Effect of Cortisone and ACTH on Blood Pressure of Hypotensive, Potassium-Deficient Rats

By S. C. Freed, M.D., R. H. Rosenman, M.D., Shirley St. George, Ph.D., and Malcolm K. Smith, A.B.

Potassium deficiency, induced in a series of rats by dietary deprivation, was associated with a depressor response. The administration of cortisone and, to a lesser extent, of corticotropin (ACTH), promptly elevated their lowered blood pressures. The possible participation of the adrenal cortex in the depressor response to potassium deficiency is discussed.

Previous studies from this laboratory have shown that both intact and hypertensive rats exhibit a gradual but progressive fall in blood pressure when deprived of dietary potassium. Further studies have shown that this depressor response is associated with a loss of body potassium and a decrease of peripheral vascular reactivity to pressor agents. The possible involvement of the adrenal cortex in this depressor response suggested itself to us previously, since the potassium-deficient rat exhibits several characteristics in common with the untreated adrenalectomized animal, including subnormal nutritional state, hypotension, decreased peripheral vascular responsiveness, and an intolerance to stress. Moreover, altered adrenocortical structure and function have been observed in potassium-deficient rats. It was therefore deemed important to determine whether or not the depressor response of the potassium-deficient state was related at least in part to consequent alteration of adrenocortical function.

Methods

Male rats (Long-Evans) were divided into two series. The first series of animals (4 weeks old) was fed a potassium-deficient ration containing 0.006 per cent potassium, as previously described. At the end of a six-week interval, blood pressures were obtained by the microphonic manometer method. Those rats having a systolic pressure below 100 mm. Hg were divided into three experimental groups and were continued on their potassium-deficient ration. During the ensuing 10-day period, the rats of group I served as controls, those of group II received 1 mg. of cortisone acetate twice daily, and those of group III received 1 mg. of corticotropin (ACTH) twice daily. Blood pressures were obtained after one, three, four, seven, and 10 days, after which determinations were made of the concentrations of potassium in the blood serum, the skeletal muscle (thigh) and the myocardium (ventricles) according to previously described methods. Three separate but similar studies were done, with comparable results, so that the data were combined for this presentation. The combined series included 26 rats in group I, 55 in group II, and 20 in group III. In addition, a small group of five potassium-deficient rats were given cortisone acetate in a smaller dose of 0.1 mg. twice daily, and their blood pressures were obtained similarly during the ensuing 10-day interval.

The second series of animals consisted of normal 10 weeks old rats fed stock ration before and during the 10 day experimental interval. Ten rats served as controls (Group IV), 10 received cortisone acetate, 2 mg. daily, and 10 received corticotropin, 2 mg. daily. Blood pressures were obtained at the onset and end of the 10-day period. The rats of group IV then were sacrificed for determination of potassium concentrations of serum, skeletal muscle, and myocardium. The hormones were administered subcutaneously in all instances.

Results

The results of the blood pressure determinations are presented in figure 1. The average blood pressure of the 26 potassium-deficient rats of the control group (I) after six weeks of the potassium-deficient diet was 83 mm. Hg.
CORTISONE AND ACTH IN K-DEFICIENT RATS

Fig. 1. The effect of cortisone and corticotropin on blood pressure of potassium-deficient rats.

(range: 52 to 100) and 10 days later was 88 mm. Hg (range: 60 to 110) (S.E. mean: ±4.0). The daily administration of 2 mg. of cortisone acetate to 55 potassium-deficient hypotensive rats (group II) was associated with a rapid and progressive rise of their average blood pressure from 85 mm. Hg (range: 56 to 100) to 106 mm. Hg (range: 90 to 114) (S.E. mean: ±3.0) at the end of 10 days. In the additional small group of five rats the daily administration of 0.2 mg. of cortisone acetate was followed by a similar elevation of blood pressure, the average rising from an initial level of 88 mm. Hg (range: 76 to 96) to 107 mm. Hg (range: 78 to 128) (S.E. mean: ±7.5). The administration of 2 mg. of corticotropin daily (group III) was also associated with a rise of blood pressure, but this was of lesser magnitude, the average rising from 81 mm. Hg (range: 52 to 96) to 98 mm. Hg (range: 82 to 100) (S.E. mean: ±2.5). The administration of 2 mg. of cortisone acetate or of corticotropin to rats fed a normal stock ration was associated with no significant change in their average blood pressures.

The untreated potassium-deficient rats (I) maintained the same average weight during the experimental period (110 Gm.). The weight of the animals receiving cortisone acetate (II) fell from an initial average of 112 Gm. to 96 Gm. during the 10-day period and those receiving corticotropin (III) fell from an initial average of 115 Gm. to 108 Gm. The prolonged dietary deprivation of potassium led to a decreased potassium content of the serum, skeletal muscle, and the myocardium (table 1). The serum potassium of potassium-deficient rats given cortisone or corticotropin was decreased to a comparable extent. The potassium content of the skeletal muscle and myocardium in the rats given cortisone or corticotropin was somewhat less than in the untreated potassium-deficient animals.

<table>
<thead>
<tr>
<th>Group</th>
<th>Regimen</th>
<th>No. Rats</th>
<th>Serum (mEq./L.)</th>
<th>Muscle (mEq./Kg.)</th>
<th>Myocardium (mEq./Kg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>K-deficient diet</td>
<td>8</td>
<td>3.5 (3.3-3.6)*</td>
<td>96 (89-101)</td>
<td>83 (72-95)</td>
</tr>
<tr>
<td>II</td>
<td>K-deficient diet plus cortisone (2 mg. daily)</td>
<td>16</td>
<td>3.0</td>
<td>80 (67-100)</td>
<td>67 (46-85)</td>
</tr>
<tr>
<td>III</td>
<td>K-deficient diet plus ACTH (2 mg. daily)</td>
<td>14</td>
<td>3.6</td>
<td>86.5 (65-98)</td>
<td>79 (74-82)</td>
</tr>
<tr>
<td>IV</td>
<td>Normal controls</td>
<td>5</td>
<td>5.6 (5.1-6.6)</td>
<td>117 (93-136)</td>
<td>91 (65-127)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate range of values.

**DISCUSSION**

These results indicate that the administration of cortisone and, to a somewhat lesser extent, corticotropin, was capable of promptly elevating the blood pressures of rats made hypotensive by dietary potassium deprivation. Similar doses of these hormones failed to raise the blood pressures of normal rats.

The mechanism of the pressor response to cortisone in the potassium-deficient hypotensive rat is not definitely established. We have previously demonstrated6 that the blood pressure fall in such rats is associated with a loss of peripheral vascular responsiveness. Since cortisone has been shown to cause an increased pressor response to l-norepinephrine,19 the possibility may be considered that cortisone has a similar effect in potassium-deficient rats. Whatever may be the nature of the effect of cortisone on the blood pressure of hypoten-
sive, potassium-deficient rats, it does not involve correction of the potassium depletion in the serum or tissues. Indeed, the potassium levels of the cortisone-treated animals were lower than in the untreated potassium-deficient rats.

Inasmuch as cortisone administration and adrenal cortical stimulation by corticotropin administration were both effective in elevating the blood pressure of hypotensive, potassium-deficient rats, it might be considered that these hormones acted by replacing a deficiency of adrenal cortical steroids.

Other investigators have demonstrated that dietary deficiency of sodium or protein induced a hypotensive response in renal hypertensive rats, with a pressor response following the administration of cortisone or corticotropin. They interpreted the depressor effect as being mediated through a suppression of adrenal cortical function, and the restitution of the blood pressure by cortisone as a replacement of the induced adrenal steroid deficiency.

On the other hand, Danford and Herrin concluded that there is inadequate evidence that sodium deficiency inactivates the adrenal cortex. Furthermore, considerable data suggest that potassium deficiency stimulates the production of Cu oxysteroids. Thus, rats on such a regime have enlarged adrenals which are depleted of ascorbic acid, involution of the thymus, decreased circulating blood eosinophils and an increased liver glycogen content. Direct measurements of adrenal cortical steroid output will be required to clarify the nature of the adrenal changes in potassium-deficient rats.

Regardless of the mechanism by which cortisone induces a pressor response in potassium-deficient rats, it is suggested that the administration of cortisone, in conjunction with definitive potassium treatment, may be of value in prophylaxis and therapy of the hypotension and circulatory collapse frequently found in clinical states of acute potassium depletion.

**Summary**

Cortisone acetate and, to a somewhat lesser extent, corticotropin, promptly elevated the blood pressures of rats made hypotensive by dietary potassium deprivation. The pressor effect of cortisone did not involve correction of the potassium depletion in the serum or tissues of the potassium-deficient rats.

Although the mechanism of its pressor effect in potassium-deficient rats was not clarified, it was suggested that cortisone may act by replacing a deficiency of adrenocorticos-teroids consequent to the chronic potassium depletion.

**Acknowledgments**

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**References**

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