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Acute Ethanol Intoxication and the Trauma Patient: Hemodynamic Pitfalls

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Abstract Many trauma patients are acutely intoxicated with alcohol. Animal studies have demonstrated that acute alcohol intoxication inhibits the normal release of epinephrine, norepinephrine, and vasopressin in response to acute hemorrhage. Ethanol also increases nitric oxide release and inhibits antidiuretic hormone secretion. This article studies the effects of alcohol intoxication (measured by blood alcohol level, BAL) on the presentation and resuscitation of trauma patients with blunt hepatic injuries. A retrospective registry and chart review was conducted of all patients who presented with blunt liver injuries at an ACS-verified, level I trauma center. Data collected included admission BAL, systolic blood pressure, hematocrit, International Normalized Ratio (INR), liver injury grade, Injury Severity Score (ISS), intravenous fluid and blood product requirements, base deficit, and mortality. From September 2002 to May 2008, 723 patients were admitted with blunt hepatic injuries. Admission BAL was obtained in 569 patients, with 149 having levels >0.08%. Intoxicated patients were more likely to be hypotensive on admission ($p = 0.01$) despite a lower liver injury grade and no significant difference in ISS. There was no significant difference in the percent of intoxicated patients requiring blood transfusion. However, when blood was given, intoxicated patients required significantly more units of packed red blood cells (PRBC) than their nonintoxicated counterparts ($p = 0.01$). Intoxicated patients also required more intravenous fluid during their resuscitation ($p = 0.002$). Alcohol intoxication may impair the ability of blunt trauma patients to compensate for acute blood loss, making them more likely to be hypotensive on admission and increasing their PRBC and intravenous fluid requirements. All trauma patients should have BAL drawn upon admission and their resuscitation should be performed with an understanding of the physiologic alterations associated with acute alcohol intoxication.

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Introduction

The correlation between alcohol use and traumatic injury has been well documented. Some studies report a rate of alcohol use as high as 47% at the time of injury, with legal intoxication in up to 15% [1–3]. Studies have also shown the immunologic effects of acute alcohol intoxication [4–7]. However, there has been little published regarding how acute alcohol affects the resuscitation of trauma patients.

Animal studies have shown that intoxicated animals were more hypotensive with fixed-volume hemorrhage compared to controls, and they required less volume of hemorrhage to produce clinically significant hypotension [7–9]. The blood pressure of intoxicated animals also responded poorly to crystalloid volume resuscitation. This physiologic difference might possibly be explained by the impairment of hemodynamic and metabolic compensatory mechanisms after acute hemorrhage. These include the inhibition of epinephrine, norepinephrine, and arginine vasopressin [7–10]. Alcohol has also been shown to depress cardiac contractility after hemorrhagic shock [10]. Although these physiologic alterations have been associated with increased hypotension following hemorrhage in

animal models, there is a paucity of literature documenting this association in humans.

We hypothesized that acutely intoxicated patients with hemorrhagic trauma would more likely be hypotensive on admission as a result of the physiologic effects of alcohol compared to those who are not intoxicated. We also expected that because of this hypotension, more of the intoxicated patients would require operative intervention, more intravenous fluid, and more blood product transfusions during initial resuscitation.

Methods

A retrospective review of the trauma registry, blood bank, and medical record data was performed for trauma patients admitted to University Medical Center/Community Regional Medical Center, a state-designated 660-bed Level I trauma center in Fresno, California, from September 2002 to May 2008.

Patients were divided into alcohol-intoxicated and nonintoxicated groups: blood alcohol level (BAL) % $\geq$0.08 and 0.0-0.08%, respectively, based on the legal limit. Although judgment and driving ability start to deteriorate at a BAL of 0.05% [11, 12], we chose 0.08% since this is the legal cutoff and therefore has the greatest practical implications with regard to loss of life, health, and resource utilization.

Patients defined as hypotensive had an initial manual blood pressure of <90 on admission to the Emergency Department. Age, mean liver injury grade, Injury Severity Score (ISS), International Normalized Ratio (INR), admission hematocrit, and base deficit were collected. Additional data included percentage of patients transfused with blood products, volume of products given, liters of intravenous crystalloid, mortality, incidence of acute respiratory distress syndrome (ARDS) and ventilator-associated pneumonia (VAP), and hospital length of stay (LOS). Data are presented as mean $\pm$ standard error. Fisher's exact and two-tailed *t*-test was used for statistical analysis, and a p value of <0.05 denoted significance.

Primary outcomes between the two groups were admission hypotension, incidence and amount of fluid and blood for initial resuscitation at 24 h, incidence of operative intervention and need for specific operative hepatic intervention, and overall mortality. Secondary outcomes were hospital length of stay and incidence of ARDS and VAP. The primary outcomes were to examine if and how alcohol intoxication affects initial trauma resuscitation, especially in regard to use of important resources, especially blood products.

Patients with blunt liver injuries were used as our primary inclusion criteria for the following reasons: (1) The liver is the most commonly affected organ in blunt trauma [13, 14]. (2) Liver injuries can be graded according to an accepted and reproducible scale: the American Association for the Surgery of Trauma (AAST) solid organ injury scale [15]. (3) Patients with documented liver injuries have objective radiographic evidence of hemorrhage. These factors allowed a direct comparison of both anatomic and physiologic severity of injury.

The project was approved by the Institutional Review Board of Community Regional Medical Centers and the University of California, San Francisco-Fresno.

Results

During the period from September 2002 to May 2008, 11,901 patients were admitted for trauma, and 9,807 (82%) had blunt mechanisms of injury. Of these, 569 patients had both confirmed liver injuries and blood alcohol concentration drawn upon admission and make up the study cohort. Four hundred twenty patients had BAL $<$ 0.08% (nonintoxicated), and 129 had BAL $\geq$ 0.08% (intoxicated).

There were no significant differences between average age, ISS, and percent with positive findings on Focused Abdominal Sonography for Trauma (FAST) between the two groups. The AAST mean liver injury grade was less (2 vs. 3, $p = 0.02$) in the intoxicated group. The admission hematocrit was slightly higher in the intoxicated group. Intoxicated patients were significantly more likely to be hypotensive on admission ($p = 0.01$) and have a worse base deficit ($p < 0.01$, Table 1). There was no significant difference in INR between the two groups.

The 24-h resuscitation outcome and blood product usage among the two groups were also compared (Tables 2 and 3). The percentage of patients who required blood product transfusion was not different between the two groups. However, despite having a lower liver injury grade and a higher admission hematocrit, intoxicated patients who were transfused required more blood products ($p = 0.02$) and more intravenous fluid ($p = 0.002$) during the first 24 h. In patients not requiring blood transfusions, the intoxicated group still required significantly more intravenous fluid (6 vs. 4 L, $p < 0.001$). Despite these differences, intoxicated patients did not have an increased likelihood of requiring laparotomy ($p = 0.08$), liver repair/resection, or hospital LOS. Although intoxicated patients received more intravenous fluid and blood products, there was no significant difference in ARDS or VAP between the intoxicated and nonintoxicated groups.

When the nonintoxicated group was further subdivided into those with an admission BAL of 0.0% ($N = 299$) and those with BAL $>$ 0.0% but <0.08% ($N = 121$), the mean BAL value of the latter group was 0.02%. Although there

Table 1 Patient characteristics

	Nonintoxicated ($n = 420$)	Intoxicated ($n = 149$)	p value
Age	33.3 ± 1.2	33.3 ± 1.6	NS
Mean liver injury grade	3	2	0.02
ISS	24 ± 0.7	24 ± 1.2	NS (0.6)
Admission hematocrit (%)	36.8 ± 0.3	38.3 ± 0.5	0.02
% with positive FAST	28%	24%	NS (0.4)
% hypotensive (SBP ≤ 90)	15%	25%	0.01
Admission base deficit	−3 ± 0.3	−6 ± 0.5	<0.01
Admission INR[a]	1.17 ± 0.43	1.15 ± 0.36	NS (0.6)

Data reported ± standard error where applicable

NS not significant, *ISS* Injury Severity Score, *FAST* Focused Abdominal Sonography for Trauma, *SBP* systolic blood pressure, *INR* International Normalized Ratio

[a] 395 nonintoxicated and 144 intoxicated patients had admission INR drawn

Table 2 Resuscitation findings

	Nonintoxicated ($n = 420$)	Intoxicated ($n = 149$)	p value
No. patients transfused	135 (32%)	51 (34%)	NS (0.7)
24-h IV crystalloid (L)	6.7 ± 0.3	9.5 ± 0.8	0.002
% exploratory laparotomy	28%	36%	NS (0.08)
% liver operation	11%	13%	NS (0.5)
Overall % mortality	11%	13%	NS (0.5)
Hospital length of stay (days)	12.2 ± 0.6	14.1 ± 1.2	NS (0.2)

NS not statistically significant

Table 3 Patients receiving transfusion

	Nonintoxicated ($n = 135$)	Intoxicated ($n = 51$)	p value
Average no. units blood products transfused	10.9 ± 1.3	18.7 ± 3.0	0.02
Average no. units PRBCs	7.6 ± 0.8	14 ± 2	0.01
Average no. units FFP	2.8 ± 0.4	4.1 ± 0.7	NS (0.1)
Average no. units platelets	1.0 ± 0.2	1.9 ± 0.5	NS (0.1)

PRBC packed red blood cells, *FFP* fresh frozen plasma, *NS* not statistically significant

was a significant difference between the two nonintoxicated subgroups ($p < 0.0001$), the mean BAL of the entire nonintoxicated group was close to negligible (0.007 ± 0.01%). Analysis of the variance (ANOVA) using post hoc analysis was used to evaluate patients with BAL of 0.0%, 0.0% < BAL < 0.08% and BAL ≥ 0.08% with respect to admission hypotension, hematocrit, base deficit, number of units of PRBC, probability of survival, and hospital days. Only base deficit was significantly different in post hoc analysis when BAL ≥ 0.08% was compared to the BAL 0.0% and BAL < 0.08% groups ($p < 0.001$ and $p = 0.028$, respectively). Also, receiver operator curve (ROC) did not show a significant dose effect with respect to BAL and admission hypotension.

Sixty-seven of the 569 patients in the study died (12%). Forty-seven were in the nonintoxicated group and 20 were intoxicated. The overall difference in mortality rate between the two groups was not significant (11% vs. 13%, respectively, $p = 0.5$). The majority of deaths (45%) in the nonintoxicated group were from closed head injury (CHI), while 38% of the same group died from documented liver hemorrhage. Forty percent of the intoxicated group died directly of liver hemorrhage, while 30% died as a result of CHI. There was no significant difference in the number of deaths by CHI or liver hemorrhage between the intoxicated and nonintoxicated patients. Also, there was no significant difference in mortality between the groups when stratified by liver injury grade. All four patients with grade 6 liver injuries died (3 nonintoxicated, 1 intoxicated).

Discussion

There is a strong association between alcohol use and injury [1–3]. While our study was limited to patients with blunt liver injuries, the effects of the physiologic derangements may be relevant to intoxicated trauma patients as a whole. Intoxicated, liver-injured patients in our study were more likely to arrive at the hospital hypotensive. Hypotension did not always indicate the presence of surgical bleeding, and the intoxicated patients in our study underwent operation no more frequently than their nonintoxicated counterparts. Also, intoxicated patients were more likely to have a greater admission base deficit (Table 1). The finding of increased base deficit in intoxicated trauma patients has been previously reported [16].

Intoxicated patients required significantly more intravenous crystalloid fluid irrespective of transfusion requirement, but they were not more likely to require transfusion. However, when intoxicated patients *did* receive blood products, they required significantly more than the nonintoxicated patients. This finding occurred despite no significant difference in the INR between intoxicated and nonintoxicated patients. Our data suggest that surgical intervention was ultimately avoided in this group due to the response to a more vigorous resuscitation.

The ANOVA and ROC analysis did not show a dose effect in regard to admission hypotension and BAL. However, the BAL values were not uniformly distributed, with the number of nonintoxicated patients who had a BAL of 0.0% being almost two and a half times greater than those nonintoxicated patients with a detectable BAL of <0.08%. The mean BAL of the nonintoxicated group as a whole was 0.007 ± 0.01%. A more uniform distribution of BAL values may have revealed a dose–effect relationship not seen in this study.

The two major causes of death in our study were CHI and liver hemorrhage. We cannot explain why the majority of nonintoxicated patients died of CHI with liver hemorrhage as a secondary cause (45% vs. 38%, respectively), while the majority of the intoxicated patients died of documented liver hemorrhage with CHI as a secondary cause (40% vs. 30%, respectively). It must be emphasized that these are multiply-injured patients with a mean ISS of 24. Principal cause of death for the purpose of this study had to be clearly stated in the operative and perioperative documentation. We are not assuming that the other injuries did not contribute to patient demise.

There is some literature implicating acute alcohol intoxication as a cause of coagulopathy [17, 18]. However, de Lange [19] demonstrated *increased* platelet aggregation in the binge-drinking population. It is interesting that when transfusion was deemed necessary, the intoxicated patients in our study did not require more platelets or fresh frozen plasma than their nonintoxicated counterparts. They did, however, receive significantly more packed red blood cells (PRBCs) compared to the nonintoxicated group despite having a significantly higher admission hematocrit compared to the nonintoxicated patients (Table 1). This attests to what may be the hemoconcentrated and relatively volume-depleted state previously observed in patients who have ingested ethanol [20]. Admission hematocrit is often available *after* clinical assessment and intervention have already been performed in the trauma bay at our institution. The decision to transfuse with PRBCs is almost always made on clinical impression alone, not initial hematocrit. As per ATLS protocol, PRBCs are the next tier of fluid resuscitation in transient or nonresponders after crystalloid infusion [21]. The question as to whether we are over-transfusing our intoxicated patients with PRBCs cannot be ignored. Both hypotension and increased fluid and blood requirements in intoxicated patients may be due to a physiologic inability to compensate for an established volume deficit and inability to respond to self-limited bleeding as opposed to actual ongoing hemorrhage.

The mechanism for the deficient catecholamine response in intoxicated trauma patients to hemorrhagic intravascular volume contraction is complex and not completely understood. Animal studies have shown that the increase in epinephrine, norepinephrine, and arginine vasopressin (AVP) normally seen during hemorrhage are all suppressed by alcohol intoxication, with norepinephrine the most significantly affected [7–9]. The finding of relative hemoconcentration in our intoxicated patients is intriguing and may be related to the impairment of AVP secretion. Alcohol-related diuresis is roughly proportional to the amount of ethanol ingested [22]. In addition to the previously described vasopressor alterations, ethanol may also predispose patients to a smaller baseline intravascular reserve [23]. This may be reflected in the hemoconcentration described previously [20] and observed in our study. The clinical ramifications of this finding may affect transfusion of PRBCs, an expensive and important resource.

This study has all the limitations of a retrospective study. Although previous physiologic studies have shown that the degree of diuresis, hemoconcentration, and vasopressor alterations may be proportional to the amount of ethanol ingested [20–22], these phenomena may not be the sole cause of clinical hypotension in trauma patients. There were not enough patients in this study to demonstrate a continuum of increasing BAL that corresponded with worsening degrees of hypotension. While there appears to be a significantly greater incidence of hypotension and resuscitative needs in our intoxicated liver trauma patients, caution must be exercised before direct cause and effect can be demonstrated. Not all trauma patients are identical in their injuries, demographics, or response to blunt trauma and the effects of ethanol.

Conclusions

Alcohol-intoxicated blunt trauma patients with liver injuries are more likely to be hypotensive on admission, have greater base deficit, and have increased resuscitative requirements of both intravenous fluid and PRBCs despite no increase in the severity of injury or difference in INR. Despite these physiologic derangements, there was no significant increase in requirement for operation, percentage of positive FAST exams, mortality, or length of hospital stay in acutely intoxicated patients with liver injuries when compared to those not intoxicated. Alcohol intoxication may impair the ability of patients with blunt liver injuries to compensate for acute blood loss.

We recommend that the resuscitation of patients with elevated blood alcohol levels be performed with an understanding of the physiologic alterations caused by acute alcohol intoxication. These alterations may impact resource (blood) usage. Further study is needed to possibly show a direct dose effect for BAL and hypotension in trauma patients.

Appropriate, aggressive resuscitation (ATLS) should be performed regardless of ethanol intoxication. However, knowledge of the physiologic impact of ethanol on trauma patient resuscitation should also be part of the surgeon's armamentarium.

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