Klin. Wschr. 52, 1173—1174 (1974)

Kurze wissenschaftliche Mitteilungen

Half-life of Plasma Renin Activity in Normal Subjects and in Malignant Hypertension

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Received April 5, 1974

Summary. Half-life of plasma renin activity (PRA) was measured in 3 normal subjects after maximal stimulation and subsequent inhibition of renin release by the intravenous administration of propranolol, as well as in a patient with malignant hypertension immediately after bilateral nephrectomy.

In the normal subjects half-life of PRA was between 10 and 15 minutes (mean 13 minutes), in the patient with malignant hypertension disappearance of renin activity from the circulation was a single exponential function with a half-life of 1 hour 22 minutes.

These results could indicate an impaired inactivation of renin in malignant hypertension and/or chronic uremia. Other possible explanations of these preliminary findings, such as contribution of the kidney to inactivation of renin under physiological circumstances or an effect and after-effect of general anaesthesia on renin inactivation will have to be excluded. The impaired extraction of renin from the circulation might be an important additional limb in the viscious circle of defective feedback control of renin characteristic of malignant hypertension.

Key words: Plasma renin activity, half-life of (PRA), liver extraction, malignant hypertension.

Die Halbwertszeit der Plasmareninaktivität bei Normalpersonen und bei maligner Hypertonie.

Zusammenfassung. An 3 Normalpersonen und 1 Patientin mit maligner Hypertonie wurde die Halbwertszeit der Plasmareninaktivität (PRA) bestimmt. Bei den Normalpersonen wurde nach maximaler Stimulation der Reninsekretion durch Induktion von Orthostase am Kipptisch die Reninsekretion durch die intravenöse Verabreichung von Propranolol supprimiert und durch Messung der PRA mittels Radioimmunoassay in 15minütigen Intervallen die Halbwertszeit der PRA bestimmt. Die Verschwinderate des Renins aus der Zirkulation wurde bei einer Patientin mit maligner Hypertonie durch Messung der PRA in 15minütigen Intervallen während und unmittelbar nach der bilateralen Nephrektomie gemessen.

Während bei den Normalpersonen die Halbwertszeit zwischen 10 und 15 min (Mittelwert 13 min) betrug, war der Abfall der PRA bei der Patientin mit maligner Hypertonie eine einfache Exponentialfunktion mit einer Halbwertszeit von 1 Std und 22 min. Die Resultate zeigen eine auf das sechsfache der Norm verlängerte Halbwertszeit der PRA bei maligner Hypertonie. Die verlangsamte Extraktion von Renin aus der Zirkulation scheint mitverantwortlich für die stark erhöhten zirkulierenden Renin- und Angiotensin II-Spiegel bei maligner Hypertonie.

Schlüsselwörter: Plasmareninaktivität, Halbwertszeit, Reninextraktion, Maligne Hypertonie.

Introduction

Most attention on the physiology of renin has been focused on the secretion of the enzyme. We are not aware that the disappearance rate of renin from the circulation has been measured in human subjects under physiological conditions, although alterations in the extraction of renin might be aqually as important determinants for actual plasma evels as are changes in the secretion rate of renin.

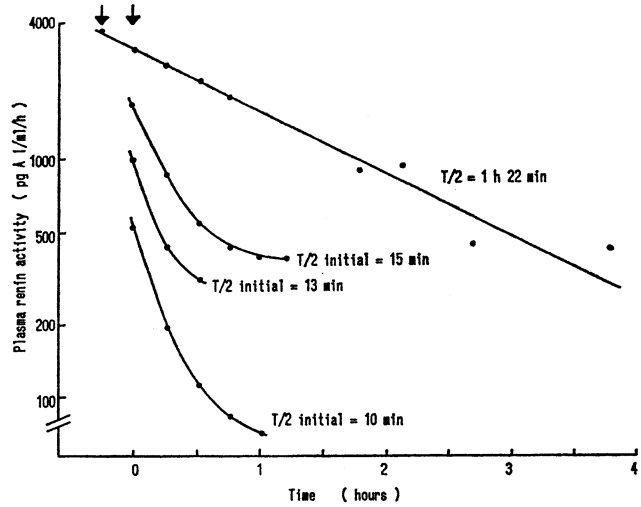

Fig. 1. The upper curve shows the disappearance of PRA from the circulation in the patient with malignant hypertension after bilateral nephrectomy; the 2 arrows indicate the time of removal of the right and left kidney respectively. The 3 curves beneath show the disappearance of PRA from the circulation in 3 normal subjects after maximal stimulation and subsequent inhibition of renin release by the intravenous administration of propranolol at time zero

Material and Methods

We have studied the disappearance rate of plasma renin activity (PRA) in 4 subjects using the method of Boyd *et al.* [1] for PRA assay, which involves extraction of generated angiotensin I onto Fuller's earth before radioimmunoassay: in a 17 year old girl with malignant hypertension immediately after bilateral nephrectomy; and in 3 normal male subjects, all aged 24 years, after maximal stimulation of renin release by inducing orthostasis on the tilting table, followed by suppression of renin release by the administration of 5 mg propranolol immediately after the subjects returned to the supine position. Since renin release in malignant hypertension does not respond to acute inhibitory stimuli it has not been possible to adopt the above protocol in the patient with malignant hypertension.

Results and Discussion

The results in the patient with malignant hypertension and in 3 normal subjects are shown in Fig. 1. The figure

shows that the decrease of PRA after bilateral nephrectomy in the patient with malignant hypertension corresponds to a single exponential function, the half-life of PRA being 1 hour 22 minutes. The initial half-lives of PRA in the 3 normal subjects were 10,13 and 15 minutes respectively. Should suppression of renin release have been incomplete by the manoeuvre adopted by us, the difference in half-lives between normal subjects and the patient with malignant hypertension would have been even more pronounced. Propranolol added in vitro to the plasma samples before incubation, did not affect the estimated plasma renin activity tested up to a concentration of 20 μg/ml plasma, which excludes an effect of propranolol on the enzyme-substrate reaction.

The half-life of PRA measured by us in normal subjects agrees closely with the value of 13 minutes calculated by Christlieb and coworkers [2] from peripheral and hepatic vein renin measurements; it is considerably shorter than the The half-life of 30 minutes measured in rats [5]. The half-life of PRA measured after bilateral nephrectomy in the patient with malignant hypertension is 6 times longer than that observed in our normal subjects and also 2 to 3 times longer than that observed in 2 subjects with hypertension of terminal renal failure measured after bilateral nephrectomy [3].

Since the protocols of investigation in the normal subjects and in the patient with malignant hypertension are different, several possible explanations of ur findings can be put forward. The longer half-life of PRA in malignant hypertension could be due to impaired mechanisms of inactivation of renin which might be the cause or the result of the disease. Other possible explanations such as contribution of the kidney to inactivation of renin under physiological circumstances or an effect of uremia and/or anaesthesia on inactivation of renin will have to be excluded.

In animal experiments high circulating angiotensin levels reduce liver blood flow and consequently in some instances the extraction of renin by the liver [4]. Since also an increase of percent extraction of renin has been observed in some experiments [6], it remains questionable whether the reduced liver blood flow caused by high circulating angiotensin levels is sufficient to explain the longer half-life of renin in the patient with malignant hypertension. Our results indicate that on impaired removal of renin from the circulation might contribute to the high circulating levels found in malignant hypertension. This might be an important additional limb in the vitcious circle of defective feedback control of renin characteristic for malignant hypertension.

Supported by the Fonds zur Förderung der wissenschaftlichen Forschung, Vienna.

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