ADRENAL FUNCTION AND CHANGES OF SODIUM AND POTASSIUM IN SERUM AND URINE IN FLUORIDE-INTOXICATED RATS

by

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SUMMARY: Administration of fluoride to intact and adrenalectomized rats reduced the serum sodium and elevated the serum potassium level. The response of serum sodium and potassium to angiotensin became more pronounced in intact rats which received fluoride than in the controls. The increased sensitivity of serum sodium to angiotensin by fluoride was associated with greater excretion of sodium. Interestingly, the elevation of serum potassium by adrenalectomy could be suppressed by angiotensin and the decreased urinary excretion of potassium induced by adrenalectomy was markedly suppressed by angiotensin. Fluoride did not alter the suppression effect of angiotensin.

Introduction

Many of the biological effects of fluoride have been extensively studied, but damage to the kidneys and adrenal glands induced by relatively large doses of fluoride has received little attention.

Schwalb et al. (1) found no pathological changes in the kidneys of a dog sacrificed a few hours after receiving a single large intravenous injection of 20-64 mg/kg fluoride (as NaF), although the volume of urine increased and excretion of urea decreased. Taylor et al. (2) reported that after administration of 20 and 30 mg sodium fluoride, the major changes in renal function were an increased volume of urine and decreased specific gravity.

Changes in physiological ion mobilization such as sodium, potassium, magnesium and calcium ions, and their related enzyme activities in the blood and kidneys were produced by a single oral dose (50 mg/kg) sodium fluoride to rats (3-6).

The following experiment was designed to study the relationship between adrenal function and changes in sodium and potassium in serum and urine during fluoride intoxication. Changes in adrenal and renal function due to fluorosis were evaluated by adrenalectomy and by the response of sodium and potassium in urine and serum to aldosterone and angiotensin.

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Materials and Methods

Treatments: Male Wistar albino rats weighing about 100g were used in this experiment. The rats were housed in an airconditioned room at 22° C. After being maintained on basal diet MF (purchased from Oriental Yeast Ind., Japan) and water ad libitum for five days, the rats were adrenalectomized. The intact rats, which served as controls, as well as the adrenalectomized rats received the same diet and water ad libitum for two additional days. All animals were fasted for 24 hours before the start of the experiment in order to minimize the effect of fluoride absorption from the bowels and to stabilize the urinary excretion on ions. Urine was collected in metabolic cages each of which housed one pair of rats.

Aldosterone (30μg/kg or angiotensin (angiotensin II) (12 μg/kg) or 0.9% saline (2 ml/kg), respectively, were administered subcutaneously twice at four-hour intervals, four hours after a single oral dose of fluoride (NaF, 50 mg/kg) or of chloride (NaCl, 69.8 mg/kg) in the control rats. The rats were sacrificed four hours after having received the last dose. Aldosterone 30 μg or angiotensin 12 μg, respectively, were contained in 2 ml. of 0.9% saline.

Analyses: The determinations of sodium and potassium in serum and urine were carried out by the method of Wills (7) by means of an Hitachi Model 518 Digital Atomic Absorption Spectrophotometer.

Materials: Angiotensin II was obtained from Protein Research Foundation (Osaka, Japan). Aldosterone was purchased from Sigma Chemical Company, (St. Louis, Missouri, U.S.A.).

Results

Adrenalectomy caused the serum sodium levels of rats to decrease significantly ($p < 0.02$). In intact rats, fluoride lowered the serum sodium to 0.9 of the control. In the adrenalectomized rats, this decrease was slight as shown in Table 1. In intact rats, treatment with aldosterone and angiotensin elevated the fluoride-induced serum sodium levels. In the adrenalectomized rats, the serum sodium was elevated by aldosterone ($p < 0.02$), in both the control and fluoride-intoxicated rats, but was not significantly elevated by angiotensin ($p > 0.05$) as shown in Table 1.

Adrenalectomy increased the urinary excretion of sodium by the rats 3.36 times above the control level in intact rats. This increase due to adrenalectomy was further enhanced to 1.81 times by fluoride. Treatment with aldosterone inhibited the increase in urinary sodium excretion when fluoride was given both in the intact and adrenalec-

tomized rats. On the other hand, angiotensin inhibited the increase of urinary sodium in intact rats which received fluoride, but failed to do so in the adrenalectomized rats given fluoride (Table 2).

Table 1

Response of Serum Sodium to Aldosterone and Angiotensin in Rats F-Intoxicated After Adrenalectomy[a]

		Intact			Adrenalectomized		
		μEq/ml	T/C	T/F	μEq/ml	T/C	T/F
Control	None	146.3±8.4	1	-	128.7±7.5	1	-
	Aldosterone	181.2±5.5	1.24[b]	-	142.5±4.7	1.11[b]	-
	Angiotensin	159.7±6.5	1.09[c]	-	125.2±5.3	1.05	-
Fluoride	None	131.3±1.9	0.90[b]	1	118.0±6.5	0.92	1
	Aldosterone	172.7±0.9	1.18[b]	1.32[d]	128.4±4.8	1.00	1.09[e]
	Angiotensin	171.5±7.5	1.17[b]	1.31[d]	123.5±0.8	0.96	1.04

Table 2

Response of Urinary Sodium to Aldosterone and Angiotensin in F-Intoxicated Rats After Adrenalectomy

		Intact			Adrenalectomized		
		μEq/12 h	T/C	T/F	μEq/12 h	T/C	T/F
Control	None	465±57	1	-	1560±152	1	-
	Aldosterone	234±21	0.50[b]	-	1027±113	0.66[b]	-
	Angiotensin	232±23	0.50[b]	-	1083±115	0.69[b]	-
Fluoride	None	1553±158	3.34[b]	1	2821±301	1.81[b]	1
	Aldosterone	1033±110	2.22[b]	0.67[d]	1728±182	1.11	0.61[d]
	Angiotensin	715±74	1.54[b]	0.46[d]	2727±294	1.75[b]	0.97

A slight elevation of serum potassium levels of adrenalectomized rats was not statistically significant (p 0.05). When fluoride was given, serum potassium in adrenalectomized rats increased significantly as shown in Table 3. Fluoride induced elevation of the serum potassium in intact rats, but this elevation was suppressed in the animals treated with aldosterone and angiotensin. The angiotensin-induced suppression of serum potassium was more pronounced in the fluoride-intoxicated rats than in the controls. In adrenalectomized rats, serum

potassium levels in control and fluoride-intoxicated rats were suppressed by aldosterone as shown in Table 3.

The urinary excretion of potassium in intact rats was increased by fluoride 1.93 times above that of the control. Urinary potassium excretion decreased 0.22 times of the control level in intact rats by adrenalectomy as shown in Table 4.

In adrenalectomized rats, the urinary excretion of potassium increased 3.38 times of the control when fluoride was given. In the intact rats, the suppressive effect of aldosterone and angiotensin on urinary potassium excretion was similar in the fluoride-intoxicated rats compared to the control. In adrenalectomized rats, treatment with angiotensin caused a twofold increase in urinary potassium excretion both in the control and in the fluoride-intoxicated rats, but aldosterone failed to alter urinary potassium excretion in control and fluoride-intoxicated rats (Table 4).

Table 3.

Response of Serum Potassium to Aldosterone and Angiotensin in Rats Fluoride-Intoxicated after Adrenalectomy[a]

		Intact			Adrenalectomized		
		μEq/ml	T/C	T/F	μEq/ml	T/C	T/F
Control	None	4.96±0.06	1	-	5.42±0.43	1	-
	Aldosterone	4.46±0.06	0.90[b]	-	4.87±0.40	0.90	-
	Angiotensin	4.48±0.15	0.90[b]	-	4.58±0.40	0.85[c]	-
Fluoride	None	5.74±0.23	1.16[b]	1	6.19±0.12	1.14[b]	1
	Aldosterone	4.74±0.30	0.96	0.83[d]	5.53±0.41	1.02	0.89[e]
	Angiotensin	3.96±0.37	0.80[b]	0.69[d]	4.58±0.04	0.85[b]	0.74[d]

Discussion

The characteristic symptoms of experimental fluorosis are mottled teeth and osteosclerosis; they represent a disorder of bone metabolism (8). Polyuria relates to renal lesions (2). In our previous papers we observed changes in ion mobilization in fluorosis (3,4).

In the present study, we were able to demonstrate a relationship between adrenal function and ion mobilization of sodium and potassium in fluoride intoxication by adrenalectomy and by treatments with aldosterone or angiotensin. Response of the serum sodium to angiotensin became much more marked by administration of fluoride in the intact

rats than in the controls, whereas fluoride did not alter the response in adrenalectomized rats. In intact rats sodium and potassium in urine did not respond to angiotensin and aldosterone after administration of fluoride. In adrenalectomized rats the response of urinary sodium to angiotensin was more noticeable when fluoride was given than in the control, but the response of urinary sodium excretion to aldosterone was not altered by fluoride. However, in the adrenalectomized rats, the response of urinary excretion of potassium to angiotensin and aldosterone was unaltered by fluoride.

Table 4.

Effect of Aldosterone and Angiotensin on Urinary Potassium Excretion in Fluoride-Intoxicated Rats after Adrenalectomy[a]

		Intact			Adrenalectomized		
		μEq/12 hr	T/C	T/F	μEq/12 hr	T/C	T/F
Control	None	457±41	1	-	101±11	1	-
	Aldosterone	325±35	0.71[b]	-	108±10	1.07	-
	Angiotensin	232±20	0.51[b]	-	198±15	1.96[b]	-
Fluoride	None	883±89	1.93[b]	1	341±35	3.38[b]	1
	Aldosterone	679±71	1.49[b]	0.77[d]	348±32	3.45[b]	1.02
	Angiotensin	685±70	1.50[b]	0.78[d]	714±72	7.06[b]	2.09[d]

[a]Rats sacrificed 12 hrs. after oral dose of 50 mg/kg NaF.
Values are averages from three pair of rats.
T/C: Values related to intact control.
T/F: Ratio of hormone treated to number of F-intoxicated rats.
[b,c]Significantly different from control (none): [b], $p<0.02$, [c], $p<0.05$.
[d,e]Significantly different from fluoride-intoxicated rats: [d], $p<0.02$, [e], $p<0.05$.

Luetscher and Axelrod (9) observed that low sodium intake augments the secretion of aldosterone. The principal adrenal steroids which affect the mineral balance (known to be aldosterone and angiotensin) stimulate aldosterone secretion from the adrenal gland (10).

From our results in this experiment and the findings of other workers described above, it is suggested that adrenal function in fluorosis plays an important role by maintaining a strong homeostasis on ion mobilization of sodium and potassium.

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