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Monocarboxylic short-chain fatty acids C_2-C_6 in serum of obese children

By

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The serum concentrations of monocarboxylic short-chain fatty acids (acetic to n-caproic) were estimated in 12 children with simple obesity aged 4—16 years and in a control group of 35 normal subjects. In the obese patients, significantly decreased values for acetic and n-caproic acid and an increased total free fatty acid level were found. The presumable causes of the phenomenon are discussed.

In obesity, the level of total plasma free fatty acids (FFA) has been shown to increase owing to their defective utilization [5, 6, 9]. On the other hand, in certain types of obesity a normal level was found [1]. In any case, the disturbance in FFA turnover appears to constitute an important factor in obesity [6].

The FFA fraction of human plasma is composed of a number of individual fatty acids with various chain length mainly C_{12} to C_{22} [3]. In most previous studies concerning obesity, FFA were considered a metabolically homogeneous entity and the behaviour of the individual fatty acids was disregarded. No attention has been devoted so far to the evaluation of short-chain fatty acids (SFA) in serum or plasma of obese patients. Since individual SFA represent important metabolic intermediates in some biochemical pathways, we have studied the C_2—C_6 SFA concentrations in serum of obese children.

Material

Twelve obese children, 7 boys and 5 girls, ranging in age from 4 to 16 years were examined. They all had simple obesity with an average overweight of 64%. The control group consisted of 35 normal children, 21 boys and 14 girls, aged 4—16 years. Their data have been described previously [10]. None of the subjects received any drug at the time of the study.

Methods

Blood was obtained by venipuncture after an overnight fast and the serum was prepared for gas-liquid chromatography after the modified method of Perry et al. [10, 12]. A gas chromatograph type G.C.H.F. 18.3 (Chromatron) equipped with flame ionisation detector was used. A single steel column 3 m × 4 mm i. d.

TABLE I

Serum concentrations of individual short chain fatty

Group		Acetic	Propionic	Iso-butyric	Butyric
Control	Range	2.12—14.71	0.0 —1.10	0.0 —1.14	0.0 —1.65
	Mean	6.98	0.50	0.40	0.73
	S. D.	3.71	0.31	0.28	0.40
	V. C. %	51.1	62.0	70.0	54.7
Obesity	Range	2.33—11.81	0.10—0.91	0.0—0.87	0.26—0.78
	Mean	4.47	0.34	0.32	0.56
	S. D.	2.74	0.23	0.22	0.16
	V. C. %	61.3	67.6	68.7	28.5

packed with 5% SP 1000 (Supelco Inc) on Chromosorb GAW DMCS 80/100 mesh was employed and maintained under isothermal conditions. The temperatures were: column, 160°C; injector and detector, 200°C. Carrier gas was N_2, 70 ml/min. The flow rates for H_2 and air were 25 ml/min and 750 ml/min, respectively. The analyses were carried out at sensitivities of 1×10^{-10} to 30×10^{-10} AFS according to the composition of the sample. Identification of separated SFA was based on the chromatograms of an artificial mixture containing acetic propionic, iso-butyric, n-butyric, iso-valeric, n-valeric, iso-caproic, and n-caproic acids (Fluka, Buchs, Switzerland) in water, at a concentration of 10 μg/ml. The peak areas were measured by planimetry. The mass correction factors were calculated by chromatographing known amounts of the investigated SFA simultaneously with 25 μg of n-heptanoic acid used as an internal standard.

The results were subjected to statistical analysis by Student's t test.

RESULTS

The serum concentrations of monocarboxylic SFA in control and obese children are presented in Table I. Acetic acid was present in all members of the control group, as well as in the obese children. N-butyric, iso-valeric and n-caproic acids were detectable in 34 control subjects, iso-butyric acid in 33, propionic and n-valeric acids in 32, and iso-capric acid in 18 subjects.

In the obese children, 6 acids (acetic, n-butyric, iso-valeric, n-valeric, propionic and n-caproic) were detectable in every sample. Iso-butyric acid was found in 11 cases and iso-caproic acid in 8 cases. The mean serum concentration of all SFA except iso-valeric acid was lower in the obese than in the control patients but only the levels of acetic and n-caproic acids were significantly decreased in comparison to the control group ($p < 0.05$). The serum level of iso-valeric acid was slightly elevated in the obese children ($p > 0.05$).

There was no correlation between the serum concentrations of individual SFA and the degree of overweight. The SFA levels scattered widely in both

acids (μg/ml) in control and obese children

Group		Iso-valeric	Valeric	Iso-caproic	Caproic
Control	Range	0.0—2.52	0.0—1.78	0.0—1.97	0.0—4.26
	Mean	0.79	0.69	0.27	1.34
	S. D.	0.62	0.48	0.51	0.72
	V. C. %	78.4	69.5	188.8	53.7
Obesity	Range	0.36—4.0	0.10—1.31	0.0—0.48	0.56—1.61
	Mean	0.98	0.54	0.18	0.79
	S. D.	1.12	0.42	0.16	0.36
	V. C. %	114.2	77.7	88.8	45.5

groups. N-butyric acid showed a low variability in obesity (V. C. = 28.5%) whereas the level of iso-caproic acid showed striking fluctuations in control sera (V. C. = 188.8%). The total serum FFA level in obese patients varied from 500 to 1499 mEq/l and its mean value of 951 ± 288 mEq/l was above that found in normal children [8].

Discussion

It is now generally agreed that the state of obesity is associated with several biochemical deviations concerning mostly the metabolism of carbohydrate and lipid [14]. Pennington [11] was the first to postulate the existence of a metabolic block beneath pyruvic acid, preventing this compound from entering the Krebs cycle. Stuchlikova et al. [13] found in obese patients that beside pyruvic acid the level of citric acid was also increased and this would suggest the presence of a block within the Krebs cycle. However, Krotkiewski et al. [7] could not confirm this hypothesis.

The high total serum FFA level observed in the majority of obese patients may result from the increased synthesis of FFA and, on the other hand, from the decreased speed of their oxidation and impaired lipolysis [2].

The low mean acetic acid level observed in our patients seems to be of interest, since this compound in the form of acetyl-coenzyme A is a common point of metabolic pathways of lipids and carbohydrates. If the above mentioned hypotheses of Pennington and Stuchlikova are valid, one migth postulate the block to be situated between the pyruvic and acetic acids. The only other possibility would be that acetic acid is utilized faster than normal in obese patients. The decreased serum level of n-caproic acid in obese children seems to be secondary to the deviation of acetic acid metabolism since this compound having an even number of carbon atoms

(C_6) is one of the intermediates on the pathway leading to the synthesis of fatty acids from acetyl-coenzyme. It seems reasonable to assume that the lower serum values for acetic and n-caproic acids in obese children as well as the increased total plasma FFA concentration reflect the subnormal rate of beta-oxidation of middle and long-chain fatty acids. This might be due to the metabolic defect based on the subnormal activity of enzymes taking part in the process of beta-oxidation. An analogous phenomenon is known to occur in G-6-PD deficiency [4]. This hypothesis would serve to explain the well-known inclination to obesity observed in some persons and families, and a normal or increased enzyme activity would prevent obesity even in overfed individuals.

The present observations do not permit to draw definite conclusions. For a reliable evaluation of the problem, simultaneous measurements of SFA, pyruvic acid and its metabolites, as well as of the tricarboxylic acids of the Krebs cycle together with the blood aminoacid pattern will be necessary.

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