Dietary ascorbic acid and muscle carnitine (β-OH-γ-(trimethylamino) butyric acid) in guinea-pigs

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Tissue ascorbic acid (AA) contents of approximately 12 and 100% saturation respectively were produced in two groups of guinea-pigs. The 'low-AA' group had significantly lower muscle carnitine concentrations than the 'high-AA' group. There was no concomitant emergence of the symptoms customarily regarded as characteristic of hypovitaminosis C. It is concluded that muscle carnitine (β-OH-γ-(trimethylamino) butyric acid) is a highly-sensitive indicator of tissue AA contents; this could account for the lassitude and fatigue reported to precede the emergence of frank scurvy in man.

Many of the classical features of frank scurvy, such as impaired healing of wounds, are theoretically explicable in terms of the basic biochemical lesion of scurvy, i.e. a defective hydroxylation of the collagen prolyl–lysyl residues (Barnes, 1975). It has proved to be less easy to accommodate within the known biochemical roles of ascorbic acid (AA) the lassitude and fatigue which, according to studies with human volunteers, would appear to precede the emergence of the more clearly definable clinical symptoms (Crandon *et al.* 1940). Lassitude was a central feature of classical descriptions. 'The signes of the Scurvie are many, as namely, a generall lazinesse and evil disposition of all the faculties...shortnesse a difficultie of breathing especially when they moove themselves...' wrote Woodall (1639). According to Lind (1753) 'The first indication of the approach of this disease is...a pale and bloated complexion; with a listlessness to action or an aversion to any sort of exercise... (which)...degenerates soon into a universal lassitude...much fatigue and upon that occasion subject to a breathlessness or panting. And this lassitude, with a breathlessness upon motion, are observed to be among the most constant concomitants of the distemper'.

The recent demonstration that AA is a co-factor for the conversion of lysine to carnitine (Hulse *et al.* 1978) provides a basis for a possible link between hypovitaminosis C and physical fatigue. Carnitine (β-OH-γ-(trimethylamino) butyric acid) has a biochemical role as a carrier molecule for the transport of fatty acid residues into the mitochondria where they may be oxidized (Bremer, 1977). By modifying the availability of skeletal muscle fatty acid for energy production carnitine may thereby influence the capacity of the muscle to maintain sustained contraction. Muscle weakness is a common feature of clinical carnitine deficiency (Engel *et al.* 1977).

An experiment was designed to determine whether dietary AA influenced the concentration of muscle carnitine.

METHODS

Two groups of eight young male albino guinea-pigs were given the scorbutogenic diet MG1 (Williams & Hughes, 1972). They received daily supplements of 25 mg AA/kg body-weight (group 1) and 10 g AA/l in their drinking water (group 2); previous studies had indicated that intakes of this order produced tissue AA contents of approximately 15 and 100% saturation respectively. A tissue AA content of approximately 15% saturation is sufficient to prevent the emergence of the diagnostic features of guinea-pig scurvy.

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Table 1. *Ascorbic acid (AA) intake (mg/kg body-weight) and muscle carnitine (μg/g) in guinea-pigs*

(Mean values with their standard errors for eight animals/group)

	Group no.	
	1	2
AA intake ...	(25 mg/kg body-wt)	(10 g/l drinking water)
Body-weight (g)		
Initial		
Mean	342	339
SE	5	6
Final		
Mean	517	531
SE	20	14
Kidney (g/kg body-wt)		
Mean	6·9	7·0
SE	0·2	0·2
Adrenals (g/kg body-wt)		
Mean	0·40	0·38
SE	0·03	0·03
AA (mg/kg)		
Liver*		
Mean	50·2	312
SE	3·5	7·6
Spleen*		
Mean	57·1	438
SE	7·5	16
Adrenals*		
Mean	203	2032
SE	20	74
Skeletal muscle		
Carnitine* (μg/g)		
Mean	0·59	1·15
SE	0·10	0·11
Triglycerides (mmol/kg)		
Mean	24·4	19·7
SE	3·1	7·1

* Differences between mean values were statistically significant; $P < 0.01$ (Student's t test).

Food was given without restriction and measurements of food consumption made. The guinea-pigs were weighed daily and killed after 28 d. AA was determined in selected organs (Williams & Hughes, 1972) and carnitine and triglycerides in samples of the gastrocnemius muscle (Marquis & Firtz, 1964; Wahlefeld, 1974).

RESULTS AND DISCUSSION

There was no significant difference between the food consumptions and gain in weight in the two groups. Relevant analytical values are summarized in Table 1.

The expected differences between the tissue AA concentrations emerged clearly. The muscle carnitine concentration in group 1 (low-AA) was significantly lower than in group 2 (high-AA). Our experiment was terminated after 4 weeks; triglyceride accumulation did not reach the level of significance reported by Khan & Bamji (1979) for carnitine deficiency induced in rats by giving them a lysine-deficient diet for 10 weeks. There were no differences between the body-weights or the organ weights (spleen, liver, kidneys and adrenals) in the two groups;

adrenal and kidney hypertrophy and failure to gain in body-weight are early features of hypovitaminosis C in guinea-pigs (Hughes, 1965).

This result suggests that in guinea-pigs muscle carnitine is a sensitive indicator of AA status and that a fall in its concentration is one of the earliest biochemical consequences of a reduced intake of AA. Carnitine has a regulatory role in skeletal muscle in the provision of energy from fatty acid sources. Its sensitivity to the AA status of an organism is therefore consistent with the early emergence of fatigue and lassitude in AA deprivation in man.

Current thought on recommended intakes of AA derives primarily from considerations of the amount required to prevent the emergence of 'clinical' scurvy; the probable existence in man of a carnitine-AA relationship similar to the one we have described in this note should perhaps stimulate a reappraisal of thought on optimal intakes of the vitamin.

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