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COMBINING THE AUDIT QUESTIONNAIRE AND BIOCHEMICAL MARKERS TO ASSESS ALCOHOL USE AND RISK OF ALCOHOL WITHDRAWAL IN MEDICAL INPATIENTS

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Abstract — Aims: Alcohol consumption is often under-reported in patients admitted to general hospitals with acute illness. For alcohol-dependent individuals hospital admission results in an enforced period of abstinence with potential alcohol withdrawal symptoms, and possible life threatening complications. Early detection of alcohol use is therefore beneficial to patients and health services. The purpose of this study was to investigate the performance of the alcohol use disorders identification test (AUDIT) questionnaire in the acute medical setting, and the effect of combining routine biological markers—glutamyltransferase, alanine aminotransferase, aspartate aminotransferase, and mean corpuscular volume (MCV) on its performance in the early identification of in-patients with alcohol use disorders and at risk of developing symptoms of alcohol withdrawal. **Methods:** Prospective study in consecutive patients admitted to an acute medical admissions ward. All patients were screened using the AUDIT questionnaire and routine blood tests. Patients were then monitored for symptoms of withdrawal using clinical institute withdrawal assessment for alcohol (CIWA-Ar). **Results:** Of the 874 patients screened using the AUDIT, 98 (11%) screened positive of whom 17 (2% of the 874) experienced clinically significant alcohol withdrawal symptoms, when using serial CIWA-Ar. The AUDIT and serial CIWA-Ar detected all patients who went on to manifest acute withdrawal symptoms. There was no loss of sensitivity at an AUDIT cut-off of 13 or more compared with the lower cut-off of 8 or more. A positive predictive value of 17.3% for an AUDIT score of 8 or more in the detection of withdrawal, increased to 47.1% when found in combination with at least two abnormal biological markers whilst maintaining a sensitivity of 94.1% and specificity of 97.9%. **Conclusion:** These findings confirm that AUDIT is a useful alcohol screen in general medical settings and that its ability to correctly predict which patients will experience alcohol withdrawal is increased when used in combination with biological markers.

INTRODUCTION

It is estimated that up to 20% of patients admitted to general hospitals during an acute medical intake are drinking above safe limits (Taylor *et al.*, 1986; Sharkey *et al.*, 1996). During hospital admission a proportion that abruptly ceases alcohol consumption may develop an alcohol withdrawal syndrome, with potentially life threatening complications (Schuckit *et al.*, 1995). Early identification of at risk patients is therefore advisable, yet many go undetected at their initial presentation (Nielsen *et al.*, 1994). Screening tools include biological parameters (Reynaud *et al.*, 2000; Sharpe, 2002) or questionnaires. Traditional biological markers include gamma glutamyltransferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and mean corpuscular volume (MCV). It has been reported that carbohydrate deficient transferrin may have higher specificity than more traditional markers but this is an expensive test and not widely available.

Over the past 30 years, a number of questionnaires have been developed to identify alcohol use disorders. The CAGE and Michigan Alcoholism Screening Test (MAST) questionnaires identify alcohol-dependent patients, with low sensitivity for those without alcohol dependence (Saunders and Kershaw, 1980). The WHO collaborative project sought to develop a questionnaire to screen for harmful drinking: the alcohol use disorders identification test (AUDIT) (Saunders *et al.*, 1993). A 10-item questionnaire covering alcohol consumption, drinking behaviour, and alcohol-related problems, it detects these end-points with high sensitivity and specificity—a score of 8 or more identifies individuals with an alcohol use disorder. Higher cut-off scores of 13, 16, and 20 or more have been suggested to improve discrimination for the severity of alcohol use disorders and in identifying alcohol-dependent patients at risk of withdrawal (Conigrave *et al.*, 1995; Babor *et al.*, 2001). However, these are yet to be established.

Hospital admission provides an excellent opportunity to screen large numbers for alcohol use disorders. There is ongoing debate as to the effectiveness of brief intervention in primary care, with very few secondary care studies conducted (Beich *et al.*, 2003). The value of questionnaires in the identification of excess alcohol consumption in hospital settings has been previously demonstrated (Canning *et al.*, 1999; Hodgson *et al.*, 2002). Many patients slip through the treatment net of alcohol management when they are admitted to hospital, often due to the clinician's oversight (DiPaula *et al.*, 1998). What objective screening test could be used on all patients to overcome this problem? This paper considers the diagnostic ability of the AUDIT questionnaire to accurately predict which patients will go on to develop a clinically meaningful alcohol withdrawal syndrome, when used in combination with traditional laboratory markers.

PATIENTS AND METHODS

The study was performed over a period of 8 weeks, on consecutive admissions to the acute medical ward at Prince Charles Hospital, Merthyr Tydfil, South Wales. This is a 434 bed district general hospital, serving a population of 150 000. The catchment population of the hospital is characterized by social and economic deprivation, in comparison to the rest of Wales.

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On admission patients aged 16 years or over were interviewed by nursing staff using the AUDIT questionnaire. Verbal consent was obtained. Nursing staff had previously attended a half-day training session on the AUDIT questionnaire, conducted by the local drug and alcohol team. Nursing staff recorded gender, age, overall AUDIT score, withdrawal symptoms, employment, and marital status in the medical admissions notebook on the ward. This information was collected and transferred to data sheets by one of the authors (J.D.) on a twice-weekly basis. Patients were excluded if they were unconscious or confused at the time of admission, refused consent, were unable to speak English, stated they had been questioned on a previous admission, or were rapidly transferred to a different ward. Patients were also excluded from the final analysis if the AUDIT questionnaire had been incorrectly completed or if not all of the relevant biological markers had been obtained at the time of admission. The total number of patients admitted to the ward over the period was 1243, of whom 369 were excluded from the study (Fig. 1).

Before the study was commenced, the local drug and alcohol team conducted a training session for nursing staff in how to apply the clinical institute withdrawal assessment for alcohol (CIWA-Ar) (Sullivan *et al.*, 1989). This well validated instrument assesses the severity of alcohol withdrawal symptoms using a 10-item scale. Patients scoring 8 or more on AUDIT were monitored by serial administration of the CIWA-Ar. Those with a CIWA-Ar score of 11 or more were treated with a benzodiazepine-based withdrawal regimen and re-assessed every 90 minutes, continuing treatment being dependent on the repeated CIWA-Ar score. If the CIWA-Ar score in these patients remained below 11, reassessment was discontinued after 12 h.

Venous blood samples were taken on the day of admission. MCV was measured on a Sysmex SE-9500, using a reference

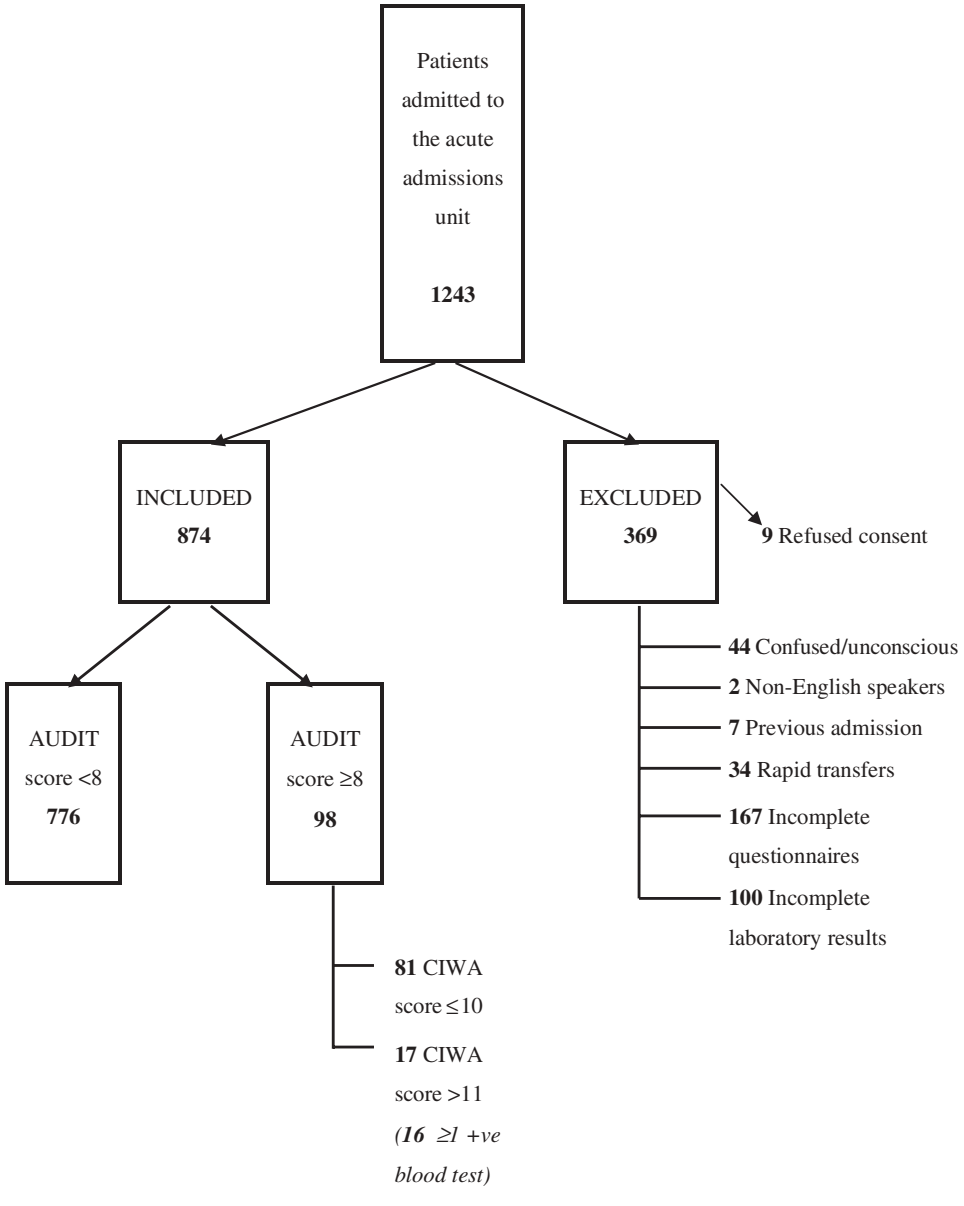

Fig. 1. Patients recruited to the study, reasons for exclusion, AUDIT, and CIWA scores.

range 80–100 fl. The parameters GGT, ALT and AST were measured on a Beckman Synchron LX-20, using a reference range suggested by the manufacturer (7–64 U/l, 5–35 IU/l, and 5–35 IU/l, respectively).

RESULTS

The sample included 874 patients (431 male, 443 female), all of Caucasian origin (Fig. 1). Average age was 61.70. Four hundred and forty-six patients were married, 132 single, 52 divorced, 15 co-habiting and 229 widowed. Five hundred and fifty-three patients were retired, 195 in current employment, 115 currently unemployed, and 11 on sick leave prior to admission. Their mean AUDIT score was 5.74 (median: zero). A total of 98 patients scored 8 or more on AUDIT, indicating alcohol use disorders—16% of men and 6.5% of women (mean AUDIT 17.74; median: 15). Of these, 17 (15 male, 2 female) experienced clinically significant alcohol withdrawal symptoms (age range 21–69 years). The extent to which biological markers were elevated is shown in Table 1. Six patients scored positive on all parameters, five of these experiencing clinically significant withdrawal symptoms. A normal screen of blood tests (i.e. normal GGT, AST, ALT and MCV) excluded all but one of the 17 patients who experienced clinically significant alcohol withdrawal (with a negative predictive value of 98.1); the AUDIT score was 19 in this patient. No patients with an AUDIT score of <8 experienced clinically significant alcohol withdrawal.

Sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) for the ability of the AUDIT questionnaire to identify patients experiencing clinically significant alcohol withdrawal were calculated using cut-off values of 8 or more and 13 or more, respectively (Table 2). Increasing the AUDIT score cut-off also increased both the specificity and the PPV of the questionnaire detecting those who later developed withdrawal symptoms.

In order to investigate the effect of combining biological parameters (MCV, AST, ALT and GGT) with the AUDIT outcome further sensitivity, specificity, PPV, and NPV calculations based on the study population were made. Incorporation of a greater number of test abnormalities increased the PPV of the questionnaire at the expense of sensitivity (Table 3). Combining two biological markers with a given AUDIT cut-off provided the optimal balance between maintaining sensitivity and increasing the PPV of the questionnaire in predicting patients who would develop withdrawal symptoms. Taking two abnormalities from the 'panel of four' achieved better sensitivity than any 'specific pair' of markers in combination above the AUDIT cut-off point, the best combination of which was AST and GGT (sensitivity 70.6%, specificity 98.8%, PPV 54.5%, NPV 99.4%).

DISCUSSION

Using a cut-off of 8, AUDIT identified an alcohol use disorder in 11% of patients admitted to the acute admissions ward. Using the AUDIT and CIWA screening, 2% of all patients assessed experienced alcohol withdrawal symptoms.

Use of the AUDIT questionnaire has the advantage of avoiding much of the disagreement in the literature surrounding the terminology and the definition of alcohol problems (Wetterling *et al.*, 1998). An AUDIT positive score alerts the clinician to the possibility of alcohol misuse. Higher cut-off scores of 13 or more and 23 or more have been suggested as better predictors of alcohol-related social problems, liver disease, or gastrointestinal bleeding, with high specificity at the expense of sensitivity (Conigrave *et al.*, 1995). We found no such fall in sensitivity using a cut-off value of 13 or more.

It is not established what AUDIT score can best predict the severity of the alcohol use disorder or the presence of dependence with physiological manifestations as defined in ICD-10 (World Health Organization, 1992). However, Reoux *et al.* (2002) tested the use of AUDIT alone as a predictor of an alcohol withdrawal syndrome in 118 alcohol-dependent patients, using CIWA-Ar to indicate a withdrawal syndrome. In their study, a cut off of 12 or more increased specificity at the cost of sensitivity. They conclude that AUDIT should be 'explored alone and in combination with other parameters to improve screening for clinically meaningful AWS in other settings'. This is what we have sought to do.

Table 1. The numbers of patients scoring 8 or more on AUDIT, and above the reference range of the biological markers

Parameter	Number of males above cut off *n* (%)	Number of females above cut off *n* (%)	Total number of patients above cut off *n* (%)
AUDIT	69 (16)	29 (7)	98 (11)
MCV	31 (7)	36 (8)	67 (8)
AST	89 (21)	84 (19)	173 (20)
ALT	80 (19)	60 (14)	140 (16)
GGT	71 (16)	76 (17)	147 (17)

Table 2. Sensitivity, specificity, PPV and NPV for AUDIT questionnaire at two different cut-off points for the detection of alcohol withdrawal syndrome in patients admitted to the acute medical ward

AUDIT score	Sensitivity	Specificity	PPV	NPV
8 or more	100	90.5	17.3	100
13 or more	100	95.6	30.9	100

Table 3. Correctly identifying an alcohol withdrawal syndrome: The effect of adding a combination of traditional biochemical screening test abnormalities to an AUDIT score above a given cut-off point

AUDIT score	Number of abnormal blood tests[a]	Sensitivity	Specificity	PPV	NPV
8 or more	+0	100	90.5	17.3	100
	+1	94.1	96.4	34.0	99.9
	+2	94.1	97.9	47.1	99.9
	+3	64.7	98.8	52.4	99.3
	+4	29.4	99.9	83.3	98.6
13 or more	+0	100	95.6	30.9	100
	+1	94.1	97.8	45.7	99.9
	+2	94.1	98.7	59.3	99.9
	+3	64.7	99.3	64.7	99.3
	+4	29.4	99.9	83.3	98.6

[a]Biological markers included MCV, AST, ALT and GGT. If any of these parameters were raised they would contribute to the 'number of abnormal tests' score i.e. +1 signifies only one out of the four was abnormal, +4 signifies that all these markers were abnormal.

A further limitation of the AUDIT questionnaire in the acute medical setting is the demand on clinical staff in terms of the time required to calculate the AUDIT score and complete serial CIWA-Ar questionnaires. Of the 98 patients identified by the AUDIT cut-off 8 or more, only 17 manifested symptoms of clinical withdrawal, that is, nursing staff had to complete CIWA-Ar forms for 81 patients who did not require treatment for alcohol withdrawal. Shorter, alternative questionnaires have already been outlined. An abbreviated form of the AUDIT exists: the three question AUDIT-C. This uses the first three questions of the longer AUDIT, appearing to be effective at screening for heavy drinking and/or active alcohol abuse or dependence (Bush *et al.*, 1998). Another way to reduce the clinical demand would be to use subsections of the AUDIT, such as the dependence questions or single questions.

The local laboratory employed a relatively high upper limit value of GGT compared with the values for ALT and AST. Previous studies (Steffensen *et al.*, 1997; Lee *et al.*, 2001) show that non-drinkers with healthy livers typically have similar levels of all three enzymes. In our study GGT provided the highest PPV, which may be influenced by this relatively high upper limit value.

The usefulness of questionnaires versus blood tests in identifying alcohol misuse has been much debated (Lock *et al.*, 1999), with a focus on the ability of the screening test, whether biological or questionnaire, to identify either alcohol misuse or dependency (Wetterling and Kanitz, 1996). One such study, conducted on behalf of the WHO, concluded that a combination of CDT, GGT and AST provided better detection of high-risk than of intermediate consumption (Conigrave *et al.*, 2002). The use of the 'panel of four' traditional biological markers with selected AUDIT cut-off scores enhanced the positive predictive value of the AUDIT questionnaire in this study population. This 'panel of 4' biological markers were chosen as they are widely available and would be applicable to the majority of patients admitted on acute medical admissions. If, given an initial AUDIT score 8 or more, a serial CIWA-Ar questionnaire were only completed if two or more out of the 'panel of 4' biological markers were abnormal, due to the increased PPV of this combined result, workload for clinical staff might be considerably reduced whilst maintaining a high sensitivity and specificity for detecting patients likely to experience withdrawal. This model using a combination of the AUDIT questionnaire and 'panel of 4' biological markers requires further validation in the clinical setting.

AUDIT has been demonstrated to be effective at identifying alcohol use disorders including dependency as well as episodic and short duration drinking patterns (Saunders *et al.*, 1993). It is possible that blood tests are raised when there is prolonged, heavy alcohol use or in the presence of co-morbidity leading to hospital admission, giving rise to an increased risk of alcohol withdrawal syndrome. This may help to explain why our results indicate that a combination of both questionnaire and biological tests increase the ability to detect and potentially prevent alcohol withdrawal.

In conclusion, the AUDIT questionnaire can be used in the acute medical setting to detect alcohol use disorders, offering opportunities for intervention in the hope of preventing alcohol withdrawal, and minimizing long-term risk. Combining routinely available biological markers with an AUDIT questionnaire enhances screening for alcohol use disorders and those patients at risk of alcohol withdrawal symptoms. Further investigation of such a combined screening tool is warranted to explore its potential in reducing the workload passed on to the clinical staff implementing the screening process.

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