The Peripheral Vascular Reactivity of Potassium-Deficient Rats

By Ray H. Rosenman, M.D., S. Charles Freed, M.D., and Meyer Friedman, M.D.

Peripheral vascular reactivity was studied in the potassium-deficient and control rats by measuring the degree of blood pressure response to intravenously injected pressor substances. The pressor response consistently was less in the potassium-deficient rats. The significance of these results with regard to the hypotensive action of potassium deprivation is discussed.

CONSIDERABLE emphasis has been given to the essential role of potassium in the maintenance of the structural and functional integrity of various body tissues. More recently, the present authors1–3 have obtained evidence that the blood pressure of normal and hypertensive rats maintained upon a potassium-deficient diet is significantly depressed. This depressor response, however, could be prevented by simultaneous deprivation of sodium.2

The mechanism by which potassium deprivation induces a lowering of the blood pressure is, as yet, not clarified. Data2, 3 obtained in this laboratory indicate that the myocardial damage which may follow potassium deficiency probably does not account for the hypotensive response that occurs in either normal or hypertensive rats. An alteration in the peripheral vascular system, however, might well be involved. The following experiments therefore were undertaken in order to test the immediate vascular response to the administration of several pressor substances in rats made potassium deficient.

METHODS

Six to 7 week old male rats (Long-Evans) were divided into three groups which were given the following dietary regimes. The first group of 12 rats (group I) was placed upon a potassium-deficient diet as described,3 and which was supplemented by an adequate vitamin intake.* A second group of 12 control rats (group II) was placed upon the identical diet except that potassium chloride, 0.5 per cent, was added to the ration. A third group of 12 control rats was fed a stock laboratory diet.

At the end of the ensuing 10 week feeding period the vascular reactivity of each rat was tested by a technic generally similar to that developed by Page and Taylor for dogs4 and adapted for rats by Masson, Page and Corcoran.5 Under ether anesthesia the abdomen was opened and a plastic cannula inserted into a branch of the inferior vena cava, providing a method for rapid intravenous injection of the test substances. The animal was then heparinized and a small cannula inserted into the distal aorta and connected to a mercury manometer. After a period of observation during which the blood pressure was allowed to stabilize at a constant level, the following substances were injected intravenously in succession, and the blood pressure changes recorded. Between each injection an adequate time interval was allowed for the return and stabilization of the blood pressure at the basal level. The test substances and their dosage were (a) commercial epinephrine, 0.1 cc. (1 µg.), (b) norepinephrine, 0.1 cc. (1 µg.), (c) angiotonin,† 0.2 cc. (5 mg. containing 2 units), and (d) renin, † 0.1 cc. (0.5 mg.). It is recognized that errors inherent in the instruments and technic employed in obtaining the blood pressures as well as the surgical trauma to which the animals were exposed prevent any conclusions from being drawn with regard to the initial pressures that were observed. Nevertheless, the method is believed reliable with regard to changes in pressure which occurred in response to injection of the pressor substances.

* We are indebted to Hoffmann-LaRoche, Inc., for generous supplies of Litriton, used to provide the supplements added to the synthetic diets.

† We are grateful to Dr. Arthur C. Corcoran and Dr. Kenneth Savard of the Cleveland Clinic Foundation for generous supplies of angiotonin and renin furnished for these studies.
Results

The rats that had been maintained upon the stock diet and upon the synthetic control diet showed comparable pressor responses to the test substances. Furthermore, the synthetic control diet was shown to be adequate since growth and weight gain in these rats were similar to growth and weight gain in rats fed the stock diet. Therefore, for simplicity, only (group II). Thus, the pressor response to all of the test substances was consistently diminished in the potassium-deficient animals (see fig. 1). There was some variation in the magnitude of this decreased response to the various test substances. The blood pressure rise after epinephrine injection in the potassium-deficient rats was about one-half as great as in the control animals, while the injection of angiotonin and

Table 1.—Changes in Blood Pressure following Intravenous Injection of Pressor Substances into Potassium-Deficient Rats

<table>
<thead>
<tr>
<th>Type of Rat</th>
<th>No of Rats</th>
<th>No of Rats</th>
<th>Weight (Gm.)</th>
<th>Weight (Gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium-Deficient</td>
<td>12 (125-233)</td>
<td>12 (125-233)</td>
<td>180 (33-96)</td>
<td>180 (33-96)</td>
</tr>
<tr>
<td></td>
<td>74 (53-118)</td>
<td>74 (53-118)</td>
<td>98 ±4.0 (4-44)</td>
<td>98 ±4.0 (4-44)</td>
</tr>
<tr>
<td></td>
<td>±4.7 ±3.0</td>
<td>±4.7 ±3.0</td>
<td>±3.9 ±4.5 ±7.0</td>
<td>±3.9 ±4.5 ±7.0</td>
</tr>
<tr>
<td></td>
<td>Initial</td>
<td>Peak</td>
<td>Increase</td>
<td>Initial</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>81 (51-100)</td>
<td>92 (63-130)</td>
<td>+11 (4-30)</td>
<td>78 (59-98)</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>79 (58-106)</td>
<td>120 (60-106)</td>
<td>+41 (30-53)</td>
<td>81 (58-106)</td>
</tr>
<tr>
<td>Angiotonin</td>
<td>98 ±4.0 (4-44)</td>
<td>98 ±4.0 (4-44)</td>
<td>98 ±4.0 (4-44)</td>
<td>98 ±4.0 (4-44)</td>
</tr>
<tr>
<td>Renin</td>
<td>79 (58-106)</td>
<td>120 (60-106)</td>
<td>+41 (30-53)</td>
<td>81 (58-106)</td>
</tr>
</tbody>
</table>

* Figures in parentheses refer to range of values obtained.
† Standard error of the mean.

Fig. 1. Average blood pressure response to intravenous injection of pressor substances into potassium-deficient rats.

The results obtained in the rats fed the synthetic diets will be presented.

Table 1 presents the blood pressure changes which followed the intravenous injection of the test substances and the figure depicts the average blood pressure responses which were observed. The average and range of values obtained in the potassium-deficient rats (group I) were in marked contrast to the control animals renin induced less than one-half, and norepinephrine only one-third of the normal pressor response.

Discussion

It has been shown recently that the motility and muscular tone of the gastrointestinal tract and urinary bladder were progressively decreased in potassium-deficient rats. These results suggested that the smooth muscle of the peripheral vascular system and, in particular, of the arterioles similarly might become atonic during potassium deprivation. The evidence obtained in these experiments lends strong support to this supposition. The consistently decreased response to the various pressor agents that was observed in the potassium-deficient rats, in contrast to that in the control animals, strongly suggests that potassium deprivation induces a decreased arteriolar tone. Although a part of its pressor action is central in the case of epinephrine, renin and angiotonin act largely by peripheral vasoconstriction. The markedly diminished response to norepinephrine is particularly significant since it has been well
shown that this substance exerts a pressor action solely by its peripheral effects, inducing arteriolar vasoconstriction, but without increasing the cardiac output. This evidence suggests that the mechanism of the decreased responsiveness of the potassium-deficient rat to pressor agents is localized to the periphery of the arterial system.

These results also suggest that the depressor effect of prolonged potassium deprivation in both normotensive and hypertensive rats is at least partly related to a reduction of peripheral vascular resistance, effected by a decreased arteriolar tone. That such a decrease in peripheral resistance actually is the cause of the hypotension which follows chronic potassium deprivation, remains, however, to be demonstrated.

Although the mechanism of decreased vascular reactivity occurring in prolonged potassium deprivation would appear to be related to a decreased arteriolar muscular tone, it must be considered that both sodium and potassium are intimately connected with the transmission of nerve impulses. It is also well known that potassium is closely related to the acetylcholine metabolism at the nerve endings. Potassium deprivation, by itself, or acting through a disturbed sodium-potassium ratio, may thus alter the arteriolar nerve-muscle system and be a factor in the induction of hypotension.

SUMMARY

Peripheral vascular reactivity has been studied in potassium-deficient and in control rats. The vascular reactivity was measured by the degree of response to intravenously injected epinephrine, norepinephrine, angiotonin, and renin.

The pressor response to all of the test substances was consistently and significantly less in the potassium-deficient rats, compared with the results obtained in the control animals. It is suggested that a decreased peripheral vascular resistance may account, in part, for the hypotensive action of potassium deprivation in both normotensive and hypertensive rats.

REFERENCES

The Peripheral Vascular Reactivity of Potassium-Deficient Rats
RAY H. ROSENMAN, S. CHARLES FREED and MEYER FRIEDMAN

Circulation. 1952;5:412-414
doi: 10.1161/01.CIR.5.3.412
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1952 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/5/3/412

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/