Original Article

Prevalence of thiamin and riboflavin deficiency among the elderly in Taiwan

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The purpose of this study was to perform biochemical assessments of the nutritional status of thiamin and riboflavin in the 2379 elderly persons (1213 males, 1166 females) participating in the Elderly Nutrition and Health Survey in Taiwan (1999-2000) (Elderly NAHSIT). Through analysis of the data we aimed to investigate possible factors related to the prevalence of vitamin deficiency. Activity coefficients of erythrocyte transketolase and glutathione reductase (ETKAC and EGRAC) were the chosen biochemical indicators for thiamin and riboflavin status. The results showed that 14.7% of men and 11.9% of women were marginally thiamin deficient, and 16.5% of men and 14% of women were thiamin deficient. The prevalence rates of marginal riboflavin deficiency were 25.7% for males and 20.1% for females, and the deficiency rates were 6.6% for elderly males and 4.1% for elderly females. Although the average dietary thiamin and riboflavin intakes reached 146% - 164% of Taiwan RDAs, the percentage of senior citizens whose thiamin or riboflavin dietary intakes were less than EARs (equivalent to 83.3% of RDAs) was around 30% for males and 40% for females. Some contributing factors to the significant prevalence of thiamin and riboflavin deficiencies are discussed in this article.

Key Words: thiamin status, riboflavin status, elderly, nutritional assessment, Taiwan, Elderly Nutrition and Health Survey in Taiwan (1999-2000)

Introduction

Thiamin and riboflavin are important coenzymes in fuel metabolism. Thiamin, in the coenzyme form of thiamin pyrophosphate (TPP), participates in the oxidative decarboxylation of α-ketoacids and the transketolation between hexoses and phosphopentose in the hexose monophosphate shunt.[1,2] Because of these biochemical functions, thiamin assists in the metabolism of carbohydrate and branched-chain amino acids as well as in the generation of ribose required for nucleic acid synthesis and NADPH required for fatty acid synthesis.[1,2] In addition, thiamin may also play a significant role in neurotransmitter functions and nerve conduction.[2] Riboflavin, in the coenzyme forms of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), catalyzes numerous oxidation-reduction reactions in intermediary metabolism.[3,4] Riboflavin also functions in the metabolism of drugs, steroids, and lipids.[3,4]

Erythrocyte transketolase (ETK, EC 2.2.1.1) and erythrocyte glutathione reductase (EGR, EC 1.6.4.2) are the TPP and FAD dependent enzymes in red blood cells respectively. Deficiency of thiamin or riboflavin results in desaturation of the respective cofactors of the two dependent enzymes. Determining the activity coefficient by measuring the stimulatory effect of *in vitro* addition of TPP or FAD to erythrocyte specimens allows the assessment of the long-term biochemical status of thiamin and riboflavin.[5,6]

Among the previous nationwide nutritional surveys, the Nutrition and Health Survey in Taiwan 1993-1996 (NAHSIT 1993-1996) was the first to use biochemical indices such as ETKAC and EGRAC together with dietary assessment and anthropometric measurements to assess the nutritional status of thiamin and riboflavin for Taiwanese aged 4 years and above.[7,8]

The NAHSIT 1993-1996 surveyed only 213 male and 194 female elderly people. The results of the survey in regards to the elderly (≥65 yrs) showed that the marginal and deficient rates of thiamin for males were 19.9% and 10.9%, and the rates for females were 9.8% and 10%, respectively.[7] The status of riboflavin was markedly worse with marginal and deficient rates of 35.6% and 43.7% for elderly men, and rates of 38.7% and 33.4% for elderly elderly women, respectively.[8] In order to continue to monitor the nutritional status of Taiwanese citizens with a

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particular emphasis on the elderly, which is a rapidly increasing population, the Elderly Nutrition and Health Survey in Taiwan (1999-2000) (Elderly NAHSIT) was carried out in 1999-2000. The purpose of this article is to report the results of thiamin and riboflavin status of Taiwanese seniors found in this most recent survey and to discuss possible contributing factors to the current situation.

Materials and methods

Study design

This survey adopted a multi-staged, stratified, clustered probability sampling scheme. The rationale and details of the study design and sampling procedures have been described in a separated article by Pan *et al*.,[9] in this issue. Taiwanese residents of 65 years old and over were the target population.

Blood sample preparation

Fasting venous blood samples were collected into heparinized vacutainers (Becton Division). Plasma was immediately separated in the field by centrifugation at 4˚C. After removal of plasma samples, packed erythrocytes were removed from the bottom of the centrifuge tubes and transferred to individual 2.0ml polypropylene cyrovials which were immersed into liquid nitrogen immediately. The erythrocyte specimens were kept and shipped on dry ice within 24 hours and then frozen at -80°C until analysis. To monitor the reproducibility of laboratory analyses, 5% split samples were prepared and blind-coded in the field as well. A total of 2,379 erythrocyte specimens (1,213 for men, 1,166 for women) were analyzed.

ETKAC and EGRAC analysis

ETKAC and EGRAC were the biochemical indices selected to evaluate the long term nutritional status of thiamin and riboflavin. The activity coefficient was determined by a ratio of respective enzyme activity stimulated with an added cofactor (TPP or FAD) to that without an added cofactor. The protocol of Mount *et al.,*[10] was employed to determine the ETKAC and EGRAC, and the semiautomatic analytical procedures were standardized to conduct the analyses on Cobas Fara II (Roche). The cut-off points for judging thiamin status were an ETKAC <1.15 for normal thiamin status, 1.15 ≤ ETKAC <1.20 for marginal deficient thiamin status, and ETKAC ≥1.20 for thiamin deficiency.[5,10] The cut-off points for determining riboflavin status were an EGRAC 1.20 for normal riboflavin status, 1.20 ≤ EGRA <1.40 for marginal deficient riboflavin status, and EGRAC ≥1.40 for riboflavin deficiency.[6,10]

Dietary thiamin and riboflavin intake

Dietary intake information was collected by trained surveyors using 24-hour recall. The dietary nutrient contents of subjects' diets, including thiamin and riboflavin, were calculated mainly by using the "Food nutrient content data base of Taiwan" and many other nutrient databases. The details of dietary nutrient intake data collection and calculation are described by Wu *et al.* in this issue.[11] Of all the 24-hour recalls collected, 955 men and 957 women had complete information. Therefore, only they were used for the analysis of dietary thiamin and riboflavin intakes.

Statistical analysis

Data were weighted for the unequal probability of sampling and analyzed by SAS for PC 8.0 and SUDAAN software in order to extrapolate the results to the whole elderly population in Taiwan. Two-way ANOVA was used for the comparison of ETKAC and EGRAC by age and sex. The details of the rationale and procedures of SUDAAN are reported by Pan *et al.,*[9] in this issue.

Results

The theoretical sample size of the Elderly NAHSIT was to include 2028 aged men and women, however, in actuality a total of 2504 participants provided blood specimens. After deletion of the disqualified or deteriorated samples, data on the ETKAC and EGRAC from 2,379 blood specimens (1,213 males, 1,166 females) were analyzed. With the standardization of assay procedures, the analysis of split samples showed a percentage of variation (%CV) of less than 5% for both ETKAC and EGRAC.

Table 1. Prevalence of thiamin and riboflavin deficiencies in elderly Taiwanese by age and sex [1]

Sex			Thiamin status[3]				Riboflavin status[4]		
Age(yr)	*N*	ETKAC[2]	Normal	Marginal	Deficient	EGRAC[2]	Normal	Marginal	Deficient
				%				%	
Male									
65-69	453	1.11 ± 0.01	66.5	15.2	18.3	1.17 ± 0.01	63.0	29.9	7.1
70-74	423	1.09 ± 0.01	69.6	15.6	14.8	1.16 ± 0.01	70.5	22.6	6.9
75-79	222	1.10 ± 0.01	70.6	13.6	15.6	1.16 ± 0.01	70.0	25.3	4.7
≥ 80	115	1.10 ± 0.02	70.0	13.1	17.0	1.17 ± 0.02	70.2	22.3	7.4
Total	1213	1.10 ± 0.01	68.8	14.7	16.5	1.17 ± 0.01	67.7	25.7	6.6
Female									
65-69	476	1.09 ± 0.01	75.6	11.4	13.1	1.13 ± 0.01	79.1	17.6	3.3
70-74	355	1.08 ± 0.01	74.8	11.3	13.9	1.14 ± 0.01	76.0	21.7	2.3
75-79	213	1.10 ± 0.01	73.0	12.8	14.2	1.15 ± 0.01	72.7	22.4	4.8
≥ 80	122	1.10 ± 0.01	70.8	13.3	16.0	1.16 ± 0.02	71.6	20.5	7.9
Total	1166	1.09 ± 0.01	74.1	11.9	14.0	1.14 ± 0.01	75.8	20.1	4.1

[1]Data were weighted for unequal probability of sampling and analyzed by SUDAAN software; [2]Means ± SE analyzed by two-way ANOVA; [3]Cutoff points of thiamin status are ETKAC 1.15 for normal status, 1.15 ≤ ETKAC < 1.20 for marginal status, and ETKAC ≥1.20 for deficient status; [4]Cutoff points of riboflavin status are EGRAC <1.20 for normal status, 1.20 ≤ EGRAC <1.40 for marginal status, and EGRAC ≥1.40 for deficient status.

The results for ETKAC and EGRAC across the various age groups of elderly men and women were within the normal range and were not significantly different either between age groups or between males and females. However, 14.7% of elderly men and 11.9% of elderly women had marginal thiamin status, and 16.5% of elderly men and 14.0% of elderly women had deficient thiamin status (Table 1). In addition, according to EGRAC results, 25.7% of men and 20.1% of women were classified as having marginal riboflavin status, and 6.6% of men and 4.1% of women surveyed were classified as being riboflavin deficient (Table 1). The average dietary thiamin and riboflavin intakes of elderly men and women did not differ significantly across the various age groups (Table 2). When compared with Taiwan RDAs (Recommended Dietary Allowances) of thiamin and riboflavin for respective sex and age groups, the mean thiamin and riboflavin intakes met the Taiwan RDAs for all age groups and both sexes (Table 2).

The results of the dietary thiamin and riboflavin intakes expressed as distributions of selected percentiles are shown in Table 3. Intakes were compared with the RDAs for males and females over 71 years old with light levels of physical activity. The range of intakes of both thiamin and riboflavin and the percentage of Taiwanese RDA (%RDA) consumed was quite large between the 5th and the 95th percentiles. The median dietary thiamin intake for both elderly men and women was very close to the RDAs, whereas the median dietary riboflavin intakes were lower than the RDAs for both elderly men and women.

Discussion

Around half of a century ago, thiamin and riboflavin deficiencies were among the most serious malnutrition problems in Taiwan. In the nutrition status survey of the civilian population in Taiwan conducted in 1954, absent ankle jerks, a sign of thiamin deficiency, was present in only 2 - 5.6% of college students and adults. However the prevalence of low excretion of urinary thiamin (less than 50 μg/g creatinine) was as high as 55.4% in the surveyed sixth grade school children, indicating high prevalence of low thiamin intake.[12] The incidence of active angular stomatitis, a clinical sign of riboflavin deficiency, was as high as 39 - 86% in all age groups of six years old and over.[12-14] The inadequate thiamin intake was related to improper rice milling processes, whereas low riboflavin intake was due to lack of food sources providing significant amounts of this vitamin.[13] In 1972, another nutrition status survey of the civilian Taiwanese population showed remarkable improvement in thiamin and riboflavin status.[15] However, the incidences of low urinary thiamin and riboflavin excretion was 9.3% and 33.7% respectively in sixth grade children, and the prevalence of active angular stomatitis was still as high as 17.5% in this age group.[15]

Although severe deficiencies of thiamin and riboflavin have been rarely seen, the presence of a substantial percentage of elderly people with low or marginal thiamin and riboflavin status has been a persistent but overlooked nutritional problem in Taiwan. The elderly persons surveyed in the NAHSIT 1993-1996 (the 1993-1996 study) were equivalent to the 70 years and older age group in the Elderly NAHSIT (the 1999-2000 study). The current survey of the elderly also reported similar rates of deficient and marginal thiamin status. Comparing the thiamin insufficiency rates in these two consecutive NAHSITs,[7] there is no indication that the thiamin status of the Taiwanese elderly has improved over the past few years.

The riboflavin status of elderly people, however, showed significant progress in the 1999-2000 study. The rates of marginal deficiency in the elderly population decreased from 34.6% in males and 38.7% in females in the 1993-1996 study[8] to 25.7% in elderly males and 20.1% in females in the current survey. The prevalence of riboflavin deficiency also greatly decreased from 43.7% in elderly males and 33.4% in females in the 1993-1996 study[8] to 6.6% in males and 4.1% in females in the 1999-2000 study. However, individuals with marginal or deficient status still accounted for one third of the male and one fourth of the female senior residents who need further improvement in their long term thiamin and riboflavin status.

The dietary thiamin and riboflavin intakes of elderly men and women from various age groups all met the RDAs established by the Department of Health in Taiwan. Although the dietary nutrient intake obtained by 24-hour recall may not fully reflect the long term dietary pattern of individual subjects, the percentile distribution of dietary nutrient intakes constructed from nearly one thousand items of data may still allow us to gain an overview regarding the dietary nutrient intake of the surveyed population. The median (50th percentile) dietary thiamin intake was 0.92 mg/day in males and 0.72 mg/day in females. This is 26% and 29% lower respectively, than the average intakes of thiamin by men and women, which reached 100% of the RDAs. Since the RDAs of thiamin and riboflavin are defined as being equal to their corresponding EARs (estimated average requirements) plus twice the coefficient of variance (assuming 10%) to cover

Table 2. Comparison of dietary thiamin and riboflavin intakes[1] of the elderly with Taiwanese RDAs[2] by age and sex

Sex / Age (yr)	*N*	Thiamin Intake (mg/day)	Thiamin % RDA (%)	Riboflavin Intake (mg/day)	Riboflavin % RDA (%)
Male					
65-69	356	1.12 ± 0.06	124	1.29 ± 0.10	129
70-74	326	1.30 ± 0.01	163	1.53 ± 0.09	170
75-79	186	1.23 ± 0.13	154	1.51 ± 0.13	168
≥ 80	87	1.36 ± 0.17	170	1.37 ± 0.19	152
Total	955	1.25 ± 0.07	156	1.42 ± 0.08	158
Female					
65-69	392	0.99 ± 0.07	124	1.28 ± 0.10	160
70-74	302	0.97 ± 0.06	139	1.37 ± 0.08	171
75-79	154	1.25 ± 0.20	179	1.31 ± 0.13	164
≥ 80	109	0.91 ± 0.09	130	1.26 ± 0.13	158
Total	957	1.02 ± 0.06	146	1.31 ± 0.06	164

[1]Values are means ± SE analyzed by SUDAAN software; [2] Taiwanese RDAs of thiamin and riboflavin for elderly people with a low level of physical activity were used as the reference: thiamin RDAs for the elderly ≤70 yrs: 0.9 mg/day for males and 0.8 mg/day for females; thiamin RDAs for the elderly ≥71 yrs: 0.8 mg/day for males and 0.7 mg/day for females; riboflavin RDAs for the elderly ≤70 yrs: 1.0 mg/day for males and 0.8 mg/day for females; riboflavin RDAs for the elderly ≥71 yrs: 0.9 mg/day for males and 0.8 mg/day for females

Table 3. Distributions of selected percentiles of dietary thiamin and riboflavin intakes[1] of the Taiwanese elderly population

Percentile	Thiamin				Riboflavin			
	Male		Female		Male		Female	
	Intake	% RDA[2]	Intake	% RDA[2]	Intake	% RDA[2]	Intake	% RDA[2]
5th	0.28	35	0.21	30	0.23	26	0.17	21
10th	0.36	45	0.28	40	0.32	36	0.23	29
15th	0.44	55	0.33	47	0.41	46	0.32	40
25th	0.59	74	0.43	61	0.56	62	0.44	55
30th	0.65	81	0.49	70	0.63	70	0.51	64
40th	0.77	96	0.60	86	0.76	84	0.68	76
50th	0.92	115	0.72	103	0.98	109	0.90	113
60th	1.00	125	0.80	114	1.24	138	1.14	143
75th	1.46	183	1.18	169	1.82	202	0.66	208
85th	1.91	239	1.59	227	2.37	263	2.26	283
90th	2.34	293	1.92	274	3.03	337	2.85	356
95th	3.31	414	2.73	390	3.85	428	3.72	465

[1]Data on dietary intakes of nutrients were obtained for the results of the 24-hour recall; [2]Taiwanese RDAs for thiamin and riboflavin for elderly persons aged 71 years and older with a low level of physical activity were used as the reference.

the needs of 97.5% of the population in a certain age group, EARs are equivalent to 83.3% of RDAs. The dietary thiamin intake of males and females ranked below the 30th percentile were less than the Taiwan EARs for thiamin (83.3% of RDAs). The median intake of dietary riboflavin was 0.98 mg/day for elderly males and 0.90 mg/day for females, both of which are slightly higher than 100% of the RDAs. The dietary riboflavin intake of elderly men and women who ranked below the 40th percentile was lower than the EARs. In contrast, the dietary thiamin and riboflavin intakes of elderly people who ranked at the higher ends of the percentile distribution were 3.3 to more than four-fold of the RDAs. Therefore, the average nutrient intakes were affected by this skewed distribution of nutrient intake and may not be able to reflect the presence of nutrient intakes far below the RDAs within the population. If evidence of a considerable portion of the population having inadequate thiamin and riboflavin intake persists, the consequential deterioration of the nutritional status of these water-soluble vitamins could continue in the future.

Nutritional status is greatly influenced by the dietary patterns and food preferences of a population. According to the analyses of dietary data by Wu *et al*.,[11] the major food source of thiamin for the elderly was pork and its products, which provided 0.38 mg/day (33.3% of average intake) of thiamin; followed by rice and its products (0.16 mg/day, 14% of total intake); dairy products (0.09 mg/day, 7.9% of total intake); wheat and flour products (0.08 mg/day, 7.0% of total); and soy beans and soy products (0.08 mg/day, 7.0% of total).[11] The remaining food categories only provided a limited amount of thiamin (less than 0.05 mg/day) to the diet of elderly people.[11] Staple foods including polished rice, wheat flour, and tubers and their products provided 0.27mg (23.7%) of dietary thiamin. Compared with the results regarding dietary thiamin sources of adults in the NAHSIT 1993-1996,[16] the patterns and percentage of dietary food sources were very similar in the two consecutive NAHSIT studies. Therefore, it seems that deriving almost 50% of dietary thiamin from very scattered food sources with low thiamin content has been a long term problem in the dietary patterns of the elderly. This may be one of the underlying factors which have contributed to the high percentage of the elderly population with inadequate dietary thiamin intakes and unsatisfactory biochemical status. Since the protein intake of the elderly already meets the recommended amount,[11] it may not be appropriate to suggest that the elderly consume more animal protein to gain more dietary thiamin. Instead, replacing portions of polished rice and products with whole grains as a staple food would greatly enhance the thiamin content of the diet, especially for those with insufficient intakes.

The major food source of riboflavin for the elderly reported by Wu *et al*., was dairy products,[11] which provided 0.52 mg/day of dietary riboflavin (equivalent to 38.5% of the average daily intake) to the elderly population. The food categories that were the next highest sources of riboflavin intake were pork and its products (0.12 mg/day, 8.9% of total intake), wheat and its products (0.11 mg/day, 8.1% of total intake), fresh fruits (0.1 mg/day, 7.4% of total diet), dark green vegetables (0.08 mg/day, 5.9% of total intake), and eggs and their products (0.07 mg/day, 5.2% of total). The remaining food categories each provided less than 3% of dietary riboflavin.[11] This pattern of dietary riboflavin intake is also very similar to the findings in the NAHSIT 1993-1996.[16] Traditionally, dairy products have not been a major food category consumed by Taiwanese adults. Probably because of the awareness of dairy consumption for the prevention of osteoporosis and the increase in popularity of dairy foods, the average consumption of dairy products has gradually increased from 0.3 cups by adult males and 0.4 cups by adult females in the 1993-1996 study[17] to 0.8 cups by elderly men and 0.9 cups by elderly women in the 1999-2000 study.[11] The increase in dairy product consumption may be the

cause of the great reduction in riboflavin deficiency that has been observed in the 1999-2000 study. Without a nutrient fortification policy, staple foods currently provide only very limited amounts (0.16 mg/day, 11.8% of total intake) of riboflavin in the diet of the elderly. In the First Nationwide Nutrition Survey held during 1980-1981, organ meat was the third major contributor of dietary riboflavin which provided 9.2% (0.10 mg/day) of the mean daily intake.[18] However, following concern about the cholesterol content and safety of organ meat, it has disappeared from the list of major food sources.

It seems that the policy of nutrient fortification in staple foods practiced by the United States guarantees a sufficient dietary intake of thiamin and riboflavin for the majority of the population.[19,20] According to the results of the Continuing Survey of Food Intakes by Individuals (CSFII) 1994-1995, food groups containing mainly fortified staple foods, such as bread and bread products, mixed foods with grain as a main ingredient, ready-to-eat cereal, pasta, rice and cooked cereal, provided about 44% of total dietary thiamin and 30% of dietary riboflavin for US adults.[19,20] Therefore, both the CSFII 1994-1995 and the NHANES III 1988-1994 showed quite agreeable results that the mean dietary thiamin and riboflavin intakes of the 5th percentile of elderly males already meet the EARs and those of the 5th-25th percentile of elderly females also meet the EARs set by the US Institute of Medicine.[19,20]

Without a nutrient fortification policy, dietary supplement use may be another choice to eliminate nutrient insufficiency. Around 30% of elderly males and 35% of elderly females use dietary supplements in Taiwan.[21] Of those who use supplements, only about 28% of men and 25% of women choose supplements containing thiamin and/or riboflavin.[21] In addition, dietary supplement use was reported to be highly correlated with urbanization, high degree of education, high monthly income, better awareness of nutrition related information, and being more health conscious.[21] These phenomena may partially explain the great discrepancy in dietary thiamin and riboflavin intakes between the means of the 95th and the 5th percentiles and the skewed distribution of the biochemical status of thiamin and riboflavin in the Taiwanese elderly population.

In addition to the prevention of vitamin deficiency, thiamin status is correlated with the cognitive function of the elderly.[22] A sufficient serum level of thiamin is required for the proper transport of TPP into the mitochondria of nerve cells[23] to ensure normal metabolism of glucose and neurotransmitters.[24] Riboflavin deficiency not only interferes with intermediary metabolism but also that of pyridoxine, folate and vitamin B_{12}. In an Asian population such as Taiwan where polished rice is the preferred staple food, dairy products are not customarily consumed by the elderly, and no nutrient fortification policy is in place, deficiency of thiamin or riboflavin may occur unless meals are well planned with wise choices of food rich in thiamin and riboflavin.

In conclusion, our study demonstrated the high prevalence of thiamin and riboflavin deficiency among elderly Taiwanese. Although the average biochemical indices and dietary intakes of thiamin and riboflavin were within the normal range, more than one third of the elderly had a dietary intake of thiamin or riboflavin less than the respective EARs. Nutritional intervention in the future is recommended to educate the target population regarding proper food choices, meal planning and dietary supplement use to correct thiamin and riboflavin deficiencies. Implementation of a food policy such as mandatory nutrient content labelling and fortification of nutrients for staple foods showing a high prevalence of deficiencies including thiamin and riboflavin should also be considered.

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