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Is thiamine deficiency in elderly people related to age or co-morbidity?

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Abstract

Objectives: to compare erythrocyte thiamine pyrophosphate concentrations in elderly people with those in healthy younger people; to determine if any differences can be attributed to age or to co-morbidities.
Design: cross-sectional and 3-year longitudinal surveys.
Setting: primary care.
Patients: 100 volunteer blood donors and 222 elderly people from a general practice register.
Measurements: thiamine pyrophosphate concentrations using high performance liquid chromatography; physical examination, medical and medication history; grip strength, body mass index and plasma albumin.
Results: the mean [95% confidence interval (CI)] thiamine pyrophosphate concentration was 152 nmol/l (147–158) in the elderly group and 224 (213–235) nmol/l in the younger group ($P < 0.001$). Ninety-six (43.4%) of the elderly subjects had thiamine pyrophosphate concentrations below the fifth percentile of the younger subjects (140 nmol/l). Over 3 years thiamine pyrophosphate concentrations fell in the elderly cohort by 20% (95% CI: 14.5–24.5%; $P < 0.01$). Thiamine pyrophosphate concentrations in 39 healthy older people were no different from those in elderly people with co-morbidity but were significantly lower than those in the younger people. Elderly people with absent vibration sense in their feet had a lower thiamine pyrophosphate concentration than the rest of the group [129 (117–142) nmol/l compared with 156 (150–162) nmol/l; $P < 0.01$)]. Thiamine pyrophosphate concentrations were not related to prevalent diseases, common medications, body mass index, grip strength or plasma albumin.
Conclusion: lower thiamine pyrophosphate concentrations in elderly people appear to be related more to age itself than to co-existent illnesses.

Keywords: *age, co-morbidity, thiamine deficiency*

Introduction

Blood concentrations of thiamine, or vitamin B_1, are lower in some elderly people compared with the standard 'normal' range, especially in housebound elderly people and those with serious illnesses [1, 2]. Other risk factors for thiamine deficiency include alcoholism [1, 3] and possibly diuretic use [4], although this is controversial [5]. People living in New Zealand may be at greater risk of deficiency as cereals and alcoholic beverages are not supplemented with thiamine.

A high prevalence of thiamine deficiency in elderly people has been found using the transketolase method. This method measures the change in the thiamine-dependent enzyme transketolase before and after addition of thiamine. Enzyme activity after addition of thiamine increases to a greater extent in people who are deficient than in normal controls. Unfortunately, this method is imprecise and the point at which it becomes abnormal is poorly defined [6]. Interpretation is complicated by a fall in transketolase activity with age [7], possibly due to ageing red blood cell progenitors. Furthermore, a direct comparison of thiamine status in older and younger people, using the transketolase effect, has shown no important differences [8]. The use of high-performance liquid chromatography (HPLC) to measure erythrocyte thiamine pyrophosphate (TPP) concentrations may be a better method for screening for thiamine deficiency [6] as it is rapid, direct and more sensitive and has a lower coefficient of variation.

The aims of the present study were to: (i) compare the range of TPP concentrations, using the HPLC method, in older people at home or rest home with those of a healthy young population and (ii) determine

if any differences with age are due to concurrent medications, co-morbidity or to age itself.

Methods

We determined the range of TPP concentrations in a healthy young adult population by analysing blood samples from 100 consecutive volunteer blood donors.

We determined the range of TPP concentrations in an elderly population by analysing blood samples from participants in a previously described community survey of people aged 65 years or more [9]. We excluded elderly subjects if they lived permanently in a nursing home providing hospital levels of care. We obtained a full medical, social and functional history, and performed an abbreviated mental test [10] and a physical examination on each elderly subject. From this information, we identified two subpopulations.

The group of 'healthy elderly people' were taking no medications (including vitamin supplements) and had none of the following: active malignancy, heart failure (treated or otherwise), angina, asthma, chronic airways obstruction, diabetes mellitus, epilepsy, hypertension, arthritis, peptic ulcer, stroke, transient ischaemic attack, peripheral vascular disease, Parkinson's disease, inflammatory bowel disease, dementia (as determined clinically or by a mental test score of 8/10 or less [10]) or depression (as determined clinically or by a score on the Short Zung Interviewer-assisted Depression Rating Scale of 70 or less [11]). Total average daily alcohol consumption was less than one standard drink (10 g) per day.

The remaining elderly subjects, who had one or more of the above medical problems and/or were taking any medication, comprised the 'elderly people with co-morbidity' group.

We measured body mass index and plasma albumin as markers of nutritional status. We assessed muscle strength by measuring grip strength in the dominant hand using a Preston handgrip dynamometer, noting the best of three recordings. We assessed daily alcohol consumption by averaging the amount consumed over a week. We also reviewed the subjects' medical records to determine if excessive alcohol consumption was under-reported by any subject.

Some of the subjects had had TPP concentrations determined 3 years earlier [9]. This made it possible to determine if there were any longitudinal changes in TPP concentrations. At that time, we also collected details on living circumstances, weight and body mass index. We made comparisons between the people who had TPP concentrations measured 3 years apart, those who died in the 3-year period and those who were not seen a second time.

We measured erythrocyte TPP concentrations directly using an HPLC method as described by Warnock [12]. The between-run coefficient of variation was 8.6% at 532 nmol/l and 12.5% at 270 nmol/l. There was no drift in the quality control reference range for samples analysed 3 years apart.

We used the χ^2 test to compare categorical variables. Because TPP concentrations had a skewed distribution, comparisons were made on log transformed data. We compared TPP concentrations between two groups by Student's unpaired *t*-test and between three groups by analysis of variance. We used Student's paired *t*-test on untransformed data to compare the change in TPP concentrations over 3 years. Results are expressed as means with 95% confidence intervals in parentheses unless otherwise specified.

The study was approved by the Canterbury Area Health Board ethics committee and all subjects gave written informed consent.

Results

Response rate

The response rate from the 407 elderly people was 55%. The 221 participants comprised 92 men and 129 women, with a mean age of 76 (75–77) years. Responders were younger than non-responders who had a mean age of 78 (77–79) years ($P < 0.05$). There were no differences in the sex ratio or place of residence between those who responded and those who declined.

TPP concentrations

Cross-sectional comparison between young and old people

The mean age of the healthy blood donor population was 41.5 (39–44) years. The distribution of TPP concentrations in young and old subjects is shown in Figure 1. The mean TPP concentration in all elderly people was 152 nmol/l (147–58) nmol/l compared with 224 nmol/l (213–35) nmol/l in the healthy blood donor population ($P < 0.001$). Ninety-six of the older subjects (43.4%) had TPP concentrations below 140 nmol/l, the fifth percentile of the healthy blood donor population (Figure 1).

Longitudinal changes in older people

TPP concentrations had been performed 3 years earlier in 200 elderly people [9]. Of these, 116 had concentrations repeated in the current study, 27 people had died and 57 were lost to follow-up. Those people who had TPP concentrations performed on both occasions were younger than those who died or

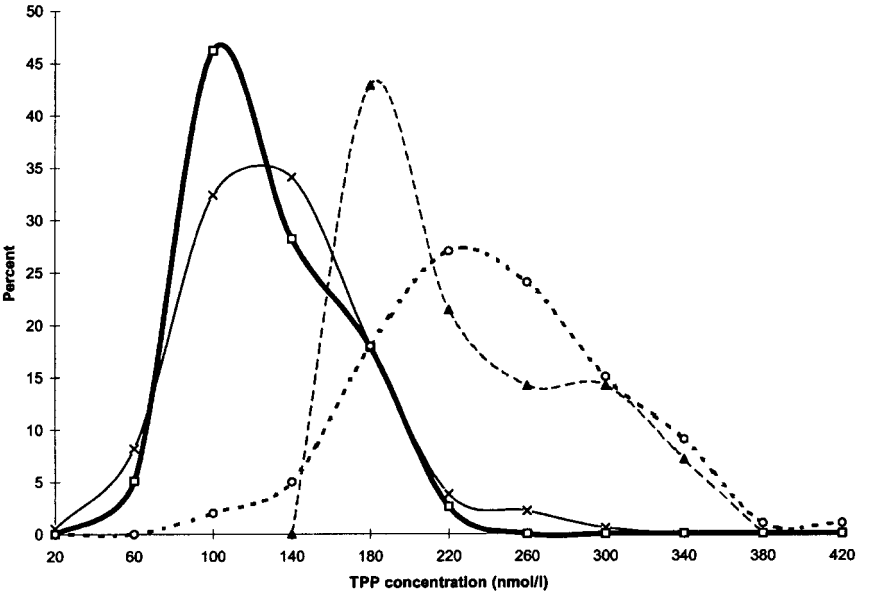

Figure 1. Thiamine concentration distributions in young people (○, $n = 100$) and in old people with (×, $n = 182$) and without co-morbidity (□, $n = 39$); ▲, 14 old people who were taking vitamin supplements.

were lost to follow-up (Table 1). There were no other significant differences between these three groups in gender, weight, body mass index or living circumstances (Table 1). The chance of dying over the 3-year period was not related to thiamine status.

Over 3 years there was a mean decrease in TPP concentrations by 20% (14.5–24.5%; $P = 0.001$) for these 116 people (Figure 2). The mean concentration fell from 204 (190.9–216.6) nmol/l to 150 (142.4–157.8) nmol/l.

Comparison between 'healthy' elderly people and those with co-morbidity

We classified 39 people as 'healthy elderly' who were taking no medications and who had no active medical problems. The TPP concentration distribution in this group was not significantly different from that seen in the 'elderly with co-morbidity' population (Figure 1). The mean TPP concentration in the 'healthy elderly' group was 149 (137–60) nmol/l compared with 153 (147–60)

Table 1. Details of elderly cohort who had erythrocyte thiamine pyrophosphate (TPP) concentrations measured 3 years earlier and their participation in the current study

	Outcome at 3 years			
	Participated	Dead	Lost to follow-up	*P*
n	116	27	57	
% female	58%	63%	75%	NS
Living arrangements (% of subjects)				
at home alone	86%	68%	72%	NS
at home with others	9%	16%	19%	
in institutional care	5%	16%	9%	
Original TPP concentration (nmol/l)[a]	204 (191–217)	207 (181–233)	211 (191–230)	NS
Age (years)[a]	76.5 (75.4–77.7)	81.0 (78.2–83.8)	78.2 (76.2–80.1)	<0.01
Body mass index (kg/m^2)[a]	25.0 (24.3–25.6)	24.5 (22.3–26.7)	25.3 (24.0–26.5)	NS
Weight (kg)[a]	67.0 (64.9–69.1)	62.7 (55.6–69.7)	65.6 (62.1–69.1)	NS

NS, not significant.
[a]Mean and 95% confidence intervals.

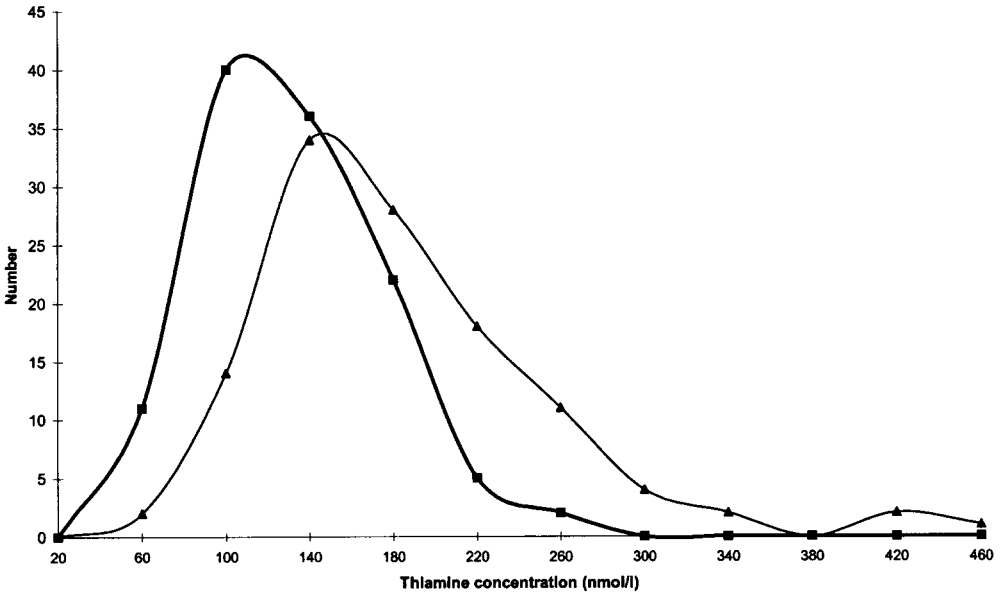

Figure 2. Change in thiamine concentrations in old people over 3 years; ▲, baseline; ■, year 3.

nmol/l in the 'elderly with co-morbidity' population (NS) but was significantly lower than that seen in the younger (blood donor) population ($P < 0.0001$).

We found no significant correlation between TPP concentrations and the prevalent diseases or medications in the study population (Tables 2 and 3). There were no significant correlations between TPP concentrations and body mass index ($r^2 = 0.005$), grip strength ($r^2 = 0.002$) or plasma albumin ($r^2 = 0.005$). Average alcohol consumption in the 'healthy elderly' group was 1.7 (0.7–2.7) g/day compared with an average of 4.8 (3.2–6.5) g/day in the remainder (differences not significant).

Effects of thiamine deficiency

Twenty-eight people, from the total population of elderly participants, had evidence of a sensory peripheral neuropathy as determined by absent vibration sense below the knees. This could have been due to many causes but TPP concentrations in this group were significantly lower [129 (117–42) nmol/l] than in the remaining 193 who did not have this abnormality [156 (150–62) nmol/l], $P < 0.01$.

Discussion

We have shown that red cell thiamine concentrations, assessed using a HPLC method, are lower in elderly people than in younger people. Low thiamine status has been found in many populations of elderly people [7, 13], although the prevalence varies between studies. We are not aware of any comparisons between

Table 2. Comparison between thiamine pyrophosphate (TPP) concentrations and prevalent diseases in older people

	Disease present				Disease absent				
		TPP (nmol/l)				TPP (nmol/l)			
	n	Mean	Median	95% CI	*n*	Mean	Median	95% CI	*P*
Cardiac failure	12	136	135	108–163	209	154	145	148–159	NS
Diabetes mellitus	19	154	143	121–188	202	152	145	147–158	NS
Hypertension	63	153	149	142–163	158	153	145	146–159	NS
Ischaemic heart disease	41	157	165	143–170	180	152	145	145–158	NS
Stroke	21	153	140	130–176	200	153	145	147–158	NS
Depression	11	149	140	119–178	210	153	145	147–159	NS
COPD	17	141	130	113–170	204	154	145	148–159	NS

CI, confidence interval; COPD, chronic obstructive pulmonary disease; NS, not significant.

Table 3. Comparison between thiamine pyrophosphate (TPP) concentrations and prevalent medications in older people

	Taking medication				Not taking medication				
		TPP (nmol/l)				TPP (nmol/l)			
	n	Mean	Median	95% CI	*n*	Mean	Median	95% CI	*P*
Aspirin	44	152	145	136–167	177	153	145	147–159	NS
β-blocker	27	147	143	132–162	194	153	145	147–160	NS
Frusemide	27	157	165	136–177	194	152	145	146–158	NS
Thiazide	17	148	135	128–169	204	153	147	147–159	NS
Digoxin	19	156	143	132–180	202	152	145	147–158	NS
NSAID	25	164	163	149–179	196	151	145	145–157	NS
Benzodiazepine	17	144	136	120–167	204	153	147	148–159	NS
Tricyclic antidepressant	21	145	140	127–163	200	153	147	147–159	NS
Laxative	29	157	149	139–176	192	152	145	146–158	NS
Multivitamin	14	198	188	163–233	207	150	145	144–155	<0.001

CI, confidence interval; NS, not significant; NSAID, non-steroid anti-inflammatory drug.

large populations of young and old people drawn from the same community. Although a cohort effect is possible, the decline in TPP concentrations with time suggests this is not the only explanation. It is not easy to determine if abnormalities seen in older people should be attributed to age itself or to the diseases associated with ageing, but an observation can be attributed to age if it is intrinsic [14], generalized, progressive and deleterious [15]. An observation is unlikely to reflect disease, if it is present in elderly people who are free of co-morbidity.

These data suggest that the lower TPP concentrations seen in older people are generalizable as the participants came from a community-based population. The observed TPP concentrations are also progressive, as shown by our longitudinal data for older people.

Subclinical thiamine deficiency is probably deleterious as:

1. TPP concentrations were lower in the group of people with an absence of vibration sense in their feet. Whilst thiamine deficiency causes peripheral neuropathy, we cannot be certain that it did so in our cases. It is possible, however, that mild thiamine deficiency may have exacerbated a neuropathy from other causes. In particular, it is possible that people with a neuropathy could have other nutrient deficiencies.
2. Replacing thiamine in older people can result in improvements in quality of life [16, 17]. In contrast, the TPP concentrations seen in older people were not associated with a greater chance of dying over a 3-year period.
3. The 12 people with cardiac failure had lower TPP concentrations. Whilst this was not statistically significant, a type II error may have occurred, and including people with ischaemic heart disease may have diluted any possible effect. Low TPP concentrations have been found in people admitted to hospital with cardiac failure, regardless of cause [18], although others have found no significant difference [19]. Similarly some have found lower thiamine activity in people taking frusemide [4], although our findings, and those of others [5], show no association with diuretic use.

It is difficult to determine if the lower TPP concentrations in older people could be intrinsic as dietary intake might be an extrinsic explanation for the findings. Reduced absorption might explain the observed decline with age, but the effect of age on thiamine absorption is controversial [20].

Prolonged alcohol consumption can cause clinical thiamine deficiency by blocking thiamine absorption and by increasing thiamine demand through its effects on intermediary metabolism [20]. Alcohol intake in our study population was generally low. It is possible that intake was underestimated, as it relied on a subject's recall; however excessive alcohol consumption would generally have been detected when reviewing the subject's medical record. It was slightly, but not significantly, lower in the 'healthy elderly' group than in the 'elderly with co-morbidity' group. Although it is possible there may be some inaccuracies in estimating alcohol consumption, it is unlikely that the amount consumed by the study population would have been sufficient to account for the high prevalence of thiamine deficiency.

The lower TPP concentrations cannot be attributed to disease as we could find no significant associations between thiamine status and the prevalent diseases or medications (Table 2), although a type II error cannot be excluded. We also found no correlation between thiamine status and crude markers of protein and calorie nutritional status such as body mass index, plasma albumin or grip strength.

The strongest evidence to suggest that co-morbidity is not an explanation for the low TPP concentrations

is the distribution of TPP concentrations seen in the 'healthy elderly' population. This is identical to that seen in a general population of older people and is significantly lower than that seen in a healthy young population.

We have found a high prevalence of subclinical thiamine deficiency in elderly people which is associated with unfavourable effects but cannot be explained by co-morbidity. It is likely, at least partially, to be related to age itself.

Acknowledgements

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Key points

- Thiamine pyrophosphate concentrations in older people are significantly lower than in younger people.
- Healthy older people without co-morbidity have significantly lower thiamine concentrations than younger people.
- Thiamine concentrations decline over time in older people.
- Thiamine status is not associated with disease or medications but is associated with absent vibration sense below the knees.

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