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Alcohol biomarkers in patients admitted for trauma

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Abstract

Background: To assess the value of blood alcohol levels (BAL) and carbohydrate deficient transferrin (CDT) in trauma patients.

Methods: A prospective study was conducted among 213 patients admitted to a university hospital after trauma. Outcomes of interest include the development of alcohol withdrawal, infections, respiratory problems, cardiac events, thromboembolism and length of stay.

Results: The majority (78%) of the trauma patients in the study were males over the age of 18. 75% reported drinking an alcohol containing beverage in the previous 30 days, 34% had ≥ 5 heavy drinking days, and 18.7% met current DSM-IV criteria for alcohol abuse and 13.1% current criteria for dependence. Twenty-two percent (n=48) had a positive blood alcohol level (BAL) and 14% (n=30) a CDT level >*2.5%*. Twelve percent (n=27) of the sample developed alcohol withdrawal and 55% (n=113) had one or more adverse health events during their hospitalization. The development of alcohol withdrawal was associated with an admission CDT >2.5% (chi-square 4.77, p<.029) and/or a positive BAL (chi-square 54.01, p<.001). The alcohol biomarkers identified 13 male and 3 female high-risk patients (7.4% of the total sample), who denied excessive alcohol use, who would have missed if these markers were not used. A composite morbidity trauma score composed of 25 adverse health events was associated with a positive BAL (p<0.022).

Conclusion: The study provides additional empirical evidence that supports the use of BAL in all patients admitted for trauma. The usefulness of CDT in trauma patients remains unclear and will require larger samples in more critically ill patients.

Keywords

trauma; biomarkers; withdrawal; adverse events; alcohol

INTRODUCTION

Excessive use of alcohol is a common cause of trauma; it complicates assessment of injury and inpatient care (Koval et al., 2008). A review of emergency department studies by Roizen (1988) found that 20-37% of the accident cases seen in trauma centers are alcohol-related. The effects of alcohol on the brain can interfere with accurate assessment of trauma (Lowenfels, 1982; Soderstorm et al., 1979) head injury, degree of pain, fractures, chest and abdominal injuries. In addition trauma patients may be reluctant to accurately self-report their alcohol use due to fear of legal implications, employment problems or payment for medical care by their health insurance company. Alcohol biomarkers may provide unique information and assist in the management of patients admitted to trauma centers.

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Traditional alcohol biomarkers include mean corpuscular volume, gamma glutamyl transferase (GGT), aspartate aminotransferase and alanine aminotransferase. However, these tests have a low sensitivity and specificity with limited clinical utility in trauma patients (Helander, 2003). Another biomarker is blood alcohol level which is used by law enforcement agencies, transplant programs, alcohol and drug treatment programs and some trauma centers.

Newer biomarkers include carbohydrate deficient transferrin (CDT) (Bortolotti et al., 2006; Savola et al., 2004), Phosphatidylethanol (PEth) (Aradottir et al., 2006; Mueller et al., 1988), and ethyl glucuronide (EtG) (Helander, 2004). These biomarkers offer potential advantages over BAL due to the rapid metabolic clearance of alcohol from blood since BAL levels fall at a rate of 15mg% (0.015g/dL) per hour. Each of these biomarkers remains positive in blood for a distinct time spectrum (Kip et al., 2008). EtG has window of 80 hrs and may be useful to detect cases of alcohol relapse (Wojcik and Hawthorne, 2007). PEth can form in vitro in the presence of ethanol (Aradottir et al., 2004) that may limit its use. CDT is widely used in Europe for screening and assessment and has specificity of 82-100% and sensitivity of (39-94%) (Hannuksela, 2007). CDT and GGT will mainly identify persons engaged in long-term heavy drinking (Spies et al., 1995; Tønnesen et al., 1999; Neumann and Spies, 2003; Neumann et al., 2008).

The purpose of this paper is to report the value of blood alcohol level and carbohydrate deficient transferrin in patients admitted for trauma. These markers have the potential to identify patients at risk of alcohol related complications.

METHODS

Design and sample

A prospective study was conducted among patients admitted with trauma to the University of Wisconsin-Madison Hospital. Two hundred and thirteen patients who met eligibility criteria were enrolled in the study. Exclusion criteria included below eighteen years of age, admitted with burns, pregnant, under police custody or inability to participate in a face-to-face interview within one week of admission. More than 90% of the sample in our study was admitted for trauma related to motor vehicle accidents with the remaining patients admitted for falls, bicycle/pedestrian accidents and penetrating trauma.

The mean injury severity score of the sample was 13.4, the median score was 10 with a range of 1-38. Critically ill patients, who were not able to participate within one week of admission, were not eligible. Due to confidentiality issues we were unable to collect any information on trauma patients who did not participate in the study. Subjects were identified each morning from the trauma admission list and approached by one of the projects research staff and invited to participate. The study was conducted in 2006-2007 over 14 month period. There were 789 potential candidates out of which 62 were excluded (5 pregnant, 52 under 18 and 5 prisoners) 187 were discharged before interview, 30 had no blood sample, 211 were too ill to consent with in one week of admission, 84 refused to take part in the study and 2 withdrew from the study.

Research procedures

All subjects who gave their written consent had a face-to-face interview within one week of admission. Family members were not contacted for collaboration due to privacy rules. Even though all trauma patients during the study period had blood drawn at the time of admission as part of routine care only those patients who consented to the study had a CDT test performed. Blood samples were stored in the refrigerator at the pathology laboratory of UW hospital until sent by FedEx to South Carolina for analysis. The CDT test was paid for by the grant and

performed in the laboratories of Dr. Ray Anton at the Medical College of South Carolina. BAL is routinely performed in all patients admitted for trauma at UW Madison. Patients with a positive BAL at UW Hospital normally receive a brief intervention by the medical staff and consultation to the addiction medicine service. The study was approved by the University of Wisconsin Health Sciences Human Subjects committee. Research subjects were paid $20 for their participation in the study.

The face to face interview included questions on alcohol use in the previous 30 days, DSM-IV criteria for alcohol abuse and dependence and socio-demographics.

Subjects were then asked if they have used any alcohol in the last 30 days. The alcoholic drinks included were beer, wine, wine coolers, gin, vodka, or other hard liquor. If patients reported any alcohol use a 30 day time line follow back procedure was employed to estimate alcohol use in the past 30 days. The time line follow back method is a calendar based recall method designed to increase the accuracy of self report. There were four DSM-IV criteria questions to detect alcohol abuse and they were further asked if any of the symptoms occurred within the last 12 months. There were seven DSM-IV criteria questions to detect alcohol dependence and they were further asked if they experienced any of the symptoms in the last 12 months. The answer to these questions was recorded as either “yes”, “no” or “NA” (not applicable). Patients needed to report one or more positive response to the abuse questions to meet a current DSM-IV diagnosis of alcohol abuse or 3 or more dependence questions to meet a current DSM-IV diagnosis of alcohol dependence. The last set of questionnaire was about gender, race, and marital status, level of education, employment status and zip code where they live.

Percent CDT levels were performed using turbidometric immunoassay method developed by Axis Shield (Oslo Norway) and distributed by Bio-Rad (Hercules California). CDT level >2.5% is considered a positive test (Anton, 2001; Fleming et al., 2004). The UW trauma data base was established in 1996 and includes a number of health variables including trauma diagnoses, blood loss, infection, respiratory problems, cardiac events, surgical procedures, development of thromboembolic events, time in the ICU, length of time on a respirator, length of stay in the hospital and post discharge plans.

Analysis

Data for the study was entered into an excel data base by members of the research team. Variables of interest included alcohol use and dependence, adverse health events during the subject hospitalization and biomarker levels. SAS was used to calculate the numbers reported in the results section. Tables 1-2 report the frequencies of the variables of interest. Table 3-4 reported associations between BAL and CDT and the outcomes of interest. Chi square analysis was used to examine the relationship between alcohol biomarkers and the development of withdrawal, adverse health events that occurred during the hospitalization and length of stay.

A composite morbidity trauma score was created to examine the relationship of BAL and CDT to adverse health events. The composite score was created as there were too few adverse health events in each category to assess the relationship of BAL and CDT levels to individual events. The events were selected based on their inclusion in the University of Wisconsin hospital trauma data base. The composite score consisted of 25 items with each event receiving a score of one. While some events are more serious than others (e.g. infarct vs. blood loss) there were too few events to weight these variables differently. The composite score ranged from 0-25. The 25 items listed in table 5 that make up the composite morbidity trauma score include blood loss (3 levels of blood loss), blood transfusion (1 event), respiratory problems (3 events), infections (4 events), wound healing (3 events), cardiac events (4 events), thromboembolism (2 events), time on ventilator (3 time periods) and a GCS score (2 events, a GCS of >10 was not included as this is considered normal).

RESULTS

Table 1 reports the consumption of alcohol during the last 30 days. Data about the alcohol consumption is presented in separate columns for males and females. They are further presented in to two sets of columns by age, in one column subjects between the ages of (18-30) and in second column subjects above 30 years of age because younger people have different drinking behavior. 12% (n=27) reported 2 or more drinks per day, 34% (n=73) had 5 or more heavy drinking days in the past 30 days, 18.7% met current DSM-IV criteria for abuse and 13.1% dependence.

Table 2 reports the relation of BAL and CDT levels with the drinkers and non-drinker. Drinkers are further separated in to three categories depending on the level of total drinks reported to the researcher during the last 30 days. There were only 30 (14%) subjects with a CDT level >2.5% all of whom were men. 48 (22.5%) subjects had a positive BAL including 6 women.

Table 3 illustrates the composite morbidity trauma score by BAL and CDT level. As explained in the methods section the composite morbidity trauma score is derived from the adverse health events recorded in the UW trauma database with the exception of alcohol withdrawal and a GCS >10. Subjects in this table were categorized into four groups based on a composite score of 0, 1-2, 3-4 and 5 or more. As noted there were 114 subjects with a score of 1 or more with 81 have a score of 1-2, 20 with a score of 3-4 and 13 a score of 5 or more.

Table 4 examines the relationship of BAL and CDT levels with the development of alcohol withdrawal, subjects with a score of one or more on the composite score and length of stay. There is a statistically significant relationship between BAL and/or CDT levels and the development of alcohol withdrawal. There is also a significant relationship of BAL and the development of other adverse health events. There was no relationship of CDT to adverse health events. There was also no relationship between the 2 biomarkers and length of hospital stay.

DISCUSSION

This paper presents new information on the clinical value of two commonly used alcohol biomarkers. The data presented supports the routine testing of BAL for all trauma patients admitted to a hospital. Nearly one in four patients had a positive BAL in a sample with mean severity score of 13.4. There was a statistically significant relationship between BAL and alcohol withdrawal and adverse hospital events. All but seven of the 27 patients who developed alcohol withdrawal had a positive BAL. The findings of this study suggest that BAL is clinically useful in patients admitted with minor trauma not just those with severe injuries who are unconscious and unable to provide alcohol information.

As noted in Table 3 Blood alcohol levels identified 16 subjects who were legally drunk but minimized their alcohol use and only reported drinking <1 drink per day. These subjects probably would not have received brief intervention counseling and/or referral for alcohol treatment if they had not had a BAL tested. BAL was also found to be a better predictor of alcohol withdrawal than patient self-report. This paper provides some of the best evidence to date that supports the current standard of care in many trauma centers – namely BAL for all trauma patients.

The routine use of CDT testing in trauma populations remains uncertain due to the limited number of patients in this study with a positive CDT (n=30, 14%), low sensitivity of %CDT in women, a sample with moderate ISS scores (mean of 13.4) and a limited number of adverse events. CDT did appear to be sensitive and specific in young men and was associated with development of alcohol withdrawal ($p<.022$). There were six women in the sample with a

positive BAL; however, none of these 6 had a positive CDT test. The addition of CDT detected two subjects not already identified by a positive BAL. Additional research with a larger sample of more critically ill patients is needed to determine the clinical utility of CDT. There were just too few patients with a positive CDT and too few adverse events in this sample. Routine CDT testing can probably be justified in men but not women.

It is important to acknowledge the varying time frames associated with BAL and CDT. Blood alcohol levels fall rapidly, are limited to acute ingestion as alcohol is metabolized at a rate of about one standard drink per hour. CDT on the other hand reflects chronic use and will remain elevated for a number of weeks after cessation of alcohol use (Fleming et al, 2004). As a result the combination of BAL and CDT offers a number of advantages over reliance on a single biomarker.

The study is in contrast with the work of Spies and colleagues who found a strong relationship of CDT and adverse events following trauma (Spies et al., 1998). They reported a strong statistical association with CDT and prolonged length of stay as well as higher rates of pneumonia, cardiac failure, sepsis and pancreatitis. Primary differences between our study and theirs was a study population which were more critically ill (ICU trauma patients only vs. all trauma patients admitted), lowers rate of employment suggesting a lower SES group, the use of a different CDT assay and a larger number of subjects with a positive CDT tests (36 out 66 ICU trauma patients had a positive CDT test).

The findings of our study are similar to the findings of the study done by (Savola et al., 2004) that blood alcohol level is the accurate indicator of hazardous drinking in trauma patients.

We find ourselves in agreement with the findings of the study by (Ryb et al., 1999) that blood alcohol level and interview screens is suggested for use in trauma patients to detect alcohol related disorders.

The study has a number of strengths including the inclusion of all patients admitted for trauma regardless of trauma severity, assessment of both blood alcohol levels and CDT testing, inclusion of illicit drug use information and state of the art laboratory and research procedures. We used a number of strategies to minimize denial that includes confidentiality, a careful interview using time line follow back procedures and multiple alcohol questions. In addition prior work in a primary care sample in Wisconsin found an abstinence rate of 40% in women and 25% in men (see Fleming M, et al. At-risk drinking in an HMO primary care sample: prevalence of health policy implications. American Journal of Public Health.1998; 88(1): 90-93).

Primary limitations include the inability to test all patients for CDT levels including those who were too ill to participate in the interview. IRB restrictions did not allow routine CDT testing of all trauma patients, since the test is not considered standard care at our hospital. Other limitations included the sample size with only 30 subjects having a positive CDT. The number of adverse events in the sample was also small with no serious cardiac events, small numbers requiring ventilatory support and no life threatening infections. There was also limited diversity in the sample with young white men compromising most of the sample and 100% of the sample with a positive CDT level. There were also too few subject with a positive BAL and/or CDT to examine potential confounding variables such as tobacco use, illicit drug use and trauma severity. Future research may want to try to include all patients admitted including those who are critically ill and try to obtain information from family members for corroborative reporting.

CONCLUSIONS

The findings of the study support the use of BAL on all patients admitted for trauma. Trauma teams may want to monitor patients closely for alcohol withdrawal and start treatment with benzodiazepines earlier than in patients with a negative BAL. Patients with a positive BAL are likely to have alcohol problems and should receive brief intervention and consultation with an addiction medicine consult service.

The clinical value of other biomarkers such as CDT levels is less clear in routine trauma patients. Since CDT reflects long term chronic use this marker has the potential to identify trauma patients whose BAL was zero as a result of delays in transportation to the hospital. Additional research, using larger samples with patients who are more critically ill, are needed to address this question.

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Table 1

Current Alcohol use & Alcohol Related Behavior (DSM-IV)

	Male		Female		Total
Age	**18–30**	**30+**	**18-30**	**30+**	
	n=64	**n=103**	**n=13**	**n=33**	**n=213**
	n %	**n %**	**n %**	**n %**	**n %**
Alcohol use last 30 days					
0 drinks	12 (19)	19 (18)	5 (38)	16 (48)	**52 (24)**
1-30 drinks	30 (47)	57 (56)	7 (53)	15 (45)	**109 (51)**
31-60 drinks	13 (20)	9 (9)	1 (7)	2 (6)	**25 (12)**
61-90 drinks	5 (8)	13 (13)	0	0	**18 (8)**
>90 drinks	4 (6)	5 (5)	0	0	**9 (4)**
Heavy drinking days, 5 or more	37 (58)	30 (29)	3 (23)	3 (9.09)	**73 (34)**
Alcohol Abuse	23 (14)	12 (7)	3 (6)	2 (4)	**40 (18.7)**
Alcohol Dependence	17 (10)	7 (4)	3 (6)	1 (2)	**28 (13.1)**

Table 2

Alcohol use, Carbohydrate Deficient Transferrin and Blood Alcohol Levels by gender

	Male				Female				Total
	Non-drinker n=32 n %	**1-30 per month n=86 n %**	**31-60 per month n=21 n %**	**> 60 per month n=28 n %**	**Non-drinker n=21 n %**	**1-30 per month n=21 n %**	**31-60 per month n=2 n %**	**> per month n=2 n %**	**n=213 n %**
CDT									
< 2.0	28 (88)	53 (62)	10 (48)	6 (21)	16 (76)	14 (67)	1 (50)	1 (50)	**129(60.5)**
2.1 - 2.5	3 (9)	24 (28)	6 (29)	7 (25)	5 (24)	7 (33)	1 (50)	1 (50)	**54(25.3)**
2.6 +	1 (3)	9 (10)	5 (24)	15 (54)	---	---	---	---	**30(14.0)**
BAL									
Zero	31 (97)	68 (79)	14 (67)	12 (43)	21 (100)	17 (81)	1 (50)	1 (50)	**165(77.4)**
0.01 - 0.02	---	1(1)	---	1(4)	---	---	---	---	**2(0.9)**
0.03 - 0.08	1 (3)	4 (5)	1 (5)	2 (7)	---	1(5)	---	1(50)	**10 (4.6)**
0.09 - 0.20	---	9 (10)	4 (19)	11 (39)	---	2(10)	---	---	**26 (12.2)**
0.21 +	---	4 (5)	2 (10)	2 (7)	---	1 (5)	1 (50)	---	**10 (4.6)**

CDT – carbohydrate deficient transferrin

BAL – Blood alcohol level

Table 3

Frequency of composite morbidity score by CDT and/or BAL level

	CDT ≤ 2.5 N=182	**CDT > 2.5 N=31**	**BAL = 0 N=164**	**BAL > 0.01 N=49**	**0 BAL and CDT <2.6 N=148**	**= BAL or CDT >2.5 N=65**	**Total N=213**
Composite Morbidity trauma score	N %	N %	N %	N %	N %	N %	N %
0	84 (46 %)	15 (48 %)	84 (51 %)	15 (31 %)	75 (51 %)	24 (37 %)	99 (46 %)
1-2	73 (40 %)	8 (26 %)	60 (36 %)	21 (43 %)	57 (39 %)	24 (37 %)	81 (38 %)
3-4	15 (8 %)	5 (16 %)	12 (7 %)	8 (16 %)	9 (6 %)	11 (17 %)	20 (18 %)
5 or more	10 (6 %)	3 (10 %)	8 (5 %)	5 (10 %)	7 (5 %)	6 (9 %)	13 (6 %)

The composite morbidity trauma score is made up of the 25 adverse health events listed in table 4 with the exception of alcohol withdrawal and a GCS score of 6 or more. Each event has an equal score of one with the potential score ranging from 0-25.

CDT – carbohydrate deficient transferrin

BAL – Blood alcohol level

Table 4

Association of CDT and BAL with the development of alcohol withdrawal, composite morbidity trauma score and length of stay

	CDT ≤2.5 N=182 n %	CDT >2.5 N=31 n %	BAL=0 N=164 n %	BAL >0.01 N=49 n %	0 BAL and CDT <2.6 N=148 n %	Either + BAL or CDT>2.5 N=65 n %	Total N=213 n %
Alcohol withdrawal	20 (11%)	**7 (26%)** [a]	6 (4%)	**21 (45%)** [b]	6 (5%)	**21 (34%)** [c]	27 (12%)
Composite morbidity trauma score of one or more	97 (52%)	16 (52%)	80 (48%)	**33 (67%)** [d]	73 (48%)	**40 (62%)** [e]	114 (55%)
Length of stay							
1-2 days	60 (34%)	13 (42%)	55 (34%)	18 (39%)	49 (33%)	24 (38%)	73 (34%)
3-4 days	42 (23%)	8 (26%)	37 (23%)	11 (24%)	34 (23%)	16 (25%)	50 (23%)
5 or more	80 (44%)	10 (32%)	71 (44%)	19 (37%)	65 (44%)	25 (37%)	90 (42%)

There was no statistical relationship between CDT and the morbidity trauma score.

There was no statistical relationship between BAL or CDT levels and length of stay.

[a] Chi square for alcohol withdrawal - comparing CDT ≤ 2.5 with those with CDT > 2.5: Chi square=4.77, p=.029

[b] Chi square for alcohol withdrawal- comparing positive BAL vs. negative BAL: Chi square=54.01, p<.001

[c] Chi square for alcohol withdrawal - comparing + BAL and/or CDT>2.5: Chi square=33.36, p<.001

[d] Chi square for morbidity composite score- comparing positive BAL vs. negative BAL: Chi square= 5.32, p<0.022

[e] Chi square for morbidity composite score- comparing positive BAL vs. negative BAL: Chi square= 4.82, p<0.029