Capillary hypertension and abnormal pressure dynamics in patients with essential hypertension


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SUMMARY

1. Pressure was measured within 28 capillaries of the nailfolds of nine patients with essential hypertension and in 33 capillaries of nine age- and sex-matched normotensive control subjects, using direct micropuncture, a dynamic servo-nulling system and computerized analysis.

2. Average pressure at the apex of the capillary was found to be elevated in the patients with hypertension (21.1 ± 4.9 mmHg compared with 13.0 ± 2.0 mmHg in the control subjects; mean ± so, P<0.01). If the two groups were combined, there was an overall correlation between average capillary pressure and mean blood pressure (r=0.68, P<0.01, n=18), but within each group separately there was no significant relation between these parameters.

3. There were also abnormalities in the waveforms of pulsations in capillary pressure in the group with hypertension, with an increased attenuation of high-frequency harmonics. Pulses appeared to be conducted more rapidly along the vascular tree in the patients with hypertension.

4. The elevation of capillary pressure in essential hypertension demonstrated in this study is in agreement with indirect evidence of capillary hyperfiltration provided by other studies which showed a reduced plasma volume and increased transcapillary escape rate of plasma proteins which cannot be explained by abnormal permeability, all point to capillary hyperfiltration. The association between hypertension and increased resistance in the postcapillary segment of the microcirculation or vascular rarefaction could cause capillary hypertension, leading to this hyperfiltration.

5. The finding of elevated capillary pressure demands the inclusion of the postcapillary segment (and possibly vascular density) in the resistance equation in essential hypertension.

Key words: blood-pressure micropuncture, capillary, hypertension, microcirculation.

INTRODUCTION

An elevation of capillary blood pressure has been put forward as an explanation for several experimental findings in essential hypertension [1–7]. The reduced plasma volume [1, 3, 7] with normal [1, 2, 4] or increased plasma protein volume [1, 3, 7] which cannot be explained by abnormal permeability [5–7, 10], all point to capillary hyperfiltration. The association between hypertension and increased resistance in the postcapillary segment of the microcirculation [11–13] or vascular rarefaction [14–18] could cause capillary hypertension, leading to this hyperfiltration.

Despite the indirect evidence, direct studies of capillary pressure have not provided confirmation of the hypothesis. There has been only one such study in humans [19] and although the capillary pressures were slightly higher in patients with hypertension, this was not significant owing to the enormous variability of the measurement. This pioneering study can be criticised in the light of more recent knowledge, as the authors included subjects with diabetes mellitus and syphilis in the (in-patient) normotensive group, and the hypertensive patients were not investigated for heart failure or renal failure, conditions that would have had an independent effect on capillary blood pressure [20–22].

More recent studies of microvascular pressures in hypertensive animals have been conflicting, with raised [23], normal [24] and low [25] values relative to normotensive controls. This variation may be explained by the different models of hypertension and anaesthetics that were used.

The aim of this study was therefore to measure capillary pressure in a small group of thoroughly investigated patients with essential hypertension and a similar group of normotensive control subjects, using a sophisticated servo-null system [27, 28] which also allows signal averaging and computerized analysis of capillary pulse waveforms [29].

METHODS

Subject selection and experimental conditions

Nine subjects with essential hypertension were recruited at random from patients attending the Blood
Pressure Unit. All had normal full blood count, sodium, potassium, creatinine, urea, plasma renin activity and aldosterone. None had clinically evident oedema or cardiac failure. All had been off medication for at least 2 weeks before the study; in seven subjects this period was at least 4 weeks, and in the other two, where the period was 2 weeks, the previous medication was nifedipine, which has a relatively short duration of action.

These subjects were matched for age (within 5 years), sex and race with individuals who were recruited from hospital visitors and laboratory staff, all of whom had blood pressures of less than 90 mmHg diastolic and 150 mmHg systolic. There was no overlap between any of these readings between the two groups. None of the control subjects was on any medication and all were free of any clinical evidence of disease. Premenopausal females were matched for the phase of the menstrual cycle, as this can affect capillary pressure [30]. All studies were performed in a temperature-controlled laboratory (21.0–22.5°C) after a period of >30 min acclimatization. The subjects lay horizontally on a chiropody chair, the height of which was adjusted hydraulically until the hand, supported outstretched on a padded bench, was at the level of the mid-axillary line.

Micropuncture and capillary pressure measurement

Nailfold capillaries were visualized using a television microscopy system [31], punctured with glass micropipettes held in a micromanipulator [28, 32] and the pressure within measured using a dynamic servo-nulling system (I.P.M. Inc., San Diego, CA, U.S.A.) [33].

For this study, only the apices of capillary loops were punctured, this being the site which causes least disturbance to capillary blood flow owing to the presence of a plasma filled ‘cap’ [34]. Skin temperature and blood pressure were noted before and after each cannulation. An electrocardiogram was recorded in all subjects.

Recording and analysis

All parameters were recorded on magnetic tape using an F.M. tape recorder (Racal ‘Store 4’) and digitized later. These records were analysed using programs incorporating routines from Imperial College ‘Engineering in Medicine’ software library. A standard period of 30 s was used for analysis of capillary pressures: mean (from the area under the curve), maximum (the highest systolic capillary pressure during the period), minimum (the lowest diastolic capillary pressure during the period) and pulse (average systolic minus average diastolic capillary pressures).

Fourier analysis was carried out for 20.48 s to determine the frequency spectrum of the capillary pulse waves. The relative amplitudes of the fundamental ($F$, the first harmonic) and the other higher harmonics ($H_2$, $H_3$, etc.) were established in both groups of subjects. Relative amplitude comparisons were carried out between $H_2$ and $F$, as higher harmonics than $H_2$ (about 2.5 Hz) were much less consistent.

The apex of the electrocardiogram R-wave was used to trigger computerized superimpositions and coherent averaging of capillary pulse waves, from which the timing of the pulse wave foot was established (in seconds after the R-wave [29]). As the R-wave has a relatively constant relation to cardiac ejection, this timing may be used as a measure of pulse wave transmission velocity down the vascular tree (see the Discussion).

All statistical comparisons were performed using the Mann–Whitney U-test, but means and SD are retained as a convenient indicator of centre and spread.

RESULTS

There were four males and five females in each group. There was no significant difference in either age or skin temperature. Average capillary pressure was established for at least 30 s in 33 capillaries in the nine control subjects and 28 capillaries in the nine patients with hypertension.

All capillary pressure and blood pressure values are summarized in Table 1.

DISCUSSION

Mean capillary pressures of normotensive subjects were about 7 mmHg lower than we (and others [32, 35]) have previously reported for measurements from the apex of the capillary. This is explained by the deliberate change in posture that was made for the present study, in which the subjects were studied when lying horizontally, so that hydrostatic influences on capillary pressure would be reduced compared with the upright posture previously used. Care was also taken to avoid factors which might cause an elevation of capillary pressure, such as inflammation from overenthusiastic cuticle trimming and high room temperatures.

The equilibrium pressure, at which there is neither net filtration nor net reabsorption of fluid, is about 16 mmHg in human subcutaneous tissue [36]. Thus, average capillary pressures of 13 mmHg in the normotensive group are weighted slightly towards reabsorption of fluid, whereas pressures of 21 mmHg in the patients with hypertension would predispose towards excessive filtration. This is therefore consistent with the findings of other studies showing a reduction in the ratio of plasma volume to extracellular fluid volume in hypertension [1–4, 7], and is also consistent with an increased transcapillary escape rate of plasma protein due to solvent drag by the flow of water across the capillary wall [3, 5, 6, 9, 10] in this condition.

Whether nailfold capillary pressures are representative for tissues in general must be questioned, but the values obtained are consistent with tissue fluid balance (in normotensive subjects) and are close to pressures obtained in muscle in normal animals with similar arterial pressures [37]. It is not possible to measure capillary pressures in other tissues in human subjects using the techniques presently available.

The finding that capillary pressure is elevated in hypertension means that an increase in precapillary (arteriolar) resistance is unlikely to be a complete explanation for the
raised total peripheral resistance in hypertension, as this would prevent the increased arterial pressures from being conducted to the capillaries [19, 38]. Capillary hypertension could result if there was: (1) volume expansion (and therefore an increase in venous pressure), (2) an increase in postcapillary resistance, or (3) a reduction in the number of vessels in parallel (rarefaction).

The first explanation is unlikely in view of the reduced resistance in plasma volume in essential hypertension, although we did not measure this parameter. The second is a plausible explanation for the results. Increased venous tone and reduced venous compliance have been reported in hypertension [7, 11-13] and although venular tone has not been measured, it has been shown that venular resistance, comprising about 20% of the total peripheral resistance, is dynamically variable and is involved in auto-regulation of tissue blood flow [39]. The third hypothesis, a structural or functional rarefaction of vessels in hypertension, has been reported in humans [14-16] and animals [17, 18].

In a preliminary study [40] we showed a 15% reduction in the number of perfused skin capillaries in patients with hypertension. If uniform, a rarefaction of that magnitude would be insufficient to explain the degree of capillary or arterial hypertension observed, without contributions from other factors. However, a rarefaction of 50% of vessels has been reported in the spontaneously hypertensive rat [17].

Structural or functional differences in precapillary vessel walls may have been responsible for the reduction in the amplitude of higher pulse wave harmonics in the capillaries of patients with hypertension, either by increased damping or alternatively due to an increased (retrograde) reflection of these frequencies at the artery/arteriole junction [41].

The finding that cardiac pulses arrive earlier in the capillaries in the patients with hypertension is probably explained by an increased pulse wave transmission velocity in this group. This is known to occur in large arteries because of the reduction in wall compliance resulting from distension by the increased transmural pressures in hypertension [42]. The timings in this study, when normalized for arm length, equate to an overall propagation velocity of 5.3 m/s in the patients with hypertension, and 4.3 m/s in the control subject.

In conclusion, this unique study has shown several abnormalities of microcirculatory haemodynamics in essential hypertension. The most important of these, capillary hypertension, provides support for several indirect findings in hypertension, and represents a marked disturbance of microcirculatory function. The consequences of these abnormalities cannot be determined, but they may be implicated in some of the complications of hypertension. In addition, these findings suggest that therapeutic measures should not be aimed purely at reducing precapillary resistance.

Table 1. Summary of all results for each group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Skin temperature (°C)</th>
<th>Blood pressure (mmHg)</th>
<th>Mean capillary pressure (mmHg)</th>
<th>Maximum capillary pressure (mmHg)</th>
<th>Minimum capillary pressure (mmHg)</th>
<th>Capillary pulse pressure (mmHg)</th>
<th>Pulse arrival time (s)</th>
<th>Harmonics relative amplitude H2/F (%)</th>
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REFERENCES


