Neurohumoral response to hospitalization in hypertensive patients

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Summary

1. To investigate whether reduced activity of pressor systems could explain the spontaneous drop in pressure upon hospitalization, 51 subjects with uncomplicated essential hypertension were admitted to hospital. Sodium intake was fixed at 55 mmol/day.

2. Blood samples for noradrenaline, adrenaline, active renin, angiotensin II and aldosterone were drawn on each morning of the first 3 days of hospitalization; blood pressure was measured at 2 h intervals and values were averaged for each day.

3. Subjects were divided in two groups depending on whether they became normotensive (group 1; \( n = 12 \)) or remained hypertensive (group 2; \( n = 39 \)). This distinction was thought to reflect mild and more severe hypertensive groups respectively.

4. Although both groups showed a comparable fall in blood pressure during hospitalization, noradrenaline levels fell more consistently in group 1, whereas adrenaline levels fell only in group 2. The components of the renin–angiotensin–aldosterone system rose, but more conspicuously in group 1.

5. It is concluded that withdrawal of sympathetic activity can only partly explain the hypotensive response to hospitalization. The renin–angiotensin–aldosterone system behaves only passively and appears to be counterproductive to alterations in blood pressure.

Key words: catecholamines, hypertension, renin–angiotensin–aldosterone system.

Introduction

Hypertensive patients often exhibit a marked fall in blood pressure when they are hospitalized.

Although the mechanisms responsible for this spontaneous reduction could provide considerable insight into the pathophysiology of essential hypertension, only very few studies have been carried out to clarify this phenomenon. In a previous study \([1]\) we have shown that part of the hospitalization effect could be explained by changes in sodium balance, but this became apparent only after the second day of admission. The present study was designed to define the role of pressor systems during the first 3 days of hospitalization.

Patients and methods

Fifty-one subjects with uncomplicated essential hypertension were hospitalized. Age ranged from 21 to 66 years (average 43 years) and mean arterial pressure from 108 to 153 mmHg (average 129 mmHg). Previous antihypertensive treatment had been withdrawn at least 3 weeks before admission. To assess habitual salt intake, patients were instructed to make 24 h urine collections on the last 3 days before admission.

Patients came into hospital between 09.00 and 10.00 hours and, after an indwelling needle had been inserted, they rested in the supine position for 30 min. Subsequently blood samples were drawn for determination of catecholamines, active renin concentration, angiotensin II and aldosterone. Thereafter patients were allowed to move freely.

On the morning of the second and the third days of hospitalization blood samples for assay of the same hormones were drawn again under the same conditions as on the first day.

Blood pressure was measured at 2 h intervals and averaged for each day. Throughout the study period dietary sodium intake was restricted to 55 mmol/day and checked by 24 h urine collections. Catecholamines were determined with a HPLC technique \([2]\). Active renin was measured by the
Fig. 1. Changes in mean arterial pressure (MAP), plasma noradrenaline (NOR), plasma adrenaline (AD) and active plasma renin concentration (APRC) during the first 3 days of hospitalization. ▲, Group 1; △, group 2.

Results

Results are summarized in Fig. 1.

For analysis, patients were divided into two groups. Group 1 (n = 12) consisted of those patients who after 3 days of hospitalization had become normotensive (mean arterial pressure ≤110 mmHg); while group 2 (n = 39) comprised the other subjects. Throughout the study patients from group 1 had lower blood pressures than those in group 2 (P < 0.01), but in both groups a similar fall in blood pressure had occurred by the third day (12 ± 2 vs 10 ± 3 mmHg; n.s.).

Plasma noradrenaline levels were consistently lower in group 1, but the difference was significant on days 1 and 3 only (P < 0.05 on both days). Noradrenaline fell constantly in group 1, and it dropped significantly (P < 0.05) during the first 24 h in group 2 to rise again thereafter. Adrenaline levels in group 1 hardly changed with time and were always significantly lower than those in group 2 (P < 0.01). In the latter group a constant fall with time was observed, which was significant (P < 0.05) at the third day. Active renin concentration rose in both groups, but much faster in patients from group 1. Moreover, at admission renin levels were significantly higher in this group (P < 0.05).

Levels of angiotensin II and aldosterone closely paralleled those of renin. However, although angiotensin II levels tended to be slightly higher in group 1, aldosterone levels on the first day of admission were significantly lower in this group (P < 0.05). The two groups were otherwise comparable with respect to age, known duration of hypertension and 24 h sodium excretion before admission.

Discussion

The present study once again shows that hospitalization of patients with essential hypertension is associated with a fall in their blood pressure.
Inasmuch as the distinction between the two groups reflected mild or borderline hypertension on the one hand (group 1) and moderate or more severe hypertension on the other (group 2), the behaviour of blood pressure in both groups was comparable. Our data further demonstrate that noradrenaline levels declined during hospitalization. This is in contrast with the findings of Hossmann et al. [4], but it should be stressed that in their study blood was drawn after patients had been lying down for only 5 min. It may well be that our patients had reached a more basal state. It is of interest that in group 2 noradrenaline fell most conspicuously during the first 24 h, although it rose again during the second day despite the fact that blood pressure fell even further.

In group 1 there was a gradual decline in noradrenaline levels, and the largest drop in pressure occurred during the first 24 h. On the other hand, adrenaline levels did not fall appreciably in group 1, but there was a gradual drop in group 2.

Combining these data we may conclude that during hospitalization a decrement in neurogenic tone or adrenal medullary activity may contribute to the pressure fall observed in hypertensive patients. Yet these factors do not fully explain the hypotensive response to hospitalization. It is also evident that the renin–angiotensin–aldosterone system does not contribute to the fall in pressure. It seems that this system behaves only passively and inversely to the changes in blood pressure. These results are fully compatible with the baroreceptor theory of renin release. The fact that the responsiveness of the system was blunted in group 2 is in good agreement with the hypothesis that renin secretion is suppressed by longstanding elevated pressure at the level of the juxtaglomerular apparatus.

Since sodium excretion in the two groups was comparable before admission, it does not seem likely that differences in sodium balance could explain the differences between the groups. In conclusion, our results suggest that the decrement in pressure during hospitalization of essential hypertensive patients can only partly be dependent on withdrawal of sympathetic tone. Still other factors have to be implicated to explain fully the hypotensive response to hospitalization.

References