Plasma Renin Activity in Acute Cerebrovascular Disease: Preliminary Communication

BY JOHN H. MORAN, M.B., B. Chir., M.R.C.P.,* AND RUTH B. LOEWENSON, Ph.D.†

Abstract: Plasma Renin Activity in Acute Cerebrovascular Disease: Preliminary Communication

A preliminary study of plasma renin activity was made in 22 patients with acute cerebrovascular disease. Eight of 12 patients with intracranial hemorrhage had plasma renin activity values above the normal range of 30 to 330 ng/100 ml plasma, but only one of ten patients with ischemic cerebrovascular disease had increased plasma renin activity. The mean values for the two groups were, respectively, 489 and 190 ng/100 ml plasma (P for difference < 0.001). Ten days later plasma renin activity was normal in each of three patients with intracranial hemorrhage. The acute increase of plasma renin activity may have been associated with altered activity of the autonomic nervous system, and may be related to posthemorrhagic vascular events such as vasospasm.

Additional Key Words
- autonomic nervous system
- angiotensin
- cerebral ischemia
- hypertension
- cerebral hemorrhage
- cerebral infarction

Introduction

Certain metabolic and pathological disturbances, for example, transient glycosuria or electrocardiographical changes in the absence of primary disease of the heart, may occur following stroke. Such phenomena are usually attributed to altered activity of the autonomic nervous system.† "

In recent years, research has shown that the renin-angiotensin system has actions other than direct vasoconstriction and the maintenance of sodium balance; in particular, it augments and modulates the autonomic nervous system.‡

This study, therefore, was undertaken to determine alterations of plasma renin activity in acute cerebrovascular disease, and to record the relationship, if any, of an increase in plasma renin activity to the type of stroke and to altered activity of the autonomic nervous system.

Methods

For assay of renin activity, blood samples (20 ml) were collected by venipuncture from the antecubital fossa and placed immediately in chilled heparin-containing tubes. The heparin and blood were mixed and immediately placed in an ice-water bath. Refrigerated centrifugation was then carried out at 2,000 rpm for ten minutes, and the plasma obtained was immediately separated and frozen, and later sent to the laboratory.

The bio-assay of Gunnells et al.§ was used for determining the plasma renin activity. This method notes the effect of intravenous injection of dialyzed and prepared plasma on the blood pressure of bilaterally nephrectomized rats.

The plasma renin activity was expressed in nanograms (ng) per 100 ml plasma. Normal values for patients in the recumbent position range from 30 to 330 ng/100 ml plasma.

Patients

All patients admitted to the Stroke Unit, Department of Neurology, Hennepin County General Hospital, Minneapolis, Minnesota, within 24 hours of an acute cerebrovascular accident were considered for this study. A division of the stroke patients into ischemic and hemorrhagic was based on the diagnosis made by staff neurologists of Hennepin County General Hospital and the University of Minnesota from clinical features, cerebrospinal fluid analysis, angiography, and other investigatory findings. Patients already receiving diuretic agents or other medication known to activate the renin-angiotensin system were excluded from the study. All patients were maintained on an intravenous dextrose/saline infusion providing approximately 100 mEq sodium per 24 hours. As far as could be determined, all patients included in this report had been on a normal dietary sodium intake (70 to 350 mEq/day)§ before admission. With the patient recumbent on the morning (8 to 9 A.M.) following admission, the blood pressure was recorded and a specimen of blood was collected for plasma renin activity and plasma electrolytes. In patients found to have an increased plasma renin

*Research Fellow, †Associate Professor, Department of Neurology, University of Minnesota Medical School, Minneapolis, Minnesota 55455.

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Reprint requests to Dr. Moran.

160

Stroke, Vol. 4, March-April 1973
activity, a further assay was performed on plasma obtained ten days after admission, provided that the specimen could be obtained under the same conditions as initially.

All patients in the study had normal electrolytes and hematocrit at the time of their renin assays.

Results
Of the 22 stroke patients studied, 12 had intracranial hemorrhage (six subarachnoid hemorrhage, two brain stem hemorrhage, and four intracerebral hemorrhage) and ten had ischemic infarcts (nine cerebral infarcts and one brain stem infarct). The values for plasma renin activity for each group are shown in figure 1. Only one patient with an ischemic infarct had an increased plasma renin activity (390 ng/100 ml), whereas the values were normal for the remaining ischemic infarct patients. In the group of patients with intracranial hemorrhage, eight had increased plasma renin activity. Four patients had values within the normal range, but two of these were “high” normal (320 and 295 ng/100 ml).

Three patients with increased plasma renin activity in the hemorrhagic group had a second renin assay ten days later, and in all of these patients the values were normal. In the only patient with increased plasma renin activity in the ischemic group, the renin activity remained elevated.

The means and standard errors of the values for renin activity (in ng/100 ml) were 190 ± 34 for the patients with ischemic infarct, and 489 ± 73 for the patients with intracranial hemorrhage. By the t-test, the difference between the two means was statistically significant with a P-value of <0.001.

The plasma renin activity did not appear to relate to the value for the blood pressure. Only three patients with increased renin activity had diastolic pressures greater than 90 mm Hg or systolic pressures above 160 mm Hg at the time blood was taken for assay, and two of these patients had additional renin assays ten days later that were normal, although their blood pressures remained elevated.

![FIGURE 1](https://stroke.ahajournals.org/)

Plasma renin activity for patients with ischemic infarcts and patients with intracranial hemorrhage. (Normal range for plasma renin activity is 30 to 330 nanograms per 100 ml.)

Stroke, Vol. 4, March-April 1973

161
Discussion

One of the possible mechanisms that can cause increased plasma renin activity is antecedent hypertension. However, the bio-assay used in this study is said to have the advantage of rarely showing increased plasma renin activity in hypertension unless it is of renovascular, malignant or accelerated form. None of the patients in the study were considered to have any of these types of hypertension.

It is thought that direct activation of the sympathetic nervous system occurs through the hypothalamus following intracranial hemorrhage and perhaps through the resulting catecholamine release, renin activity is increased. Animal experiments have shown a direct relationship between brain stimulation and increases of plasma renin activity. In dogs, stimulation of electrodes placed in the dorsal portion of the medulla oblongata produces a definite increase in plasma renin activity, provided the renal nerves are intact. In rats, stimulation of the hypothalamus produces consistent increases in plasma renin levels. These experiments indicate that the central nervous system plays a role in the regulation of renin secretion. Furthermore, the increase of renin secretion produced by brain stem stimulation can be almost completely abolished by the prior administration of beta-adrenergic blocking agents, suggesting that a link exists between the brain, the activity of the sympathetic nervous system and the secretion of renin.

It is appreciated that individual responses to a given renin level may be variable and that plasma renin activity is influenced by many factors. However, the finding of increased plasma renin activity in a number of patients with acute hemorrhagic stroke warrants further study. In particular, activation of the renin-angiotensin system may be important in the production of vasospasm after subarachnoid hemorrhage, or in the transient rise of blood pressure and disturbances of the autonomic nervous system that may occur after acute strokes. A study of a larger series of patients is under way to assess these possibilities.

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References

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