Thiamin and Riboflavin Status of Medical Inpatients†

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Abstract

Thiamin status was assessed by erythrocyte transketolase activity (ETKA) and thiamin pyrophosphate effect (TPPE) and riboflavin status by erythrocyte glutathione reductase activity (EGRA) and activity coefficient (AC) in 165 medical inpatients in Ramathibodi Hospital. Based on TPPE >15 per cent, 9 per cent of the medical inpatients had thiamin depletion. Most of them were patients with renal, cardiovascular, hematological and infectious diseases. Based on AC ≥ 1.2, 17 per cent of these inpatients had riboflavin depletion. Most of them were patients with pulmonary, cardiovascular and hematological diseases. Only one patient with pulmonary disease had both thiamin and riboflavin depletion. The proportion of thiamin depletion (2/37) in subjects with thiamin supplementation (mean 32.4, median 6, mode 2 md/d) tended to be less than those without (9/98). But, subjects with riboflavin supplementation (mean 3.3, median 4, mode 1 md/d) had the proportion of riboflavin depletion (0/31) significantly (Z-test, p< 0.005) lower than without supplementation (23/104). The data suggested that although the usual dose of vitamin supplementation in medical inpatients is beneficial thiamin depletion can still be present in catabolic patients.

Malnourished patients are known to have a higher risk of developing medical complications, a prolonged hospital stay and a higher mortality rate(1-6). Clinical studies have shown that malnutrition is a more important problem than had been considered earlier. About 30-50 per cent of patients in the U.S.A. and UK have evidence of protein and calorie malnutrition(1-4). In Thailand, Tanphaichitr et al (1980) showed that 73 per cent of adult hospitalized medical patients and 79 per

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cent of adult surgical inpatients in Ramathibodi Hospital had protein-energy malnutrition (PEM) according to weight-height parameters. Besides, anemia and vitamin deficiencies were also present in some patients(5,6). Chuntrasakul et al (1989) reported that 33 per cent of hospital inpatients in Siriraj Hospital were PEM by weight-height(7). The information on vitamin and mineral status was not available. The aim of this study was to determine thiamin and riboflavin status in medical inpatients in Ramathibodi Hospital and to monitor vitamin prescriptions in these patients.

SUBJECTS AND METHOD

Subjects

From November 1994 to February 1995, a cross-sectional study was carried out in 165 patients (78 women and 87 men) admitted to the medical wards of Ramathibodi Hospital. Physical examination, anthropometric assessments, dietary record, prescription of vitamin and mineral supplements and doses were investigated by the nutritional support team. The mean (±SEM) ages were 53.7 ± 2.0 years in males and 51.6 ± 2.1 years in females, mean body mass indices (BMI) were 20.4 ± 0.4 and 21.6 ± 1.2 kg/m^2, respectively.

Biochemical assessment

Venous blood was obtained from each patient after 12 to 14 hour fast on the next day after the ward round. The sample was centrifuged and frozen at -40°C until analysis. Thiamin status was assessed by using the erythrocyte transketolase activity (ETKA) and thiamin pyrophosphate effect (TPPE)(8). Values higher than 15 per cent for TPPE were considered as thiamin depletion(9). Riboflavin status was assessed by using the erythrocyte glutathione reductase activity (EGRA) and activity coefficient (AC). Equal or greater value of AC than 1.2 indicated riboflavin depletion(10).

Statistical analysis

The chi-square test of association and Z-test for proportion test were used(11).

RESULTS

One hundred and seventy-six patients were studied. Their age and sex distribution with disease categories are shown in Table 1. Forty-one per cent of patients were 60 years of age or over.

Prevalence of thiamin and riboflavin depletion in medical inpatients by diseases and age-groups is shown in Table 2. Nine per cent of the total patients had thiamin depletion, determined by TPPE >15 per cent and 17 per cent of them had riboflavin depletion, determined by AC ≥1.2. Detail of vitamin supplementation in various diseases is shown in Table 3 (including preparation). Table 4 shows the relationship between thiamin status and thiamin supplementation. The data shows no asso-

Table 1. Age group of patients by sex and disease categories.

	No. in age-group (%)			
	<40 y	40-59 y	≥60 y	Total
Sex				
Male	22	23	42	87
Female	24	28	26	78
Total	46 (28)	51 (31)	68 (41)	165
Disease categories				
Pulmonary	1	4	9	14
Renal	4	7	4	15
Infectious	11	8	15	34
Malignancy		5	6	11
Neurological	4	3	5	12
Cardiovascular	7	6	12	25
Psychiatric	3	1		4
Metabolic and endocrine	3	4	3	10
Autoimmune	1	4		5
GI and hepatic	1	4	10	15
Hematological	11	5	4	20

Table 2. Frequency of thiamin and riboflavin depletion in medical inpatients by diseases and age-groups.

		TPPE > 15%*			AC ≥ 1.2 **		
Disease / age-group	No	<40 y (n=40)	40-59 y (n=42)	60-80 y (n=59)	<40 y (n=40)	40-59 y (n=42)	60-80 y (n=59)
Pulmonary	12	-	-	1	1	-	3
Renal	14	-	1	1	-	-	1
Infectious	29	-	1	2	1	1	-
Malignancy	9	-	-	1	-	-	-
Neurological	8	-	-	-	1	-	1
Cardiovascular	22	-	-	2	2	1	1
Psychiatric	4	-	-	-	1	-	-
Metabolic and endocrine	7	-	1	-	-	1	-
Autoimmune	4	1	-	-	-	-	-
GI and hepatic	13	-	-	-	-	1	2
Hematological	19	1	1	-	4	1	1
Total	141	2	4	7	10	5	9

* Total no. of thiamin depletion = 13 (9.2 %)
** Total no. of riboflavin depletion = 24 (17 %)

Table 4. Distribution of thiamin status of patients in relation to thiamin supplementation*

	Thiamin supplementation		
Thiamin status	No suppl	Suppl	Total
Normal	89	35	124
Depletion	9	2	11
Total	98	37	135

* Thiamin status and thiamin supplementation are not association ($\chi 2$ test, $p > 0.05$)

Table 5. Distribution of riboflavin status of patients in relation to riboflavin supplementation*

	Riboflavin supplementation		
Riboflavin status	No suppl	Suppl	Total
Normal	81	31	112
Depletion	23	0	23
Total	104	31	135

* Riboflavin status and riboflavin supplementation are associated ($\chi 2$ test, $p < 0.005$)

ciation between thiamin status and thiamin supplementation ($\chi 2$ test, $p > 0.05$). Table 5 shows the relationship between riboflavin status and riboflavin supplementation. Statistical analysis revealed an association between riboflavin status and riboflavin supplementation ($\chi 2$ test, $p < 0.005$). The proportion of riboflavin depletion (0/31) with riboflavin supplementation was significantly lower than the proportion of riboflavin depletion (23/104) without riboflavin supplementation (Z-test, $p < 0.005$).

DISCUSSION

The nutritional status of patients in medical wards is quite often neglected. Patients in a hypercatabolic state will require more nutrients than the normal recommended daily allowance. Clinically, unless it is severe, malnutrition is frequently unrecognized or ignored. Vitamin deficiency should be considered as a progressive process that has begun long before the apparition of overt clinical manifestations, which are preceded by a depletion of body stores and biochemical alterations of cell metabolism[12].

Thiamin status

In the present study, thiamin depletion was noted in 9 per cent (13/141) of medical inpatients in Ramathibodi Hospital and occurrence increased with age (15% in <40, 30% in 40-59

Table 3. Types of vitamin supplementation* by disease categories.

Disease	No suppl	MUL-TAB bid	B-complex bid	B1-6-12 bid	Z-BEC od	Centrum od	FBC tid	Vitamin K 10 mg IV.	Vitaral bid	Folic acid bid	Total
Pulmonary	10	1	-	-	-	-	-	1	-	-	12
Renal	11	1	-	-	-	-	1	1	-	-	14
Infectious	20	3	2	1	1	-	3	-	1	1	32
Malignancy	4	3	2	-	-	-	1	1	-	-	11
Neurological	9	1	-	1	-	-	1	-	-	-	12
Cardiovascular	16	2	1	1	-	-	2	2	-	-	24
Psychiatric	2	-	-	1	-	-	-	1	-	-	4
Metabolic & endocrine	5	2	2	-	-	1	-	-	-	-	10
Autoimmune	2	1	1	-	-	-	-	-	-	-	4
GI and hepatic	6	2	1	2	-	-	-	4	-	-	15
Hematological	15	-	-	-	-	-	1	3	-	1	20
Total	100	16	9	6	1	1	9	13	1	2	158

*MUL-TAB: vit A 2500 iu, vit D 300 iu, vit B_1 mononitrate 1 mg, vit B_2 0.5 mg, vit C 15 mg, nicotinamide 7.5 mg;
B-complex: vit B_1 mononitrate 5 mg, vit B_2 2 mg, vit B_6 2 mg, nicotinamide 20 mg;
B1-6-12: thiamine mononitrate 100 mg, pyridoxine hydrochloride 5 mg, cyanocobalamin 65 mcg;
Z-BEC: vit B_1 15 mg, vit B_2 10.2 mg, vit B_6 10 mg, vit B_{12} 6 mcg, vit C 600 mg, vit E 45 iu, niacin 100 mg, pantothenic acid 25 mg, Zn 22.5 mg;
Centrum: vit A 5000 iu, vit B_1 2.25 mg, vit B_2 2.6 mg, vit B_6 3 mg, vit B_{12} 9 mcg, vit C 90 mg, vit D 400 iu, vit E 30 iu, folic acid 400 mcg, niacinamide 20 mg, biotin 45 mcg, cal pantothenate 10 mg, cal 162 mg, phosphorus 125 mg, iodine 150 mcg, iron 27 mg, mag 100 mg, copper 3 mg, manganese 7.5 mg, pot 7.5 mg, Zn 22.5 mg;
FBC: ferrous fumarate 200 mg, vit B_1 2 mg, vit B_2 2 mg, vit B_{12} 5 mcg, niacin 10 mg, vit C 20 mg, folic acid 100 mcg, cal phosphate 100 mg;
Vitamin K: Konakion 1 mg;
Vitaral: vit A 4000 iu, vit D 400 iu, vit B_1 1 mg, vit B_2 2 mg, vit B_6 0.125 mg, vit B_{12} 0.001 mg, vit C 30 mg, vit E 0.25 mg, folic acid 0.2 mg, niacinamide 10 mg, rutocide 5 mg, dehydrocholic acid 5 mg, cal phosphate 200 mg, iodide 0.065 mcg, iron 16.75 mg, mag 1.25 mg, copper 0.0025 mg, manganese 1.35 mg, pot 0.275 mg, zinc 0.075 mg;, cobolt 0.0235 mg, molybdate 0.005 mg,
Folic acid: folic acid 5 mg

and 54% in 60-80 years old). Most of them were patients suffering from renal, infectious, cardiovascular and hematological problems. Woo J et al also reported that thiamin status was poorer in the older age group (> 40 yrs) of Chinese medical inpatients. Elderly patients, and those with infections, malignancies, heart failure, and chronic obstructive airways disease had poorer nutritional status(13). Disease can affect thiamin status by the following ways:- 1) decreasing the intake; 2) preventing normal absorption: individuals at greater risk of deficiency such as patients with cancer; 3) interfering with utilization: this is encountered in diseases associated with liver dysfunction; 4) increasing requirements,such as fever, infection or conditions with diuresis in which excretion is increased(14).

Riboflavin status

In this study, we found that 17 per cent of medical inpatients in Ramathibodi Hospital had riboflavin depletion. Most of them were patients with pulmonary, cardiovascular and hematological diseases. Only one patient with pulmonary disease had both thiamin and riboflavin depletion. Many diseases have profound effect upon riboflavin metabolism and physiology. Riboflavin absorption is decreased in hyperthyroidism and increased in hypothyroidism(15). In one investigation, reduced EGRA could be corrected with riboflavin administration even in those who shortly thereafter succumbed to liver failure(16). Chronic stress may lead to riboflavin deficiency, especially if the dietary intake of the vitamin is marginal(17). Komindr et al reported that inadequate thiamin, riboflavin, ascorbic acid and α-tocopherol status were presented in 4-30 per cent in chronic hemodialysis (HD) patients, and should receive vitamin supplements except vitamin A(18). Descombes E et al also reported that the α-ETK (the ratio of enzyme activity after/before vitamin addition) was insufficient in 5 per cent and marginal in 16 per cent of HD patients and thiamin supplementation rapidly normalized the α-ETK values in almost all patients(19). A supplement of 200 to 300 mg/wk of thiamin hydrochloride (30-45 mg/d) restored ETK activity to satisfactory levels in most patients. Pfitzenmeyer et al reported that 12 per cent of elderly hospital inpatients with cardiac failure was thiamin deficient and vitamin treatment (7 days of 200 mg thiamin/d) permitted a significant improvement in thiamin status(20).

Our study revealed that only 37 per cent (58/158) had vitamin prescription with various types (Table 3). No systematic supplement seems to be indicated for vitamins and minerals in Ramathibodi Hospital. The vitamin status in an individual patient depends on several different interacting factors including sex, age, actual vitamin intake and severity of disease. It should be noted that subjects with thiamin supplementation (mean 32.4, median 6, mode 2 mg/d) had the proportion of thiamin depletion (2/37) less than those without (9/98). There were two subjects who continued to have thiamin depletion while on supplementation (Table 4). One of them was a 60 year-old patient suffering from cancer with spine metastatis and post laminectomy receiving B-complex (10 mg thiamin/d) and the other one was a 58 year-old patient suffering from cancer with chronic duodenal ulcer and strongyloidiasis receiving MULTAB (2 mg thiamin/d). Bozzetti et al measured resting metabolic expenditure in 65 cancer patients and found it to be elevated in 60 per cent of these patients(21). Lundholm et al concluded that high glucose turnover may account for over 40 per cent of the increased oxygen consumption seen in cancer cachexia(22). So thiamin intake should be increased in cancer patients because thiamin is essential for the metabolism of carbohydrates and branched-chain amino acids (0.5 mg/1000 kcal). Ideally, vitamin prescription should be based on individual monitoring. But, subjects with riboflavin supplementation (mean 3.3, median 4, mode 1 mg/d) had a proportion of riboflavin depletion (0/31) significantly lower than without supplementation (23/104). The requirement levels for riboflavin, in contrast to those for thiamin, are not raised when energy utilization is increased. The prescription of 1-10 mg/d of riboflavin was sufficient in these patients. The data suggested that vitamin supplementation in medical inpatients tend to be more beneficial to patients than without supplementation. Unfortunately, since this study was a cross-sectional survey we did not assess the pre and post treatment status of vitamins.

In conclusion, 9 and 17 per cent of 165 medical inpatients in Ramathibodi Hospital had thiamin and riboflavin depletion, respectively. Only one patient with pulmonary disease had both thiamin and riboflavin depletion. Subjects who had received thiamin supplementation suffered from a lower rate of thiamin depletion than those who had not. In addition, subjects with riboflavin supplementation also had a lower rate of riboflavin depletion than those without supplementation ($p < 0.005$). The data suggested that vitamin supplementation in medical inpatients tend to be more beneficial to patients than without supplementation. However, thiamin depletion can still be present in catabolic patients.

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ภาวะโภชนาการของวิตามินบีหนึ่งและบีสองในผู้ป่วยในของหอผู้ป่วยทางอายุรกรรม†

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ได้ประเมินภาวะโภชนาการของวิตามินบีหนึ่งและบีสองในผู้ป่วยในของหอผู้ป่วยทางอายุรกรรมในโรงพยาบาลรามาธิบดีจำนวน 165 คน ประเมินภาวะโภชนาการของวิตามินบีหนึ่งโดยการวัด erythrocyte transketolase activity (ETKA) และ thiamin pyrophosphate effect (TPPE) ส่วนภาวะโภชนาการของวิตามินบีสองประเมินโดยการวัด erythrocyte glutathione reductase activity (EGRA) และ activity coefficient (AC) เมื่อใช้ค่า TPPE >15% เป็นเกณฑ์ตัดสิน พบว่าร้อยละ 9 ของผู้ป่วยในของหอผู้ป่วยทางอายุรกรรมมีภาวะพร่องของวิตามินบีหนึ่ง ส่วนใหญ่ของผู้ป่วยที่ขาดวิตามินบีหนึ่งเป็นโรคไต โรคหัวใจ โรคโลหิตและโรคติดเชื้อ เมื่อใช้ค่า AC $\geq$ 1.2 เป็นเกณฑ์ตัดสิน พบว่าร้อยละ 17 ของผู้ป่วยในมีภาวะพร่องของวิตามินบีสอง ส่วนใหญ่ของผู้ป่วยที่ขาดวิตามินบีสองเป็นโรคปอด โรคหัวใจและโรคโลหิต มีผู้ป่วยเพียงคนเดียวซึ่งเป็นโรคปอดที่ขาดทั้งวิตามินบีหนึ่งและบีสอง จากการสำรวจพบว่าผู้ป่วยในกลุ่มที่เสริมวิตามินบีหนึ่ง (mean 32.4, median 6, mode 2 md/d) มีสัดส่วนของการพร่องของวิตามินบีหนึ่ง (2/37) ต่ำกว่ากลุ่มที่ไม่ได้เสริม (9/98) แต่ผู้ป่วยในกลุ่มที่เสริมวิตามินบีสอง (mean 3.3, median 4, mode 1 md/d) มีสัดส่วนของการพร่องของวิตามินบีสอง (0/31) ต่ำกว่ากลุ่มที่ไม่ได้เสริม (23/104) อย่างมีนัยสำคัญทางสถิติ (Z-test, $p < 0.005$) ผลการศึกษาแสดงให้เห็นว่า แม้ว่าการเสริมวิตามินในปริมาณที่ใช้กันทั่วไปจะมีประโยชน์ต่อผู้ป่วยใน แต่ยังสามารถพบภาวะพร่องของวิตามินบีหนึ่งในผู้ป่วยที่มี catabolic state

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