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Title

Increased thiamine intake may be required to maintain thiamine status during weight loss in patients with type 2 diabetes.

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Running title: Thiamine status during weight loss

Abstract

During weight loss, erythrocyte thiamine pyrophosphate (TPP) decreased (221 ± 52 to 195 ± 39 nmol/L, $P < 0.05$) on a diet with adequate thiamine (1.1mg/day) but was unchanged (217 ± 55 vs 218 ± 52 nmol/L, NS) on a high thiamine diet (2.8mg /day). Attention to thiamine status may be required in patients with diabetes after weight loss.

Introduction

Thiamine deficiency is not a common condition but well may become more common as bariatric surgery particularly for people with diabetes becomes more common. About 15% of obese patients before bariatric surgery have been shown to have low plasma thiamine levels [1]. Mild thiamine deficiency, as assessed by decreased plasma thiamine concentrations, occurs in those with diabetes possibly related to enhanced urinary thiamine excretion [2]. The implications of low plasma thiamine are unclear but high doses of thiamine have been shown to reduce urinary albumin excretion and improve neuropathy [3-5]. Higher carbohydrate diets (>50% of energy) may require enhanced thiamine intake to maintain normal thiamine status which during energy restriction may be difficult to achieve. Pork is naturally high in thiamine therefore a higher protein diet containing pork may offer an alternative approach to achieve weight loss while also maintaining thiamine status. The aim of this study was to determine the effects of a high protein, high thiamine weight loss diet compared with a high carbohydrate, adequate thiamine diet on thiamine status in participants with type 2 diabetes (T2DM).

Methods

Participants were overweight/obese men and women with T2DM. They were not eligible if they had known proteinuria, malignancy, a history of liver, kidney, cardiovascular, respiratory or gastrointestinal disease, uncontrolled hypertension or were pregnant, lactating, a smoker or were on insulin. The study was approved by the Human Research Ethics Committees of the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Participants provided written informed consent. The trial was registered with the Australian New Zealand Clinical Trials Registry (<http://www.anzctr.org.au>), ACTR No: 12608000206325.

In a parallel design, participants were blocked matched for age, gender and weight, before randomisation to one of two energy-restricted (6-7 MJ/day) diets for 16 weeks, high thiamine (HT) (carbohydrate 43%, protein 33% and fat 22% of energy, 2.8mg thiamine/day) or adequate thiamine (AT) (carbohydrate 53% protein 19% and fat 26% from energy, 1.1mg thiamine/day). Sources of thiamine in HT were 180g lean pork (raw weight) for 4 meals per week and 50g lean ham (cooked weight) for 4 meals per week and thiamine fortified breakfast cereals. The AT diet excluded pork, ham and thiamine fortified cereal foods. Participants were seen at baseline and every 2 weeks by a qualified dietitian. Key foods (~50% of total energy) were supplied fortnightly. Baseline dietary intake was assessed using a validated food frequency questionnaire [6]. Participants kept a daily semi-quantitative food record. Dietary intake on 7 days every 2-weeks was analysed using a computerized dietary analysis package (Food Works Professional Edition, version 4 software, 1998; Xyris Software, Highgate Hill, Australia).

At baseline and week 16 participants attended the CSIRO Clinic after an overnight fast for measurement of height, weight and blood pressure (BP) and to have a blood sample taken for the measurement of thiamine. A 24-hour urine sample was collected for the measurement of urea, creatinine, albumin, potassium and sodium.

Biochemical Analyses

Thiamine and 24-hour urinary urea, creatinine, sodium, potassium and albumin analysis was performed in a single assay at a commercial laboratory (Institute of Medical and Veterinary Science (IMVS), Adelaide, Australia).

Statistical Analysis

Statistical analyses were performed using PASW Statistics 18 (Version 18.0, SPSS, Chicago, IL). Changes over time in the treatment groups were assessed using repeated measures ANOVA with time as the within-subject factor and diet as the between-subject factors.

Pearson's correlation coefficients were used to determine the relationships between variables. Statistical significance was set at $P < 0.05$, data are presented as means $\pm$ SD, unless otherwise stated.

Results

One hundred participants commenced the study (HT $n=60$, age 55 ± 9 yr, BMI 35.3 ± 4.3 kg/m², AT $n=40$ age 55 ± 8 yr, BMI 35.5 ± 4.8 kg/m²). Forty-nine participants on the HT diet (age 56 ± 7 yr, BMI 35.5 ± 4.2 kg/m²) and 35 participants on the AT diet (age 56 ± 8 yr, BMI 35.1 ± 4.9 kg/m²) completed the study. Compliance to the diets was good as assessed by a significant diet effect ($P < 0.001$) for the urinary urea:creatinine ratio (**Table 1**). Weight decreased similarly in both diet groups (103.3 ± 14.5 to 92.6 ± 12.4 kg vs 102.3 ± 17.0 vs 92.4 ± 15.1 , HT vs AT respectively, $P < 0.001$ for time).

At baseline dietary thiamine intake estimated by FFQ was not different between diet groups (HT 2.0 ± 1.2 vs AT 1.7 ± 0.7 mg/d). During the intervention thiamine intake from food records was higher in HT compared to AT (2.8 ± 0.3 vs 1.2 ± 0.2 , $P < 0.001$) before and after adjustment for baseline thiamine intake.

Whole blood TPP was not different at baseline (Table 1). After weight loss TPP did not change in HT (0.14 ± 52.6 nmol/L) but decreased in AT (-25.7 ± 53.2 nmol/L) ($P < 0.05$ for interaction). The change in TPP was negatively correlated with baseline TPP ($r = -0.53$, $P < 0.01$ HPHT, $r = -0.72$ $P < 0.01$ HCAT). There were no correlations between change in TPP and change in any other variable. TPP concentrations were not different between the diet groups at baseline (222.8 ± 62.4 nmol/L versus 218.6 ± 50.8 nmol/L HP, $n=60$ and AT, $n=40$, respectively). If an intention to treat analysis is used with the baseline value carried forward for the subjects who dropped-out the difference remained significant ($p < 0.05$ time by diet interaction, 222.8 ± 62.4 nmol/L to 222.9 ± 66.4 nmol/L, 218.6 ± 50.8 to 199.3 ± 55.4 nmol/L, HP, $n=60$ and AT, $n=40$, respectively).

Urinary albumin excretion did not change. Urinary albumin:creatinine ratio, sodium excretion and blood pressure decreased with time ($P<0.01$), with no effect of diet composition. There was no relationship between the change in weight or sodium excretion and the change in mean arterial pressure (MAP).

In conclusion, values for whole blood TPP remained within the normal range of 120-240 nmol/L [7-8]. However neuropathy could occur at lower levels of TPP before transketolase activity is significantly reduced so thiamine status in people with type 2 diabetes, particularly those who have lost weight, may become marginal. Painful peripheral neuropathy may well be mistaken for diabetic neuropathy when thiamine deficiency may well play a role [9]. We have shown in this study that even with relatively modest weight loss less than the usual range of bariatric surgery induced weight loss, cellular thiamine levels decreased even when consuming thiamine supplemented carbohydrate-rich foods. These results suggest that clinicians should be aware that thiamine concentrations may fall after weight loss and it may be wise to recommend a diet high in thiamine or a multivitamin supplement for patients commencing a weight loss program. The clinical significance is if a patient with diabetes has lost weight and has a painful neuropathy whole blood TPP levels should be measured.

Authors' contributions: J.B.K, M.N and PMC developed the concept and study design, J.B.K. & PMC performed the data analyses . T.P.W and G.D.B coordinated the study. J.B.K, M.N. & X.C. designed the dietary intervention, X.C. coordinated the implementation of the dietary protocols. J.B.K. wrote the first draft of the manuscript and all authors critically reviewed the manuscript & data interpretation.

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The authors declare that they have no conflict of interest.

Table 1 Outcome variables before and after weight loss

	HT (n,49)	HT (n, 49)	AT (n, 35)	AT (n, 35)
	Wk 0	Wk 16	Wk 0	Wk 16
Whole blood TPP nmol/L [*]	217.4 ± 54.8	217.6 ± 52.2	221.1 ± 52.4	195.3 ± 39.5
Urine albumin excretion ug/min	21.3±47.8	11.5±21.1	12.0±22.0	10.2±21.3
Urine albumin:creatinine mg/mmol [*]	1.5±2.8	0.9±1.7	1.1±1.5	0.8±1.2
Urine creatinine excretion mmol/24hr [†]	17.9±6.4	16.4±5.5	17.5±5.6	15.9±5.0
Urine urea excretion mmol/24hr	524±211	520±152	495±176	414±140
Urine urea:creatinine ratio [‡]	30.0±8.0	33.2±8.5	29.5±8.0	26.0±5.5
Urine sodium excretion mmol/24hr [†]	212±94	176±78	211±89	182±79
MAP mmHg [‡]	102±8	90±8	101±8	91±7

HT, High thiamine diet

AT, Adequate thiamine diet

MAP, Mean arterial pressure

TPP, Thiamine pyrophosphate

TPP *P<0.05, diet by time interaction

Urine albumin:creatinine mg/mmol *P<0.05, main effect time

Urine creatinine excretion mmol/24hr [†]P<0.01 main effect time

Urine urea excretion mmol/24hr *P<0.05, main effect time, P=0.064 diet by time interaction

Urine urea:creatinine ratio [‡]P<0.001 diet by time interaction

Urine sodium excretion mmol/24hr [†]P<0.01, main effect time

MAP [‡]P<0.001, main effect time

Data are Mean±SD

- [1] Carrodegua L, Kaidar-Person O, Szomstein S, Antozzi P, Rosenthal R. Preoperative thiamine deficiency in obese population undergoing laparoscopic bariatric surgery. *Surg Obes Relat Dis.* 2005; 1: 517-522; discussion 522
- [2] Thornalley PJ, Babaei-Jadidi R, Al Ali H, *et al.* High prevalence of low plasma thiamine concentration in diabetes linked to a marker of vascular disease. *Diabetologia.* 2007; 50: 2164-2170
- [3] Rabbani N, Alam SS, Riaz S, *et al.* High-dose thiamine therapy for patients with type 2 diabetes and microalbuminuria: a randomised, double-blind placebo-controlled pilot study. *Diabetologia.* 2009; 52: 208-212
- [4] Stracke H, Gaus W, Achenbach U, Federlin K, Bretzel RG. Benfotiamine in diabetic polyneuropathy (BENDIP): results of a randomised, double blind, placebo-controlled clinical study. *Exp Clin Endocrinol Diabetes.* 2008; 116: 600-605
- [5] Thornalley PJ. The potential role of thiamine (vitamin B1) in diabetic complications. *Curr Diabetes Rev.* 2005; 1: 287-298
- [6] Hodge A, Patterson AJ, Brown WJ, Ireland P, Giles G. The Anti Cancer Council of Victoria FFQ: relative validity of nutrient intakes compared with weighed food records in young to middle-aged women in a study of iron supplementation. *Aust N Z J Public Health.* 2000; 24: 576-583
- [7] Warnock LG, Prudhomme CR, Wagner C. The determination of thiamin pyrophosphate in blood and other tissues, and its correlation with erythrocyte transketolase activity. *J Nutr.* 1978; 108: 421-427
- [8] Lu J, Frank EL. Rapid HPLC measurement of thiamine and its phosphate esters in whole blood. *Clin Chem.* 2008; 54: 901-906
- [9] Rudnicki SA. Prevention and treatment of peripheral neuropathy after bariatric surgery. *Curr Treat Options Neurol.* 2010; 12: 29-36