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ORIGINAL ARTICLE

The relationship between plasma and red cell B-vitamin concentrations in critically-ill patients

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Summary
Background and aims: Low vitamin B-complex status has been associated with poorer outcome in critically-ill patients. However, these findings have been based on indirect methods. Using direct methods for assessing vitamin status, we examined the effect of B-complex vitamin supplementation by measuring plasma and red blood cell B1, B2 and B6-vitamin concentrations in critically-ill patients.
Methods: Thiamine diphosphate (TDP), flavin adenine dinucleotide (FAD) and pyridoxal phosphate (PLP) concentrations were measured in plasma and red cells of normal subjects ($n = 49$) and ITU patients ($n = 41$).
Results: Compared with the normal subjects, critically-ill patients had higher C-reactive protein and lower albumin concentrations ($P < 0.001$). Also, plasma FAD and PLP were lower ($P < 0.001$) and red cell concentrations of both were higher ($P < 0.01$) in critically-ill patients. Critically-ill patients were grouped according to whether ($n = 23$) or not ($n = 18$) they had been supplemented with B-complex vitamins. Compared with non-supplemented group, the supplemented group had significantly higher red cell TDP and PLP concentrations ($P < 0.01$). Plasma FAD and PLP concentrations did not differ significantly between the groups.
Conclusions: The results of the present study suggest that direct measurements of red cell FAD and PLP are more responsive to supplementation than plasma measurements in the critically-ill patient.

Introduction

It has been recognised for some time that vitamin B deficiencies are associated with complications and

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poor survival in patients with critical illness. For example, thiamine (vitamin B1) deficiency may lead to Wernicke–Korsakoff syndrome[1] and compromised immune and antioxidant status has been observed after B2 and B6 vitamin deficiencies.[2] Also, Cruickshank and coworkers[3] reported poorer outcome in critically-ill patients with whole blood thiamine status below normal values. Whole blood riboflavin status (vitamin B2) has also been found to be lower in critically-ill patients who died in intensive care unit (ITU) compared with patients who survived.[4] Although these observations were made using indirect functional assays, usually functional tests that are prone to error, critically-ill patients in some centres are routinely supplemented with B-complex vitamins.

It is now generally accepted that, rather than functional assays, laboratory measurement of circulating B vitamins are more reliable for assessing status. However, it has become clear that plasma concentrations of many vitamins are transiently decreased as part of the systemic inflammatory response and therefore such concentrations may not reflect tissue levels.[5,6] Indeed, recent work has highlighted the discrepancy between plasma and red cell vitamin PLP concentrations in patients with acute and chronic inflammatory diseases.[7,8] The aim of the present study was to examine the relationship between plasma and red cell FAD (vitamin B2) and PLP (vitamin B6) concentrations in critically-ill patients with and without B-complex vitamin supplementation.

Materials and methods

Patients and study design

A cross-sectional study of patients in ITU who had respiratory failure requiring ventilatory support, were $\geqslant$18 years old, and who had evidence of the systemic inflammatory response syndrome as per Bone's criteria,[9] was under taken. Patients received B-complex vitamin supplementation if they were considered malnourished or had a history of excessive alcohol intake.

Healthy (non-smoking, non-supplemented) subjects were also studied as a control group.

Venous blood samples (lithium heparin/EDTA) were withdrawn for the analysis of analysis of plasma and/ or red cell vitamins B1, B2, B6 and C-reactive protein and albumin. In the critically-ill patients this was at various times during the ITU stay (Table 1). APACHE II, predicted mortality and B-complex vitamin supplementation were recorded. Enteral feeding was usually instituted on the second day in ITU.

B-complex vitamin supplementation was recorded from the drug cardex and given as Pabrinex (Link Pharmaceuticals Ltd., West Sussex, UK) one dose of which contains 500 mg ascorbic acid, 160 mg nicotinamide, 50 mg pyridoxine hydrochloride, 4 mg riboflavin, 250 mg thiamine hydrochloride. In those patients who received vitamin B supplementation a single dose of pabrinex was given on the morning of day 1 and daily to day 7 and

Table 1 Characteristics and B complex vitamins of normal subjects and critically ill patients.

	Normal subjects	Critically-ill patients		ANOVA, *P*-value
	No supplementation ($n = 49$)	No supplementation ($n = 18$)	Supplementation ($n = 23$)	
Age (yr)	57 (35–72)	65 (23–85)	60 (22–82)	0.697
Sex (M/F)	26/23	10/8	14/9	0.824
Apache II		24 (13–38)	25 (10–42)	0.298
Predicted mortality (%)		38.6 (5.8–78.9)	57.4 (5.6–93.9)	0.028
Day of sampling (Day 0/1/2/3/4/5/$\geqslant$6)		11/2/1/1/1/0/2	0/3/4/2/2/2/10	0.002
C-reactive protein (mg/l)	$<$10 ($<$10–$<$10)	140 (20–290)	134 (16–255)	$<$0.001
Albumin (g/l)	42 (37–49)	22 (13–33)	25 (10–31)	$<$0.001
Red cell haemoglobin (g/l)	261 (231–324)	269 (240–310)	270 (230–310)	0.961
Red cell TDP (ng/gHb)	437 (294–647)	600 (320–1252)	906 (390–2420)	$<$0.001
Plasma FAD (nmol/l)	94 (63–159)	38 (22–76)	44 (16–74)	$<$0.001
Red cell FAD (nmol/gHb)	2.1 (1.10–3.70)	2.6 (1.3–4.7)	2.8 (0.9–4.6)	0.010
Plasma FAD/red cell FAD	45.9 (26.9–80.0)	15.4 (4.9–39.2)	15.7 (8.6–56.7)	$<$0.001
Plasma PLP (nmol/l)	43 (26–154)	13 (3–63)	20 (2–121)	$<$0.001
Red cell PLP (pmol/gHb)	371 (278–774)	363 (209–883)	1000 (267–8491)	$<$0.001
Plasma PLP/red cell PLP	0.121 (0.082–0.199)	0.035 0.009–0.165)	0.020 (0.002–0.157)	$<$0.001

Median (range).