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EFFECTS OF VASOPRESSIN ON SWEAT RATE AND COMPOSITION IN PATIENTS WITH DIABETES INSIPIDUS AND NORMAL CONTROLS*

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ABSTRACT

Baseline sweat rate and concentrations of sodium, chloride, and potassium, and the effect of exogenous vasopressin on these parameters were determined in 13 patients with acquired diabetes insipidus (ADI), four patients with nephrogenic diabetes insipidus (NDI), three subjects with cystic fibrosis, and age- and sex-matched controls.

The four patients with NDI did not differ from the controls with respect to baseline sweat rate, but baseline sodium, chloride, and potassium concentrations were significantly elevated. In addition, parenteral vasopressin caused a significant decrease in sweat rate ($p < .01$) while the electrolyte concentrations remained unchanged. This indicates that vasopressin may also have an effect on electrolyte reabsorption in NDI patients. Alternatively, the amount of sweat precursor fluid may have been reduced.

The patients with ADI did not differ from the controls with respect to baseline data, and parenteral vasopressin had no effect on their sweat rate and composition. Likewise, vasopressin had no effect in controls or patients with cystic fibrosis.

We conclude that, except in patients with NDI, vasopressin does not play a significant role in the regulation of human eccrine sweating. Sweat gland physiology appears to be different in patients with NDI and in them vasopressin may have a significant effect on sweat.

Considerable controversy exists concerning the actions of antidiuretic hormone (ADH) on sweat rate and composition. While several studies [1–4] have demonstrated significant effects of exogenous vasopressin on sweat, other investigators [5–12] have been unable to detect any such actions. Even the few studies [1–3] with positive results have differed from each other with respect to the observed effects of vasopressin on sweat. In an attempt to resolve some of these conflicts and to determine the role, if any, of ADH in sweat gland physiology, we studied sweat rate and electrolyte composition before and after the exogenous administration of aqueous vasopressin in the following groups: (1) patients with acquired diabetes insipidus (ADI) who had severely decreased or absent endogenous ADH; (2) patients with nephrogenic diabetes insipidus (NDI) with peripheral (renal) unresponsiveness to ADH; (3) patients with cystic fibrosis, a disease associated with abnormally elevated sweat electrolytes; and (4) normal controls.

MATERIALS AND METHODS

Thirteen patients, aged 7 to 28 years, with ADI due to idiopathic causes (4 cases) or Hand-Schüller-Christian disease (9 cases) and four patients with NDI, aged 8 to 28 years, were studied; all NDI subjects and seven of the 13 ADI patients were males. NDI was diagnosed as described previously [13] for these same patients. Eight of the nine patients with Hand-Schüller-Christian disease had concomitant growth hormone deficiency as an isolated anterior pituitary hormone defect [14]. Adrenal and thyroid function were normal in all patients with both forms of diabetes insipidus. The three patients with cystic fibrosis were 20, 26, and 28 years old with moderate to advanced disease; none had any history suggestive of ADH deficiency. Baseline sweat data on all patients were compared to results obtained from 36 age- and sex-matched controls who had no history of significant diseases and no family history of cystic fibrosis. All patients on vasopressin replacement had discontinued vasopressin tannate-in-oil for at least 48 hours and vasopressin snuff and spray for 24 hours. Only one patient with NDI was taking medication and he discontinued the chlorthiazide and potassium therapy 4 days prior to testing.

Sweating was stimulated by iontophoresis of a 0.2% pilocarpine nitrate solution according to a slight modification of the method of Gibson and Cooke [15]. The sites for stimulation of sweating (in all cases the arms) were washed with distilled water and dried. Iontophoresis was performed for exactly 5 minutes at a current of 2 to 2.5 mA. After completion of the iontophoresis, the skin site was again washed with distilled water and dried. A piece of preweighed filter paper with extremely low sodium content (Whatman #44, Arthur H. Thomas Co., Philadelphia, Pa.) was placed on the area, covered with parafilm (previously washed in distilled water), and the edges sealed with tape to prevent evaporation. Sweating was allowed to proceed for exactly 45 minutes at which time the filter paper was rapidly removed, placed in a preweighed flask, and the weight of the sweat determined. The sweat was eluted from the filter paper with

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distilled water. Sodium and potassium concentrations were determined by atomic absorption spectrophotometry (Perkin-Elmer 303, Perkin-Elmer Corp., Norwalk, Conn.) and chloride concentrations were determined with a chloridometer (Buchler-Cotlove, American Instrument Co., Silver Spring, Md.). No sweat sample of less than 100 mg was accepted for study.

All sweat collections were done in a cool environment (temperature of 74° F, relative humidity of 30–50%). The subjects were resting and were allowed fluids ad lib, although the amount ingested was not quantitated. All sweat tests were run in duplicate (i.e., for those subjects receiving vasopressin, 2 tests were done before giving the hormone and 2 after, all at different sites to prevent effects from the previous iontophoresis).

At the conclusion of the control sweat tests, 5 units of aqueous vasopressin (Pitressin ®, [Parke, Davis, & Co., Detroit, Mich.]) were given intramuscularly to 12 of 13 patients with ADI, all NDI patients, the three patients with cystic fibrosis, and five control subjects, aged 19 to 21 years. The injection site was distant from the sweat collection areas. To determine whether the vasopressin had been absorbed from the injection site, a 60-minute sample of urine was collected before giving vasopressin for determination of volume, osmolarity, and concentrations of sodium and chloride, and a similar sample was collected beginning one hour after vasopressin injection. The post-vasopressin sweat tests were started one hour after giving the vasopressin. Informed consent was obtained from all patients and there were no adverse effects from the tests.

RESULTS

Nephrogenic diabetes insipidus (NDI). The four patients with NDI did not differ significantly from normal controls with respect to baseline sweat rate (Table I), but baseline sweat sodium concentrations were significantly elevated in all four patients when compared to age-matched normals ($p < 0.01$ and < 0.02 for the two age groups) and chloride concentrations were significantly higher ($p < 0.02$) in the two older patients with NDI; chloride concentrations in the younger NDI patients were not significantly higher (Table I). Potassium levels were significantly higher in the younger patients with NDI ($p < 0.05$) but were not measured in the two older patients (Table I). Serum sodium levels in the two older patients with NDI were 148 and 151 mEq/1 and chloride levels were 109 and 111 mEq/1.

Acquired diabetes insipidus (ADI). Comparing the baseline data from the 13 patients with ADI with age- and sex-matched controls, the only significant difference was the sweat rate for the patients 11 to 20 years of age. Otherwise, the patients with ADI did not differ significantly from the controls with respect to sweat rate and sodium, chloride, and potassium concentrations (Table I). Since baseline urine values for the ADI patients revealed very high volumes and low osmolarities, it is unlikely that any effects from previous therapy with vasopressin were still present at the time of testing. Serum electrolyte levels were normal.

Effects of vasopressin. In all patients with ADI, the three patients with cystic fibrosis, and the control subjects, vasopressin had a marked renal effect as evidenced by a significant fall in urine volume and rise in osmolarity and concentrations of sodium and chloride. The NDI patients demonstrated no renal response to the exogenous vasopressin (Table II).

A significant decrease in sweat rate after vasopressin administration was noted in all patients with NDI ($p < 0.01$); the sweat sodium, chloride, and potassium concentrations remained the same before and after vasopressin (Table III) in these four patients. Vasopressin had no effects on sweat rate and sweat sodium, chloride, and potassium concentrations in normal subjects, patients with ADI, and patients with cystic fibrosis (Table III).

Sex had no influence in any group on any of the parameters studied.

DISCUSSION

Elevated sweat electrolytes previously have been reported in NDI, but the few patients described were all under one year of age [16]. It was suggested [16] that sweat analysis may aid in the diagnosis of NDI, but occasionally similarly elevated values may be found in normals. Our findings of elevated baseline sodium, chloride, and potassium levels in the patients with NDI tend to confirm these previous reports and indicate that the sweat abnormality in NDI may persist into adulthood. The increased baseline salinity of sweat in patients with NDI also suggests that these patients, especially infants, may be at an increased risk of salt depletion, dehydration, and so-called heat prostration on exposure to excessive heat and exercise. A similar situation has been well described by di Sant'Agnese, Darling, Perera, and Shea [17] for cystic fibrosis, a disease with elevated sweat sodium and chloride concentrations. It is unclear why the baseline chloride values for the two younger NDI patients were not as elevated as they were for the two older patients; these results suggest that another anion, such as lactate, may appear in higher concentrations in sweat in some of these patients.

The patients with NDI also showed a significant decrease in sweat rate after receiving parenteral vasopressin but the sweat electrolyte concentrations remained the same, indicating that vasopressin also may have some effect on electrolyte reabsorption in the sweat ducts in these patients. Alternatively, the amount of sweat precursor fluid may have been reduced secondary to vasopressin-induced vasoconstriction. If this second mechanism is responsible for the changes noted, then this alone is of interest since the NDI patients were the only group to respond in such a dramatic manner; they decreased their mean sweat rate by 39 percent. Although we allowed our patients ad lib fluids we did not perform detailed water balance studies and therefore the patients with NDI, who are usually in a state of chronic dehy-

TABLE I

Baseline sweat rate and composition

	Sweat rate (gm/m²/45 min)		Sodium (mEq/l)		Chloride (mEq/l)		Potassium (mEq/l)	
Normals (5–10 years)	145.9 ± 55.2* (4)†	(N.S.‡)	16.8 ± 2.2 (6)	(N.S.)	13.9 ± 3.7 (5)	(N.S.)	7.1 ± 0.8 (6)	(N.S.)
Acquired Diabetes Insipidus (5–10 years)	88.6 ± 9.8 (3)		27.7 ± 7.3 (3)		16.3 ± 4.4 (3)		7.9 ± 0.1 (2)	
Normals (11–20 years)	113.2 ± 14.0 (14)	(p <.05)	30.3 ± 4.1 (15)	(N.S.)	21.0 ± 2.4 (14)	(N.S.)	7.8 ± 0.8 (12)	(N.S.)
Acquired Diabetes Insipidus (11–20 years)	68.1 ± 11.5 (8)		42.6 ± 6.8 (8)		26.7 ± 5.6 (8)		10.4 ± 1.1 (8)	
Normals (21–30 years)	117.4 ± 15.9 (13)	(N.S.)	33.0 ± 3.3 (15)	(N.S.)	21.4 ± 2.8 (14)	(N.S.)	N.D.§	
Acquired Diabetes Insipidus (21–30 years)	101.4 ± 51.0 (2)		53.7 ± 28.5 (2)		41.5 ±27.1 (2)			
Normals (5–10 years)	145.9 ± 55.2 (4)	(N.S.)	16.8 ± 2.2 (6)	(p <.01)	13.9 ± 3.7 (5)	(N.S.)	7.1 ± 0.8 (6)	(p <.05)
Nephrogenic Diabetes Insipidus (5–10 years)	115.8 ± 0.7 (2)		44.4 ± 7.4 (2)		30.8 ± 9.4 (2)		11.6 ± 2.3 (2)	
Normals (21–30 years)	117.4 ± 15.9 (13)	(N.S.)	33.0 ± 3.3 (15)	(p <.02)	21.4 ± 2.8 (14)	(p <.02)	N.D.	
Nephrogenic Diabetes Insipidus (21–30 years)	132.6 ± 10.4 (2)		57.9 ± 3.4 (2)		42.0 ± 0.6 (2)			

* Mean ± standard error of the mean

† Number of subjects in parentheses

‡ N.S. = difference of means not significant

§ N.D. = not done

TABLE II

Urine findings before and after vasopressin

Group	Pre-Vasopressin				Post-Vasopressin			
	Volume (cc)	Osmolarity	Sodium (mEq/L)	Potassium (mEq/L)	Volume (cc)	Osmolarity	Sodium (mEq/L)	Potassium (mEq/L)
Acquired Diabetes Insipidus	249*	176	29	36	67	558	102	113
Nephrogenic Diabetes Insipidus	749	89	41	49	663	90	15	23
Cystic Fibrois	87	647	107	153	55	810	113	166
Normal Controls	131	N.D.†	91	65	65	N.D.†	163	130

* All values in the table are means

† N.D. = not done

TABLE III

Effects of vasopressin on sweat rate and composition

	Pre-vasopressin	Post-vasopressin	p values
Normal Controls			
Rate (gm/m²/45 min)	107.5 ± 16.5* (5)†	106.0 ± 11.2 (5)	N.S.‡
Sodium (mEq/l)	28.5 ± 4.6 (5)	29.3 ± 4.8 (5)	N.S.
Chloride (mEq/l)	19.4 ± 4.2 (5)	22.2 ± 5.1 (5)	N.S.
Potassium (mEq/l)	8.7 ± 0.3 (5)	7.7 ± 0.4 (5)	N.S.
Acquired Diabetes Insipidus			
Rate (gm/m²/45 min)	77.9 ± 10.0 (13)	82.4 ± 12.2 (12)	N.S.
Sodium (mEq/l)	40.9 ± 5.9 (13)	41.3 ± 5.9 (12)	N.S.
Chloride (mEq/l)	26.6 ± 5.1 (13)	27.9 ± 5.2 (12)	N.S.
Potassium (mEq/l)	9.4 ± 1.0 (11)	9.8 ± 0.9 (10)	N.S.
Nephrogenic Diabetes Insipidus			
Rate (gm/m²/45 min)	124.2 ± 6.4 (4)	76.3 ± 5.4 (4)	<.01
Sodium (mEq/l)	51.2 ± 5.1 (4)	50.1 ± 4.7 (4)	N.S.
Chloride (mEq/l)	36.4 ± 5.0 (4)	37.2 ± 3.9 (4)	N.S.
Potassium (mEq/l)	11.6 ± 2.3 (2)	11.6 ± 2.6 (2)	N.S.
Cystic Fibrosis			
Rate (gm/m²/45 min)	122.5 ± 18.6 (3)	98.5 ± 20.7 (3)	N.S.
Sodium (mEq/l)	96.8 ± 11.2 (3)	97.9 ± 11.5 (3)	N.S.
Chloride (mEq/l)	101.4 ± 7.3 (3)	104.2 ± 10.4 (3)	N.S.
Potassium (mEq/l)	15.1 ± 5.4 (3)	14.2 ± 4.6 (3)	N.S.

* Mean ± standard error of mean

† Number of subjects in parentheses

‡ N.S. = not significant

dration and negative water balance, may have remained in this condition during the tests. The high serum sodium and chloride levels in the two NDI patients in whom serum electrolytes were measured indicate that this may have been the situation. Increased sweat water retention due to this dehydration or increased electrolyte secretion would seemingly be reasonable explanations for the high baseline sweat electrolyte concentrations. However, dehydration would be expected to produce elevated levels of aldosterone which would lead to a decreased excretion of sweat sodium and chloride [18]. Dehydration also has been shown to cause a decrease in sweat rate [7]. The baseline data for our NDI patients revealed the opposite: normal sweat rate and elevated excretion of electrolytes. It is likewise difficult to postulate that an increased retention of water in the sweat ducts is due to the high endogenous vasopressin levels common in NDI [19] since the baseline sweat rates for the NDI patients did not differ from normal. Thus, it is unclear at present why patients with NDI have higher baseline sweat electrolyte values and why exogenous vasopressin affects their sweat rate and sweat electrolyte concentrations.

Our studies have demonstrated that patients who lack ADH (ADI subjects) produce sweat at the same rate and with a similar composition as normal subjects. The only significant difference in the ADI subjects was the sweat rate for the age group 11–20 years; this was an isolated finding and we conclude that, as a group, the ADI patients did not differ significantly from the

control population. In addition, parenteral vasopressin had no effect on sweat from ADI and cystic fibrosis patients and controls. It should be noted that we measured gross sweat rate (i.e., rate over 45 min) in contrast to minute rates. It is possible that vasopressin has an effect on sweat stimulated by iontophoresis during the very early phases of sweating before the sweat rate declines [20, 21]. If this is the situation, then the vasopressin effects are only transient. We conclude that normally vasopressin does not play a major role in the regulation of either pilocarpine-induced or physiologic sweating.

Our findings of a lack of an effect of vasopressin on sweat in normal situations are similar to the results from other studies. Ladell [5] and Ladell and Whitcher [8] found no effects of vasopressin on sweat rate as measured by loss of body weight in subjects exercising in moderate heat; Amatruda and Welt [6] detected no differences in the rate of secretion and electrolyte composition of thermally induced sweat in two subjects given vasopressin; and Pearcy, Robinson, Miller, Thomas, and De Brota [7] also found no difference in sweat rate after vasopressin administration to hydrated men working in the heat. Ratner and Dobson [9] could not demonstrate any change in sweat osmolarity after giving vasopressin, and Cage and Dobson [10] noted no effects of 30 units of vasopressin on sweat sodium excretion and free water clearance in six normal men. Allen and Roddie [12] and Senay and van Beaumont [11] found no decrease in the rate of thermally induced sweat after vasopressin.

Conversely, Hankiss [1] found a significant decrease in sweat rate but no change in the absolute value of sodium and potassium excretion in sweat after giving vasopressin to a patient with vasopressin-deficient diabetes insipidus; they concluded that vasopressin had no effect on sweat electrolyte excretion. In their study, sweat was collected from palms, and such sweat is known to be influenced by emotional stimuli. More recently, Fasciolo, Totel, and Johnson [2] demonstrated that vasopressin given subdermally to humans significantly reduced sweat rate (measured over the vasopressin injection sites) and independently stimulated the active reabsorption of sodium. Quatrale and Speir [3] also noted that vasopressin decreased the rate of sweating and sodium excretion from the footpads of the rat. It is difficult to compare all these investigations because of differences in the general designs of the studies, the methods of stimulating sweating, the collection of the sweat, and the amounts of vasopressin used.

We attempted to avoid the effects of emotion, dehydration, heat, and exercise on endogenous ADH secretion and the mechanism of sweating by using a simple, harmless technique (iontophoresis) on resting, hydrated subjects in a controlled, cool environment. It is unlikely that the normal subjects and patients with cystic fibrosis had high endogenous serum levels of ADH prior to testing. Local vasoconstrictive effects of vasopressin were minimized by giving the hormone intramuscularly at sites distant from the sweat collection areas. Although the maximal effects of exogenous aqueous vasopressin may occur before one hour (the time at which we began our experimental set of sweat tests), activity has been shown to last 3 to 4 hours [22]. In addition, 1-hour urine samples collected during the experimental sweat tests in ADI patients, cystic fibrosis patients, and normals revealed that the vasopressin was still having considerable renal action.

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