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Plasma ammonia is the principal source of ammonia in sweat

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Summary. Sweat contains ammonia. However, neither its source nor factors affecting its concentration in the sweat are known. The aim of this study was to examine the effect of plasma concentrations of ammonia and urea on the concentration of ammonia in the sweat. Four groups of male volunteers were examined: one control, two after ingestion of ammonium chloride, three cirrhotic, hyperammonaemic, four uraemic. Sweat was collected from each subject from the palmar side of the forearm using gauze pads, after previous iontophoresis of pilocarpine. Ammonia and urea concentrations were determined in the sweat and in the plasma. It was found that elevated plasma ammonia concentration in healthy subjects after ingestion of ammonium chloride as well in the cirrhotic patients resulted in an increase of ammonia concentration in the sweat. High plasma and sweat urea concentration in the uraemic subjects did not affect the concentration of ammonia in the sweat. It was concluded that plasma ammonia was the principal source of ammonia in the sweat.

Key words: Ammonia – Urea – Sweat – Plasma – Man

Introduction

Sweat contains ammonia (Robinson and Robinson 1954). The concentration of ammonia in the sweat has been reported to be about 50–150 times higher than in the plasma (Robinson and Robinson 1954; Czarnowski and Górski 1991). However, both the source of the ammonia and the factors affecting its concentration in the sweat remain unknown. Mosher (1933) has suggested that sweat ammonia was a product of bacterial catabolism of sweat urea. Lobitz and Mason (1948) have hypothetized that ammonia present in the sweat was produced by the sweat glands whereas according to Emrich and Oelert (1966) ammonia diffuses passively to sweat from the plasma. The results presented in this work provided indirect evidence that the plasma ammonia is the principal source of ammonia in the sweat.

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Methods

Subjects

All subjects volunteered for the study. They were informed about the purposes and details of the experiment and consent was obtained. The project was accepted by the Ethics Committee of the Medical School, Białystok.

Procedures

Four experimental groups were used:

Group 1. Ten healthy medical students, aged 21–23 years, were examined 3–4 h after breakfast. Local sweating was stimulated with iontophoresis of pilocarpine on the palmar side of the forearm. The forearm was washed with soap, rinsed with distilled water and sterilized with 70% ethyl alcohol. After drying, a 10-ply gauze 5 × 15 cm, soaked with 10 ml of a 1% aqueous pilocarpine hydrochloride solution (pilocarpinum 1%, Polfa, Warsaw) was put on the skin and covered with an electrode of the same size connected to the positive pole of an apparatus for iontophoresis (COTM, Białystok). Another gauze pad soaked with solution of H_2SO_4 0.02 mol·l^{-1} was put on the skin of the same arm, and covered with an electrode connected to the negative pole of the apparatus. The intensity of the electrical current was increased gradually – to 2 mA during the 1st min, to 4 mA during the 2nd min and to 6 mA during the 3rd min and was maintained at this level for 7 min. Next, the electrodes and gauze were removed and the forearm was again washed with alcohol. After drying, a sterile 5-ply gauze, 5 × 15 cm, was put on the skin with a pair of forceps and covered with alcohol-cleansed plastic. The plastic was taped to the skin. The gauze was removed after 30 min, placed in a centrifuge tube, and centrifuged for 10 min at 3000 rpm, at 4° C. The tubes had diaphragms with holes which enabled the collection of the sweat. Blood was taken before and after the collection of sweat with a plastic catheter located in the antecubital vein.

Group 2. The same group of students was examined again at least a week after the first examination and 3–4 h after the breakfast, they were given ammonium chloride orally (Polfa), 150 mg·kg^{-1}

dissolved in distilled water; they were then given distilled water to drink, if they so desired. It was found in a preliminary study that plasma ammonia concentration was raised 30 min after the ingestion of the compound, peaked at 45 min and returned to the control value at 90 min. Accordingly, iontophoresis with pilocarpine was begun 15 min after ingestion of ammonium chloride and the procedure for sweat collection was performed as above. Blood from the antecubital vein was taken (by means of a plastic catheter) three times: before ingestion of ammonium chloride, and 45 and 60 min after. Four subjects had no side-effects after ingestion of the compound. In the remaining five subjects mild nausea developed and one subject vomited and he was excluded from the study.

Group 3. Hyperammonaemic patients. Four men (aged 38–55 years) with advanced hepatic failure, hospitalized in the Department of Infectious Diseases, Medical School, Białystok, participated in the study. Blood samples were collected from the antecubital vein in the morning after an overnight fast. Thereafter, iontophoresis of pilocarpine and collection of sweat was performed as in group 1.

Group 4. Uraemic patients. Ten male uraemic patients (aged 19–51 years) were examined. They were chronically dialysed (three times a week for 4–5 h) in the Department of Nephrology, Medical School, Białystok. The sweat was collected after iontophoresis of pilocarpine (as in group 1) twice: before and after blood dialysis. Blood samples were collected from the arterio-venous Cimino-Brescia fistula before and after dialysis. In the plasma and sweat, the concentrations of ammonia and urea were determined immediately after collection of samples. Ammonia was determined enzymatically (Da Fonseca-Wollheim 1973) using "Monotest Ammoniak" (Boehringer Mannheim, GmbH, Mannheim) and urea by the urease method (Richterich 1971). The gauze itself had previously been found to contain ammonia (Czarnowski and Górski 1991). Therefore, the gauze pads were applied to the skin of six resting healthy subjects as in experiment 1, but without previous iontophoresis with pilocarpine. They were removed after 30 min, soaked in ammonia-free water, centrifuged as above and the amount of ammonia eluted from each pad was measured. The mean amount of ammonia was 1.62 µmol and the intergauze differences were negligible. This value was considered as a "blank" value and was subtracted from each individual value obtained. The concentration of ammonia in the sweat sample obtained from each subject was then recalculated.

Satistics

The results were evaluated statistically using the Wilcoxon's rank sum test. A P value <0.05 was considered to be statistically significant.

Results

The results are presented in lable 1. The concentration of ammonia in the sweat of the control subjects was about 22-times higher than in the plasma and the concentration of urea was 1.8 times higher. Iontophoresis had no effect on the concentration of ammonia or urea in the plasma. Ingestion of ammonium chloride resulted in an elevation of ammonia concentrations both in the plasma and the sweat. The concentration of urea in both fluids remained unchanged. In the cirrhotic patients, the plasma ammonia concentration was over two times higher than in the controls. The concentration of ammonia and urea in the sweat was higher than in the controls. In uraemic subjects, the concentration of ammonia in the plasma and the sweat was similar to that of the control group and it was not affected by the dialysis. The concentration of urea in the plasma and in the sweat were several times higher than the respective control values. They were reduced by about 50% after dialysis.

Table 1. Sweat and plasma concentration of ammonia and urea

Group		Time of sampling	Ammonia (µmol·l^{-1})		Urea (mmol·l^{-1})	
			mean	SD	mean	SD
Control	sweat		827.0	103.0	7.6	0.7
($n=10$)	plasma	1	35.6	5.2	4.2	0.4
		2	37.2	5.8	4.3	0.4
Ingestion	sweat		1359.0	198.0[d]	7.9	0.8
of ammonium	plasma	1	34.2	5.2	4.3	0.5
chloride		2[A]	53.8	10.7[b]	5.0	0.7
($n=9$)						
Cirrhotic	sweat		1304.0	73.0[d]	11.6	0.6
($n=4$)	plasma	1	79.8	5.8[d]	4.7	0.4
		2	samples not taken			
Uraemic	sweat	before	886.0	141.0	61.3	9.5[d]
($n=10$)	plasma	dialysis	35.9	7.4	30.1	5.0[d]
	sweat	after	884.0	155.0	34.0	5.1[d,a]
	plasma	dialysis	37.3	7.2	15.5	4.7[d,a]

1, before; 2, after examination
[A], In a sample taken at the end of the sweat collection, i.e. 60 min after ingestion of ammonium chloride. The concentrations 45 min after the ingestion were: ammonia, 72.6 (SD 11.1)[b] µmol·l^{-1} and urea, 4.9 (SD 0.7)[c] mmol·l^{-1}. [d] $P<0.001$ versus the value in the control group, [c] $P<0.02$, [b] $P<0.001$ versus the value before iontophoresis, [a] $P<0.001$ versus the value before dialysis

Discussion

Ammonia is a weak base. In aqueous solutions, ammonia remains in equilibrium with the ammonium ion (Cooper and Plum 1987). The pK for ammonia is 9.1–9.2 (Cooper and Plum 1987) and thus at the physiological pH of the blood it exists mainly in the form of the ammonium ion and less than 5% in the form of ammonia (Mutch and Banister 1983). The permeability of cell membranes for ammonia is similar to water whereas the permeability for the ammonium ion is small (Hindfelt 1975; Visek 1968). Therefore, the pH gradient between water compartments directs the movement of ammonia across the membranes and thus its distribution (Stabenau et al. 1959). As a result, ammonia diffuses from a solution of higher to lower pH (Stabenau et al. 1959). The pH of the sweat ranges from 4.0 to 6.8 (Robinson and Robinson 1954) and this factor undoubtedly facilitates diffusion of ammonia from the blood to the sweat. The concentration of ammonia in the sweat after iontophoresis of pilocarpine was much lower than has been found previously in this laboratory in thermal sweat (Czarnowski and Górski 1991).

The pH of sweat induced by cholinergic stimulation of the sweat glands has been found to be less acid than that of the thermal sweat (Herrmann and Mandol 1955). This factor may have been responsible for the difference between the concentration of ammonia in the sweat obtained after iontophoresis of pilocarpine (the present data) and in sweat after a sauna-bath (Czarnowski and Górski 1991). It remains an open question whether the different sites selected for sweat collection [forearm in the present study and hypogastric region for the thermal sweat in the study of Czarnowski and Górski (1991)] could have an effect on the sweat ammonia concentration. Ingestion of ammonium chloride resulted in an elevation of both plasma and sweat ammonia concentration, whereas the plasma and sweat concentration of urea remained unchanged. This would indicate that the "extra" amount of ammonia in the sweat could not have come from a breakdown of urea, although there was also no reason to presume that the sweat glands produced more ammonia after ingestion of the compound. Therefore, the most likely conclusion is that the "extra" ammonia in the sweat must have come from the plasma. This conclusion is supported by the results obtained in cirrhotic patients. They had elevated concentrations of ammonia not only in plasma but also in sweat.

Sweat has been shown to contain considerable amounts of urea (Robinson and Robinson 1954; Quinton 1983). The sweat urea comes from the plasma and the amount of urea lost in this way may be so great that it has to be taken into account when nitrogen balance in the body is considered (Brusilow and Gordes 1965; Consolazio et al. 1975; Lemon and Mullin 1980; Schwartz et al. 1953). The concentration of urea in the sweat obtained from uraemic patients was shown to be markedly elevated in studies by Brusilow and Gordes 1965 and Schwartz et al. 1953. We have examined uraemic patients to find out if high plasma and sweat urea concentrations effect ammonia concentration in the sweat. We found that the sweat ammonia concentration in these patients was the same before and after dialysis and did not differ from the control value. This would indicate that excretion of ammonia with sweat is not influenced by the presence of urea, even in a very high concentration.

References

Brusilow SW, Gordes EH (1965) Secretion of urea and thiourea in sweat. Am J Physiol 209:1213–1218

Consolazio CF, Johnson HL, Nelson RA, Dramise JG, Skala JH (1975) Protein metabolism during intensive physical training in the young adult. Am J Clin Nutr 28:29–35

Cooper AJL, Plum F (1987) Biochemistry and physiology of brain ammonia. Physiol Rev 67:440–519

Czarnowski D, Górski J (1991) The sweat ammonia excretion during submaximal cycling exercise. J Appl Physiol 70:371–374

Da Fonseca-Wollheim F (1973) Direkte Plasmaammoniakbestimmung ohne Enteiweibung. Z Klin Chem Klin Biochem 11:426–431

Emrich HM, Oelert H (1966) pH-Wert und Gesamtammoniak im menschlichen Schweiß. Pflügers Arch 290:311–314

Herrmann FMD, Mandol LBA (1955) Studies of pH of sweat produced by different forms of stimulation. J Invest Dermatol 24:225–246

Hindfelt B (1975) The distribution of ammonia between extracellular and intracellular compartments of rat brain. Clin Sci 48:33–37

Lemon PWR, Mullin JP (1980) Effect of initial muscle glycogen levels on protein catabolism during exercise. J Appl Physiol 48:624–629

Lobitz WC Jr, Mason HL (1948) Chemistry of palmar sweat. VII. Discussion of studies on chloride, urea, glucose, uric acid, ammonia, nitrogen and creatinine. Arch Dermatol Syph 57:907–915

Mosher HH (1933) Simultaneous study of constituents of urine and perspiration. J Biol Chem 99:781–790

Mutch BJC, Banister EW (1983) Ammonia metabolism in exercise and fatigue: a review. Med Sci Sports Exerc 15:41–50

Quinton PM (1983) Sweating and its disorders. Ann Rev Med 34:429–452

Richterich R (1971) Clinical chemistry. Theory and practice. PZWL, Warsaw, pp 255–258

Robinson S, Robinson AH (1954) Chemical composition of sweat. Physiol Rev 34:202–220

Schwartz IL, Thaysen JH, Dole VP (1953) Urea excretion in human sweat as a tracer for movement of water within the secreting gland. J Exp Med 97:429–437

Stabenau JR, Warren KS, Rall DP (1959) The role of pH gradient in the distribution of ammonia between blood and cerebro-spinal fluid, brain and muscle. J Clin Invest 38:373–383

Visek WJ (1968) Some aspects of ammonia toxicity in animal cells. J Dairy Sci 51:286–295