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EVALUATION OF A CLINICAL SCREENING INSTRUMENT TO IDENTIFY STATES OF THIAMINE DEFICIENCY IN INPATIENTS WITH SEVERE ALCOHOL DEPENDENCE SYNDROME

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Abstract — **Aims:** To develop a Thiamine Deficiency Questionnaire (TDQ), and to assess its reliability in the identification of Thiamine deficiency, in patients with severe alcohol dependence. **Methods:** 58 severely alcohol dependent patients underwent socio-demographic, medical, psychiatric, and alcohol use assessment, including administration of the Thiamine Deficiency Questionnaire (TDQ). The Red Blood Cell Thiamine Pyrophosphate concentration provided the 'gold standard' to test the validity of the instrument. Univariate 2 × 2 diagnostic test tables and multivariate analysis were performed. **Results:** A set of eight questionnaire items had an overall predictive power of 73.7%. Two of these were highly specific: '*missed meals due to lack of funds*', and the clinical co-occurrence of medical conditions potentially related to poor nutrition. The Michigan Alcohol Screening Test and serum gamma glutamyl transferase were moderately predictive. **Conclusions:** Screening that combines socio-demographic, clinical and biological factors, and/or standardized questionnaires, could improve early recognition of thiamine deficiency.

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INTRODUCTION

Thiamine is present in all natural foods (Thurnham, 2000) and was the first member of the vitamin B complex to be chemically identified. Thiamine is absorbed mainly by the upper-intestine (Thurnham, 2000), and is rapidly converted predominantly to its active form, thiamine diphosphate (pyrophosphate, TPP), which functions as a co-enzyme in carbohydrate metabolism (Chaney, 2002). A serious deficiency of thiamine leads to neurological and cardiovascular disturbances that give rise to Wernicke–Korsakoff Syndrome (WKS), peripheral neuritis, and beriberi heart disease (Somogyi, 1976).

As a water-soluble vitamin, thiamine stores in the body are limited to ~30 mg with a biological half-life of 9–18 days (Ariaey-Nejad *et al*., 1970). In underdeveloped countries thiamine deficiency is generally the result of poor dietary practices, but in the UK and other developed countries it is most often related to chronic alcohol dependence syndrome (Leevy *et al*., 1982; Thomson *et al*., 1987).

The most dramatic complication of thiamine deficiency in the population with alcohol related problems is Wernicke's Encephalopathy (WE), which in its classic form is characterized by the triad of ocular abnormalities, ataxia, and a global confusional state (Victor, 1993). Unfortunately the classic triad is neither consistently nor frequently encountered, and the onset of the syndrome may be acute or gradual (Victor *et al*., 1989; Blansjaar *et al*., 1992). In a recent literature review, Thomson *et al*. (2002) concluded that since only about 10% of patients present with the classical triad of signs, we might be failing to make the diagnosis of WE in up to 90% of patients. This conclusion is supported by post-mortem and other studies (Harper *et al*., 1986, 1995; Cook *et al*., 1998).

A number of biochemical measurements, both direct and indirect, have been used to assess thiamine status as an aid to clinical diagnosis. Earlier methods, such as the measurement of blood pyruvate concentration (Morgan *et al*., 1968) were not specific, and indirect or functional methods, such as the measurement of the activity of the erythrocyte enzyme transketolase (ETKA) or the thiamine pyrophosphate effect (TPP effect; Warnock, 1975) may be influenced by factors other than thiamine deficiency (Baines, 1985; Baines *et al*., 1988). In this study, we have used direct high performance liquid chromatographic (HPLC) measurement of the principal physiological form of thiamine, thiamine pyrophosphate, in erythrocytes, a tissue which has been shown to be a good indicator of body stores (Brin, 1964).

Diagnosis of WE remains a difficult medical task because it is mainly based on clinical findings, complemented by laboratory testing, and is confirmed only by post-mortem histopathological examination (Victor *et al*., 1989; Victor, 1993). However, failure to diagnose WE can result to serious amnesic syndrome (Korsakoff Syndrome, KS), or irreversible brain damage, or death (Victor *et al*., 1989; Victor, 1993). Early diagnosis, and treatment of WE can prevent the development of KS. Unfortunately, a standardized instrument for early detection of thiamine deficiency related to alcohol dependence is lacking. Thus, it is desirable to obtain a standardized questionnaire, which could be used as a screening tool in clinical settings for the identification of patients with alcohol-related disorders and likely associated thiamine deficiency. This instrument would enhance the clinician's ability to diagnose such a diverse, and sometimes insidious, condition as WE, promptly.

This paper reports on the development of such an instrument, as well as evaluating its predictive capability to identify the state

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of thiamine deficiency in patients with alcohol dependence syndrome. Thiamine deficiency is not an isolated feature of malnutrition related to alcohol dependence (Thomson *et al*., 1987; Bunout, 1999) and it can be hypothesized that a questionnaire detecting a generalized nutritional deficiency may be used as a proxy measure to the thiamine deficiency associated with alcohol dependence. This type of instrument could complement clinical and laboratory testing, in early diagnosis of patients at risk for WE.

SUBJECTS AND METHODS

Study population

Patients admitted to the inpatient unit of the local Substance Misuse Department for detoxification, who were between 18–65 years of age and had a history of either Harmful Use or Dependence Syndrome due to alcohol, as defined in ICD-10 (World Health Organisation, 1994) were invited to take part in the study. Patients who were suffering from diabetes mellitus, or other medical conditions such as end-stage cancer or chronic renal failure that have been associated with development of thiamine deficiency were excluded (Saito *et al*., 1987; Hung *et al*., 2001; Togay *et al*., 2001; Ogershock *et al*., 2002). Diagnosis of diabetes mellitus was determined by World Health Organisation criteria (Oxford Handbook of Clinical Medicine, 2001). We excluded patients who had a history of anaphylactic shock due to IV administration of vitamin B1, or any other drug, and also patients suffering from any medical or psychological condition which in the opinion of the investigator should preclude entry to the study.

Development of the Thiamine Deficiency Questionnaire

Literature was reviewed to identify important nutritional and clinical parameters. We developed a Thiamine Deficiency Questionnaire (TDQ), consisting of 16 items (Appendix A). The Nutritional Information (NI) questions were adopted from a nutrition-screening tool being used with clients with learning disabilities and mental health problems (Bryan *et al*., 1998).

Methodology

The Local Research Ethics Committee approved the protocol. Three psychiatrists in training and a staff grade psychiatrist, all with at least 2 years of experience in the assessment and management of psychiatric patients, completed interviews and medical examinations, supervised by the principal investigator.

Each participant signed informed consent and completed a questionnaire on socio-economic status, lifestyle, alcohol use history, and self-reported alcohol consumption during a typical week. All subjects, within 48 h of entering the study, received a full medical and psychiatric evaluation, which followed a structured format developed by the investigators, and included Medical and Psychiatric history, Mental State Examination, Physical and Neurological examination, Mini Mental State Examination (MMSE), Severity of Alcohol Dependence Questionnaire (SADQ; Stockwell *et al*., 1983), and Michigan Alcohol Screening Test (MAST; Zung *et al*., 1975). The TDQ was administered at that stage. Height and weight, and blood alcohol concentration, measured with a standard breath analyser, were recorded on admission to the unit. Body Mass Index (BMI) was calculated as weight (kg) divided by squared height (m^2).

Fifteen subjects (25% of sample population) presented on admission with symptoms and signs of alcohol intoxication and/or had blood alcohol concentration >0.035 mg/100 ml. These patients were thought to be incapable of giving informed consent on admission to the unit. Consent was obtained when symptoms and laboratory evidence of intoxication subsided, which was within 6 h of the initiation of treatment. We routinely perform the laboratory investigations presented below, apart from measurement of Red Blood Cell Thiamine Pyrophosphate (RBCTPP), on all patients admitted to the inpatient unit for detoxification. Blood for measurement of RBCTPP from these fifteen subjects was stored until final informed consent was obtained.

Blood analyses and treatment with parenteral thiamine

Blood samples were obtained on admission, before the beginning of treatment of the withdrawal syndrome, for measurement of RBCTPP, serum electrolytes (Na^+, K^+ and Ca^{++}), urea and creatinine, liver function tests (alanine aminotransferase, ALT; aspartate aminotransferase, AST; alkaline phosphatase; total bilirubin; gamma-glutamyl transferase, GGT), non-fasting blood glucose, and a full blood count. Urine samples for measurement of glucose were also collected at that stage.

The RBCTPP concentration before initiation of treatment provided the 'gold standard' to judge the criterion validity of the new instrument. RBCTPP was measured in washed red cells by the HPLC method of Baines (Baines, 1985). The reference range was 165–286 nmol/l and the inter-batch precision was 5.7% at a concentration of 223 nmol/l.

Assessment of withdrawal symptoms was carried out on admission, and subsequently 6-hourly, by a clinical interview and administration of the Addiction Research Foundation Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar; Sullivan *et al*., 1989; Stuppaeck *et al*., 1994). Treatment of alcohol withdrawal, with diazepam and symptomatic medication, began for all participants within 2 h after admission and followed a standard protocol. All subjects also received two pairs of Pabrinex® intravenous (IV) high potency multi-vitamin injection, by IV infusion over 15–30 min in 100 ml of 0.9% sodium chloride, every 8 h for a period of 48 h. On completion of the Pabrinex administration, a second blood sample for measurement of RBCTPP was obtained.

Statistical Analysis

A database of 26 variables containing demographic details, laboratory measurements, and relevant questionnaire scores was created. Demographic variables were age, gender, marital and occupational status; laboratory variables were GGT, mean red cell volume (MCV), and pre- and post-treatment RBCTPP. Individual TDQ item scores, sub-category scores as well as total questionnaire scores (SADQ, MAST) were included. All statistical computations including descriptive statistics were carried out using SPSS for Windows (SPSS, 1999).

Subjects were identified as Cases of Thiamine Deficiency (CTD) if their pre-treatment RBCTPP values were <165 nmol/l. Non-Cases of Thiamine Deficiency (NCTD), had RBCTPP values $\geqslant$165 nmol/l. The univariate 2×2 diagnostic test table for each variable was computed so that individual variable sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) could be calculated. The mid-point score was used as the cut-off point to identify cases

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of thiamine deficiency, for all TDQ items apart from item 14 (see Appendix A).

For multivariate analysis, a logistic regression was applied to the database to select variables that were significantly associated with caseness. This type of regression has been shown by Rosenberg *et al*. (1998) to be successful in selecting significant groups of variables for predicting cases. The Receiver Operating Characteristic (ROC) curve (Altman, 1991; Cloves, 1999) was used to determine the predictive power of various combinations of significant variables as chosen by the regression.

RESULTS

Sixty subjects entered the study. Two were found to have diabetes mellitus and were excluded from the final analysis. There were no participants with a history of anaphylactic shock, or suffering from cancer or chronic renal failure, or any other medical or psychiatric condition that precluded entry to the study. The remaining 58 patients were between 21–65 years old, with average age of 42.36 (SD ± 11.65) years, mostly males (62.7%) and unemployed (88.1%). Only 31% of the patients were married or living with a partner, and 50% were living alone. All patients reported more than 10 years of alcohol misuse and related problems. They consumed 40–952 units (1 unit equivalent to 8 g of ethanol) of alcohol per week (mean: 228.16±182.90 SD), in the last month before admission, mainly in a regular pattern of use. Fifty of our subjects (86.2%) presented with clinical and/or laboratory evidence of liver dysfunction [presence of abdominal pain and tenderness and/or hepatomegaly and/or splenomegaly and/or jaundice and/or abnormal Liver function tests (ALT > 40 u/l, AST > 40 u/l, GGT > 50 u/l, alkaline phosphatase >100 u/l, or total bilirubin > 17 μmol/l)] but none had ascites or other clinical signs of cirrhosis (skin manifestations or ecchymotic lesions).

Only 13.8% of the patients could be categorized as being 'underweight' (BMI < 20), with 34.5% having a BMI within recognized normal limits (20–24) for their age and height, and 51.7% a BMI > 24. The distribution of SADQ and MAST scores indicated a severe level of dependence in our study cohort with mean scores of 34.9 (SD ± 12.97) and 36.1 (SD ± 8.74) respectively. Table 1 shows some descriptive statistics of demographic, laboratory and questionnaire variables. A ranking of variables/items based on their sensitivity and specificity with corresponding Positive Predictive Value (PPV) and Negative Predictive Value (NPV) is shown in Table 2. Table 3 contains the computational detail and results of logistic regression.

Thirty-one subjects (53.4%) had pre-treatment RBCTPP values <165 nmol/l and hence were identified as cases of thiamine deficiency. Only 11 subjects (19.0%) were identified as cases after the treatment with Pabrinex. To confirm that the change of RBCTPP levels between pre- and post-treatment is significant the paired samples *t*-test was applied to the RBCTPP values for the pre- and post-treatment. The two-tailed significance was <0.001 ($P < 0.001$, df = 57), indicating that the change of RBCTPP levels between pre- and post-treatment is significant. However, eight of the subjects had post-treatment RBCTPP values lower than their pre-treatment values, with five actually having pre-treatment values within the reference normal range, which became 'abnormal' after treatment with Pabrinex (see Table 4). The latter subjects were between 23–42 years old, had a higher ratio of females (3/5) than in the total sample, and had relatively high serum GGT activity (mean 540.80 UI/l) and MCV (mean 101.14 fl) values. Two of these subjects had BMI values > 30. Mean TDQ and MAST total scores (68.80 and 35.20 respectively) were similar to the means on these scales in the total sample.

A comparison between Table 2 and Table 3 highlighted two main groups of variables selected by the logistic regression. The first group contains variables such as TDQ items 1, 4 and 8 that

Table 1. Summary statistics of variables

Variables	Min	Max	Mean	S.D.
Age (years)	21	67	42.36	11.65
TDQ total score	44	82	64.69	6.98
BMI	15	43	24.40	5.00
TDQ NI sub-score	7	25	18.69	4.37
TDQ AU sub-score	4	20	17.29	3.15
TDQ CE sub-score	0	10	3.86	2.55
SADQ score	3	58	34.97	12.97
MAST score	14	53	36.05	8.74
RBCTPP (nmol/l) 1*	95	274	169.59	46.76
RBCTPP (nmol/l) 2**	120	604	257.22	98.11
GGT (UI/l)	10	2835	446.19	554.75
MCV (fl)	84.0	119.60	101.71	7.70

TDQ, Thiamine Deficiency Questionnaire; BMI, Body Mass Index; NI, Nutritional Information; AU, Alcohol Use; CE, Clinical Examination; SADQ, Severity of Alcohol Dependence Questionnaire; MAST, Michigan Alcohol Screening Test; RBCTPP, Red Blood Cell Thiamine Pyrophosphate; GGT, gamma-glutamyl transferase; MCV, mean corpuscular volume
*Pre-treatment RBCTPP **Post-treatment RBCTPP.

Table 2. TDQ items with highest Specificity and Sensitivity with corresponding Positive Predictive Value (PPV) and Negative Predictive Value (NPV)

Items	Sensitivity (%)	PPV (%)	NPV (%)	Items	Specificity (%)	PPV (%)	NPV (%)
Item 8	96.77	52.63	0.00	Item 5	100	100.00	48.21
Item 9	96.77	53.57	50.00	B.M.I.	92.59	81.81	53.19
Item 10	93.54	53.70	50.00	Item 14	85.18	73.33	53.49
Item 1	87.10	52.94	42.85	Item 15	77.77	71.42	56.75
Item 4	80.64	59.52	62.50	Item 11	51.85	60.60	56.00

Table 3. Logistic Regression for questionnaire items and laboratory measurements that best identify cases

Parameters used in the regression	Items selected by the regression	SE	Significance of log LR
Sample size = 58	MAST score	0.049	0.257
Computational	GGT	0.001	0.016
method = Backward	TDQ item 1	1.169	0.329
stepwise & Forward	TDQ item 2	1.148	0.046
stepwise	TDQ item 3	0.794	0.430
% correctly predicted:	TDQ item 4	0.919	0.243
85.2%	TDQ item 5	36.602	0.751
	TDQ item 8	60.438	0.876
	TDQ item 13	0.849	0.119
	TDQ item 15	0.950	0.007

MAST, Michigan Alcohol Screening Test; GGT, gamma-glutamyl transferase; TDQ, Thiamine Deficiency Questionnaire; SE, Standard Error; log LR, Logistic Regression.

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Table 4. Pre- and Post Treatment RBCTPP values in subjects with lower post-treatment values (reference range 165–286 nmol/l)

	Pre-treatment RBCTPP (nmol/l)	Post-treatment RBCTPP RBCTPP (nmol/l)
1	209	122
2	196	156
3	259	190
4	274	175
5	238	221
6	176	127
7	263	120
8	231	164

RBCTPP, Red Blood Cell Thiamine Pyrophosphate.

Table 5. ROC curve areas for different combinations of variables

Combination of variables	Area under the ROC curve	Asymptotic 95% CI	
		Lower bound	Upper bound
Combination 1	0.837	0.722	0.951
Combination 2	0.697	0.552	0.841
Combination 3	0.737	0.603	0.870
Combination 4	0.779	0.650	0.908
Combination 5	0.834	0.718	0.950

Combination 1: BMI, MAST, GGT, CE sub-score, TDQ total score, TDQ items 1–5,8,13,15.
Combination 2: BMI, MAST, GGT, CE sub-score.
Combination 3: TDQ items 1–5, 8, 13, 15.
Combination 4: BMI, MAST, GGT, TDQ items 1–5, 8, 13, 15.
Combination 5: BMI, MAST, GGT, CE sub-score, TDQ items 1–5, 8.
ROC, Receiver Operator Characteristic; CI, Confidence Interval; BMI, Body Mass Index; MAST, Michigan Alcohol Screening Test; GGT, gamma-glutamyl transferase; CE, Clinical Examination; TDQ, Thiamine Deficiency Questionnaire.

have high sensitivity while the second group contains variables such as TDQ items 5, 14 and BMI that have high specificity. The remaining items/variables were selected to enhance the predictive power. If area under the ROC curve is used to represent the predictive power of the TDQ items and variables as summarized in Table 5, it may be seen that the combination between the selected TDQ items and measured variables provides high predictive power. For example, the overall combination of all selected items and variables has predictive power of 0.837 (83.7%). We notice however, that if only the TDQ items were used to predict cases, the predictive power (0.737 or 73.7%) is higher than the predictive power (0.697 or 69.7%) of the measurement variables (BMI and GGT) combined with MAST and CE sub-score. This result implies that further development and refinement of TDQ may lead to an effective screening tool with high predictive power.

DISCUSSION

The Thiamine Deficiency Questionnaire (TDQ) has been developed to identify patients with alcohol related conditions who are also nutritionally deficient, and might require treatment with parenteral thiamine in clinical settings. The importance of early treatment of thiamine deficiency was emphasised in the Royal College of Physicians recent report entitled 'Alcohol — can the NHS afford it?' which also contains recommendations for the treatment of WE in the Accident and Emergency department (Report of Royal College of Physicians, 2001, Appendix 3). The current widely accepted practice, nationally and internationally, is to administer parenteral (usually intravenous) replacement therapy to all high-risk patients undergoing treatment of alcohol withdrawal syndrome in inpatient settings, especially if they show signs of chronic malnutrition (Report of Royal College of Physicians, 2001, Appendix 3; Thomson *et al*., 2002).

Although this 'treat all' policy has many advantages, there are drawbacks. The albeit small risk of anaphylaxis is well documented and can be fatal (Stephen *et al*., 1992; British National Formulary (BNF), 2003). A 'treat all' policy can be expensive, since intravenous administration of any drug is a logistically demanding clinical procedure that also causes discomfort to many patients. The BNF, recognising the risk of anaphylaxis, advises, 'use be restricted to patients in whom parenteral treatment is essential'. There is neither a clinical assessment protocol nor a laboratory investigation method that can, rapidly, predict the need for treatment with Pabrinex. Our study demonstrates that a standardized questionnaire instrument could be invaluable in assisting clinicians in treatment decisions.

The RBCTPP concentration before initiation of treatment provided the 'gold standard' to judge the criterion validity of the new instrument. Thirty-one subjects (53.4%) were identified as cases of thiamine deficiency, which is not dissimilar to the percentage that had been previously reported in the literature (30–80%; Thomson *et al*., 1987). In a recent paper, Mancinelli *et al*. (2003) described an HPLC method for the simultaneous determination of thiamine, and the mono- and diphosphates in red cells. Other such methods have been previously published (Tallaksen *et al*., 1991, 1993; Herve *et al*., 1994). Whilst these studies are interesting, and provide research data helpful in the understanding of thiamine utility, they are at present research methods and not generally available for routine use. Further, they confirm the pivotal role that RBCTPP has as an indicator of thiamine status, though studies using methods such as the above may provide data on the handling of thiamine by the alcoholic patient. However, we believe that RBCTPP will remain the primary biochemical diagnostic test of thiamine status.

In our results, selected items with high sensitivity and/or specificity, grouped together, can predict thiamine deficiency in ~80% of cases. Nutritional and clinical examination items had higher predictive capability than alcohol use variables (apart from *frequency of alcohol use*), which suggests that malnutrition contributed more to the development of vitamin deficiency in our population than their drinking *per se*. Item 5 (*missed meals due to lack of funds*) and item 14 (*co-occurrence of other nutritional related conditions*) had particularly high Positive Predictive Values (PPV, 100% and 73.33% respectively). These items could be useful minimal assessment tool for clinicians who assess patients in emergency or other settings, since they can fairly confidently detect a high proportion of true thiamine-deficient cases.

The high specificity of a low BMI possibly reflects its distribution in our sample (52% had a BMI > 24).

Further refinement and evaluation of the TDQ are needed to improve the instrument's validity. In particular, the generalizability

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of the instrument requires further investigation. Our sample came from a population with a long history of heavy drinking with severe social and occupational dysfunction. It would be important to test this instrument in a larger and more varied population such as patients attending Accident and Emergency Departments.

Logistic regression was used to regress our independent variables toward the binary outcome. We used the total MAST score as one of the independent variables, as shown in Table 3. Although MAST is a detailed instrument compared to individual TDQ items (see Table 3), it has less statistical significance than these items, when it comes to the prediction of thiamine-deficient cases. This is understandable since MAST was not intended for this. The total MAST score was selected by multivariate analysis as a moderately strong factor and it would be of interest to combine selected items of the MAST with selected items of the TDQ. Taking into account that most of the items of the latter are denoting self-report judgements, it would seem more appropriate to add or replace items with MAST items that are based on more objective evidence. Skinner (1979), in his multivariate evaluation of the MAST, identified five important *dimensions* (subsets of items). In the study's factor analysis, the second subset of items (Factor II: *legal, work and social problems*) had internal consistency reliability of 0.76 and eigenvalue of 3.71, which were second only to the Factor I (*recognition of alcohol problems by self or others*) values. All these items denote specific, objective, alcohol-related events and consequences (e.g. arrests, fights, occupational or marital difficulties, other social events, *delirium tremens* events) and can be incorporated into the TDQ.

GGT was also selected by logistic regression as a moderately strong factor. GGT is a routinely used laboratory marker of liver dysfunction, and is also a widely used marker of the severity of alcohol dependence (Reynaud *et al*., 2000; Conigrave *et al*., 2002). Patients who present with high values may present with more severe liver pathology, which may lead in reduced ability to store vitamins. Reduced hepatic storage has been identified as one of the mechanisms of thiamine deficiency in chronic alcoholism (Hoyumpa, 1980) and therefore this result may indicate a significant effect of alcoholic liver disease on thiamine levels.

Treatment was effective in alleviating thiamine deficiency ($P < 0.0001$), which may reflect a clinically significant treatment effect. Relatively high doses of Pabrinex were used. Nevertheless, a small number of the subjects had post-treatment RBCTPP lower than their pre-treatment values, with five actually having post-treatment values lower than the reference normal range. There are no demographic, physical or mental health, nutritional, or alcohol use factors, in our sample that appeared to explain this. The precision of the HPLC method used for determination of RPCTPP values (inter-batch precision 5.7%) should not be a factor (see Table 4). Moreover, all participants in the study received the same dose of thiamine, other vitamins, and anhydrous glucose during parenteral treatment with Pabrinex. They also had the same daily number of meals during the treatment. This finding poses a puzzling question which needs further investigation in a larger sample, because it may be an isolated finding. Possible explanations might be a defect with the uptake of the parenteral thiamine by the red cell, or defects with the phosphorylation of the administered thiamine within the cell. Another might be that 'rebound' erythropoiesis occurs on instigation of treatment as the suppressive effect of alcohol is removed (Hourihane *et al*., 1970), but there is no evidence of this in our results. Finally, these subjects might be 'fast utilizers' of thiamine, a concept that has not been sufficiently investigated in the literature.

In conclusion, the development of a screening tool that will enable clinicians to quickly and correctly identify alcohol dependent patients at risk of thiamine deficiency, and associated WE, is certainly desirable. This evaluation of a new questionnaire demonstrates that early recognition of thiamine deficiency with a standardized tool is possible. Further evaluation and refinement of the tool is necessary in order to determine its usefulness and validity when used in different population samples and clinical settings.

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Statement — Dr X. Sgouros was responsible for the design, execution, data collection and interpretation, and preparation of the manuscript. Dr M. Baines helped with the design of the project, biochemical analysis, data interpretation and preparation of the manuscript. The study framework was derived from Dr Bloor's original idea, who also was the overall advisor of the project. Dr McAuley was involved in the protocol design, execution and data collection stage and Dr L. O. Ogundipe helped with protocol design, and also submitted the project for ethical approval. Dr Willmott performed the statistical analysis and was involved in the preparation of the manuscript.

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APPENDIX A

A brief description of the TDQ items:

1. Frequency of eating carbohydrates (1a), or fruit and vegetables (1b), or meat, fish or poultry (1c) in the past year (per day)
2. Frequency of meal completion
3. Weight loss in the past year (in kg)
4. Weight gain in the past year (in kg)
5. Frequency of missed meals because of lack of funds (per week)
6. Frequency of reduced appetite with avoidance of meals (per month)
7. Frequency of eating breakfast (per week)
8. Frequency of alcohol use
9. Units of alcohol in a typical drinking day
10. Frequency of having 6 or more units of alcohol on one occasion
11. Frequency of occurrence of 'blackouts' (defined as transient circumscribed memory deficit episodes that occur during periods of severe intoxication)
12. Frequency of early morning drinking due to withdrawal symptoms
13. Total number of episodes of vomiting in the past month
14. Co-occurrence of other nutritional-related conditions (poluneuropathy, amblyopia, pellagra, anaemia or subacute combined degeneration, *yes or no*)
15. General Clinical Impression about nutritional status scale (based on clinical judgement)
16. Body Mass Index

Nutritional Information Variables (NI): Items 1–7, range 0–3, cut-off scores: Items 1 and 4 $\leqslant 2$, Items 3, 5–7 $\geqslant 2$).

Alcohol Use Variables (AU): Items 8–12, range 0–4, cut-off score $\geqslant 2$.

Clinical Examination Variables (CE):Items 13–15 (Item 13, range 0–3, cut-off score $\geqslant 2$), (item 14, rated as either 0 or 3, cut-off score = 3), (item 15, range 0–4, cut-off score $\geqslant 2$).
Total score = BMI plus NI, AU and CE sub-scores.

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