The role of vascular capacitance in the genesis of essential hypertension

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Summary

1. Analysis of relationships between blood volume, vascular capacitance, cardiopulmonary and peripheral blood volumes, labelled albumin disappearance rate, plasma renin activity, blood pressure and age was performed in essential hypertensive males.

2. The results indicate that capacitance bed constriction probably occurs with age in essential hypertension leading to an increase in the product blood volume $\times$ vascular capacitance tone even in the presence of low blood volume.

3. A metabolic defect in the venous vascular bed along with an abnormality of regulation of renal sodium excretion is postulated.

Key words: albumin, blood volume, capacitance, haemodynamics, hypertension, plasma renin activity.

Introduction

The leading theme of the Borst–Guyton–Ledingham concept is that the circulatory overload caused by renal retention of fluid leads to transiently increased cardiac output, which through the tissue blood flow autoregulation is converted into increased total peripheral resistance and hypertension (Guyton, 1961; Borst & Borst-De Geus, 1963; Ledingham & Cohen, 1963). Although the concept is compatible with normovolaemic or hypervolaemic hypertension it can hardly in its present form be applied to uncomplicated essential hypertension because in this condition blood volume has repeatedly been shown to be mildly or even severely reduced (for review see Ulrych, 1973). The present knowledge of self-regulating systems makes it unlikely that this results from a marked over-correction. Laragh (1974) has popularized the equation: blood pressure = volume $\times$ vasoconstriction. It is important to realize that the expression 'volume' in the above equation should be substituted by the term 'circulatory filling', which is the relation between the amount of fluid and constriction of vessels around it or, in other words, blood volume $\times$ vascular capacitance tone. We have shown recently that the disappearance rate of labelled albumin may very well reflect the state of this crucial function (Ulrych & Ulrych, 1976).

Methods

Data were obtained on fifteen normotensive control subjects and forty-nine patients with arterial hypertension (thirty-seven without complications of hypertension, four with renal artery stenosis, two with uraemia, four with congestive heart failure and uraemia and two with congestive heart failure only). Plasma volume, labelled albumin disappearance rate, packed cell volume and blood volume were measured in principle by injecting Evans Blue and frequent sampling over the next 1–2 h. Blood pressures were measured either by an automatic recording device or directly; mean blood pressure was calculated as diastolic plus 1/3 of pulse amplitude. Cardiac output and cardiopulmonary blood volumes were measured by indicator dilution technique, injecting into the right atrium and sampling in the ascending aorta. Detailed descriptions of these methods were published in Ulrych, Frohlich, Tarazi, Dustan & Page (1969) and Ulrych (1973). Plasma renin activity was measured by immunoassay of angiotensin I. Studies were carried out only
with informed consent, and protocols of studies were approved by the Institutional Human Investigations Committee.

Results

In uncomplicated essential hypertension blood volume was decreased in proportion to the blood pressure increase \( (r = -0.493, P < 0.001) \). Blood volume was increased in those with complications of the disease (uraemia, congestive heart failure or both). Distribution of blood volume between pulmonary and peripheral circulation was altered in hypertensive patients with much wider variance than the normotensive control subjects and in both there was an inverse correlation between cardiopulmonary and peripheral blood volume when influence of body size was excluded by partial correlation technique \( (r = -0.543, P < 0.025) \).

There was a direct correlation between labelled albumin disappearance rate and blood pressure \( (r = 0.447, P < 0.05) \). There was a highly significant inverse linear relationship between the disappearance rate and ln(plasma renin activity), with a significantly steeper slope in the essential hypertensive group than in control subjects \( (r = -0.956, P < 0.015; r = -0.963, P < 0.001 \) in normotensive and essential hypertensive groups respectively). Blood volume corrected for body size correlated inversely with age \( (r = -0.596, P < 0.001) \). Blood pressure had a significant negative relationship with plasma renin activity \( (P < 0.05) \). In multiple regression analysis age seems to exert a more important influence on blood volume than blood pressure itself.

Discussion

It is obvious that the data do not conform with either Borst–Guyton–Ledingham or the Laragh concepts as simply as they are usually understood. It is also clear that 'circulatory filling' can be expressed as blood volume x capacitance tone and this expression should be substituted for volume in both of the previously mentioned concepts. This seems to be important especially in view of the inverse correlations between either peripheral or total blood volume on one hand and cardiopulmonary blood volume on the other hand. This strongly supports the idea that when the peripheral capacitance vascular bed constricts it pushes blood into the heart and lungs. Esler, Julius & Randall (1975) have shown that increased cardiopulmonary blood volume correlated with low plasma renin activity. Similarly we have shown that there is a very close inverse linear relationship between labelled albumin disappearance rate and plasma renin activity and that albumin disappearance rates correlate directly with blood volume and blood pressure changes. All this evidence supports the idea that labelled albumin disappearance rate most likely expresses the state of 'circulatory filling' which might be reflected by the size of cardiopulmonary blood volume. With a low blood volume it is very difficult to accept the present concepts emphasizing the important role of volume overload, but the present data are compatible with the idea of primary importance of vasoconstriction in certain components of the capacitance bed. This is really the mechanism of circulatory overload and leads to a decrease in blood volume. This is compatible with the finding of an exaggerated reaction of cardiac output to infusion of fluids (Ulrych, Hofman & Hejl, 1964) and also with the findings of an exaggerated natriuresis in relation to plasma renin activity (Krakoff, Goodwin, Baer, Torres & Laragh, 1970; Schalekamp, Krauss, Schalekamp-Kuyken, Kolsters & Birkenhager, 1971).

Decreases in blood volume and plasma renin activity with age in hypertensive patients (M. Ulrych & Z. Ulrych, unpublished observations) are possibly indicative of capacitance bed constriction becoming greater as a patient with hypertension ages. Since the incidence of hypertension increases with age one could imagine this might be a consequence of delayed penetrance of inherited biochemical defect similar to that shown by Greenberg (1975) in spontaneously hypertensive rats. Prostaglandin synthetase activity changes in them with age whereas it does not change in normotensive rats. This might be the biochemical reason for increased sensitivity of the vessels to constriction. It is thus possible to speculate that a similar defect might be present in the vessels of essential hypertensive humans, leading to increased constriction of the capacitance bed and thus to overloading of the circulation due to postulated abnormality of kidney or regulation of its function.

References

Vascular capacitance in hypertension


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