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Relationship of taurine and other amino acids in plasma and in neutrophils of septic trauma patients

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Summary. Recently, an interdependency of plasma taurine and other amino acids as well as metabolic and clinical variables implicating therapeutic options was reported. This result may be an indication that plasma taurine levels are directly related to intracellular levels. Therefore, the aim of this study was to analyse the possible relationship between taurine levels in plasma and in neutrophils, the relationship to other amino acids, and variables quantifying metabolic impairment and severity of sepsis in multiple trauma patients developing sepsis. After multiple trauma taurine decreased significantly in plasma in thirty-two patients as well as within the neutrophil and does not recover in sepsis. Lower individual levels in the neutrophil did not follow lower individual levels in plasma and no correlation of taurine in plasma and in the neutrophils could be observed. In sepsis, only plasma showed an interdependency of taurine, aspartate, and glutamate. No association between taurine plasma or intracellular levels and SOFA score as indicator for severity of sepsis or metabolic variables was observed. After multiple trauma and in sepsis, taurine uptake in cells (which is regulated in different ways), and intracellular taurine (which serves e.g. as an osmolyte) can be influenced. Therefore a prediction of the neutrophil taurine pool seems not fully possible from taurine plasma levels. Intracellular taurine has some unique properties explaining the missing interdependency despite some similarities in osmoregulation and metabolic interactions to other amino acids. The association of taurine, aspartate, and glutamate in plasma cannot be simply transferred to the neutrophils intracellular level. The clinical meaning of the plasma correlation remains unclear. A dependency of plasma and neutrophil taurine to severity of sepsis and to metabolic variables seems not possible because of the multifactorial pathophysiology of sepsis.

Keywords: Taurine – Amino acids – Neutrophil – Sepsis

Introduction

In previous decades, investigation of amino acids in critical illness has predominantly focused on some individual amino acids such as glutamine or arginine. In the more recent past, relevance of taurine in trauma and sepsis for host defence and antioxidant protection has been recognised (Redmond et al., 1998; Stapleton et al., 1998; Watson et al., 1995).

Little is known about the relationship between changes in taurine to other amino acids levels, and to clinical variables in critical illness. Chiarla et al. (2000) recently demonstrated that in trauma patients plasma taurine levels in sepsis were directly related to levels of glutamate, aspartate. Moreover, decreasing plasma taurine was associated with worsening of metabolic plasma and clinical variables (Chiarla et al., 2000). They conclude that these results might also have therapeutic implications in as much as an augmented plasma taurine availability delivered by nutritional solutions may be associated with a better preservation of cell function and a decreased susceptibility to host tissue damage. This result might be possible if plasma taurine levels are directly related to intracellular taurine levels of stress-affected cells in sepsis.

Neutrophils play a major role in host defence after trauma and in sepsis. The aim of this study was therefore to analyse the relationship between taurine levels in plasma and in neutrophils using a ''one cell level'' technique. Furthermore, we also looked for a relationship between taurine and other amino acids, and for variables quantifying metabolic impairment and severity of sepsis in multiple trauma patients developing sepsis.

Methods

Thirty-two critically ill patients after multiple trauma who developed sepsis were retrospectively included into the study (Table 1). Patients were excluded when no informed consent was obtained from the patients' closest relatives, they were under 18 or over 65 years of age, Injury Severity Score (ISS) was <30 points, and patients had no consuming illness or gravidity.

Table 1. Demographic data of patients

	All patients (n = 32)	Survivors (n = 23)	Non-survivors (n = 9)
Age (yrs)	38.9 ± 13.3	38.5 ± 13.0	40.3 ± 14.3
Height (cm)	177 ± 9	177 ± 9	177 ± 10
Weight (kg)	82.9 ± 13.5	82.2 ± 14.7	85.0 ± 10.8
ISS (baseline)	43 ± 9	43 ± 9	44 ± 10
Catecholaminergic support (no. [%])	26 [81]	19 [63]	7 [77]
Focus of infection (no. [%])			
Respiratory tract	13 [40]	9 [30]	4 [44]
Intra-abdominal/Pelvis	7 [22]	5 [16]	2 [22]
Skin/Wound	4 [12]	3 [10]	1 [11]
Other	3 [9]	1 [3]	2 [22]
Sepsis onset (days [median, range])	5 (2–10)	4 (2–10)	5 (2–10)
Death (days [median, range])	15 (10–27)		15 (10–27)
ICU LOS (days [median, range])	23 (10–48)	23 (10–48)	
Energy Requirement (Indirect Calorimetry [Kcal/24 h])	2330 ± 725	2241 ± 662	2599 ± 914
Energy delivered (% of requirement)	102 ± 33	107 ± 35	90 ± 29
Protein delivered (% of requirement [1.0 g/kg BW])	117 ± 58	120 ± 58	108 ± 58

ISS, Injury Severity Score; *ICU LOS*, Length Of Stay in Intensive Care Unit; *BW*, body weight

Table 2. SOFA and metabolic variables in plasma for septic trauma patients (n = 32)

Variables	Post-trauma	Sepsis
SOFA	7.6 ± 4.0	8.2 ± 2.2
Glucose (mmol/l)	7.8 ± 1.2	8.3 ± 2.5
Lactate (mmol/l)	1.55 ± 0.50	1.56 ± 0.46
Urea (mmol/l)	11.8 ± 5.6	12.8 ± 6.8
Creatinine (μmol/l)	110 ± 40	110 ± 21
Glycerine (mmol/l)	0.70 ± 0.51	0.89 ± 0.58
Free fatty acids (mmol/l)	0.20 ± 0.20	0.31 ± 0.27
Ammonia (mmol/l)	34 ± 7	34 ± 7
CRP (mg/l)	125 ± 66	171 ± 84*

SOFA, Sequential Organ Failure Assessment; *CRP*, C-reactive protein; *$p < 0.05$

During the time course at the intensive care unit (ICU), all patients received a standard infusion- and transfusion-therapy, and antibiotics were given according to microbiological testing. All patients were mechanically ventilated and sedated with midazolam or propofol. Analgesia was induced with fentanyl.

The patients received enteral nutrition from day 1 in the ICU over a gastric tube. Enteral nutrition consisted of a standard isocaloric, polymeric diet (Fresubin® plus, Fresenius, Bad Homburg, Germany; 1000 kcal/L, 15% protein, 30% lipids, 55% carbohydrates). If energy requirements could not be covered enterally, a parenteral supplementation until target rate with standard products (Glucose 40%, Fresenius Kabi, Bad Homburg, Germany; Aminoplasmal® 10%, B.Braun, Melsungen, Germany; Intralipid® 20%, Fresenius Kabi, Bad Homburg, Germany) was performed. Of all amino acids delivered, part of branched chain amino acids reached 17%, acid amides (asparagine, glutamine) and acid amino acids (aspartate, glutamate) 25%.

For determination of the target rate, energy expenditure was measured daily by indirect calorimetry for 90 min between 08:00 and 12:00 am (Deltatrac II, Datex, Finland).

Within 24 hrs of arrival at the surgical ICU, initial blood samples for routine laboratory analyses were taken, and clinical data, including diagnostic and therapeutic interventions, drug and infusion therapy, SOFA (Sequential Organ Failure Assessment)-Score (Vincent et al., 1998), and cardiopulmonary monitoring data was recorded. Sepsis was assumed if the criteria proposed by the members of the American College of Chest Physicians/Society of Critical Care Medicine (1992) were fulfilled. The clinical course was recorded until either transfer to a general ward or death in the ICU.

Before the onset of sepsis 1–2 measurements per patient were performed and the results were averaged. This period lasted 5 ± 3 days. Thereafter the study was carried out until criteria for persistent sepsis were fully met, or until death in septic state occurred, i.e. 5 ± 3 days. In this period also 1–2 amino acid analyses, taken at 08:00 am, per patient were accomplished.

Amino acid determination in whole blood samples

The method to analyse intracellular amino acid content using the ''one cell level'' technique is different to other methods referring to other biological parameters such as intracellular water or intracellular protein or DNA content (Canepa et al., 1989; Metcoff, 1986). The technique of neutrophil separation used in this study is a further development of the methods described by Eggleton et al. (1989) which allows a very rapid and selective enrichment of neutrophil, preserving high cellular viability and integrity from small quantities of whole blood (Mühling et al., 1999). Hereby, 4 mL of the cooled and heparinised whole blood samples were overlaid into a previously prepared and precooled (4°C) Percoll® gradient (Pharmacia, Uppsala, Sweden), followed by several centrifugation steps at 350 g (Biofuge®, Heraeus, Hanau, Germany), lysing the erythrocytes, and resuspension in PBS buffer. Purity and viability of the neutrophil samples were verified subsequently by light microscopy (Zeiss, Oberkochen, Germany), discarding samples both with purity less than 96% and viability less than 96%. Immediately after withdrawal and preparation, the extracted and cooled neutrophil samples were frozen at −80°C before lyophilisation (CIT-2®, Heraeus, Germany). This allowed a metabolically preserving and non-chemically mediated neutrophil lysis, as well as a long stability during storage.

Amino acids in neutrophil and plasma were quantified using high-performance liquid chromatography (HPLC). Amino acids were determined (Mühling et al., 1999) according to the strict guidelines of the FDA validation workshops 2001 (Crystal City, VA) for ultra sensitive, comprehensive amino acid analysis.

Table 3a. Free taurine, acid amide, acid amino acid, and basic amino acid concentrations in plasma and in neutrophils for septic trauma patients

Amino acid	Plasma (μmol/l), n = 32			Neutrophil concentration (μmol/l), n = 32			Neutrophil content (10^{-16} mol/cell), n = 32		
	PV	Post-trauma	Sepsis	PV	Post-trauma	Sepsis	PV	Post-trauma	Sepsis
Taurine (Tau)	*114 ± 21*	54 ± 38$^{\#\#\#}$	58 ± 37$^{\#\#\#}$	*9207 ± 2929*	6909 ± 1249$^{\#\#\#}$	7150 ± 1678$^{\#\#}$	*41.8 ± 13.3*	34.36 ± 6.12$^{\#\#}$	31.75 ± 7.52$^{\#\#}$
Acid amides									
Asparagine (Asn)	*58 ± 11*	54 ± 25	46 ± 17$^{\#\#}$	*90 ± 46*	176 ± 129$^{\#\#\#}$	100 ± 71*	*0.41 ± 0.21*	0.88 ± 0.65$^{\#\#\#}$	0.44 ± 0.33*
Glutamine (Gln)	*536 ± 81*	486 ± 182	433 ± 124$^{\#\#\#}$	*667 ± 242*	979 ± 594$^{\#\#}$	728 ± 519*	*3.03 ± 1.10*	4.86 ± 2.84$^{\#\#}$	3.24 ± 2.36*
Acid amino acids									
Aspartate (Asp)	*12 ± 3*	6 ± 5$^{\#\#\#}$	5 ± 3$^{\#\#\#}$	*566 ± 383*	482 ± 345	306 ± 256$^{*,\#\#}$	*2.57 ± 1.74*	2.40 ± 1.71	1.37 ± 1.20$^{*,\#}$
Glutamate (Glu)	*31 ± 14*	69 ± 31$^{\#\#\#}$	65 ± 25$^{\#\#\#}$	*1284 ± 387*	1401 ± 748	1231 ± 582	*5.83 ± 1.76*	7.03 ± 3.85	5.46 ± 2.55*
Basic amino acids									
Ornithine (Orn)	*42 ± 19*	79 ± 36$^{\#\#\#}$	72 ± 28$^{\#\#\#}$	*99 ± 66*	197 ± 180$^{\#}$	122 ± 114*	*0.45 ± 0.30*	0.99 ± 0.92$^{\#\#}$	0.54 ± 0.50*
Lysine (Lys)	*191 ± 50*	155 ± 67$^{\#}$	129 ± 43$^{\#\#\#}$	*121 ± 68*	176 ± 190	90 ± 59	*0.55 ± 0.31*	0.88 ± 0.48$^{\#\#}$	0.40 ± 0.26*
Arginine (Arg)	*84 ± 13*	65 ± 29$^{\#\#}$	51 ± 20$^{*,\#\#\#}$	*101 ± 55*	121 ± 127	36 ± 28$^{*,\#\#}$	*0.46 ± 0.25*	0.61 ± 0.65	0.16 ± 0.13$^{*,\#}$
Citrulline (Cit)	*32 ± 9*	17 ± 6$^{\#\#\#}$	16 ± 8$^{\#\#\#}$	*33 ± 17*	24 ± 17	19 ± 13$^{\#\#}$	*0.15 ± 0.08*	0.12 ± 0.09	0.08 ± 0.06$^{*,\#}$
Histidine (His)	*88 ± 23*	55 ± 16	50 ± 17	*244 ± 132*	89 ± 61$^{\#\#\#}$	33 ± 34$^{*,\#\#\#}$	*1.11 ± 0.60*	0.44 ± 0.31$^{\#\#\#}$	0.15 ± 0.15$^{*,\#\#\#}$

Concentrations are given in μmol/l, content as 10^{-16} mol/cell (mean ± SD); *PV*, physiological values of healthy volunteers; neutrophil cell volumes decrease significantly from $596 \pm 186 \cdot 10^{-18}$ m^3 after multiple trauma to $483 \pm 132 \cdot 10^{-18}$ m^3 in sepsis (PV: $454 \pm 118 \cdot 10^{-18}$ m^3). $^{*}p < 0.05$ comparing post-trauma with sepsis; $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ comparing with PV

Table 3b. Free branched chain amino acid (BCAA), neutral amino acid, aromatic amino acid, and methionine concentrations in plasma and in neutrophils for septic trauma patients

Amino acid	Plasma (μmol/l), n = 32			Neutrophil concentration (μmol/l), n = 32			Neutrophil content (10^{-16} mol/cell), n = 32		
	PV	Post-trauma	Sepsis	PV	Post-trauma	Sepsis	PV	Post-trauma	Sepsis
BCAA									
Isoleucine (Ile)	*66 ± 15*	68 ± 30	74 ± 27	*102 ± 61*	101 ± 78	57 ± 53$^{*,\#}$	*0.46 ± 0.28*	0.50 ± 0.39	0.26 ± 0.24$^{*,\#}$
Leucine (Leu)	*127 ± 32*	127 ± 44	136 ± 49	*114 ± 51*	221 ± 175$^{\#\#}$	109 ± 100*	*0.52 ± 0.23*	1.10 ± 0.88$^{\#\#\#}$	0.49 ± 0.46*
Valine (Val)	*215 ± 41*	254 ± 74$^{\#}$	264 ± 86$^{\#\#}$	*143 ± 90*	198 ± 126	111 ± 71$^{*,\#\#\#}$	*0.65 ± 0.41*	0.99 ± 0.64$^{\#}$	0.50 ± 0.32*
Neutral amino acids									
Serine (Ser)	*121 ± 21*	85 ± 32$^{\#\#\#}$	70 ± 23$^{*,\#\#\#}$	*513 ± 200*	396 ± 226	293 ± 229$^{*,\#\#\#}$	*2.33 ± 0.91*	1.98 ± 1.13	1.30 ± 1.05$^{*,\#\#\#}$
Glycine (Gly)	*253 ± 42*	213 ± 64$^{\#\#}$	149 ± 44$^{*,\#\#\#}$	*709 ± 268*	624 ± 343	565 ± 277	*3.22 ± 1.22*	1.98 ± 0.41$^{\#\#\#}$	2.51 ± 1.23
Threonine (Thr)	*134 ± 36*	160 ± 87	116 ± 47*	*273 ± 129*	194 ± 107$^{\#}$	127 ± 99$^{*,\#\#\#}$	*1.24 ± 0.59*	0.97 ± 0.55	0.57 ± 0.46$^{*,\#\#\#}$
Alanine (Ala)	*357 ± 83*	350 ± 148	252 ± 137$^{*,\#\#}$	*412 ± 216*	677 ± 342$^{\#\#}$	506 ± 337*	*1.87 ± 0.98*	3.36 ± 1.66$^{\#\#\#}$	2.24 ± 1.48*
Aromatic amino acids									
Tyrosine (Tyr)	*56 ± 14*	83 ± 41$^{\#\#}$	70 ± 32	*133 ± 81*	132 ± 97	56 ± 44$^{*,\#\#\#}$	*0.73 ± 0.39*	0.66 ± 0.49	0.25 ± 0.20$^{*,\#}$
Tryptophane (Trp)	*65 ± 14*	46 ± 19$^{\#\#\#}$	36 ± 16$^{*,\#\#\#}$	*37 ± 20*	53 ± 48	32 ± 33*	*0.17 ± 0.09*	0.26 ± 0.24	0.14 ± 0.14*
Phanylalanine (Phe)	*69 ± 16*	97 ± 25$^{\#\#\#}$	96 ± 34$^{\#\#\#}$	*207 ± 129*	122 ± 64$^{\#\#\#}$	102 ± 60$^{\#\#\#}$	*0.94 ± 0.59*	0.60 ± 0.32$^{\#\#\#}$	0.45 ± 0.26$^{*,\#\#\#}$
Methionine (Met)	*23 ± 6*	35 ± 14$^{\#\#\#}$	29 ± 11	*40 ± 18*	90 ± 99$^{\#\#}$	39 ± 34*	*0.18 ± 0.08*	0.45 ± 0.50$^{\#\#}$	0.17 ± 0.15*
Total amino acids	*2674 ± 564*	2558 ± 1013	2217 ± 828$^{\#}$	*15095 ± 5588*	13362 ± 5345	11812 ± 4691$^{\#}$	*68.7 ± 25.4*	65.5 ± 24.8	52.5 ± 21.1$^{*,\#\#}$

Concentrations are given in μmol/l, content as 10^{-16} mol/cell (mean ± SD); *PV*, physiological values of healthy volunteers; neutrophil cell volumes decrease significantly from $596 \pm 186 \cdot 10^{-18}$ m^3 after multiple trauma to $483 \pm 132 \cdot 10^{-18}$ m^3 in sepsis (PV: $454 \pm 118 \cdot 10^{-18}$ m^3). $^{*}p < 0.05$ comparing post-trauma with sepsis; $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.001$ comparing with PV

Free intracellular amino acid content of a single neutrophil was obtained by dividing the result of the amino acid analysis with the number of neutrophils in this sample. Cell volume was determined using a lysing reaction method (COBAS®, Roche Diagnostics, Basel, Switzerland).

Amino acid reference ranges for healthy volunteers ($n = 29$, age 29 ± 6 years, height 177 ± 7 cm, weight 80 ± 10 kg) at our institute in a single neutrophil and in plasma are presented in Tables 3a, 3b. Cell volume was $454 \pm 118 \cdot 10^{-18}$ m^3.

The study has been approved by the hospital's ethics committee. Informed voluntary consent by the patients' next of kin was obtained.

Statistical analysis

Mean and standard deviation or median and range were calculated for all variables. Statistical analysis was performed by using one-factor ANOVA. Nonparametric data were analysed by Mann-Whitney U-test, otherwise Student's t-test was used. For nominal variables the Chi^2 test was utilised. Spearman's rank correlation was used to determine the relationship between plasma and intracellular amino acids. A $p < 0.05$ was considered as statistically significant.

Results

After multiple traumas taurine decreases significantly in plasma as well as within the neutrophil (Table 3a). This reduced level does not change in sepsis neither in plasma nor intracellular. No correlation of taurine in plasma and in the neutrophils can be observed, neither after multiple trauma nor in sepsis (Fig. 1).

A correspondent course shows no other amino acid (Tables 3a, 3b). In sepsis, a significant decrease in plasma as well as in the neutrophil is observed beneath taurine only in aspartate, serine, arginine, and citrulline (Tables 3a, 3b). Additionally, aspartate, arginine, citrulline, and serine also decrease significantly in plasma after trauma (Tables 3a, 3b), maintaining, however, normal levels in the neutrophil. Despite a reduction of taurine levels in the neutrophil after multiple trauma, total amino acid content does not change in comparison to levels in healthy volunteers (Table 3b). This is due to the fact that several amino acids rise within the cell (asparagine, glutamine, ornithine, lysine, leucine, valine, alanine, methionine) and beneath taurine only four amino acids decrease (histidine, glycine, threonine, phenylalanine) (Tables 3a, 3b). However in sepsis, total intracellular amino acid content

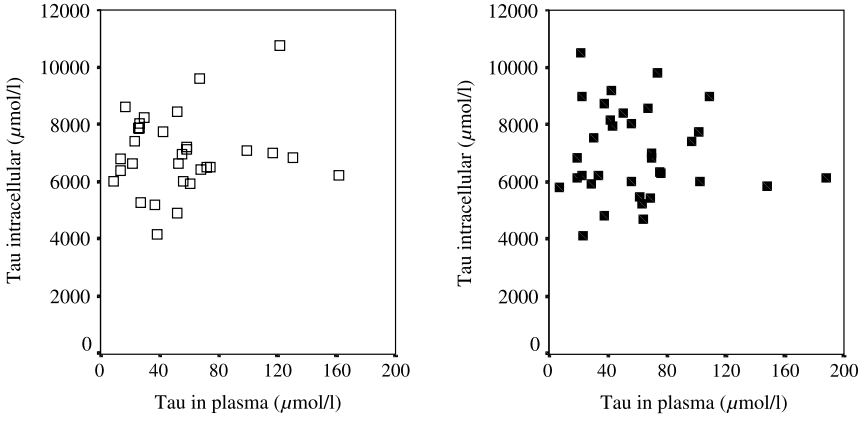

Fig. 1. Correlation of taurine (Tau) concentrations in plasma and in neutrophils after multiple trauma (open squares, $r = 0.119$, $b = 4.273$, $beta = 0.119$, $p = 0.524$) and in sepsis (full squares, $r = 0.151$, $b = -7.101$, $beta = -0.151$, $p = 0.386$)

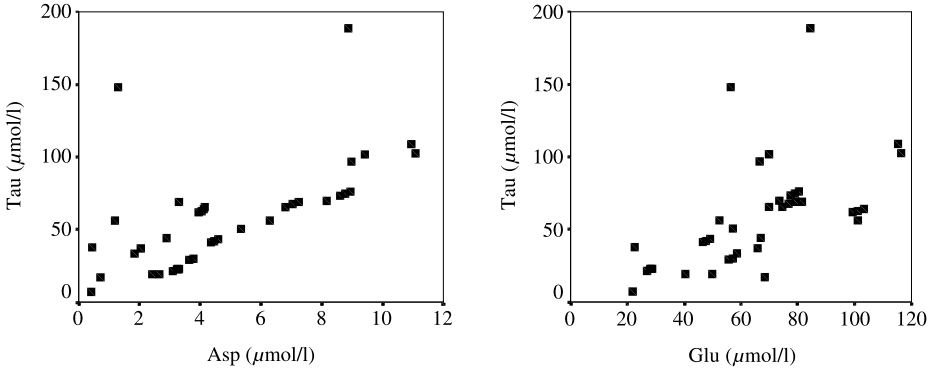

Fig. 2. Correlation of plasma taurine (Tau) with plasma aspartate (Asp) ($r = 0.617$, $b = 7.598$, $beta = 0.617$, $p = 0.000$), and with plasma glutamate (Glu) ($r = 0.576$, $b = 0.846$, $beta = 0.576$, $p = 0.000$) in sepsis

decreases significantly (Table 3b). No single amino acid is elevated. Ten out of 20 amino acids are within the normal range (Tables 3a, 3b). A correlation is only found in plasma between taurine and aspartate, and between taurine and glutamate during sepsis (Fig. 2).

SOFA as an indicator for the severity of sepsis shows a tendency to increase in sepsis (Table 2). Normally after multiple traumas, elevated SOFA score decreases as a sign of recovery. Metabolic variables such as glucose, lactate, and free fatty acids do not change when comparing trauma and sepsis (Table 2). However, C-reactive protein increases in sepsis (Table 2). No interdependency is observed between taurine plasma or intracellular levels and SOFA score or metabolic variables.

Discussion

For taurine, there is no correlation observed between plasma and neutrophil taurine levels neither after multiple trauma nor in sepsis. After trauma, taurine in plasma decreased significantly below the range of healthy individuals and did not recover in sepsis. Intracellular taurine concentrations also show a significant lower range during the ICU stay compared to a healthy state. However, lower individual levels in the neutrophil do not follow lower individual levels in plasma.

Intracellular taurine levels do not depend on a passive incorporation of extracellular taurine from plasma. Taurine uptake in cells is regulated in various ways. A high and a low affinity uptake as well as a diffusion system are described (Wersinger et al., 2001). Up- and down-regulation of taurine uptake is accompanied by an increase respectively decrease of taurine transporters (Kang et al., 2002; Shimizu et al., 2000; Shioda et al., 2002). Taurine uptake is stimulated by TNF-α (Kang et al., 2002), as a reaction to hypertonicity (Shimizu et al., 2000) with and without LPS (Romio et al., 2001), and in a taurine-deprived medium. In contrast, a taurine release is observed in a hypotonic medium (Schaffer et al., 2000; Scheller et al., 2000).

All these situations are observed after multiple trauma and in sepsis. After multiple trauma mediators and cytokines display an undulatory form of activation and compensatory counter-regulation culminating in sepsis (Oberholzer et al., 2000). Also, volume status may change resulting from volume loading dosage and diuresis or filtration.

Hydration state and volume of the neutrophil may vary in response to nutrient supply and stress. Such hydration changes act as an independent signal, which regulates cellular metabolism, and represent a mechanism for adaptation of cell function towards environmental changes (Häussinger et al., 1993). Taurine serves as an osmolyte to regulate and protect cells against osmotic stress (Schaffer et al., 2000; Scheller et al., 2000; Shimizu et al., 2000). Hereby, taurine is one of the most important organic osmolytes rarely interfering with the physico-chemical situations at cellular level. Therefore, intracellular taurine contents and concentrations may alter depending on cell volumes. The averaged cell volumes decrease over time from ICU admission after multiple trauma to sepsis.

As taurine plays a regulatory role within the cell, a prediction of the intracellular neutrophil taurine pool based on taurine plasma levels seems not entirely possible. This may be one of the reasons why no correlation between plasma and intracellular taurine levels is observed.

Relationships of plasma taurine with other plasma components are described in experimental and clinical settings (Becquet et al., 1993; Chiarla et al., 2000; Griffith, 1986). Chiarla et al. (2000) described the relationships of taurine and aspartate and taurine and glutamate in human sepsis. However, recognition of these effects seems to be limited by a high inter-patient variability (Chiarla et al., 2000). Therefore, Chiarla et al. performed repeated measurements in a single patient, monitoring only a small number of patients.

Furthermore, we were able to demonstrate in plasma an association between taurine and aspartate, and taurine and glutamate in human sepsis in a larger number of patients. These relationships are explained by osmoregulation as the underlying mechanism (Schaffer et al., 1995). A metabolic relationship is suggested by the metabolic balance existing between glutamate and aspartate, and by the fact that glutamate may serve as a substrate for the taurine synthesis (Hayes, 1988; Skeie et al., 1990). Within the neutrophil, taurine, glutamate, and aspartate account for 73% of the free intracellular amino acids pool (taurine alone for 60%). Co-variations in their plasma levels are interpreted by shifts in the intracellular-extracellular amino acid pools to maintain osmotic balance. However, intracellular taurine has in contrast to other amino acids some unique properties. For example, taurine is not incorporated into proteins. Moreover, taurine is dependent on the intracellular amino acid transport system β and not in other transport systems such as system A, which are major determinants of changes in the plasma amino acids pool in sepsis.

Therefore, at the cellular level of the neutrophil, we cannot find an interdependency of changes in taurine, aspartate, and glutamate, regarding either concentrations or contents. Aspartate and glutamate are both involved in

energy delivering pathways highly necessary in the neutrophil after trauma and in sepsis. This is reflected by the fact that intracellular levels of glutamate and aspartate are maintained after trauma, and only aspartate declines in sepsis, possibly as a form of exhaustion.

A role in host-defence is suggested by the maintaining of high concentrations in neutrophils and lymphocytes. Neutrophils are important components of the host defence system, which protects human organism from invading bacteria. Their importance becomes particularly apparent when their numbers are reduced or their functions become impaired. However, considering the outcome of sepsis in the polytraumatised patient, the role of taurine cannot be focused on the neutrophils alone. A dependency of plasma and neutrophil taurine to severity of sepsis as measured with the SOFA score and to metabolic variables seems not possible for the multifactorial pathophysiology of sepsis.

We did not differentiate between patients with sepsis and those with septic shock. Characterisation of pathophysiological effects, such as sepsis on taurine and amino acids in experimental settings, is clearer than in human critical illness, because clinical conditions may change in short episodes and more than one stimulus has an effect to the patient. To compare results, it is necessary to compare the setting (experimental, clinical) and the studied patient population. For example, in septic medical patients Druml et al. (2001) found with the exception of lysine, methionine, glutamate, ornithine, phenylalanine, and tyrosine all other 11 measured amino acids in the plasma lowered. In our investigation, only 5 out of these 11 lowered amino acids have declined in plasma below the normal range. Komarov et al. (1998), who investigated plasma free amino acids in a murine model of septic shock, found out of Druml's six unchanged amino acids only glutamate and phenylalanine not decreased, but four other amino acids unchanged. Patient age and morbidity also influence plasma amino acid concentrations. Druml et al. patients' aged 53.6 ± 4.3 years with an average weight of 66.3 ± 4.8 (Druml et al., 2001), whereas in our investigation patients' age is 38.9 ± 13.3 years with an average weight of 82.9 ± 13.5. The trauma population in our study represents a relatively homogenous patient cohort of young, healthy individuals in a good nutritional state (body mass index 26.5) with few comorbidities. This is reflected by a decline of total amino acid plasma concentration in sepsis in Druml et al. study (Druml et al., 2001) by 35% and in ours by only 18%.

In conclusion, no correlation between plasma and neutrophil taurine levels in septic trauma patients has been found. In sepsis a dependency of taurine, aspartate, and glutamate in plasma exists. The clinical meaning of this dependency remains unclear. In the neutrophil no association of taurine to other amino acids, to severity of sepsis, and to metabolic plasma variables has been observed.

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