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Serum concentrations of individual monocarboxylic short-chain fatty acids $C_2 - C_6$ in underweight children

By

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The serum concentrations of individual short-chain fatty acids containing 2–6 carbon atoms were studied in 12 underweight children. Mean n-butyric and iso-valeric acid levels were significantly elevated in underweight children, while those of n-valeric and iso-caproic acids were not significantly higher than in the control group. The level of total free fatty acids was also increased in the underweight group. A reduced enzymatic activity in fatty acid synthesis is supposed to be the factor underlying the impaired lipogenesis.

In children, underweight is more common than obesity. The failure to gain weight is usually due to exogenous factors, mainly to an insufficient caloric supply. In some cases it is the result of disturbances of biological autoregulation systems, especially vegetative centres [16] or of changes in the activity of anabolic and catabolic enzymes when the metabolic equilibrium is shifted towards catabolism leading to decreased weight gain or even to understature.

As fatty acids are an important source of energy and their metabolism is abnormal in obesity [10], it seemed interesting to study the serum concentration of individual short-chain fatty acids (SFA) containing 2—6 carbon atoms in underweight children.

Material

Twelve children, 6 boys and 6 girls, aged 6 to 14 years were examined. Their deficit varied from 20% to 42.3% (mean 33.5%). In 8 cases there was a growth deficit of 8.1%–38%; 3 of these were diagnosed as pituitary dwarfism. The history revealed insufficient caloric intake in 6 cases and a low birth-weight in 5 cases. The control group consisted of 35 apparently healthy children, 21 boys and 14 girls, 4 to 16 years of age [9] of normal weight and height and free from metabolic disorders.

Methods

Five ml blood was obtained by venipuncture after an overnight fast and the serum was prepared for analysis after the method of Perry et al. [11] in our own modification [9]. For separation and quantitation of individual SFA, gas chromatography was employed.

The results were subjected to statistical analysis by means of Student's *t*-test.

Results

The serum concentrations of individual SFA in both groups are summarized in Table I. Acetic, propionic, iso-valeric and n-caproic acid were present in the sera of all the underweight children, iso-butyric acid was detectable in 11 cases and iso-caproic acid in 6. In the control group, only

Table I

Serum concentration of individual short-chain fatty acids (μg/ml) in normal and underweight children

Group	Number of subjects	Age		Acetic	Propionic	Isobutyric	Butyric
Underweight	12	5—13	n	12	12	11	12
			Range	3.55—22.1	0.19—1.51	0—1.08	0.44—1.86
			Mean	9.10	0.76	0.56	1.01
			S. D.	5.90	0.38	0.30	0.49
			V. C.	64.8	50.0	53.5	48.5
Control	35	4—16	n	35	32	33	34
			Range	2.12—14.71	0—1.10	0—1.14	0—1.65
			Mean	6.98	0.50	0.40	0.73
			S. D.	3.71	0.31	0.28	0.40
			V. C.	53.1	62.0	70.0	54.7
				$p < 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$

Group	Number of subjects	Age		Isovaleric	Valeric	Isocaproic	Caproic
Underweight	12	5—13	n	12	12	6	12
			Range	0.7—1.98	0.22—1.91	0—2.25	0.74—1.97
			Mean	1.25	0.70	0.41	1.27
			S. D.	0.48	0.52	0.68	0.41
			V. C.	39.2	74.3	165.8	32.3
Control	35	4—16	n	34	32	18	34
			Range	0—2.52	0—1.78	0—1.97	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
				$p < 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$

n = number of cases with detectable levels of individual SFA

acetic acid was found in every child, whereas the other SFA were not always detectable [9].

The average values for all SFA except n-caproic acid were higher in underweight children but only the n-butyric and iso-valeric acid concentrations were significantly elevated in comparison to the control group ($p < 0.05$). The mean serum n-caproic acid level was insignificantly lower in underweight patients ($p > 0.05$). There was no correlation between the serum concentration of individual SFA and the degree of underweight and/or understature. The SFA levels in pituitary dwarfism did not differ markedly from those found in the other underweight subjects. In both groups the serum SFA levels showed a wide individual variability except the n-caproic acid level in the underweight group (V.C. = = 32.3%), whereas the iso-caproic acid level showed striking fluctuations in both groups (V.C. = 165% and 188%, respectively). The total free fatty acid (FFA) concentration in underweight children varied from 333 μE/l to 1692 μE/l and its mean of 1004 $\pm$ 388 μE/l was above the normal 694 $\pm$ 153 μE/l.

Discussion

The FFA fraction of tissue or plasma lipids represents an important source of energy [1, 6, 16]. Adipose tissue is considered to be the main source of blood FFA [6, 8]. The circulating FFA level is an algebraic summation of the rate of release from fat stores and the rate of utilization in tissues [5]. Lean subjects display a steeper rise of blood FFA under fasting conditions than normal or obese persons do [5]. This may be caused by an accelerated FFA mobilization from lipid stores, their decreased utilization by tissues, or both. There are many factors including hormonal ones stimulating the mobilization of FFA from adipose tissue [16]; one of them is malnutrition both in infants [2] and in animals [3]. It was postulated that in kwashiorkor a metabolic block would prevent the coenzyme-A derivatives of short-chain fatty acids from entering the Krebs cycle [7]. The elevated serum total FFA level in our material also supports that observation [2, 3].

Increased serum levels of short-chain fatty acids, especially those with an even number of carbon atoms, seems to reflect an impaired synthesis of long-chain fatty acids from acetyl-CoA by reversed beta-oxidation, which takes place in the mitochondrial system [13, 14, 15]. The concentration of n-caproic acid was, however, somewhat lower in underweight patients than in the control group, but much higher than in obese children [10]. The elevated propionic acid level could be regarded as the result of an impaired utilization of propionyl-CoA for the formation of palmitate via malonyl-CoA in the non-mitochondrial system of FFA synthesis, beside the main pathway through acetyl-CoA [13].

According to Robb et al. [12] the

majority of infused SFA, especially acetate, propionate and butyrate, is utilized for lipogenesis and fattening in sheep. On the basis of our observation one may postulate that there is an inclination to accumulation of these compounds in the blood of underweight children, which could explain the impaired lipogenesis and insufficient weight gain. It seems reasonable to suggest that the impaired FFA synthesis and the subsequent diminished lipogenesis may primarily result from the decreased activity of enzymes responsible for the functioning of mitochondrial and non-mitochondrial systems. The increased serum acetic and n-butyric acid levels indicate that predominantly the mitochondrial system is involved [13]. On the other hand, the rate of enzymatic conversion of individual SFA to their acyl-CoA derivatives may be subnormal or even the formation of acylcarnitine complexes transportable through mitochondrial membranes [15] may be insufficient. It is difficult to establish whether these presumably enzymatic changes are constitutional or acquired. In some cases they seem to be determined genetically as some persons [5] and some strains of mice [4] are inclined to remain lean despite overfeeding.

Another problem is presented by the increased concentrations of isobutyric and iso-caproic acids in underweight children, as these acids are not intermediates in FFA synthesis. In obese children the serum levels of these acids are low [10], a fact suggestive of differences in their turnover depending on the nutritional state. The explanation of the elevated iso-valeric acid level remains obscure, as this compound was elevated also in the serum of obese children [10].

In summary, a decreased utilization of SFA for the synthesis of long-chain fatty acids and subsequently for lipogenesis in connection with the increased release of FFA from adipose tissue results in reducing the lipid stores and leads to a loss of weight.

References

1. Braun, J. S.: Freie Fettsäuren im Serum. Z. klin. Chem. **5,** 387 (1971)
2. Dogan, F., Bilger, M., Hatemi, N., Tumay, S. B.: Le taux des acides gras libres (A. G. L.) dans la malnutrition après hyperglycémie provoquée par voie orale et test à l'adrenaline. Pédiatrie **28,** 519 (1973)
3. Engel, F. L., White, J. E.: Some hormonal influence in fat mobilization from adipose tissue. Amer. J. clin. Nutr. **8,** 619 (1960)
4. Fenton, P. F.: Studies on genetically determined metabolic patterns. Amer. J. clin. Nutr. **8,** 748 (1960)
5. Gordon, E. S.: Non-esterified fatty acids in the blood of obese and lean subjects. Amer. J. clin. Nutr. **8,** 740 (1960)
6. Gordon, R. S., Jr., Cherkes, A.: Unesterified fatty acids in human blood plasma. J. clin. Invest. **35,** 206 (1956)
7. Hadden, D. K.: Glucose, free fatty acids and insulin interrelations in kwashiorkor and marasmus. Lancet **2,** 589 (1975)
8. King, K., Adam, P. A. J., Laskowski, D. E., Schwarz, R.: Sources of fatty acids in the newborn. Pediatrics **47,** 192 (1971)
9. Papierkowski, A., Gawdzik, J., Trocewicz, J., Gundłach, A.: The concentration of individual monocarboxylic short-chain fatty acids in serum of normal children. Acta paediat. Acad. Sci. hung. **16,** 271 (1975)

10. Papierkowski, A., Kowalczuk, J., Torcewicz, J., Gundłach, A.: Monocarbloxylic short-chain fatty acids C_2—C_6 in serum of obese children. Acta paediat. Acad. Sci. hung. **16,** 277 (1975)
11. Perry, T. L., Hansen, S., Diamond, S., Bullis, B., Mok, Ch., Melancon, S.: Volatile fatty acids in normal human physiological fluids. Clin. chim. Acta **29,** 369 (1970)
12. Robb, J., Reid, J. T.: Energetic efficiency of the utilization of acetate and glycerol by fattening sheep. Brit. J. Nutr. **28,** 249 (1972)
13. Wakil, S. J.: The mechanism of fatty acid synthesis. Amer. J. clin. Nutr. **8,** 630 (1960)
14. Wakil, S. J.: Lipid metabolism. Academic Press, New York 1970
15. White, A., Handler, P., Smith, E. L.: Principles of Biochemistry. McGraw Hill, New York 1968, p. 57
16. Williams, R. H.: Disorders in carbohydrate and lipid metabolism. W. B. Saunders Co., Philadelphia 1962

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