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ORIGINALARBEIT

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Plasma and whole blood taurine concentrations respond differently to taurine supplementation (humans) and depletion (cats)

Taurinkonzentration in Plasma und Gesamtblut bei normaler Ernährung sowie nach Taurinsupplementierung (Menschen) und Taurinmangel (Katzen)

Summary In the present study the relationship between plasma and whole blood taurine was examined under normal physiological circumstances in humans and cats. In addition, the effect of taurine supplementation on plasma and whole blood taurine was evaluated in humans and the depletion of taurine pools after a taurine-deprived diet was studied in cats. The normal plasma taurine concentration in humans was 44 ± 8 μmol/L and the whole blood taurine concentration was 227 ± 35 μmol/L. Under normal physiological conditions plasma and whole blood taurine were not correlated (r = 0.092). Plasma taurine responded rapidly to dietary supplementation in humans or the taurine depletion in cats. In contrast, the whole blood taurine pool was more inert and varied only under extremes of depletion (cats) or sustained taurine supplementation.

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Zusammenfassung Die vorliegende Studie untersuchte die Beziehung zwischen der Taurinkonzentration in Plasma und Gesamtblut unter normalen physiologischen Bedingungen bei Menschen und bei Katzen sowie nach oraler Taurinsupplementierung beim Menschen und nach taurinfreier Fütterung bei Katzen. Beim Menschen betrug die durchschnittliche Taurinkonzentration im Plasma 44 ± 8 μmol/L und im Gesamtblut 222 ± 35 μmol/L. Unter diesen „physiologisch normalen“ Bedingungen bestand zwischen der Taurinkonzentration in Plasma und Gesamtblut keine Korrelation (r = 0.092). Die Plasmataurinkonzentration stieg nach oraler Taurinsupplementierung beim Menschen rasch an bzw. fiel schnell nach taurinfreier Ernährung bei Katzen ab. Die Taurinkonzentration im Gesamtblut war dagegen mehr inert und änderte sich erst nach anhaltender Taurinzufuhr beim Menschen bzw. nach andauerndem Taurinmangel bei Katzen.

Key words Taurine – plasma – whole blood – depletion – supplementation

Schlüsselwörter Taurin – Plasma – Gesamtblut – Taurinmangel – Supplementation

Introduction

Interest in taurine metabolism and its nutritional importance for humans has increased in the past 20 years since its first association with retinal degeneration and blindness in taurine-deficient cats (3, 4) and the observed depression in plasma and urine taurine concentrations in infants fed taurine-free formulas, as well as in children and adults undergoing long-term parenteral nutrition (2, 3, 13–15). A dietary requirement for taurine may exist under these circumstances in humans.

Although plasma taurine concentration is considered to be an adequate index of taurine status, the most reliable estimation of body taurine status is based on plasma and whole blood taurine concentrations (10). Although the much greater taurine concentration in blood cells relative to plasma is remarkable (100 times higher in lymphocytes, 300 times higher in granulocytes, and 400 times higher in platelets) (1, 5, 13), the utility of the whole blood taurine concentration has only been appreciated recently (10).

Assessing whole blood taurine introduces less chance for technical error than assaying plasma or the taurine pools in specific blood cells. The "physiologic normal" plasma taurine concentration is in the range between 35 and 60 μmol/L, with any excess being readily excreted via the kidneys in the urine (10). Plasma taurine levels below 30 μmol/L may signal the onset of taurine depletion, although it is not exactly known at what point a "low" plasma taurine concentration signals depletion of whole blood or tissue stores in humans. Plasma taurine concentrations of 1 to 10 μmol/L are common in taurine-depleted cats (8, 12). In humans plasma taurine concentrations exceeding 80 μmol/L suggest "spillage" of intracellular taurine under normal circumstances or occur after extended dietary taurine supplementation. Normal whole blood taurine in humans ranges between 160 and 320 μmol/L (10).

The present studies examined the relationship between plasma and whole blood taurine under normal physiological circumstances in humans and in cats, the latter being the only species with a definite dietary taurine requirement. The response of plasma and whole blood taurine to taurine supplementation in humans (a single supplement of 50 mg and a 400 mg/day supplement for 8 days) as well es a prolonged taurine depletion in cats was examined.

Materials and methods

Human studies

Study 1 (normal taurine status)

To demonstrate a relationship between plasma and whole blood taurine concentrations, data of plasma and whole blood taurine concentrations from a total of 32 subjects were combined. A single blood sample was taken from 22 subjects. From 10 subjects blood was drawn on 3 days within a 10-day period to examine intra-individual variation. These data have been recently published elsewhere (10). Blood samples were drawn either after an overnight fast or before lunchtime after a taurine-free, light breakfast.

Study 2 (taurine-supplemented breakfast)

A blood sample was taken on two separate mornings from seven subjects, both before and after eating a taurine-free or a taurine-supplemented (50 mg of taurine) breakfast. Blood was collected 90, 180, and 270 min after completing breakfast.

Study 3 (taurine supplementation with 400 mg per day for 8 days)

A fasting blood sample was taken from four males and three females prior to supplementation and at days 1, 4 and 8 after supplementation with 400 mg taurine per day. The taurine supplement was given as a powder and taken in one single dose. In a subgroup of four subjects (two males and two females) taurine supplementation with 400 mg per day was repeated again for 7 days and then plasma and whole blood taurine concentrations as well as urinary taurine excretion were measured before and at days 4 and 7 of supplementation.

Cat studies

Study 4 (taurine-free and taurine-supplemented feeding)

Plasma and whole blood taurine concentrations were determined in cats fed either taurine-supplemented diets (both a purified diet based on 35 % casein supplemented with 0.05 % taurine or a commercial dry cat food containing 0.12 % taurine) or fed a taurine-free purified diet for up to 250 days. The cats used in these studies represent a closed colony of 18 domestic shorthairs (nine males and nine females). For details about the diets and the experimental design see (12).

All experimental animal procedures were approved by the Brandeis University Animal Case and Use Committee.

Blood collection

Venous blood was drawn into a dry, sterile disposable plastic syringe and immediately transferred into EDTA-treated plastic tubes (10 μL/mL) and kept at room temperature. An aliquot of whole blood (200–400 μL) was transferred for analysis of whole blood taurine. Plasma was separated from the remaining blood by centrifugation for 15 min at 1500 x g at room temperature to minimize plasma contamination from the release of intracellular taurine (taurine from blood cells).

Sample preparation

For whole blood taurine analysis the whole blood samples were quickly frozen on dry ice and thawed using an ultrasonic bath. This procedure was repeated three times to achieve maximum taurine release from blood cells. Whole blood samples were deproteinized with TCA (50 μL of 100 % TCA to 200 μL of whole blood to yield a final concentration of 20 %) vortexed and centrifuged for 5 min at 12 000 x g to obtain a clear supernatant. Plasma was deproteinized by adding TCA (40 μL of 100 % TCA to 400 μL of plasma making a final concentration of 9 %), vortexed and centrifuged for 5 min at 12 000 x g. An aliquot (200–300 μL) of the deproteinized supernatant from the whole blood and plasma samples was filtered through an ion-exchange clean-up column to remove amino acids that interfere with the taurine analysis by HPLC (for details about the method see ref 11). Taurine recovery from the ion-exchange column was 96 ± 2.7 µmol for a 100 µmol taurine solution and 10 ± 0.9 µmol for a 10 µmol taurine solution (10). Columns (0.5 cm ID) were prepared by layering 2 cm AG 50W-X8 200/400 mesh (Bio-Rad, Richmond, California) in the hydrogen form over 2 cm AGI-X8 100/200 mesh (Bio-Rad) in the formate form. The prepared columns were washed with 10 mL water just before use. After loading the sample onto the column, the taurine eluant was collected by flushing with 3.0 mL water (6, 11).

Taurine analysis with HPLC

Taurine was analyzed by HPLC after precolumn derivatization with o-phthalaldehyde (OPA) using 44 % of 0.05 mol monosodium phosphate buffer/L, pH 5.3, combined with 56 % of 0.05 mol monosodium phosphate buffer containing 75 % methanol (by volume)/L as mobile phase. The mobile phase was pumped at a flow rate of 2 ml/min. The absorbance of the OPA-taurine aduct was monitored at an excitation wavelength of 360 nm and an emission wavelength of 455 nm. The taurine concentration of the sample was calculated based on the peak area from known concentrations of standard solutions (11).

Statistical procedures

Statistical differences were evaluated using one-way ANOVA and Fisher's protected least significant difference test or a paired *t*-test when appropriate.

Results

Study 1: Taurine status under normal physiological circumstances

The mean plasma taurine concentration in humans (n = 52 from 32 subjects) was 44 ± 8 µmol/L ranging from 29 to 69 µmol/L. Whole blood taurine concentrations ranged between 159 and 318 µmol/L with a mean of 227 ± 35 µmol/L. Under these normal physiological conditions plasma and whole blood taurine concentrations were not correlated (Fig. 1).

Study 2: Plasma taurine response after breakfast with or without taurine

After a taurine-free breakfast, plasma taurine concentrations decreased progressively (-23 %, not significant) from the fasting baseline level. In contrast, after the same breakfast supplemented with 50 mg taurine, plasma taurine concentrations revealed a significant (20 %) increase 90 min after completing the meal. After 180 and 270 min the plasma taurine concentration had declined to the fasting baseline level (Tab. 1).

Table 1 Plasma taurine response to a breakfast with or without taurine supplementation (50 mg)

Status	Time after breakfast (min) 0	90	180	270
	µmol/L			
Taurine-free breakfast	53±14	49±8	46±7	41±10
range	(37–73)	(38–61)	(34–54)	(27–56)
% change		-8	-13	-23
p value*		ns	ns	ns
Taurine-suppl. breakfast	44±8	53±10	47±10	45±10
range	(35–61)	(41–71)	(42±53)	(34±65)
% change		+20	+7	±
p value*		< 0.01	ns	ns

Values are mean ± SD (n = 7)
* paired *t*-test

Table 2 Changes in plasma and whole blood taurine concentration during taurine supplementation (400 mg/day) of humans for 8 days

	Day 0	Day 1	Day 4	Day 8
Plasma µmol/L	44±12[a, b]	60±11[c]	70 ± 13[a, d]	101 ± 31[b, c, d]
Whole blood µol/L	257±30	239±33	248±40	274±41

Values are mean ± SD (n = 7).
[a,b,c] Values sharing a common superscript are significantly different ($p < 0.05$) using one-factor repeated measures ANOVA and Fisher's least significant difference test

Table 3 Changes in plasma and whole blood taurine concentration during taurine supplementation (400 mg/day) of humans for 7 days

	Day 0	Day 4	Day 7
Plasma µmol/L	61±6[a, b]	92±15[a]	102±13[b]
Whole blood µmol/L	313±27[a]	313±29[b]	341±12[a, b]
Urine µmol/24 h	724±217	2467±369	1955±541
µg/g creatinine	61±14[a]	218±53[a]	163±42

Values are mean ± SD (n = 4).
[a, b] Values sharing a common superscript are significantly different ($p < 0.05$) using one-factor repeated measures ANOVA and Fisher's least significant difference test

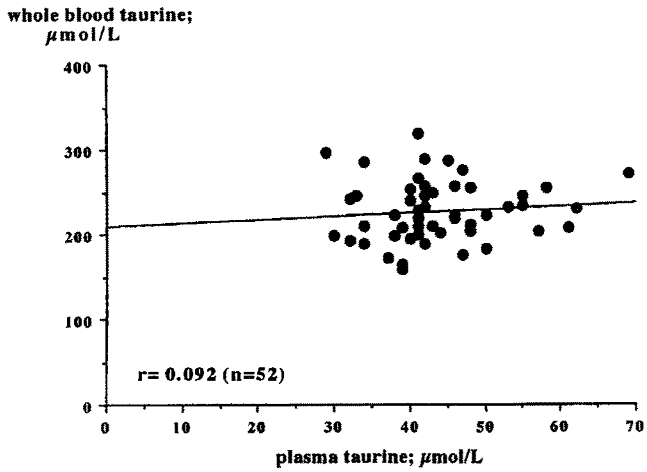

Fig. 1 No correlation exists between plasma taurine (µmol/L) and whole blood taurine (µmol/L) concentration in humans under normal physiological circumstances.

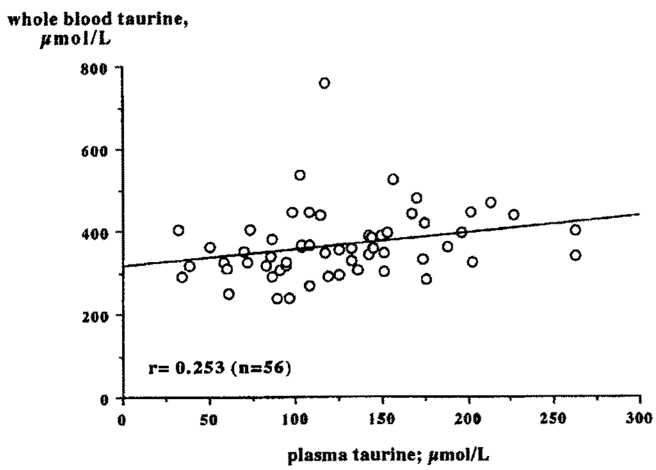

Fig. 2 Relationship between plasma taurine (µmol/L) and whole blood taurine (µmol/L) concentrations in cats fed taurine-supplemented diets.

Study 3: Plasma and whole blood taurine response and urinary taurine excretion after taurine supplementation for 7 or 8 days, respectively

Plasma taurine increased rapidly during dietary taurine supplementation, whereas whole blood taurine increased only minimally and only after 8 days of supplementing with 400 mg taurine per day (Table 2). Plasma taurine was already increased by 38 % after 1 day of supplementation. At day 4 plasma taurine was increased by 67 % (significantly different from baseline $p < 0.05$) and at day 8 plasma taurine was increased by 159 % (significantly different from baseline $p < 0.0001$). In contrast, the whole blood taurine concentration did not change until day 8 when a 7 % increase (not significant) was noted (Table 2). Similar changes in plasma and whole blood taurine concentrations were observed in the second supplementation study (Table 3). After 4 days of supplementing 400 mg taurine, urinary taurine excretion was increased 3.4 fold compared to basal taurine concentration. After 7 days of supplementation the urinary taurine concentrations was somewhat lower, but still a 2.7 fold increase compared to baseline taurine excretion was examined (Table 3).

Study 4: Plasma and whole blood taurine in taurine-supplemented and taurine-depleted cats

The mean plasma taurine concentration in cats fed the taurine-supplemented diets (purified diet or commercial cat food) was 125 ± 53 µol/L with a range between 32 and 262 µmol/L. The whole blood taurine concentration ranged from 237 to 757 µmol/L with a mean of 368 ± 84 µmol/L. Plasma and whole blood taurine concentrations revealed no correlations in cats fed taurine-supplemented diets (Fig. 2).

In cats fed the taurine-free diet, plasma taurine decreased rapidly, whereas the decline in whole blood taurine lagged behind the flux in plasma taurine. After 40 days plasma taurine was already decreased to 6 ± 4 µmol/L. In contrast, whole blood taurine had decreased to 99 ± 67 µmol/L after 40 days and decreased further to 67 ± 54 µmol/L after 100 days of depletion (Fig. 3). During the period of taurine-depletion a positive relationship between plasma and whole blood taurine developed (Fig. 4).

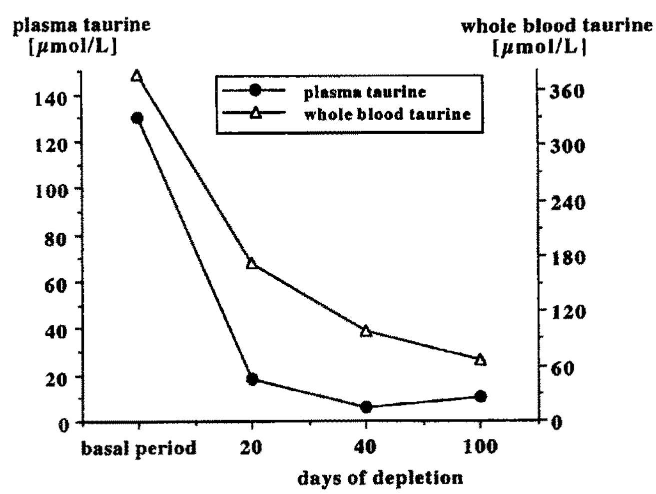

Fig. 3 Plasma and whole blood taurine concentration in taurine-depleted cats during a 100-day feeding period.

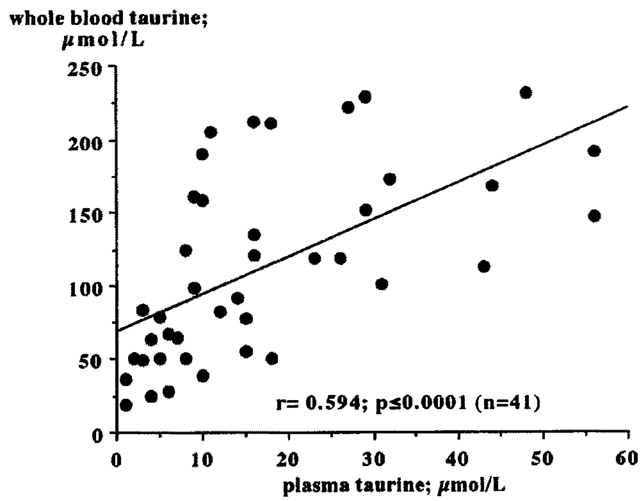

Fig. 4 Correlation between plasma taurine (µmol/L) and whole blood taurine (µmol/L) concentrations in cats during a period of taurine-free feeding.

Discussion

The current set of studies was intended to examine the relationship between plasma and whole blood taurine under opposing physiological circumstances, i.e., after taurine supplementation with a single meal supplement of 50 mg and a supplement of 400 mg per day for 1 week or after prolonged taurine depletion in cats. The actual daily intake of taurine in humans is estimated to range between 40 and 400 mg on a dietary basis (3), so both supplements can be considered within the normal range of dietary intake. However, the input of a continued high dietary taurine intake on plasma and intracellular taurine has not been adequately investigated in humans. In light of now available taurine-rich energy drinks which can contain between 250 and 4 000 mg/L, the effect of excess taurine doses on blood taurine pools need to be evaluated.

Under normal physiological circumstances the whole blood taurine pool which represents both the intracellular (i.e., taurine in leucocytes, platelets and erythrocytes) and plasma taurine, is relatively independent of the plasma taurine pool. No correlation was revealed between the whole blood and plasma taurine concentrations under these conditions in humans as well as in cats (Fig. 1 and 2). Previous studies with humans and cats also did not demonstrate a correlation between plasma and platelet taurine concentrations under normal circumstances (5). However, plasma and platelet taurine concentrations were positively correlated in children receiving long-term parenteral nutrition without supplemental taurine where both concentrations were low (14). In addition, a significant correlation was found in taurine-supplemented humans where plasma and platelet taurine concentrations had increased and in taurine-depleted cats with decreased plasma and platelet taurine concentrations (5). This corroborates the present data where during extended taurine depletion in cats plasma and whole blood taurine concentrations decreased and a positive correlation between this two parameters existed (Fig. 4). These observations suggest that only under extremes of taurine depletion or prolonged taurine supplementation does a relationship between whole blood and plasma taurine exist. Again, these findings confirm our previous opinion that taurine status is most reliably assessed by measuring both plasma and whole blood concentrations (10, 11).

A single taurine dose of 50 mg with a low-calorie breakfast, representing approximately one-half of the average daily taurine consumption, caused only a transient but significant increase in the plasma taurine concentration. This increase was observed 90 min after the taurine-rich meal, whereas after 180 and 270 min plasma taurine declined to the normal plasma concentration. The kinetics of the plasma taurine increase after oral taurine administration corroborates the results from previous taurine tolerance tests with epileptic patients (7), cystic fibrosis patients, and control subjects (9). Apparently, plasma taurine concentration peaks about 60–90 min after administration, whereas after about 4 h plasma taurine concentration is down to normal.

Obviously, an occasional high taurine intake has only a temporary effect on plasma taurine, whereas the intracellular taurine pool is not affected by this dietary manipulation. Moreover, plasma taurine increased rapidly during 1 week of supplementing with 400 mg taurine per day, whereas whole blood taurine was only minimally altered (+ 7 % increase) after 8 days of supplementation. These findings emphasize again that the whole blood taurine pool is remarkably stable and unlike the flux in plasma taurine which reflects acute changes in taurine availability.

However, the current supplementation period (8 days) may not have been long enough to reveal significant changes in whole blood taurine. Further studies are needed to focus on a long-term dietary taurine supplement and its impact on plasma and especially whole blood taurine.

Under normal nutritional conditions, excess dietary taurine is excreted in the urine because the kidney is firmly regulating the total body pool of taurine. In fact, urinary taurine excretion was increased 3.4 times after 4 days of supplementing 400 mg/d taurine compared to taurine excretion before supplementation (Table 3). Interestingly, despite the ongoing supplementation urinary taurine excretion decreased somewhat after 7 days of taurine supplementation and a slight increase (+ 9 %) in whole blood taurine was determined at the same time. Taurine is a major urinary amino acid in humans because of a limited renal tubular reabsorption and urinary taurine excretion is usually high, ranging from 200 to 2 000 μmol/L, or roughly 2 to 10 times the plasma taurine concentration (3).

In summary, these data indicate that an occasionally high taurine intake has only a temporary effect on plasma taurine concentration, whereas whole blood taurine representing intracellular taurine is not affected. However, a prolonged taurine supplementation (at least longer than 1 week) could result in an increase in whole blood taurine concentration, despite the fact that the major part of dietary taurine is excreted in the urine. The degree of such an increase needs to be evaluated in further investigations.

References

1. Ahtee L, Boullin DJ, Paasonen MK (1974) Transport of taurine by normal human blood platelets. Br J Pharm 52:245–251
2. Hayes KC (1988) Taurine nutrition. Nutr Res Rev 1:99–113
3. Hayes KC, Trautwein EA (1994) Taurine. In: Shils ME, Olson JA, Shike M (eds) Modern Nutrition in Health and Disease. Lea & Febiger, Philadelphia, S 477–485
4. Hayes KC, Carey RE, Schmidt SY (1975) Retinal degeneration associated with taurine deficiency in the cat. Science 188:949–951
5. Hayes KC, Pronczuk A, Adessa AE, Stephan ZF (1989) Taurine decreases platelet aggregation in cats and humans. Am J Clin Nutr 49:1211–1216
6. Larsen BR, Grosso DS, Chang SY (1980) A rapid method for taurine quantitation using high performance liquid chromatography. J Chromatogr Science 18:233–236
7. Mantovani J, DeVito DC (1979) Effects of taurine on seizures and growth hormone release in epileptic patients. Arch Neurol 36:672–674
8. Messing JM, Sturman JA (1993) Evaluation of taurine status in cats consuming diets containing different amounts of taurine by determination of plasma and whole blood taurine concentrations. J Nutr Biochem 4:168–171
9. Thompson GN (1988) Excessive fecal taurine loss predisposes to taurine deficiency in cystic fibrosis. J Pediatr Gastroenterol Nutr 7:214–219
10. Trautwein EA, Hayes KC (1990) Taurine concentrations in plasma and whole blood in humans: estimation or error from intra- and interindividual variation and sampling technique. Am J Clin Nutr 52:758–764
11. Trautwein EA, Hayes KC (1991) Evaluating taurine status: determination of plasma and whole blood taurine concentration: J Nutr Biochem 2:571–576
12. Trautwein EA, Hayes KC (1991) Gender and dietary amino acid supplementation influence the plasma and whole blood taurine status of taurine-depleted cats. J Nutr 121:S173–S174
13. Vinton NE, Laidlaw SA, Ament ME, Kopple JD (1986) Taurine concentrations in plasma and blood cells of patients undergoing long-term parenteral nutrition. Am J Clin Nutr 44:398–404
14. Vinton NE, Laidlaw SA, Ament ME, Kopple JD (1987) Taurine concentration in plasma, blood cells and urine of children undergoing long-term total parenteral nutrition. Pediatr Res 21:399–403
15. Zelikovic I, Chesney RW, Friedman AL et al. (1990) Taurine depletion in very low birth weight infants receiving prolonged total parenteral nutrition: role of renal immaturity. J Pediatr 116:301–306