30% were observed whereas TPR decreased by 30% owing to

the mechanical distension of blood vessels by the increased BP. Qualitatively similar results were obtained in two other models of volume-loading hypertension: aldosterone infusion and Goldblatt 1 kidney - 1 clip hypertension.

Conclusions: From the simulations one may conclude that autoregulation limits the amount of fluid retention required to increase BP in order to achieve salt balance, but does not affect the final level of BP.

Keywords: hypertension, blood flow autoregulation, computer simulations