Choline supplementation reduces urinary carnitine excretion in humans[1–3]

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ABSTRACT Two experiments were conducted to determine the effects of supplementary choline and/or pantothenate on the carnitine and lipid status of free-living humans. Analyses of carnitine and cholesterol fractions, triacylglycerols, and creatinine were determined in serum and/or urine. In experiment 1, adults receiving 13.5 mmol choline plus 1.4 mmol pantothenate/d had a significant decline in urinary carnitine excretion and renal clearance with nonesterfied carnitine (NEC) declining the most dramatically, 84%. Additionally, serum NEC and total carnitine concentrations decreased significantly. No changes were observed in any of the serum lipids examined. In experiment 2, subjects took 0.20 mmol and 0.02 mmol/kg choline or pantothenate, respectively. Choline, but not pantothenate, supplementation significantly decreased urinary carnitine excretion, renal clearance, and fractional clearance of NEC. We conclude that supplementary choline maintained serum carnitine concentrations by conserving urinary carnitine. Moreover, these observations merit additional investigation to determine metabolic and functional consequences of choline and carnitine interactions in humans. *Am J Clin Nutr* 1996; 63:904–10.

KEY WORDS Choline, pantothenate, carnitine, humans, renal clearance

INTRODUCTION

We are concerned about the carnitine status of subjects who are self-dosing or taking therapeutic amounts of choline singularly or in combination with other compounds or nutrients, such as pantothenate. Carnitine is not generally recognized as essential in the diet even though it is indispensable for the translocation of long-chain fatty acids into the mitochondria. Its function in the transport of long- and short-chain fatty acids and organic acids within and among body compartments is critical in intermediate metabolic processes.

Pharmacologic doses of choline, lecithin, and pantothenate are widely used in clinical trials for a variety of neurologic (1) and hyperlipidemic (1, 2) conditions. Additionally, these compounds are commercially available in supplement form for persons to consume as desired. The side effects and safety of pharmacologic doses of choline and pantothenate have been reviewed (1, 3, 4), but their interactions with other nutrients have not been fully elucidated in humans or animals.

It has long been known that the addition of choline chloride to a choline-deficient diet in rats significantly increases carnitine concentrations in the liver and muscle while significantly lowering the urinary carnitine concentrations (5–7). Recently, Sheard and Krasin (8) confirmed that in rats fed a choline-deficient diet, serum and urinary carnitine concentrations are not reflective of tissue concentrations. Although many studies are directed toward the effect of choline-deficient diets, there are no complete reports of the effects of supplementary choline and/or pantothenate on the serum and urinary carnitine concentrations of free-living humans consuming regular diets.

Because choline, carnitine, and pantothenate are of pragmatic and clinical interest, it is important that the effects are documented. The purpose of this investigation was to examine the effects of choline and pantothenate on serum and urinary carnitine concentrations in free-living humans. The objectives of experiment 1 were to *1*) determine the effects of supplementary choline plus pantothenate (Ch+Pa) on the serum and urinary carnitine concentrations, *2*) determine whether supplementary Ch+Pa alters the serum and urinary response to L-carnitine supplementation, and *3*) assess the effects of the supplements on serum triacylglycerol and cholesterol concentrations in adults. The objectives of experiment 2 were to *1*) confirm observations in experiment 1, and *2*) determine whether the decreases in serum and urinary carnitine concentrations were due to supplementary choline or pantothenate, or to a combination of the two.

SUBJECTS AND METHODS

Experiment 1

Healthy adults aged 23–52 y, with no known clinical disease, were recruited from the faculty and graduate student population of The University of Tennessee, Knoxville, to participate in this study. The study was approved by the Human Subject Review Board of the university. The control and experimental groups consisted of 10 and 20 subjects, respectively, with an equal number of males and females in each group. One of the control males developed a respiratory infection requiring med-

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Received August 11, 1994.

Accepted for publication January 19, 1996.

TABLE 1
Daily dietary intake of selected nutrients[1]

Dietary factor	Control group (n = 9)	Experimental group (n = 20)
Energy (MJ)	8.5 ± 1.2	7.9 ± 0.6
Protein (g)	76 ± 11	75 ± 8
Carbohydrate (g)	265 ± 39	226 ± 16
Fat (g)	73 ± 13	70 ± 8
Cholesterol (mg)	218 ± 56	237 ± 37
Pantothenate (mg)	4.5 ± 0.6	3.9 ± 0.5
Carnitine (mg)	46.3 ± 14.5	37.7 ± 9.7
Choline chloride (mg)	138.9 ± 3	103.0 ± 19.9
Lecithin (g)	2.3 ± 0.3	1.9 ± 0.2

[1] $\bar{x}$ ± SEM. The molecular weights of cholesterol (386.6), pantothenate (219.2), carnitine (161.2), choline chloride (139.6), and lecithin (800) may be used to convert from grams to moles.

ication that lead to his withdrawal from the study. There was no requirement for subjects to adopt or adapt to a single diet or lifestyle. Individuals were specifically instructed to follow their usual dietary pattern and refrain from skipping meals, eliminating commonly consumed foods, binging, and adding novel foods or nutrient supplements for the duration of the experiment. Likewise, the subjects were instructed to maintain their usual lifestyle patterns of exercise, work, and recreation.

The control group took no supplements the first 7 d whereas the experimental group took 13.5 mmol choline by mouth, supplied as choline bitartrate (Twin Laboratories, New York) and 1.4 mmol pantothenate supplied as D-calcium pantothenate (Nature Made Nutritional Products, Los Angeles) daily. The source and amount of supplementation for this study were typical of that prescribed in a medical facility and used over-the-counter. The manufacturers maintain that these supplements have a purity ≥ 98.6% and consist of US Pharmacopeia (USP)-grade ingredients. From day 7 until day 10 both the control and experimental groups took 6.2 mmol L-carnitine/d (Kendall McGaw Laboratories, Irvine, CA). The experimental group continued to take the supplementary Ch+Pa during days 7–10. Subjects could either take all the supplements at one time or in several doses throughout the day. We determined previously that the supplements gave similar responses whether taken at one time or in several doses throughout the day. If subjects chose to take the supplements in doses, they were required to take some of all the supplements at each interval. Furthermore, supplements were suspended 10–12 h before blood collection.

Blood, 24-h urine, and food records were collected from subjects on days 0, 3, 7, and 10. Measurements of height and weight were made on day 0. Fasting blood samples were collected by venipuncture into evacuated tubes containing no anticoagulant and processed to obtain sera. Thymol was used as a preservative for urine. The NUTRITIONIST III computer program (N Squared Computing, Silverton, OR) was used to estimate dietary intake of nutrients. Dietary choline, lecithin, and carnitine intakes were estimated from published sources (9–13).

Carnitine in blood and urine was assayed according to the procedure of Cederblad and Lindstedt (14) as modified by Sachan et al (15). The nonesterifed carnitine (NEC), total acid-soluble carnitine (ASC), and acid-insoluble acylcarnitine (AIAC) were directly determined by assay, and acid-soluble acylcarnitine (ASAC) was the difference between the NEC and the ASC

TABLE 2
Serum carnitine concentrations[1]

Carnitine fraction and day of study	Control group (n = 9)	Experimental group (n = 20)
	μmol/L	
NEC		
0	34.4 ± 2.9	36.5 ± 1.8
3	35.1 ± 3.4	35.0 ± 2.5
7	34.5 ± 3.3	31.6 ± 2.4[2]
10	41.6 ± 3.6[3]	41.3 ± 2.2[3]
ASAC		
0	8.7 ± 0.7	7.0 ± 0.7
3	9.1 ± 0.9	7.4 ± 0.6
7	7.6 ± 0.8	6.6 ± 0.5
10	9.4 ± 1.2	7.7 ± 0.5
AIAC		
0	2.6 ± 0.2	2.1 ± 0.1
3	2.5 ± 0.2	1.9 ± 0.1
7	2.2 ± 0.2	1.8 ± 0.2
10	2.6 ± 0.3	1.8 ± 0.1
Total carnitine		
0	45.7 ± 3.3	45.6 ± 1.8
3	46.7 ± 3.9	44.3 ± 3.0
7	44.3 ± 3.8	40.0 ± 2.6[2]
10	53.7 ± 4.6[3]	50.8 ± 2.3[3]

[1] $\bar{x}$ ± SEM. NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine; AIAC, acid-insoluble acylcarnitine.
[2] Significantly different from days 0 and 3 for carnitine fraction, $P < 0.05$.
[3] Significantly different from day 7 for carnitine fraction, $P < 0.05$.

TABLE 3
Urinary carnitine concentrations[1]

Carnitine fraction and day of study	Control group (n = 9)	Experimental group (n = 20)
	μmol/mmol creatinine	
NEC		
0	11.4 ± 1.7	10.5 ± 1.5
3	9.6 ± 1.5	2.5 ± 0.4[2]
7	9.3 ± 1.7	1.7 ± 0.3[2]
10	64.2 ± 6.7[3]	24.4 ± 3.5[3]
ASAC		
0	10.0 ± 1.2	10.2 ± 0.9
3	9.9 ± 0.9	6.1 ± 0.6[2]
7	9.0 ± 1.0	5.2 ± 0.5[2]
10	26.0 ± 2.8[3]	14.2 ± 1.5[3]
AIAC		
0	1.2 ± 0.1	0.8 ± 0.1
3	1.1 ± 0.1	0.7 ± 0.1
7	1.1 ± 0.1	0.6 ± 0.1
10	2.0 ± 0.2[3]	1.2 ± 0.2[3]
Total carnitine		
0	22.6 ± 2.7	21.6 ± 2.0
3	20.5 ± 1.9	8.9 ± 1.0[2]
7	19.5 ± 2.7	7.6 ± 0.6[2]
10	92.2 ± 9.1[3]	39.7 ± 4.7[3]

[1] $\bar{x}$ ± SEM. NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine; AIAC, acid-insoluble acylcarnitine.
[2] Significantly different from day 0 for carnitine fraction, $P < 0.05$.
[3] Significantly different from day 7 for carnitine fraction, $P < 0.05$.

fractions. Total carnitine is the sum of NEC, ASAC, and AIAC. Carnitine clearance was calculated according to a standard renal clearance formula (16). Total cholesterol and high-density-lipoprotein (HDL)-cholesterol concentrations were determined by Sigma procedure nos. 352 and 352–3 (Sigma Chemical Co, St Louis), respectively. Triacylglycerols were determined by the method of Giegel et al (17), and the low-density-lipoprotein (LDL)-cholesterol concentrations were derived from the formula of Friedewald et al (18) before values were converted to Syst[grav]eme International units. Urinary creatinine was determined by the alkaline-picrate method (19). A standard biochemical profile of 18 tests was completed on selected subjects.

Data were examined in two sets and analyzed by using the general linear models procedure of SAS (20). Because there was a change of treatments during the experiment, data were divided into two data sets to reflect treatments. Data set 1 included observations on days 0, 3, and 7, and data set 2 included observations for days 7 and 10. Each data set was analyzed by using a completely randomized design with repeated measures. Between-subjects variation was negligible compared with within-subject variation ($P > 0.30$); accordingly, these two sources of variation were pooled in the analysis. If significant effects ($P < 0.05$) were found by the F test analysis of variance (ANOVA), subgroup means were separated using Fisher's protected least-significant-difference test (21, 22). We were interested in only a selected number of comparisons and these differed between serum and urine. For the serum, comparisons between days 0 and 7 and 7 and 10 were the most important. Serum carnitine concentrations change slowly if at all; therefore, a longer observational period is needed. Urinary carnitine concentrations change abruptly; thus, comparisons between days 0, 3, 7, and 10 were the most important.

Experiment 2

Twenty-two subjects (11 males, 11 females) were recruited from a university population similar to that in experiment 1. They ranged in age from 20 to 62 y and represented diverse ethnic groups (African, Chinese, Indian, Korean, and American). The subjects were randomly assigned to the supplementary choline or to the pantothenate group. The supplements were purchased from the Department of Pharmacy, University of Tennessee Medical Center, Knoxville. Choline (Rexall, Fort Lauderdale, FL) and pantothenate (Nature Made Nutritional Products) were administered at doses of 0.20 mmol and 0.02 mmol/kg body wt, respectively. Subjects served as their own controls and were instructed to standardize their lifestyles by eating and exercising as uniformly as possible throughout the 14-d period. In experiment 1, we had recognized that it takes a few days for individuals to standardize their lifestyles; therefore, baseline data were collected on days 0 and 3 and this was called time period (TP) 1. At TP 2 (days 4–7) a supplement of choline or pantothenate was taken by the choline and pantothenate groups, respectively; for TPs 3 and 4 (days 8–14), both groups took supplementary Ch+Pa.

A blood sample, 24-h food record, and 24-h urine sample were collected on days 0, 3, 7, 10, and 14. After a fast of 10–12 h, venous blood was collected from 0600 to 0900. Serum and urinary carnitine and urinary creatinine were determined as in experiment 1. In addition, serum creatinine was determined by the method of

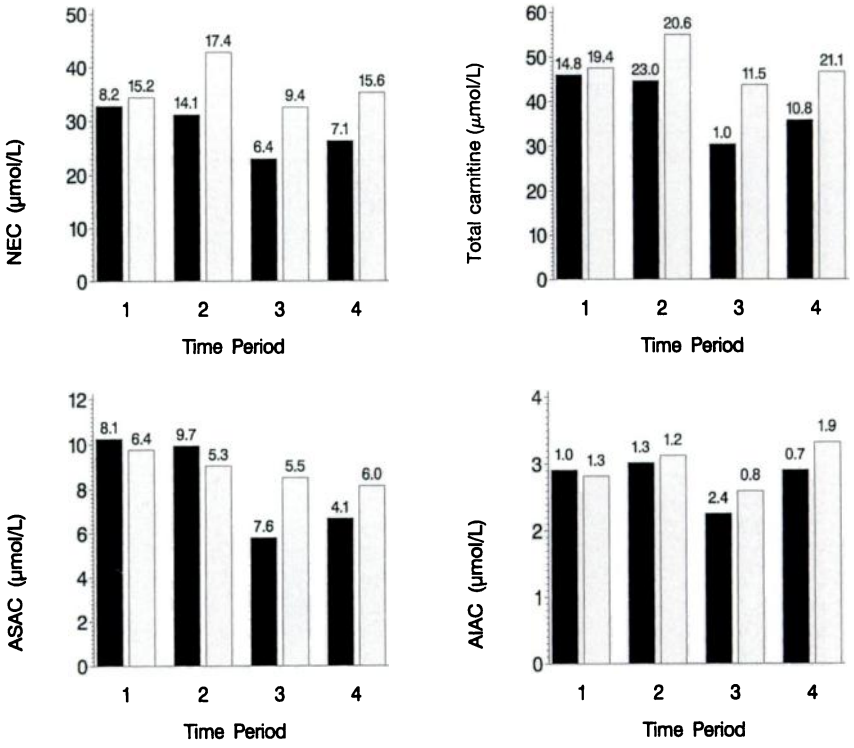

FIGURE 1. Serum carnitine concentrations observed over a 14-d period in the choline group (solid bars) and the pantothenate group (open bars). NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine, which is the difference between NEC and the total acid-soluble carnitine fraction; AIAC, acid-insoluble acylcarnitine; total carnitine is the sum of NEC, ASAC, and AIAC. $\bar{x} \pm$ SD.

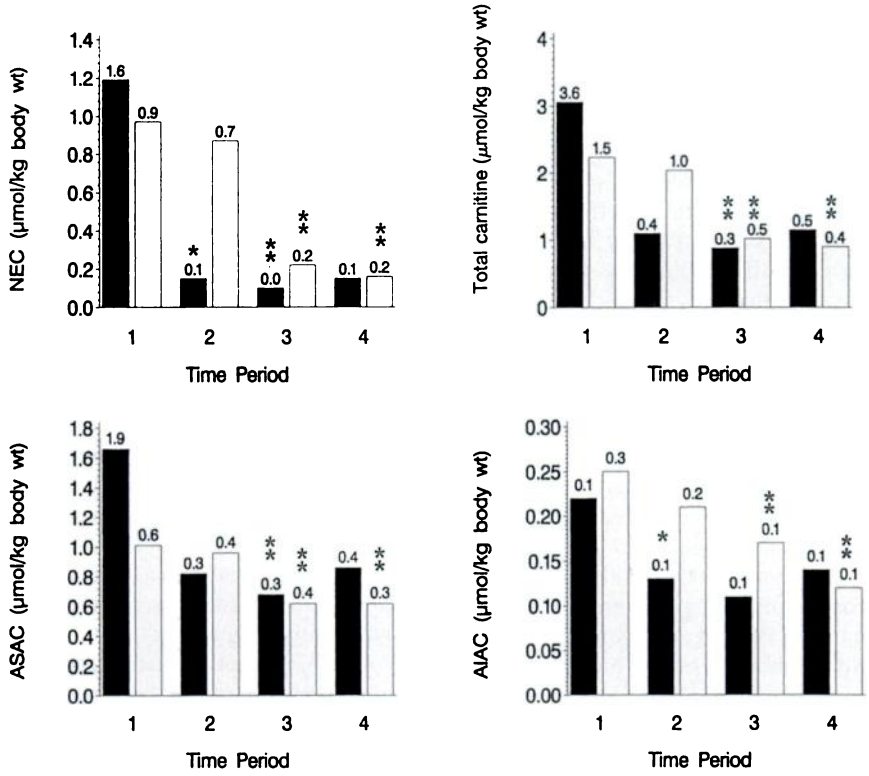

FIGURE 2. Urinary carnitine concentrations observed over a 14-d period in the choline group (solid bars) and the pantothenate group (open bars). NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine, which is the difference between NEC and the total acid-soluble carnitine fraction; AIAC, acid-insoluble acylcarnitine; total carnitine is the sum of NEC, ASAC, and AIAC. $\bar{x} \pm$ SD. * Significantly different from time period (TP) 1, $P < 0.05$. ** Significantly different from TP 2, $P < 0.05$.

Raphael (23), fractional carnitine clearances were calculated according to the formula of Ohtani et al (24), and statistical analyses were performed in the same manner as in experiment 1. In the first data set, TPs 1 and 2 (days 0–7) were compared; and in data set 2 comparisons were made among TPs 2, 3, and 4 (days 7–14). The comparisons of greatest interest were TPs 1 and 2, TPs 2 and 3, and TPs 2 and 4. Comparisons of TPs 1 and 2 indicated whether a single supplement was responsible for observed change, and comparisons of TPs 3 and 4 with TP 2 indicated whether a combination of the supplements produced the effect and if the effect was sustained for 7 d.

RESULTS

Experiment 1

The mean ages of the control group (no Ch+Pa supplementation) and the experimental group (Ch+Pa supplementation) were 39.6 ± 3.4 and 34.8 ± 1.8 y, respectively. Height, weight, body mass index, and body surface area were within the standard range and did not differ significantly between the two groups. Despite the free-living conditions, the groups achieved a remarkable degree of uniformity in diet and lifestyle. The average daily dietary intake of macronutrients, choline, pantothenate, and carnitine were similar for both groups (**Table 1**). The mean intake of pantothenate was 4.5 ± 0.6 and 3.9 ± 0.5 mg/d for control and experimental groups, respectively, which is at the lower end of the estimated safe and adequate daily dietary intake (ESADDI). After supplementation, pantothenate intake was 43 times the highest ESADDI (25). The estimated dietary choline intake was lower than the 600-1000-mg range suggested as the usual choline intake for adults by Zeisel (26). Choline supplementation increased the intake to ≈1800 mg/d. Dietary carnitine intake was estimated to be 37–46 mg/d and in the moderate range of consumption (27). Both dietary choline and carnitine consumption are difficult to estimate because of limited food-composition data.

During the first 7 d of experiment 1, supplementary Ch+Pa exerted only a slight influence on the overall serum carnitine concentrations (**Table 2**). The NEC and total carnitine concentrations of the experimental group were significantly lower on day 7 than at baseline, day 0. No significant changes occurred in the control group, which confirmed that the experimental conditions did not significantly alter serum and urinary carnitine concentrations.

In contrast with serum, supplementary Ch+Pa triggered a dramatic decrease in all urinary carnitine fractions except AIAC by day 3 (**Table 3**). The decrease in urinary carnitine fractions was sustained, and by day 7 there was a decline of 84%, 49%, and 65% in NEC, ASAC, and total carnitine, respectively. These percentages were calculated by dividing the concentrations on day 0 by the concentrations on day 7. The carnitine clearances followed a pattern similar to those of the urine data (data not shown).

Supplementary L-carnitine significantly increased the serum NEC and total carnitine (Table 2) and the excretion of all fractions of carnitine in both groups (Table 3). The

increase in excretion was highest in the NEC fraction with a 7- and 14-fold increase in the control and experimental groups, respectively. However, when the percentage change in NEC between days 0 and 10 was calculated, the control group had a 5.6-fold increase whereas the experimental group had only a 2.3-fold increase.

The serum lipid profile of the groups did not change significantly during the experiment. No significant differences were observed within or among the groups for any lipid fraction (data not shown). Similarly, no differences were seen in blood chemistry profiles of selected subjects.

Experiment 2

Of the 22 people consenting to participate, 20 completed the study. Personal obligations unrelated to the study hindered two individuals from finishing the study. The mean ages for the choline and pantothenate groups were 35.8 ± 4.3 and 35.8 ± 2.8 y, respectively. The mean body mass indexes (in kg/m^2) were 22.8 ± 1.5 and 24.7 ± 1.2 for the choline and pantothenate groups, respectively. The mean energy and nutrient consumption for the groups did not differ significantly among TPs and was similar to data presented in Table 1. Although many ethnic dietary patterns were represented, the calculated nutrient intakes did not differ between the two groups.

As shown in **Figure 1**, neither choline nor pantothenate supplementation alone or in combination produced significant changes in any of the serum carnitine fractions. In contrast with serum, dynamic changes occurred in urine for both the choline and pantothenate groups. After 4 d of choline supplementation, urinary NEC and AIAC concentrations were significantly decreased at TP 2 (**Figure 2**). When Ch+Pa was administered a significant decrease occurred in all fractions of carnitine at TP 3 in the choline group. However, the effect was not sustained in TP 4; thus, the addition of pantothenate to the choline group did not produce a sustained decrease in urinary carnitine fractions.

In the pantothenate-supplemented group, no decreases occurred in any urinary carnitine fraction at TP 2 (Figure 2). The addition of supplementary choline to the pantothenate group resulted in a significant decrease in all fractions of urinary carnitine at both TP 3 and 4. Therefore, choline but not pantothenate supplementation produced the effects observed here. The decrease in urinary carnitine excretion was observed consistently whether the data were expressed as μmol/24 h, per kg body weight, or per mmol urinary creatinine.

Urinary clearances and fractional clearances were calculated to further examine renal handling of carnitine. After 4 d of choline supplementation, only renal NEC clearance decreased significantly (**Figure 3**), which was not significantly altered after Ch+Pa supplementation (TPs 3 and 4). However, Ch+Pa supplementation of the pantothenate group resulted in significant decreases in both NEC and total carnitine clearance at TPs 3 and 4. The fractional clearances followed the same pattern as the renal clearances (**Figure 4**), indicating that the renal reabsorption of NEC was significantly greater with than without choline supplementation.

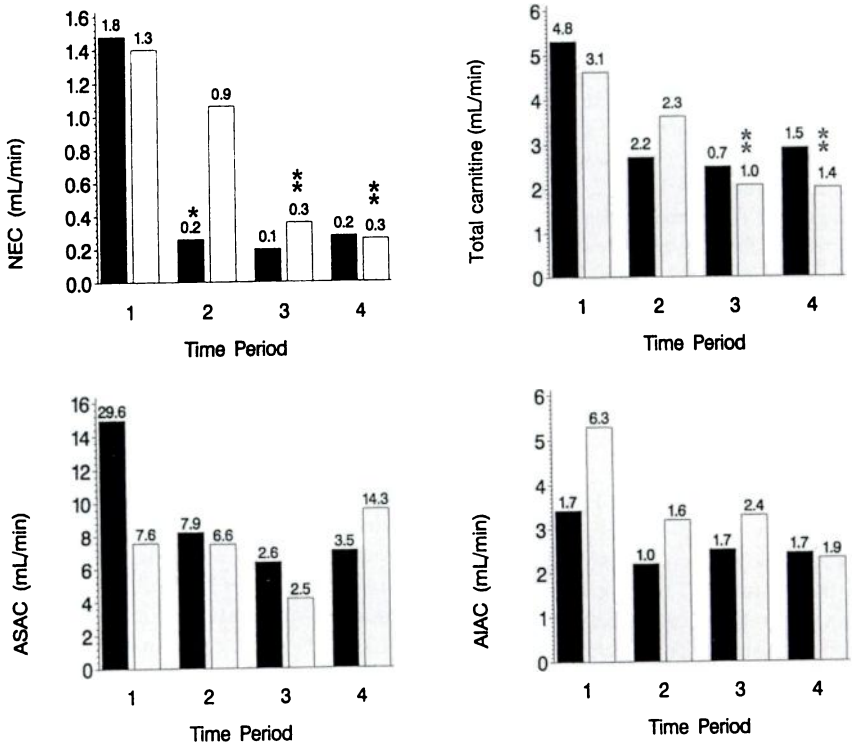

FIGURE 3. Renal carnitine clearance observed over a 14-d period in the choline group (solid bars) and the pantothenate group (open bars). NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine, which is the difference between NEC and the total acid-soluble carnitine fraction; AIAC, acid-insoluble acylcarnitine; total carnitine is the sum of NEC, ASAC, and AIAC. $\bar{x}$ ± SD. * Significantly different from time period (TP) 1, $P < 0.05$. ** Significantly different from TP 2, $P < 0.05$.

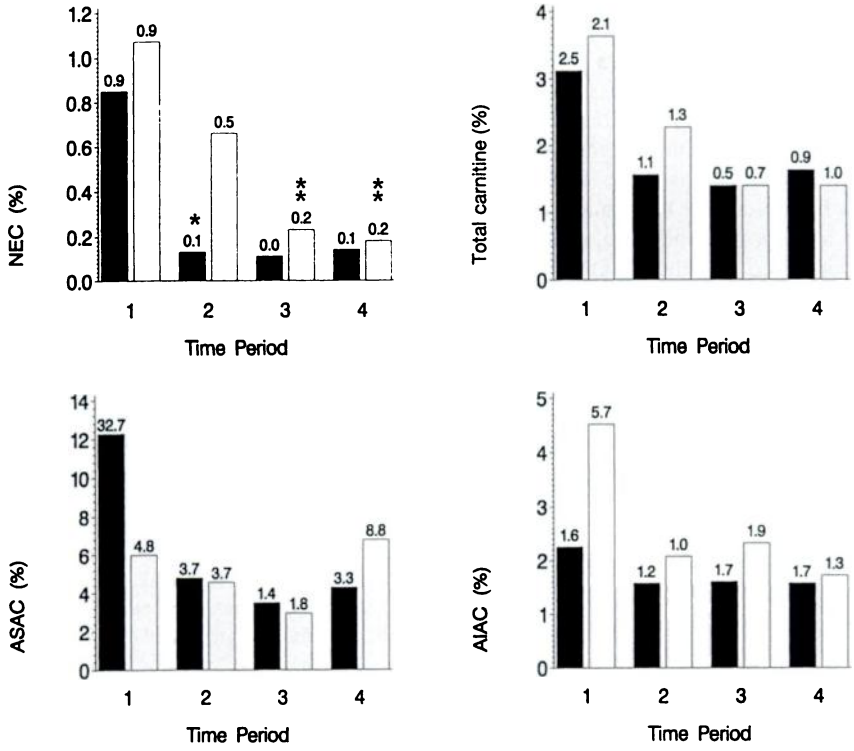

FIGURE 4. Fractional carnitine clearance observed over a 14-d period in the choline group (solid bars) and the pantothenate group (open bars). NEC, nonesterified carnitine; ASAC, acid-soluble acylcarnitine, which is the difference between NEC and the total acid-soluble carnitine fraction; AIAC, acid-insoluble acylcarnitine; total carnitine is the sum of NEC, ASAC, and AIAC. $\bar{x} \pm$ SD. * Significantly different from time period (TP) 1, $P < 0.05$. ** Significantly different from TP 2, $P < 0.05$.

DISCUSSION

These experiments indicate that free-living humans respond to supplementary choline by conserving carnitine through decreased urinary excretion of most fractions of carnitine and through a decreased renal clearance and fractional clearance of NEC. Supplementary pantothenate alone did not significantly alter urinary carnitine concentrations. At TP 3, Ch+Pa supplementation in the choline group resulted in a significant reduction in urinary carnitine fractions; however, the effect was transitory and was not sustained until day 14. It is quite clear that choline is responsible for carnitine conservation even in groups of people who have varied and diverse food habits and ethnic backgrounds.

The decreased clearance and excretion of urinary carnitine was necessary to maintain normal serum carnitine concentrations. The kidney plays an important role in carnitine homeostasis, and it is important to examine not only urinary excretion (renal clearance) but fractional carnitine clearance as well. Fractional clearance indicates the percentage of cleared and filtered carnitine that is being excreted. The percentage of carnitine reabsorption is the difference between the percentage excreted and 100%. Decreased renal clearance and excretion may occur independently of a change in fractional clearance; therefore, a significant change in all three of these processes indicates a concerted effort by the kidneys to maintain serum carnitine concentrations.

The mechanism for increased renal reabsorption of filtered carnitine is less apparent than the phenomenon. Choline does not inhibit or promote carnitine transport across the renal brush border when carnitine and choline are of equal molar concentrations (28). Because carnitine and choline were most likely of unequal concentrations, there is a possibility that choline may increase reabsorption at the brush border. Additionally, carnitine reabsorption is likely to be a multistep process (28); therefore, choline has the opportunity to enhance carnitine transport through the tubular cells or the basolateral membrane into the circulation. Zeisel (26) suggested the possibility that choline is needed to position the carnitine carrier on the plasma membrane. Therefore, choline may aid the transport of carnitine into cells.

To further support the choline effect, we can rule out several factors that are known to influence carnitine concentrations. Dietary carnitine intake was maintained at a fairly constant amount, and two baseline measurements indicated that experimental conditions had no significant effect on urinary carnitine concentrations. Despite normal dietary carnitine consumption, the choline group's urinary carnitine concentrations mimicked those of strict vegetarians (29). Additionally, the urinary NEC response of the choline group was about one-ninth that expected for the effect of a low-protein or high-carbohydrate diet (30). A decrease in glomerular filtration rate mediates the renal effect of low-protein, high-carbohydrate diets, but it is unlikely that choline affects creatinine clearance (31). No significant differences were observed in creatinine clearance at any TP.

Serum total carnitine is most often used to evaluate the carnitine status of humans. Although a significant decrease in serum NEC was observed in experiment 1, it was not confirmed in experiment 2, which may be because of the heterogenous population or other factors inherent in the latter study. Therefore, supplementary choline would not affect the carnitine status of most individuals. However, it is important to

mention that there were individuals in both experiments who had precipitous drops in serum NEC and total carnitine concentrations. For example, in one case the serum NEC concentration dropped from 32.99 to 17.46 μmol/L and the total carnitine declined from 41.57 to 25.73 μmol/L after 7 d of supplementary choline. Such an individual might be assessed as carnitine deficient. It seems reasonable to conclude that some individuals have a fragile control mechanism for carnitine homeostasis that is lost during choline supplementation. Other investigators (7) concluded that choline enhances transport rather than carnitine biosynthesis in rats. However, the rat model has limitations in explaining carnitine homeostasis in humans; the guinea pig is an appropriate model for studying choline-carnitine interactions in humans consuming a self-selected diet (32, 33).

Neither supplementary choline, pantothenate, nor L-carnitine had an effect on serum lipids or acylcarnitine concentrations. The lack of change in serum triacylglycerols and lipoprotein cholesterol concentrations was not totally unexpected because the subjects were normolipemic. However, a significant increase in triacylglycerols and a decrease in cholesterol were reported in the postprandial state for choline-supplemented individuals (34). Perhaps our studies were not of sufficient duration for changes to be manifested.

In conclusion, supplementary choline, not pantothenate, significantly reduced serum and urinary carnitine concentrations under usual free-living dietary conditions and promoted carnitine conservation. The urinary response was rapid and stabilized in 3–4 d. Choline supplementation improved the efficiency of NEC reabsorption and may have precipitated drops in serum carnitine concentrations simulating carnitine deficiency in some individuals. These observations merit additional investigation to delineate the metabolic and functional consequences of choline and carnitine interactions in humans.

We thank Kendall McGaw (Irvine, CA) for providing L-carnitine; Carolyn Boyle, Harriet Foley, and Patrick Gerard for performing the statistical analyses; and Youn Soo Cha for assistance with carnitine analysis in experiment 2.

REFERENCES

1. Zeisel SH. "Vitamin-like" molecules (A) choline. In: Shallowest ME, Young VR, eds. Modern nutrition in health and disease. 7th ed. Philadelphia: Lea & Febiger, 1988:440–52.
2. Rubba R, Postiglione A, DeSimone B, Lamenza F, Montefusco S, Mancinie M. Comparative evaluation of the lipid-lowering effects of fenofibrate and pantethine in type II hyperlipoproteinemia. Curr Ther Res Clin Exp 1985;38:719–27.
3. McCormick DB. Pantothenic acid. In: Shallowest ME, Young VR, eds. Modern nutrition in health and disease. 7th ed. Philadelphia: Lea & Febiger, 1988:383–7.
4. Wood JL, Allison RG. Effects of consumption of choline and lecithin on neurological and cardiovascular systems. Bethesda, MD: Life Sciences Research Office, Federation of American Societies for Experimental Biology, 1981.
5. Tsai AC, Romsos DR, Leveille GA. Significance of dietary carnitine for growth and carnitine turnover in rats. J Nutr 1974;104:782–92.
6. Tsai AC, Romsos DR, Leveille GA. Determination of carnitine turnover in choline-deficient and cold-exposed rats. J Nutr 1975;105: 301–7.
7. Carter AL, Frenkel R. The relationship of choline and carnitine in the choline deficient rat. J Nutr 1978;108:1748–54.
8. Sheard NF, Krasin B. Restricting food intake does not exacerbate the effects of a choline-deficient diet on tissue carnitine concentrations in rats. J Nutr 1994;124:738–43.
9. Wurtman JJ. Sources of choline and lecithin in the diet. In: Barbeau A, Growden JH, Wurtman RJ, eds. Nutrition and the brain. New York: Raven Press, 1979;5:73–81.
10. Zeisel SH. Dietary choline: biochemistry, physiology, and pharmacology. Annu Rev Nutr 1981;1:95–121.
11. Weihrauch JL, Son YS. The phospholipid content of foods. J Assoc Off Chem 1983;60:1971–8.
12. Rebouche CJ, Engel AG. Kinetic compartmental analysis of carnitine metabolism in the human carnitine deficiency syndromes. J Clin Invest 1984;73:857–67.
13. Rudman D, Sewell GW, Ansley JD. Deficiency of carnitine in cachectic cirrhotic patients. J Clin Invest 1977;60:716–23.
14. Cederblad G, Lindstedt S. A method for the determination of carnitine in the picomole range. Clin Chim Acta 1972;37:235–43.
15. Sachan DS, Rhew TH, Ruark RA. Ameliorating effects of carnitine and its precursors on alcohol-induced fatty liver. Am J Clin Nutr 1984;39:738–44.
16. Faulkner WR, King JW. Renal function. In: Tietz N, ed. Fundamentals of clinical chemistry. Philadelphia: WB Saunders, 1976:975–1014.
17. Giegel JL, Ham AB, Clema W. Manual and semi-automated procedures for measurement of triglycerides in serum. Clin Chem 1975;21: 1575–81.
18. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
19. Henry RJ. Determination of creatine and creatinine. In: Henry RJ, ed. Clinical chemistry: principles and technique. New York: Harper & Row, 1967:292–6.
20. SAS Institute, Inc. SAS user's guide: statistics, version 6.03. Cary, NC: SAS Institute, Inc, 1990.
21. Carmer SG, Walker WM. Pairwise multiple comparisons of treatment means in agronomic research. J Agron Ed 1985;14:19–26.
22. Fisher LD, Van Belle G. Biostatistics a methodology for the health sciences. New York: John Wiley & Sons, Inc, 1993.
23. Raphael SS. Estimation of plasma or serum creatinine. In: Lynch's medical laboratory technology. 3rd ed. Philadelphia: WB Saunders, 1976;1:165–6.
24. Ohtani Y, Nishiyama S, Maytsuda I. Renal handling of free and acylcarnitine in secondary carnitine deficiency. Neurology 1984;34:977–9.
25. National Research Council. Recommended dietary allowances. 10th ed. Washington, DC: National Academy Press, 1989.
26. Zeisel SH. Choline deficiency. J Nutr Biochem 1990;1:332–49.
27. Borum PR. Carnitine. Annu Rev Nutr 1983;3:233–59.
28. Rebouche CJ, Mack DL. Sodium gradient-stimulated transport of L-carnitine into renal brush border membrane vesicles: kinetics, specificity, and regulation of dietary carnitine. Arch Biochem Biophys 1984;235:393–402.
29. Lombard KA, Olson AL, Nelson SE, Rebouche CJ. Carnitine status of lactoovovegetarians and strict vegetarian adults and children. Am J Clin Nutr 1989;50:301–6.
30. Stadler DD, Chenard CA, Rebouche CJ. Effect of dietary macronutrient content on carnitine excretion and efficiency of carnitine reabsorption. Am J Clin Nutr 1993;58:868–72.
31. Mudd S, Poole JR. Labile methyl balances for normal humans on various dietary regimens. Metabolism 1975;24:721–33.
32. Daily JW, Sachan DS. Supplementary choline causes decreased urinary carnitine excretion in guinea pig. FASEB J 1993;7:A615(abstr).
33. Daily JW, Sachan DS. Choline supplementation alters carnitine homeostasis in humans and guinea pigs. J Nutr 1995;125:1938–44.
34. Hirsch MJ, Growdon JH, Wurtman RJ. Relations between dietary choline or lecithin intake serum choline levels, and various metabolic indices. Metabolism 1978;27:953–60.