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Parenteral thiamine use in the prevention and treatment of Wernicke–Korsakoff syndrome

AIMS AND METHOD

A pre-/post-intervention audit of 163 case notes was conducted to assess the efficacy of printing information about the identification and treatment of the Wernicke–Korsakoff syndrome on the hospital alcohol detoxification sheet.

RESULTS

Parenteral thiamine was indicated in 42 of 163 patients; 26 had symptoms suggestive of Wernicke's encephalopathy and 16 were at risk. The intervention increased the chance of appropriate parenteral treatment by an odds ratio of 5.9 (95% CI 1.3–27.8). Admission to a

specialist alcohol unit increased the chance of appropriate treatment by an odds ratio of 7.0 (95% CI 1.52–32.25). The mean number of doses rose from 3.08 to 4.62.

CLINICAL IMPLICATIONS

A simple intervention may lead to improved treatment of patients with Wernicke–Korsakoff syndrome.

The Wernicke–Korsakoff syndrome is due to thiamine (vitamin B₁) deficiency and can be precipitated by alcohol withdrawal. Wernicke's encephalopathy is classically defined by a triad of symptoms (confusion, ophthalmoplegia and ataxia), but it is increasingly recognised that few cases will present in this way, many presenting with non-specific acute confusional states. Korsakoff's psychosis is an amnesic syndrome which may be preceded by a clear-cut episode of Wernicke's encephalopathy or may result from a series of subclinical encephalopathies in which the classical features are absent (Cook & Thomson, 1997). Recent work has categorised Korsakoff's psychosis and alcoholic dementia as part of the same disorder, with thiamine deficiency having a role (Chick, 1997). It is therefore important to have a low threshold for treatment in people at risk, such as patients undergoing alcohol detoxification.

Alcohol misuse is being increasingly recognised as having significant comorbidity in psychiatric populations and many people with a primary alcohol problem will accrue psychiatric diagnoses (Weaver *et al*, 2003).

The incidence of Korsakoff's psychosis is rising in Scotland (Ramayya & Jauhar, 1997). In 1992 Parentrovite preparations were discontinued. In 1989 the Committee on Safety of Medicines published a report warning of adverse reactions to Parentrovite (Committee on Safety of Medicines, 1989). There was a 9-month gap during which no parenteral preparation was available. It has been suggested that psychiatric practice then changed to favour oral preparations, even in malnourished patients with alcoholism (O'Brien, 1995).

The incidence of anaphylactic reactions to injectable thiamine preparations has been quoted as 4 per million pairs of intravenous ampoules sold in the UK and 1 per 5 million intramuscular ampoules sold in the UK. These are reports to the Committee on Safety of Medicines on Parentrovite (Cook & Thomson, 1997) and are far lower than the incidences reported for streptokinase or penicillin. It is now suggested that psychiatric practice requires refocusing on the use of parenteral thiamine preparations.

The Royal Edinburgh Hospital has a specialised 12-bedded alcohol detoxification ward (the Alcohol Problems Clinic) and six 25-bedded adult general psychiatric wards, which cover different geographical areas of Edinburgh. The Alcohol Problems Clinic admits patients with a primary diagnosis of alcohol dependence for detoxification on a voluntary basis, and does not accept detained patients or those who require a high level of nursing observation. Patients in these latter categories undergo detoxification on the general adult wards, which also detoxify patients referred by local community healthcare teams.

The Royal Edinburgh Hospital devised a guideline for the treatment of Wernicke–Korsakoff syndrome in 1999. This identified patients in whom the presence of the syndrome should be considered (those with symptoms of ataxia, confusion, ophthalmoplegia/nystagmus, memory disturbance, hypothermia and hypotension or coma/unconsciousness) and patients 'at risk' (those with diarrhoea, vomiting, poor diet, weight loss or physical illness). Dosing schedules of parenteral vitamins were provided.

Method

Information from the hospital guideline on Wernicke–Korsakoff syndrome was integrated into the hospital alcohol detoxification sheet, a fixed chlorthalidone reducing regimen (Fig. 1). This was printed on bright yellow card and distributed to all wards in January 2002. Guidance on the identification and treatment of Wernicke–Korsakoff syndrome was printed on the reverse of the chart.

The pre-intervention phase of the study involved all patients undergoing detoxification on general wards between 10 September 2001 and 31 January 2002. The post-intervention period included patients undergoing detoxification between 1 May 2002 and 31 October 2002. Patients were identified by clinical pharmacists working on the wards. Between September 2001 and 31 January 2002 there were 128 admissions to the alcohol



CHLORDIAZEPOXIDE REDUCING DOSE CHART

NHS Lothian January 2002

Name:		DoB	Ward	Unit No.	Consultant
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Day	Date	Drug	Dose	Route	Administration Times Given by (initials *)				Prescriber's Signature
					8am	1pm	6pm	10pm	
1		Chlordiazepoxide	20 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	
2		Chlordiazepoxide	10 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	
3		Chlordiazepoxide	20 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	
4		Chlordiazepoxide	10 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	
5		Chlordiazepoxide	10 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	
6		Chlordiazepoxide	10 mg	Oral	✓ ----- *	✓ ----- *	✓ ----- *	✓ ----- *	

PRESCRIBE On main prescription sheet: chlordiazepoxide according to reducing dose chart
and chlordiazepoxide 10 or 20 mg as required (including maximum dose in 24 h); review use daily

CONSIDER Prophylaxis of Wernicke–Korsakoff syndrome: 1 pair IM or IV ampoules Pabrinex daily for 3 days
Treatment of Wernicke's encephalopathy: 1 pair IM or IV ampoules Pabrinex twice daily for 2 days
If symptoms respond ⇒ continue 1 pair ampoules daily for a further 3 days
If no response ⇒ discontinue and consider referral to a neurologist

OR If no indication for parenteral supplementation: Thiamine orally 100 mg three times daily for 5–7 days, then review

Fig. 1. Detoxification schedule.



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detoxification unit, and between 1 May 2002 and 31 October 2002 there were 140 admissions. These numbers were outside the resources of the study, so consecutive admissions were numbered and cases selected randomly by computer (SAS, version 8.2).

Case notes were audited using a standard proforma, based on symptoms described in the hospital guideline which accorded with a recent national guideline (Scottish Intercollegiate Guidelines Network, 2003). Basic demographic data were collected. Symptoms of Wernicke–Korsakoff syndrome were recorded, as well as the timing and number of vials of parenteral thiamine administered.

The main area of interest was whether patients received better treatment pre or post intervention. A good outcome was defined as those who were treated according to the guideline. The analysis also took into account the ward to which patients were admitted (general ward v. alcohol problems clinic).

Results

A total of 70 pre-intervention and 93 post-intervention patients were included. The two groups were similar in terms of gender (50/70 v. 67/93 male), age (median age group 41–50 years in both groups) and length of admission (median stay 8 days and 11 days respectively).

From the 163 case notes studied, parenteral thiamine was indicated for 17 (24%) of the pre-intervention cases and 26 (28%) of the post-intervention cases. Among the pre-intervention cases, 11 patients had symptoms of Wernicke–Korsakoff syndrome and 6 had symptoms placing them at risk. In the post-intervention group, 15 patients had symptoms indicative of Wernicke–Korsakoff syndrome and 10 had symptoms that placed them at risk.

In a quarter of the pre-intervention cases patients were treated as per guideline; in the post-intervention group this rose to over 60%. Pre intervention 13 patients received thiamine, post intervention this rose to 21. Logistic regression was used to investigate change in adherence to the guideline, which was modelled as a binary dependent variable. The independent variables included whether patients were part of the pre-intervention or post-intervention group and whether or not they had been admitted to the Alcohol Problems Clinic. There is a significant effect for the intervention taking into account ward of admission: odds ratio 5.9; 95% CI 1.3–27.8 (Table 1).

Using logistic regression to look at admissions to the Alcohol Problems Clinic gave an odds ratio of 7.0 (95% CI 1.52–32.25), showing that admission to a specialist alcohol treatment unit had a stronger effect than the

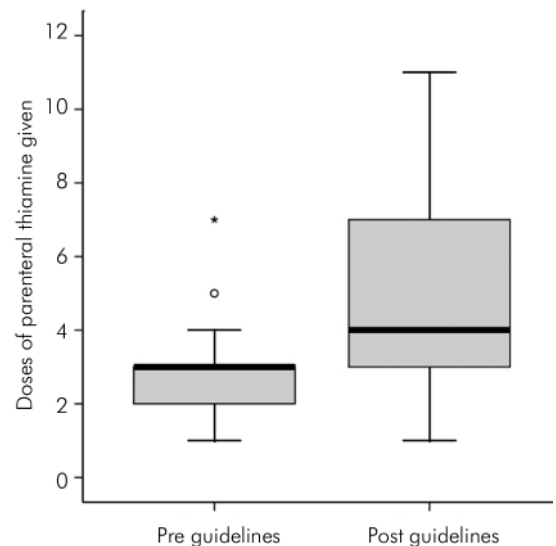


Fig. 2. Number of doses of parenteral thiamine before and after the intervention.

intervention on adherence to the protocol. Following the intervention, the average number of doses of parenteral thiamine rose from 3.08 to 4.62 (Fig. 2).

Discussion

In this study a quarter of patients undergoing detoxification required parenteral treatment with thiamine. The intervention of printing information from a guideline on the standard detoxification prescription sheet, and therefore having the guidance available at the time of prescribing, appeared to improve adherence to the guideline. Adherence was more common in a specialised alcohol treatment unit.

This study was a retrospective case-note analysis and as such its results should be interpreted cautiously. A standard proforma was used to minimise bias. Signs and symptoms were documented where recorded in case notes; because of this method of ascertainment it is likely that the incidence of patients requiring treatment was underestimated. The patient populations from the general ward and the specialist alcohol treatment unit may differ; however they are both likely to neglect their diet and to be at risk of alcohol-related memory impairment.

Parenteral vitamin replacement can prevent and treat the Wernicke–Korsakoff syndrome. There are increasing

	β (s.e.)	P	Adjusted odds ratio	
			OR	(95% CI)
Intervention	1.78 (0.79)	0.024	5.94	1.27–27.80
Alcohol Problems Clinic	1.94 (0.78)	0.013	7.00	1.52–32.25



numbers of patients requiring alcohol detoxification in a psychiatric setting; it is therefore important that psychiatric teams have access to appropriate information and guidance to ensure the patients' outcomes are optimised by appropriate use of parenteral vitamins. The risk of anaphylaxis is extremely low and they are on essential life and memory saving treatment.

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