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The Carbohydrate Metabolism of Normal Subjects during Potassium Depletion

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Summary. A potassium loss of 3–11% (6.0 ± 2.7%) of total body potassium was produced in 6 normal subjects during the course of a metabolic balance study of 13–16 days duration using a supplemented formula diet. This resulted in the development of a marked hypokaliaemic alkalosis. There were no significant changes of blood sugar, free fatty acid and plasma insulin concentrations during intravenous (0.5 g/kg) or oral (100 g) glucose tolerance tests for control and experimental periods.

Métabolisme des hydrates de carbone chez des sujets normaux au cours de la déplétion en potassium

Résumé. Une perte de potassium de 3–11% (6.0 ± 2.7%) du potassium total du corps a été observée chez 6 sujets normaux au cours d'une étude de bilan métabolique d'une durée de 13–16 jours en utilisant un régime enrichi. Ceci eut pour résultat le développement d'une alcalose hypokaliémique. Il n'y avait pas de modifications significatives de la glycémie, des acides gras libres et des concentrations d' insuline plasmatique, au cours des tests de tolérance au glucose intraveineux (0.5 g/kg) ou oral (100 g) par rapport au contrôle des périodes expérimentales.

Der Kohlenhydratstoffwechsel von Normalpersonen im Kaliummangel

Zusammenfassung. Bei 6 normalen Versuchspersonen wurde im Rahmen einer 13–16-tägigen Bilanzstudie ein Kaliumdefizit von 3–11.0% (6.0 ± 2.7%) des Gesamtkörperkaliums erzeugt. Dabei entwickelte sich eine ausgeprägte hypokaliämische Alkalose. Obwohl im K-Mangel eine leichte Verminderung der Plasmainsulinkonzentration nach intravenöser Glucosezufuhr und ein verminderter Anstieg und verzögerter Abfall des Blutzuckers und der Plasmainsulinkonzentration nach oraler Glucosezufuhr zu beobachten war, kam es insgesamt zu keinen signifikanten Veränderungen des Kohlenhydratstoffwechsels in Richtung auf eine diabetische Stoffwechsellage. Es kann daraus die Schlußfolgerung gezogen werden, daß andere zusätzliche Faktoren für die Entstehung einer diabetischen Stoffwechsellage im K-Mangel hinzutreten müssen.

Key-words: Potassium deficiency, plasma insulin, glucose tolerance.

Numerous studies *in vitro* and animal experiments have shown that carbohydrate metabolism may be affected by potassium [4–7, 10, 11, 12]. Clinical observations during potassium deficiency have shown the occurrence of hyperglycaemia and of deterioration of glucose tolerance. The changes in carbohydrate metabolism during periods of potassium deficiency have been attributed to impairment of insulin secretion [1, 2, 15] or of peripheral glucose utilization [19]. In a potassium balance study in humans, Sagild *et al.* found a decreased glucose assimilation when potassium was deficient [15, 16]. Since there is no information on the changes of insulin secretion in normal subjects during potassium deficiency, we have studied the problem during the course of a potassium balance study.

Methods

Experimental subjects were 6 healthy male medical personel between the ages of 26 and 36 years. For the 13 to 16 days of the study they were engaged in their usual activities and were fed a formula diet of 2870 calories (18% protein, 30% fat, and 52% carbohydrate, enriched with vitamins, iron and calcium). The potassium content of this basic diet was 9 meq per day. The body weight of the subjects remained constant.

During the initial control period (Period I) of 4–5 days duration, 40 meq potassium per day (3 × 1 Kalinor®) was added to this diet. This was replaced during the potassium-deficiency period (Period II), by the oral administration of 30 g of a cation exchange resin (Resonium®). Four days before the end of Period II, the subjects were given 50 mg of hydrochlorothiazid (2 tbl. Esidrix®). Potassium excretion was estimated by collecting 24 h urine samples and 2 pools of faeces, one during the control and one during the potassium-deficiency period. The urinary corticosteroid excretion was measured during the last 2 days of the control period and during days 7 and 8 of the potassium-deficiency period. At the end of the control and the potassium-deficiency periods, respectively, serum sodium, potassium and chloride were measured; pH, bicarbonate and base excess in capillary blood were determined and ECG's were recorded. Intravenous glucose tolerance tests (0.5 g/kg) were

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performed at the end of the control period and at the end of the potassium-deficiency period, respectively, the latter 48 h following the intake of 50 mg hydrochlorothiazid. Oral glucose tolerance tests with 100 g glucose were also performed during each period. The tests were performed in the morning 10 h after the last meal.

Blood sugars were measured using glucose oxidase [8], free fatty acids with the autoanalyzer [9] and plasma insulin modified according to Yalow and Berson [20]. Sodium and potassium in serum, urine, faeces and in samples of the diet were measured by flame photometry, chloride concentration was determined potentiometrically. Bicarbonate, pH, and base excess were measured according to Astrup. Corticosteroids were determined according to Reddy and co-workers [13]. Means (m) and standard deviations (s) were calculated. For statistic analysis the Student test was used.

Table 1. *K^+-balance in the K^+-deficiency period*

Subject	Weight	Height	Days of experiment	K^+ intake	K^+ output/period		K^+ balance	Total[a] body K^+	Loss of K^+
					Urine	Faeces			
	kg	cm		meq	meq	meq	meq	meq	%
Br	54	167	11	99	199	250	350	3186	11.0
El	70	179	11	99	109	193	203	4830	4.2
He	80	182	11	99	128	249	277	5520	5.0
Ka	67	171	9	81	124	273	316	4623	6.8
Kü	65	180	11	99	102	131	134	4485	3.0
Ne	73	181	12	108	128	291	311	5037	6.1
				7.5	*132*	*231*	*265*		*6.0*
				±8.8	±34.7	±59.1	±81.3		±2.7

[a] Calculated according to (3)

Table 2. *Serum electrolytes during experiment*

Subject	Days	Control period			Days	K^+-deficiency period		
		K^+	Na^+	Cl^-		K^+	Na^+	Cl^-
		(meq/l)	(meq/l)	(meq/l)		(meq/l)	(meq/l)	(meq/l)
Br	5	3.65	127	100	11	2.6	136	96
El	4	3.85	138	108	11	3.1	140	96
He	4	3.75	139	106	11	2.8	141	97
Ka	4	4.15	140	108	9	2.7	137	98
Kü	4	4.30	140	104	11	3.4	148	96
Ne	4	3.90	139	102	12	2.6	142	96
		3.93	137	104		2.86	140.6	96.5
		±0.24	±5.0	±3.2		0.32	4.2	0.8
				$p < 0.001$				
						$p < 0.2$		
							$p < 0.001$	

During the control period potassium balance was maintained. Intake was 204 ± 25 meq, output was 202 meq (urinary excretion 142 ± 42 and faecal excretion 60 ± 26). The potassium loss during the experimental period amounted to 134 — 340 meq (265 ± 81). During this period faecal excretion of potassium (231 ± 59 meq), contrary to that of the control period, was higher than urinary excretion (132 ± 35 meq) (Table 1). Assuming a total body potassium of 69 meq/kg body weight [3] the potassium loss was 3—11% (6 ± 2.7%) of total body potassium. During the experimental period serum potassium fell from 3.93 ± 0.24 meq/l to 2.86 ± 0.32 meq/l ($p < 0.001$), whereas serum sodium increased slightly (Table 2). There was a significant fall of serum chloride concentration from 104.6 ± 3.2 meq/l to 96.5 ± 0.8 meq/l at the end of the experimental period. There were also marked changes of the acid-base balance, characterized by an increase of pH from 7.34 ± 0.02 to 7.47 ± 0.03 ($p < 0.001$), of bicarbonate concentration from 25.0 ± 0.3 meq/l to 30.2 ± 3.4 meq/l ($p < 0.01$) and of base excess from 1.12 ± 0.52 meq/l to 6.8 ± 2.9 meq/l ($p < 0.01$) corresponding to a metabolic alkalosis. With exception of subject Kü, who had a potassium loss of only 3%, there were ECG changes typical of potassium deficiency in all experimental subjects. There was no change in urinary excretion of corticosteroids during the potassium-deficiency period (4.0 ± 0.8 mg/24 h) compared with the control period (4.7 ± 1.4 mg/24 h). At the end of the potassium-deficiency period, there were in all subjects complaints of headache, fatigue, weakness, irritability, polydipsia and polyuria.

K values for glucose assimilation during the control period ranged from 1.38—1.91 (1.62 ± 0.23) (Table 3).

Results

During the intravenous glucose tolerance tests, free fatty acids fell from 724 ± 68 meq/l to 270 ± 47 meq/l after 54 min. Plasma insulin concentrations rose from 12.8 ± 0.5 mU/ml to 44.5 ± 5.6 mU/ml after 4 min, and then decreased to 28.8 ± 3.0 mU/ml after 64 min. There was no change of glucose assimilation and of the course of free fatty acids during the intravenous glucose tolerance tests in the experimental period. The peak insulin concentration was slightly lower (40.1 ± 4.5 mU/ml). The fall of the plasma insulin concentration during the potassium deficiency was delayed, with a second peak between 44 and 54 min following glucose administration (Fig. 1).

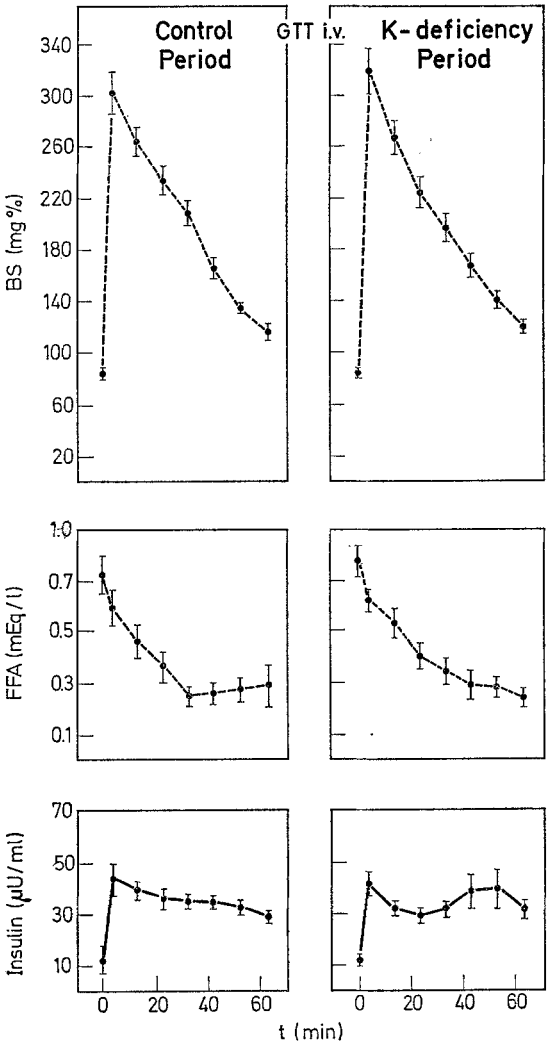

Fig. 1. Blood sugar, NEFA and plasma insulin concentration after oral administration of 100 g glucose during control periods and potassium deficiency periods, respectively

Upon oral glucose tolerance testing, in the control period the peak blood sugar after 30 min was 170.0 ± 14.8 mg% (Fig. 2). During the potassium-deficiency period, the peak blood sugar concentration was lower (162 ± 6.2 mg%) and the fall of the blood sugar concentration was delayed. Changes of plasma insulin concentration during the potassium-deficiency period were characterized by a slightly delayed rise compared with the control period. This was, however, not statistically significant. There were no changes of the time course of free fatty acids between the two tests.

Table 3. *Coefficients of glucose assimilation (following 0.5 g/kg glucose i.v.)*

Subjects	Control period K-Values	K^+-deficiency period K-Values
Br	1.64	1.65
El	1.86	1.64
He	1.38	1.54
Ka	1.91	1.53
Kü	1.38	1.38
Ne	1.53	1.56
	1.62	1.55
	± 0.23	± 0.09

Discussion

Potassium balance was maintained during the control period of 4 to 5 days duration. Potassium intake was 204 meq, potassium excretion 202 meq. During the potassium-deficiency period of 9 to 12 days duration, there was a loss of potassium ranging from 134—350 meq/l (265 ± 81 meq/l). This amount corresponds to a loss of total body potassium of 3—11% (6.0 ± 2.7%). Consequently, there was a marked hypokaliaemic, hypochloraemic alkalosis.

Study of the carbohydrate metabolism revealed that glucose utilization following intravenous and oral glucose administration was not affected significantly by potassium depletion. K values were, for the control period, 1.62 ± 0.23 and for the experimental period 1.55 ± 0.09. There were no significant changes of plasma insulin concentrations during the period of potassium deficiency. An impaired rise and delayed fall followed by a second peak during intravenous glucose testing, was suggestive of an impaired insulin secretion, which has been found in animal experiments, and which would correspond to the findings of Conn [2] in patients with primary aldosteronism and in patients with uraemia [17]. Contrary to our results, Sagild *et al.*, in 5 normal subjects, observed a reversible deterioration of glucose tolerance during potassium depletion. However, in his study only potassium excretion was measured, and in spite of a calculated potassium deficiency of 6.17% of body weight, serum potassium was 3.0 meq/l or below only in 3 cases. There were no symptoms or ECG changes except in one subject [15].

Similarly, following oral glucose administration, contrary to findings in patients with uraemia [18], there were no significant changes in glucose tolerance.

An increased rise and delayed fall of blood sugar and plasma insulin concentrations were suggestive of an impaired intestinal glucose absorption [14]. There

were no indications of a loss of effectiveness of insulin such as observed in animal experiments [1] and in a clinical study by Weinges [19].

In conclusion, a loss of body potassium ranging from 3—11% (6.0±2.7%) in normal subjects, does not result in significant changes in carbohydrate metabolism. In cases of potassium deficiency, where such changes are observed, other mechanisms must in addition be operating.

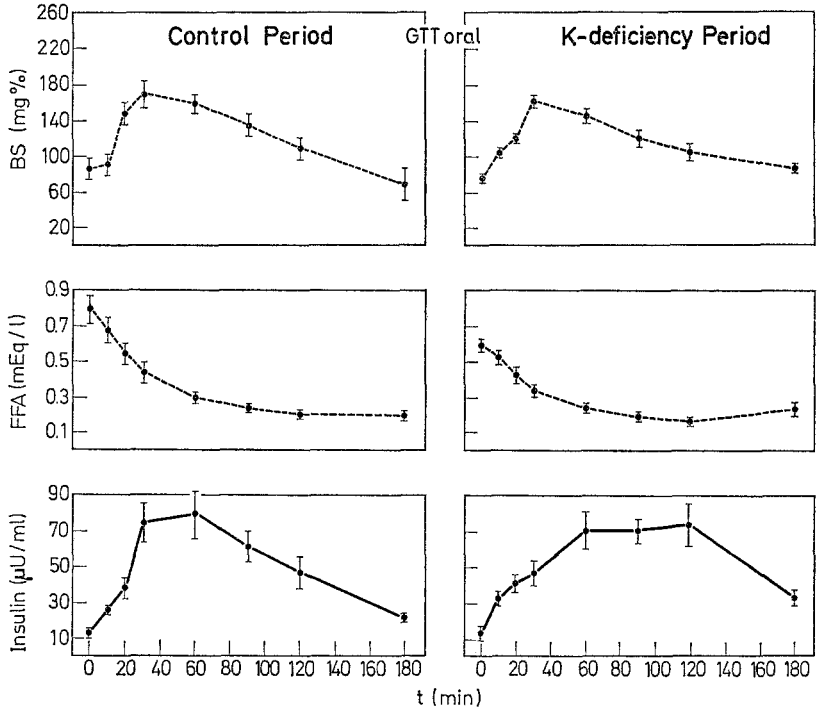

Fig. 2. Blood sugar, NEFA and plasma insulin concentration after i.v. administration of 0.5 g/kg glucose during control periods and potassium-deficiency periods, respectively

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