EFFECTS OF CARNITINE ADMINISTRATION, FASTING, AND EXERCISE ON URINARY CARNITINE EXCRETION IN MAN

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Summary 1. In this study, the carnitine level in 24-hr urine has been determined in males, (a) before and after a single oral dose of 500 mg (as carnitine) of DL-carnitine chloride, (b) during fasting, and (c) before and after a severe running program (3 × 2,000 m/8-8.5 min).
2. After the administration of DL-carnitine chloride, the urinary carnitine excretion was increased by only approximately 10% of the dose, suggesting a large body pool size of carnitine.
3. Urinary carnitine excretion was significantly increased during five-day fasting; a maximum level of 2.17 ± 0.24 (mean and SD) mmol/day was 4.6 times higher than the usual level of 0.47 ± 0.10 mmol/day (p<0.001). Respiratory quotients (RQ) decreased significantly (p<0.01) from the control value of 0.81 ± 0.03 to the value of 0.75 ± 0.02 after five-day fasting and was significantly correlated with urinary carnitine levels (r = −0.62, p<0.05).
4. The urinary excretion of carnitine increased slightly with heavy running exercise.
5. The results are discussed in relation to the physiologic regulation of the rate of carnitine synthesis.

Carnitine (3-hydroxy-4-N-trimethylaminobutyrate) plays a major role in the oxidation of long-chain fatty acids by transferring the free fatty acids into the mitochondria (1). It has been established that carnitine can be synthesized primarily by the liver from lysine (2-4) and methionine (5) in the rat and occurs in high concentration in cardiac and skeletal muscles in most animal tissues (6).

The carnitine content of the rat tissue has been shown to be elevated in conditions with high rates of fatty acid oxidation, such as high fat feeding (7,8), fasting (8), and cold-acclimation (9,10). The carnitine content of sheep liver

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also increases markedly with starvation (11). Our previous report has shown that a marked increase in total carnitine concentration in rat skeletal muscle occurs on swimming exercise as well as on fasting in the rat (12). In alloxan-diabetes, however, the concentration of carnitine is strikingly increased in sheep liver (11, 13) and halved in rat skeletal muscle (14).

The present study on man shows the effect of fasting, exercise, and carnitine administration on urinary carnitine excretion.

**EXPERIMENTAL**

**Subjects.** Eleven physical education students between the ages of 21 and 23 served as subjects. Most of them had only limited training.

**Carnitine administration experiment.** Four subjects, weighing 57–75 kg, were fed normal controlled meals (2,866 kcal: protein 69.8, fat 106.8 and carbohydrate 392.9 g) for three days. At 9 a.m. on the 3rd day, they were orally administered with a single dose of 500 mg (as carnitine) DL-carnitine chloride (Monocamine: generously provided from Tanabe Pharmaceutical Tokyo Co., Tokyo). Twenty-four hour urine was collected before and after administration.

**Fasting experiment.** Four subjects, weighing 56–65 kg, were given normal controlled diets (2,688 kcal: protein 93.3, fat 72.5 and carbohydrate 401 g) for three days and then fasted for five days. On the first day and the days following the fasting period, the subjects were given meals of rice gruel (348 kcal: protein 5.2, fat 1 and carbohydrate 78 g and 1,382 kcal: protein 47.5, fat 14.7 and carbohydrate 263.8 g) and thereafter controlled meals which had the same compositions as those ingested prior to fasting. During the fasting period, they were allowed to drink water ad libitum.

Twenty-four hour urine was collected two days before fasting, daily during fasting, and one, 7 and 8 days following the fasting period. Respiratory quotients were measured at between 9:30 and 11:30 a.m. on the previous day and on the 3rd and 5th day of the fasting period and the 4th day following fasting.

**Exercise experiment.** Three subjects, weighing 53–60 kg, were given controlled meals (described in carnitine administration experiment) for three days. On the 3rd day they ran a distance of 2,000 m for 8–8.5 min before breakfast, lunch, and dinner. Twenty-four hour urine was collected prior to the first run and after it.

**Urinary carnitine analysis.** Purification and separation of carnitine in the urine was carried out by eluting the urine sample through a column of Amberlite CG-120 (H+, 100–200 mesh) ion-exchange resin with 2N ammonia according to MEHLMAN and WOLF (15). Carnitine was chemically determined by analyzing the eluate by the method of FRIEDMAN (16).

**Expired gas analysis.** Collections and analysis of expired gas for measurement of respiratory quotients were carried out using a “Expired Air Successive
Collector-Respirizer” (Fukuda Medical Physics Lab., Ltd., Tokyo).

RESULTS

Carnitine administration experiment (Table 1)

Urinary carnitine levels were significantly increased by the oral administra-

<table>
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<th>Urinary carnitine</th>
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<td></td>
<td>mg per day (mean ± SD)</td>
<td>87.1±11.9</td>
<td>132.1±15.3</td>
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* Subjects were administered with a single dose of 500 mg (as carnitine) of dl-carnitine chloride (Monocamin).

![Graph](image)

Fig. 1. Effect of fasting on body weight, RQ, and urinary carnitine excretion in man. a and b: Significantly different ($p<0.01$ and $p<0.001$, respectively) from values for the days 1 and 2. c: Significantly different ($p<0.05$) from values for the day 7. d and e: Significantly different ($p<0.01$ and $p<0.05$, respectively) from values for the day 2.
tion of DL-carnitine chloride \(p<0.01\), however, the average value of 45 mg/day of the increased carnitine excretion accounted for less than 10% of the dosed amount.

**Fasting experiment (Fig. 1)**

Body weights were reduced about 5 kg by five-day fasting. The average whole body RQ decreased significantly during fasting \(p<0.01\), on the 5th of the fasting) and increased markedly on the 4th day following fasting \(p<0.05\) as compared to the control value of 0.81 ± 0.03.

The urinary carnitine excretion was significantly increased by fasting \(p<0.01\) and \(p<0.001\), values for the 2nd and 3rd to 5th day of the fasting period vs. the control mean value for two days before fasting, respectively) and nearly reached at a maximum level on the 3rd day of fasting. The level of urinary carnitine was markedly dropped by the ingestion of rice gruel meals \(p<0.05\), the value for the 1st day after fasting vs. the value for the 5th day of the fasting) and recovered to the usual levels on the 7 day after fasting.

**Exercise experiment (Fig. 2)**

A very severe running exercise increased slightly the urinary carnitine excretion from the average control value of 0.34 ± 0.12 (SD) mmoles/day to 0.58 ± 0.16 (SD) mmoles/day.

**DISCUSSION**

The very low recovery of the dosed carnitine was observed after the oral administration of a single large dose of DL-carnitine chloride (Table 1). D-Carnitine is not a naturally occurring isomer of carnitine and can not be utilized by the organism (17). As the employed chemical method of carnitine assay determines both L- and D-carnitine isomers and the efficiency of carnitine absorption at intestine and carnitine content of fed diets were not examined, so it is very difficult to evaluate a meaning of the finding. However, if the absorption efficiency of DL-carnitine is high and the D-isomer of carnitine is excreted greatly faster than the L-isomer as was indicated in the rat (18,19), the present result would suggest a large body carnitine pool size in man.

Our previous study indicated that carnitine concentrations in gastrocnemius muscle of rat were increased by approximately 65 and 17% with five-day fasting and one- or three-hour swimming exercise (12). Fröberg et al. also observed the elevated carnitine concentrations in the red parts of gastrocnemius muscle from rats subjected to a 15 week running training (20). The present study in man also showed that the urinary carnitine excretion was significantly and slightly increased with fasting and heavy exercise, respectively (Fig. 1, 2). Furthermore, as shown in Fig. 3, the increase of urinary carnitine excretion was significantly correlated with the decrease of RQ during fasting \(p<0.05\). These findings in
man may clearly indicate that the rate of carnitine synthesis in animals is extremely stimulated in fasting with high rates of fatty acid oxidation, considering that the rat tissue carnitine concentrations were elevated with fasting (8,12).

The mechanism of physiologic regulation of the rate of carnitine synthesis is not known. It has been observed that the glucocorticoid (dexamethasone) and
insulin treatment \textit{in vivo} increase the tissue carnitine concentrations in lactating cows \((21)\) and alloxan-diabetic \((14)\) and choline-deficient alloxan-diabetic rats \((22)\), respectively. These observations are seemed to suggest that the endocrine functions may play an important role in the regulation of the rate of carnitine synthesis in animals.

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\textbf{REFERENCES}