Nutr. Hosp. (2002) XVII (6) 262-270
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Nutrición Hospitalaria

Revisión

Taurine: a conditionally essential amino acid in humans? An overview in health and disease

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Abstract

Taurine, a sulphur containing amino acid, is the most abundant intracellular amino acid in humans, and is implicated in numerous biological and physiological functions. This comprehensive overview explores areas, from its characterisation to its potential clinical benefit as a conditionally essential amino acid and a pharmaconutrient. In healthy individuals the diet is the usual source of taurine; although in the presence of vitamin B_6 it is also synthesised from methionine and cysteine. Taurine has a unique chemical structure that implies important physiological functions: bile acid conjugation and cholestasis prevention, antiarrhythmic/inotropic/chronotropic effects, central nervous system neuromodulation, retinal development and function, endocrine/metabolic effects and antioxidant/antiinflammatory properties. Taurine is an essential amino acid for preterm neonates and is assured by breast milk. Specific groups of individuals are at risk for taurine deficiency and may benefit from supplementation, e. g. patients requiring long-term parenteral nutrition (including premature and newborn infants); those with chronic hepatic, heart or renal failure. Further studies are required to determine the benefits of replenishing taurine pools as well as the need to include taurine routinely in parenteral nutrition regimens.

(*Nutr Hosp* 2002, 17:262-270)

Keywords: *Cholestasis. Parenteral nutrition. Preterm neonates. Taurine. Taurine deficiency.*

LA TAURINA, ¿UN AMINOÁCIDO CIRCUNSTANCIALMENTE ESENCIAL PARA EL SER HUMANO? DESCRIPCIÓN DE SU IMPORTANCIA PARA LA SALUD Y LA ENFERMEDAD

Resumen

La taurina, un aminoácido que contiene azufre, es el aminoácido intracelular más abundante del ser humano e interviene en numerosas funciones biológicas y fisiológicas. En esta amplia revisión se exploran distintos campos, desde su caracterización hasta su posible utilidad clínica como aminoácido circunstancialmente esencial y como farmaconutriente. La dieta de las personas sanas es la fuente habitual de taurina; no obstante, en presencia de vitamina B_6, también se sintetiza a partir de la metionina y de la cisteína. La taurina posee una estructura química singular que facilita funciones fisiológicas importantísimas: conjugación de los ácidos biliares y evitación de la colestasis, efectos antiarrítmicos/inotropos/cronotropos, neuromodulación del sistema nervioso central, desarrollo y función de la retina, efectos endocrinometabólicos y propiedades antioxidantes/antiinflamatorias. La taurina es un aminoácido esencial para los prematuros y su presencia queda asegurada con la leche materna. Algunos grupos concretos de personas corren riesgo de sufrir carencia de taurina y pueden mejorar con los suplementos, por ejemplo, los pacientes que precisan nutrición parenteral prolongada (incluidos los prematuros y recién nacidos), los enfermos con hepatopatía crónica, insuficiencia cardíaca crónica o insuficiencia renal. Se requieren nuevos estudios para conocer las ventajas derivadas del llenado de los depósitos de taurina así como de la necesidad de incluir la taurina de forma sistemática en los tratamientos de nutrición parenteral.

(*Nutr Hosp* 2002, 17:262-270)

Palabras clave: *Carencia de taurina. Colestasis. Nutrición parenteral. Prematuros. Taurina.*

Introduction

Taurine is a sulphur containing amino acid implicated in numerous biological and physiological functions in the human body; first isolated from ox bile in

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Recibido: 29-IV-2002.
Aceptado: 22-VI-2002.

1827, it is non-essential in the rodent, essential in the cat and may be conditionally essential in humans[1]. Recent interest ensued from several animal and human studies that did emphasise its importance in clinical nutrition and as potential pharmaconutrient[2].

In the embryo, taurine deficiency has been associated with various lesions, e.g. cardiomyopathy, retinal degeneration and growth retardation[3-5]. Taurine is probably an essential amino acid for neonates; due to enzymatic immaturity they have a limited capacity for its synthesis, and due to the immature kidney there is a relative inability to conserve taurine[6-7]. Deficiency in neonates appears to have a deleterious effect on the developing brain and retina, hence supplementation is required for neonates on parenteral nutrition (PN)[8, 9].

Both in children and adults, long-term PN is often associated with hepatobiliary dysfunction[10, 11]. Because taurine is involved in the formation of bile acid conjugates, its deficiency is likely to play a role in the pathogenesis of PN-associated cholestasis[10-14]. In guinea pigs, Guertin et al.[13] observed that the addition of taurine to PN solutions prevented biliary dysfunction associated with the infusion of standard amino acid solutions; the supplementation modified the pattern of bile acid conjugation and secretion whilst promoting bile flow, thereby preventing hepatotoxic bile acids' stasis[13]. In adults, taurine plasma concentrations are known to decrease in response to starvation, surgical injury and a variety of clinical conditions, e.g. cancer, trauma and sepsis[12]. Overall, taurine seems to be essential in neonates and conditionally essential in certain adult patients requiring long-term PN[10, 15].

Since taurine plays an important role in cell membrane stabilisation, modulation of intracellular calcium levels, osmoregulation and detoxification [16-19], it is likely to modulate various physiological functions, which are disturbed in a broad range of clinical situations. Although its mechanism of action is poorly understood, it appears to have important cardiovascular effects and to influence platelet aggregation, central nervous system (CNS) neuromodulation, retinal photoreceptor activity, endocrine functions, antioxidant activity and control of growth and cell differentiation[1, 2].

Our objective is to provide a comprehensive, yet brief, overview of taurine, from its characterisation to its potential role in humans as a conditionally essential amino acid with possible pharmacological benefits.

Biosynthesis and metabolism

Taurine is a neutral β-amino acid; both the amine and sulphonic groups can undergo ionisation, the dissociation constant of the latter confers its biological and functional specificity[1, 12].

Taurine synthesis

In healthy humans, dietary foodstuffs are the main sources of taurine: high concentrations are found in animal sources whilst undetectable in vegetables (table I)[2, 20]. Since vegetarians have no dietary intake of taurine and often eat low sulphur amino acid diets, plasma concentrations are lower in vegetarians[20, 21]. Methionine and cysteine are precursors of taurine, however synthesis ability varies widely amongst species[1]; the maximal human synthesis rate is unknown. The average daily synthesis in adults ranges between 0.4-1.0 mmol (50-125 mg)[1]; under stress the synthesis capacity may be impaired; therewith some authors consider taurine as a conditionally essential amino acid, whereas for others it remains nonessential[1, 2, 12].

Table I
Taurine content of foodstuffs[2, 20]

Meat	
Beef/raw	43
Pork/raw	61
Chicken/raw dark meat	169
Turkey/raw dark meat	306
Lamb/raw dark meat	47
Ham/baked	50
Seafood	
Tuna/canned	42
White fish/raw	151
Mussels/raw	655
Oysters/fresh	70
Cod/frozen	31
Clams/fresh	240
Clams/canned	152
Milk and derivatives	
Pasteurized milk	6
Cheddar cheese	not detected
Yogurt/low fat plain	3.3
Ice cream/vanilla	1.9
Fruit, vegetables, seeds, nuts, grain, beans peanuts, cereals	not detected

Taurine content is expressed in mg (mean)/100 g wet weight.

Endogenous taurine synthesis occurs mainly in the liver and brain[22], and requires several steps involving enzymatic oxidation and conversion of cysteine, either directly or following conversion of methionine into cysteine (figure 1)[2]. Cystathionine synthase, cystathionase and cysteinesulphinic acid decarboxylase are the three involved enzymes, all of which require vitamin B_6 as a co-factor; vitamin B_6 deficiency, due to poor intake, drug antagonism or disease-altered metabolism[23, 24] reduce taurine synthesis. The activity of the hepatic rate-limiting enzyme cysteinesulphinic acid decarboxylase is also influenced by other factors, e.g. age and sex[1, 22, 25]. Humans have a relatively low enzyme activity; enzymatic immaturity stresses the deficiency risk for neonates[15, 26]. In general, men have a higher enzymatic activity than women, a phenomenon that may explain the higher incidence of gallstones in

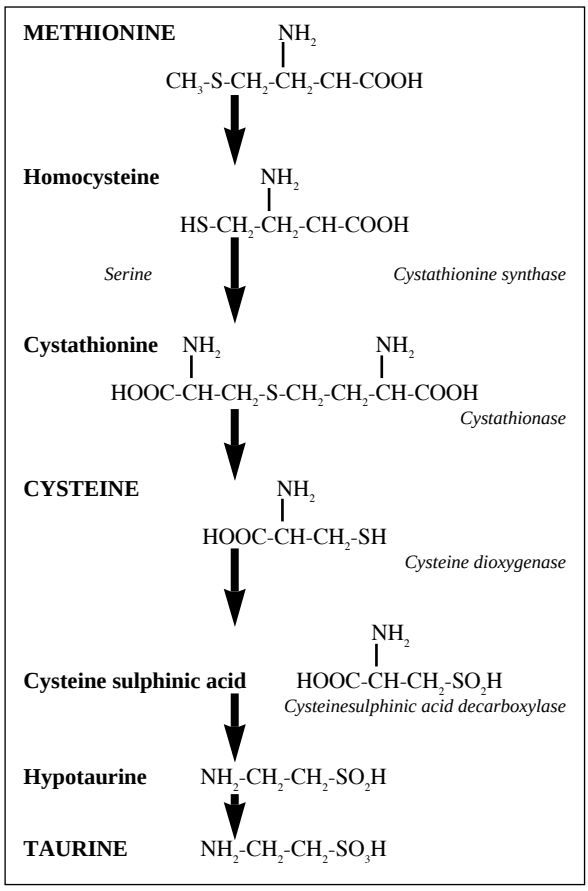

Fig. 1.—Biosynthetic pathway of taurine. The main pathway includes cysteine oxidation to cysteinesulphinic acid, a subsequent decarboxylation to hypotaurine and then oxidation to taurine (adapted/from 2).

women, given the taurine involvement in bile acid conjugation[13].

Taurine distribution

Taurine is the most abundant intracellular amino acid in the human body; although most is free, it is not incorporated into proteins, only a small amount is present as small peptides in the brain[1, 2]. A 70 kg human contains about 560 mmol (70 g) of taurine with an intracellular concentration in the range of 5-50 mM, whereas the plasma concentration is about 100 μM[1]. Tissues that are excitable and prone to generate free radicals, such as the retina, white blood cells, platelets, brain, CNS, heart, skeletal muscle, and liver, have higher concentrations; the distribution being shown in table II[1]. Taurine takes part in several biochemical reactions; cell membrane protection seems to be the major physiological role either by reducing toxic substances or by acting as an osmoregulator[18, 27, 28]. Plasma concentrations are maintained by a homeostatic control comprising a low renal tubular reabsorption threshold, relevant during periods of dietary restriction; unlike whole blood concentrations plasma

Table II
Taurine distribution in the human body[1]

	µmol/g (wet weight)		*µmol/l (concentration)*
Brain	0.8-5.3	Bile	200
Erythrocytes	0.05-0.07	Liquor	5-36
Heart	6	Milk	337
Kidney	1.4-1.8	Saliva	16-65
Liver	0.3-1.8		
Lung	1-5		
Muscle	2.2-5.4		
Platelets	16-24		
Retina	30-40		
Spleen	11.4		
White blood	20-35		
Cells	20-35		

concentrations vary rapidly in response to intake[1, 2]. Sturman et al.[29] characterised taurine turnover by two exchangeable pools, a small (2.0 mmol or 0.25 g) and a large one (100 mmol or 12.5 g). The former is not a good indicator of individual tissue concentrations and most likely reflects dietary intake and urinary excretion, is rapidly miscible/exchangeable, with a half-life of 0.1 h; it includes bile, CNS and other tissues, most of which actively take up taurine against a concentration gradient. The large pool has a slow turnover rate and a half-life of 70 hours; it is yet unclear whether the large hepatic is readily available as a donor for other tissues, given its primary role on bile acid synthesis[29]. Taurine is actively transported to all tissues by a transporter protein that is coupled to the transport of sodium and chloride ions and is regulated by the activation of two calcium sensitive enzymes: protein kinase C (transporter inhibitor) and calmodulin (transport stimulator)[30, 31].

Taurine excretion

While taurine is excreted through urine and bile[32], it is the kidney that regulates the total body pool by altering tubular reabsorption[33]; taurine is filtered through the glomerulus and partially reabsorbed in the tubules through a high affinity, low capacity, sodium dependent, β-amino acid specific transport system[2]. The amount of taurine excreted daily varies from individual to individual, and in the same individual from day to day; it may reach 0.22-1.85 mmol and is influenced by various factors including genetics, age, sex, current dietary intake, renal function and clinical conditions[1, 20, 21, 34]. Patients with tubular dysfunction are at increased risk of deficiency. During periods of inadequate dietary intake or reduced availability of precursor amino acids, taurine renal reabsorption is increased favouring the maintenance of tissue stores[33]. Conversely, high dietary intake and conditions inducing taurine release from cells, e.g. surgery, muscle

disease/damage or radiation therapy, increase its renal excretion[12, 34, 35].

Taurine physiological functions

Bile acid conjugation and prevention of cholestasis

The two primary bile acids, cholic and chenodeoxycholic, are synthesised in the hepatocytes from cholesterol through cholesterol 7-α-hydroxylase activity[36]; these acids are excreted into the bile and from there into the duodenum. Secondary bile acids, deoxycholic acid and lithocholic acid, are derived from primary bile acids by exposure to intestinal bacteria, and later reabsorbed in the ileum, returning to the liver via the portal vein. During this enterohepatic circulation, bile acids undergo numerous structural modifications, including conjugation with taurine and glycine and sulfation, to diminish their hepatotoxicity[36]; besides, conjugation is essential to maintain bile acids' solubility in the aqueous intestinal environment[36]. In healthy adults, the tauro-conjugated:glyco-conjugated bile acid ratio is 3:1; this ratio varies from individual to individual and is influenced by the taurine hepatic pool[33]. Neonates are exclusive tauro conjugators; glyco-conjugates are not usually present until the 3rd week of life, though they may appear earlier in taurine deficient neonates[37, 38]. The efficiency of tauro-conjugated bile acids is due to the sulphonic acid group that facilitates its ionisation, thereby enhancing their detergent action and solubility, and also reduces reabsorption. In addition, tauro-conjugated bile acids have a choleretic effect and prevent cholestasis, unlike unconjugated or glycine-conjugated bile acids[36,38]. Data support the protective action of sulphation of taurolithocholate but not of glycolithocholate[39]. In vitro, at physiologic concentrations, sulphated glycolithocholate is readily precipitated by calcium, by contrast sulphated taurolithocholate prevents calcium precipitation as well as cholestasis[39]. Taurine supplementation enhances hepatic cholesterol 7-α-hydroxylase activity, the rate-limiting enzyme for bile acid synthesis[39].

In summary, taurine promotes bile flow, increases bile acid production and prevents cholestasis[13, 14, 40, 41].

Cardiovascular effects

Over 50% of the total amino acid pool of the heart is taurine[42], which has been shown to have positive antiarrhythmic, chronotropic and inotropic effects, to enhance digitalis inotropy[3, 16, 43], and may reduce blood pressure both in animals and humans[44-46]. These properties appear to be mediated by taurine binding to membranes in the sarcolemma, promoting calcium transport; specific effects on phospholipids or its binding to high and low affinity protein receptors in the membrane are not yet known[12]. Taurine may improve chronic heart failure through several mechanisms[47-52]: 1) taurine promotes natriuresis and diuresis, through its osmoregulatory activity in the kidney, its modulation of atrial natriuretic factor secretion and its putative regulation of vasopressin release; 2) taurine modulates calcium fluxes and enhances inotropic and beta-adrenergic activation through its influence on cyclic AMP regulation; 3) taurine attenuates angiotensin II effect on calcium transport, protein synthesis and angiotensin II signalling, thereby taurine may minimise many adverse actions of angiotensin II, e.g. induction of cardiac hypertrophy, volume overload and myocardial remodelling. Other publications suggest that the increased cytokine activity in heart failure may increase the need for cysteine and taurine[50-52]. After myocardial infarction, taurine supplementation helps to stabilise electrical membrane excitability by modulating calcium ion concentration, whilst reducing platelet aggregation[43, 53].

Central nervous system neuromodulation

In the nervous system and during brain development, taurine affects cell migration, modulates neurotransmission[5, 54], and can speed brain development; on the contrary, glutamic, gamma-amino butyric and aspartic acids slow brain development[54, 55]. Some low-molecular-weight peptides isolated from brain synaptosomes contain taurine; the most abundant of these peptides, glutaurine, appears to act as a neurotransmitter[54, 55]. Furthermore, by controlling the mobilisation of calcium ions during depolarisation, taurine stabilises membranes and influences glutamate generation, an important neurotransmitter[56]. Recent research suggests that taurine depletion may be associated with epileptic seizures and supplementation has been reported as beneficial[57]; however the effectiveness of taurine supplementation is probably limited due to its poor diffusion across the blood-brain barrier. Taurine may inhibit nerve stimulation, and has been reported to control motor tics, such as uncontrollable facial twitches[57]. Taurine may act as well as a neuromodulator in central respiratory control, in response to acute hypoxia[58].

Retinal photoreceptor activity

Taurine is the most abundant amino acid in the retina, it appears essential for normal vision and deficiencies are linked with retinal degeneration[4, 59]. In cats, where taurine is an essential amino acid, deficiency leads to retinal degeneration and eventual blindness along with low retinal and plasma concentrations[60, 61]. In infant monkeys, deficiency was associated with growth retardation but retinal function seemed unimpaired[62]. In more recent studies on taurine-deficient primates, Huxtable et al.[63] reported retinal lesions, impaired visual acuity and degenerati-

ve structural changes in photoreceptor outer segments, particularly in younger animals. In infants and children raised on taurine-free long-term PN, retinal abnormalities[64] and immature brainstem auditory evoked responses[65, 66] were demonstrated by ophthalmoscopy and electrophysiology, respectively. There was an attenuation of the b-wave on the electroretinogram associated with low plasma taurine concentrations; the electroretinogram normalised after taurine supplementation. The mechanisms involved in the complex function are still unclear though modification of calcium ion fluxes and inhibition of protein phosphorylation and/or osmoregulation changes may be involved[65, 66].

Endocrine and metabolic effects

Another role for taurine may be the maintenance of euglycemia by enhancing insulin activity via stimulation of insulin receptors[30, 67]. Low plasma and platelet taurine have been reported in diabetes mellitus, supplementation restores plasma concentrations and corrects blood platelet dysfunction[68, 69]. In a diabetic rat model, taurine improved glucose and fat metabolism along with reduced insulin resistance. The reduced serum cholesterol and triacylglycerol content may reflect greater cholesterol transformation into bile acids and/or reduced cholesterol synthesis[70]. Thus, taurine may be helpful in the management of human hypercholesterolemia[70].

Taurine may prevent diabetes-associated microangiopathy; it seems to attenuate hyperglycaemia-induced endothelial cell apoptosis, through reactive oxygen species inhihition and intracellular calcium concentration stabilisation[71].

Antioxidant/detoxifying activity

It has been suggested that taurine may act as an antioxidant or oxidant scavenger[19]. In the hamster, prophylactic dietary taurine can prevent acute NO_2-induced bronchioles injury and may avert other oxidant-induced lung injuries[72]. The exact mechanism of action is unknown, it may relate to taurine's membrane-stabilising properties by promoting potassium, sodium, calcium and magnesium fluxes[72].

In vitro, taurine through the formation of taurochloramine, appears to facilitate the removal of hypochlorous acid, a strong oxidant that causes DNA damage[73, 74]. Taurochloramine may also have a regulatory role in inflammatory processes[75, 76] through the inhibition of the production of interleukins 6 and 8, presumably as a consequence of diminished activity of the major transcriptional cytokine gene regulators[76]. Taurine metabolic precursor, hypotaurine (figure 1) may also have antioxidant properties[28].

Moreover, taurine conjugates secondary bile acids, retinoids and certain xenobiotics, increasing their polarity, aqueous solubility and clearance from the body[77], a potential detoxifying activity.

Other effects

Taurine may be important in preventing cirrhosis, depression and male infertility due to low sperm motility[57]. It has been shown to heal damaged colon cells[78] and acute gastric ulcers[79]. In cystic fibrosis taurine supplementation ameliorates steatorrhea, perhaps due to enhanced bile salt reabsorption[80, 81]. In Alzheimer's disease, low acetylcholine concentrations are related to memory loss; in experimental animals taurine administration increases acetylcholine in the brain[82]. Taurine concentrations are decreased in Gaucher patients; it has to be established whether taurine availability is an important regulator of macrophage function in the liver[83]. It has been hypothesised that taurine enhances the bioavailability of lipid soluble vitamins, probably by promoting easily hydrolyzable complexes[84].

Patients at risk for taurine deficiency

Given taurine's considerable biological significance, deficiency clearly has the potential to cause clinical consequences. Deficiency may be due to inability to synthesise or conserve taurine or to an inadequate supply relative to requirements[1, 2]. In theory, the provision of sufficient methionine or cysteine should guarantee adequate synthesis. But this assumes efficient metabolic pathways and adequate enzymatic function, including enough vitamin B_6[29]. If endogenous synthesis is not enough, if dietary intake of taurine is severely limited or absent for extended periods, or if there are increased demands[15], depletion is likely. As a consequence there are specific groups at risk for taurine depletion and these individuals may benefit from supplementation. These risk groups include preterm neonates, patients requiring long-term PN and patients with hepatic or chronic renal failure.

Preterm neonates

Preterm neonates (gestational age ≤ 32 weeks) have a limited capacity to convert methionine to cysteine and hence to taurine, due to an enzymatic immaturity of liver enzymes responsible for the biochemical pathway shown in figure 1[10, 85, 86]. Premature neonates have greater requirements because of their growth rate and the needs of their developing nervous and visual systems[4, 5, 54, 87]. In addition, premature neonates are born with lower stores of taurine, the kidney β-amino acid transport system is immature and lacks the capacity to conserve taurine by increased reabsorption[7]. This homeostatic failure is reflected in the premature neonates' markedly elevated urinary content, with fractional excretion ranging from 38 to 60%, compared to below 10% in term neonates[7]. Whether mature neonates require extra taurine is uncertain, they seldom show a deficiency because of its presence in breast milk[87, 88]. Formula-fed neonates may benefit from supplementation[89].

Parenteral nutrition

Parenteral amino acid solutions usually contain little or no cysteine, because cysteine is rapidly converted to cystine, which is insoluble in aqueous solution[90]. Moreover, most amino acid solutions used in PN do not contain taurine; certain neonatal solutions are the exception[90, 91]. Furthermore, the synthesis of cysteine and taurine from methionine is restricted when the liver first-pass metabolism is bypassed by PN. For these reason patients receiving long-term PN have a unique nutritional requirement for supplemental taurine[15,92-94]. Depleted status has been well documented in neonates on taurine free long-term PN, they have low concentrations in the plasma, platelets and urine[7, 9, 12, 15]. In very low birth weight neonates, the lack of taurine in PN and the inability of the immature kidney to upregulate tubular reabsorption, lead to depleted body pools. This may have deleterious effects on the developing brain and retina as well as on bile acid conjugation, thereby increasing the risk of cholestasis[10, 95].

Taurine supplementation may be justified in trauma, as depletion in these patients persists longer than other hypoaminoacidemias, because of depressed renal tubular reabsorption[33, 96]. A study comprising a cohort of adult patients submitted to long-term PN without taurine, revealed decreased plasma, platelet, lymphocyte and erythrocyte concentrations without changes in the granulocyte content[94]. In a similar study, where granulocyte concentrations were decreased as well, supplementation with daily intravenous 10 mg of taurine/kg body weight normalised plasma and blood cell status[92]. In addition, in critically ill mechanically ventilated septic patients under PN, decreases in taurine were significantly correlated with increases in pulmonary artery pressure and pulmonary vascular resistance, and deterioration of pulmonary dysfunction[97, 98].

Patients with short bowel syndrome do not normally reabsorb bile salts; hence, they have increased losses of bile acids' tauro-conjugates[92], which further compounds the need for exogenous taurine especially if they are on long-term PN. Those patients are at increased risk of liver dysfunction because of long-term PN, as such, they may benefit from taurine supplementation.

Desai et al.[35] and Dilley[99] observed a profound taurine deficiency after intensive chemotherapy and whole-body irradiation. This was more severe in patients receiving taurine free PN than in orally-fed patients. The plasma precursor amino acids, methionine and cysteine, were not affected but a marked increase in urinary taurine was observed; the latter was attributed to the massive lymphocyte destruction due to irradiation[35]. Subnormal taurine concentrations commonly occur in malnourished postoperative cancer patients; possible explanations include decreased synthesis, increased renal excretion or shifts between intracellular and extracellular compartments[93]; supplementation may be appropriate.

Hepatic dysfunction

The liver is the pivotal metabolic organ and the major site for enzymatic reactions involved in taurine synthesis. Hepatic dysfunction disturbs amino acid synthesis and adversely affects sulphur amino acid status. Patients with severe liver damage or cirrhosis have low plasma taurine, cysteine and glutathione concentrations, an elevated plasma cystathionine concentration, decreased urinary taurine excretion, and increased cysteine and cystathionine excretion[95, 100, 101]. Vitamin B_6 deficiency may also concur, especially in alcoholics'[23]. All these factors contribute to disturb the taurine enzymatic pathway.

Chronic renal failure

Low plasma and muscle intracellular taurine concentrations are often found in patients with chronic renal failure, even though the precursor amino acids are normal or elevated. This suggests a metabolic block in the synthesis, probably linked to a decreased activity of the key enzyme, cysteine sulphinic acid decarboxylase. Intracellular taurine depletion may be responsible for muscle fatigue, a common symptom in uraemia; supplementation may be appropriate in chronic renal failure[12, 102, 103]. A recent cross-over trial suggests that nocturnal hemodialysis may increase taurine and improve uraemia[104].

Conclusion

Several observations suggest a clinical role for taurine. Firstly, taurine is one of the most abundant intracellular free amino acid in the human body but there is little correlation between circulating taurine and total body stores. The incidence of intracellular taurine deficiency may be much higher than suggested bv plasma concentrations. Secondly, taurine is not incorporated into plasma proteins; therefore, its deficiency cannot be evaluated through nitrogen balance or other sophisticated methods to evaluate protein synthesis; nevertheless, taurine is highly relevant for a wide range of biomedical functions both at the cellular and subcellular level. Thirdly, the human body has a limited capacity to synthesise taurine. Altogether, there is enough data to support taurine as an essential amino acid in neonatology and probably a conditionally essential amino acid in some adult syndromes. Appropriately designed, controlled and prospective clinical studies are required to search for potential benefits of replenishing taurine pools as well as the need to include taurine routinely in PN regimens.

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