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Relationship Between Blood Alcohol Concentration and Hepatic Enzymes in an Emergency Department

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Abstract

Objective: Hepatic enzymes can be used as a predictor of hepatic injury. The present study investigated the relationship between blood alcohol concentration (BAC) and hepatic enzymes in patients intoxicated with ethanol at an emergency department (ED).

Materials and Methods: To determine whether BAC is an independent predictor of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, we retrospectively reviewed the medical data for patients who were intoxicated and whose BAC and hepatic enzyme levels were measured. Patients who had hepatitis caused by viruses or traumatic hepatic injury, as well as patients with a normal BAC, were excluded.

Results: Of the 1432 patients, 298 were female and 1134 were male. The average age of males was 41.4±11.7 years and that of females was 35.6±11.8 years. Mean serum AST and ALT levels were 78±88 IU/L and 51±67 IU/L in males, while those in females were 63±110 IU/L and 40±83 IU/L, respectively. Mean BACs were 199.6±99.0 mg/dL for males and 175.1±101.1 mg/dL for females. Log BAC had a high positive correlation with log ALT (r=0.208; p<0.001) and log AST (r=0.086; p=0.001) when BAC was above 50 mg/dL (0.05%). Multivariate linear regression showed that BAC was an independent predictor of AST and ALT (r^2=0.057 and 0.056, respectively).

Conclusion: The high correlation of BAC with serum AST and ALT levels in patients intoxicated with ethanol when their BAC was above 50 mg/dL can be used to predict serum AST and ALT levels. However, a high BAC only appears to be associated with a slight elevation in hepatic

enzymes. Therefore, in patients with acute alcohol intoxication at the ED, an elevation in AST and ALT levels should be considered as a result of hepatic injury rather than an effect of alcohol. (*Tzu Chi Med J* 2010; 22(1):24–28)

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1. Introduction

Hepatic enzymes are conventional biomarkers of hepatocyte injury (1) and they have recently aroused the interest of researchers when used in studies of damage to the liver caused by alcohol (2–4). However, knowledge about the relationship between the quantity, frequency, and patterns of drinking and alcoholic liver disease is limited (5). In previous studies, not only has alcohol consumption been found to influence serum hepatic enzyme levels (6–8), but also age and body mass index have been reported to be associated with hepatic enzymes (9–11). However, the relation between the blood alcohol concentration (BAC) and hepatic enzymes in patients with acute alcohol consumption is not well known.

The relationship between hepatic enzyme levels and the consumption of alcohol has been found to be valuable when exploring the complications of drinking such as comorbid conditions that may be affected by drinking and their prognosis (11–13). Previous studies have focused on the amount of chronic or acute consumption of alcohol and the time and condition at which the BAC was elevated (14,15). However, some studies have reported that alcohol consumption is insignificantly or weakly related with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels (10). Therefore, controversy remains with regard to the relationship between hepatic enzymes and alcohol consumption.

In this cross-sectional study, we retrospectively reviewed the medical records of 2416 adults who were intoxicated and whose blood was drawn and tested for BAC and hepatic enzymes soon after arrival at our emergency department (ED). We utilized the BAC of patients rather than the amount of alcohol they had consumed. This study aimed to investigate the association between BAC and hepatic enzymes in intoxicated subjects.

2. Materials and methods

2.1. Study design and setting

This retrospective cross-sectional analysis was done in an urban academic medical center that had approximately 80,000 adult visits per year to the ED between January 1, 2005 and June 30, 2008. The dataset was collected from the ED registry database, and the protocol was approved by the hospital's institutional review board.

2.2. Selection of participants and data collection and processing

We included all adult patients aged 18 years and over who had been admitted to our ED. Patients who were suspected to have consumed alcohol by a physician or with impairment of their conscious level were tested for BAC, hepatic enzymes and other laboratory data as needed. In total, 2416 patients suspected of being intoxicated had their blood drawn soon after arrival at our ED and these patients were recruited as subjects. Twenty-six patients who had been transferred from outside hospitals and another 148 patients where there was incomplete data collection were excluded. Two hundred forty-six patients were found to have blunt abdominal injury and 78 patients who had a medical history of hepatitis were also excluded. Four hundred sixty-five patients with an unclear consciousness had a BAC within normal levels and were confirmed to have not consumed alcohol; these patients were also excluded. Finally, 21 patients who were diagnosed from their medical chart as having chronic hepatitis or pancreatitis due to chronic alcohol consumption were also excluded. After these exclusions, a total of 1432 patients formed our study population. We collected data on their age, sex, BAC and hepatic enzyme results.

Venous blood samples were obtained and analyzed within 1 hour after patients arrived at our ED. AST and ALT levels were analyzed using an automated biochemistry spectrophotometric analyzer (Hitachi 747; Roche Diagnostics, Tokyo, Japan). Elevated levels of AST and ALT were based upon the standard cut-points utilized by our laboratory (>42 IU/L and >40 IU/L respectively). The normal ethanol level used by our laboratory was <6 mg/dL.

2.3. Statistical methods

Data are reported using percentage, mean, median, and standard deviation, depending on the type of

variable. The continuous variables AST, ALT and BAC were abnormally distributed. After logarithmic transformation of the raw data to obtain symmetrical distributions, the relationships between AST and ALT with BAC and age were assessed using bivariate correlational statistics (Pearson's *r* for continuous variables). Sex differences in these variables were compared by Student's *t* test. Multivariate linear regression analysis was performed using AST and ALT as the dependent variables to determine whether BAC was an independent predictor of ALT and AST while controlling for potential confounding factors. Covariates (age and sex) were chosen based upon their clinical relevance and their impact on mean AST and ALT in the Student's *t* test and bivariate correlational statistics. Using a stepwise selection method, individual covariates were retained in the final model based on a maximization of the model fit (r^2), while taking into account each additional covariate selected. For all statistical tests, $p<0.05$ was considered significant. All statistical operations were performed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA) for Windows.

3. Results

Of the 1432 patients, 298 were female and 1134 were male. Their average age was 40.2±12.0 years. The mean serum levels of AST and ALT were 74±93 IU/L and 49±71 IU/L, respectively. The mean BAC was 194.5±99.9 mg/dL. The men were older than the women; the mean ages were 41.4±11.7 and 35.6±11.8 years, respectively ($p<0.001$). The men's and women's mean serum levels of AST were 78±88 IU/L and 63±110 IU/L ($p=0.020$), respectively, ALT levels were 51±67 IU/L and 40±83 IU/L ($p=0.015$), respectively, and BACs were 199.6±99.0 mg/dL and 175.1±101.1 mg/dL ($p<0.001$), respectively; all of these were higher in men than in women. Overall, in 35.1% of our patients, the AST-to-ALT ratio was greater than 2.

After logarithmic transformation of AST, ALT and BAC data, ALT was found to be positively correlated with AST ($r=0.828$; $p<0.001$) and BAC ($r=0.135$; $p<0.001$), and AST was found to be positively correlated with BAC ($r=0.067$; $p=0.001$; Fig. 1). However, because of the distribution of BAC, a low BAC did not appear to be correlated with AST or ALT. When patients with a BAC below 50 mg/dL were deleted from the dataset, we found the strongest correlation between AST ($r=0.208$) and ALT ($r=0.086$). This finding suggests that a BAC below 50 mg/dL may not affect AST and ALT levels. There was also a significant correlation between BAC and age ($r=0.067$; $p=0.011$).

An increase in BAC was found to positively affect the levels of hepatic enzymes. Multiple regression analyses were performed to evaluate the effects of AST and ALT. Multivariate linear regression was used to determine independent predictors of AST and ALT. The final model was a good predictor of AST ($r^2=0.057$) and ALT ($r^2=0.056$) with residuals normally distributed around a mean of zero. Using this model, BAC was found to be an independent determinant of ALT and AST (Table 1, both values of $p<0.001$).

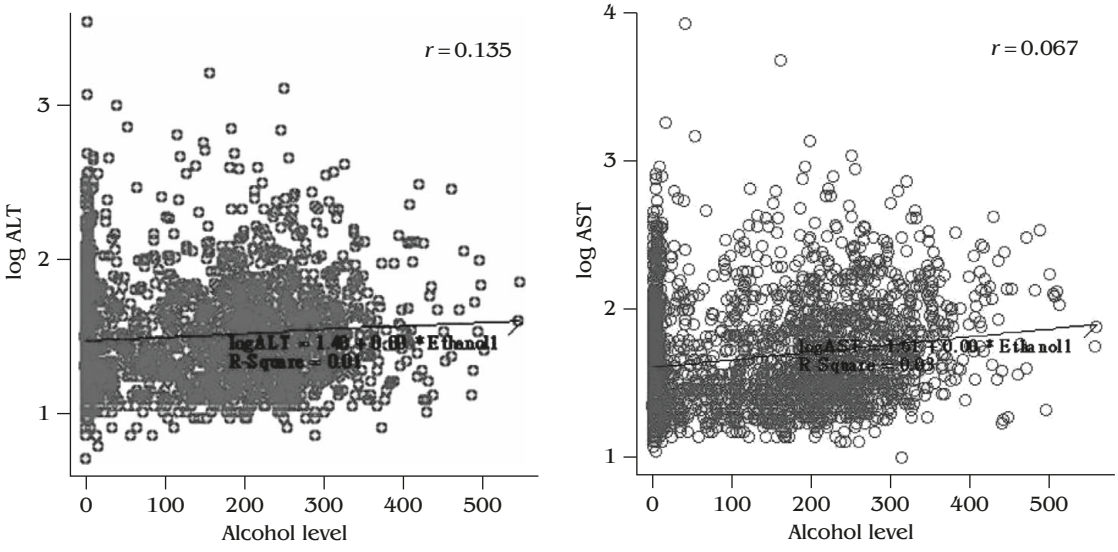

Fig. 1 — Scatter diagrams showing the relationship between blood alcohol concentration and the log-transformed biochemical markers (aspartate aminotransferase and alanine aminotransferase, $p<0.001$ and $p=0.001$, respectively). *r*=Pearson's correlation coefficient; ALT=alanine aminotransferase; AST=aspartate aminotransferase.

Table 1 — Analysis of the independent variables AST and ALT using a multivariate linear regression model

Independent predictors	Log AST*		Log ALT†	
	Beta±SE	*p*	Beta±SE	*p*
Sexes	0.168±0.018	<0.001	0.184±0.017	<0.001
Log BAC	0.045±0.008	<0.001	0.017±0.008	<0.001

*The variables included in the multivariate linear regression model were sex, age, and log blood alcohol concentration; †the variables included in the multivariate linear regression model were sex, age and log blood alcohol concentration. The reference group of sex was male. AST=aspartate aminotransferase; ALT=alanine aminotransferase; SE=standard error; BAC=blood alcohol concentration.

4. Discussion

AST and ALT levels are used to predict the existence of liver injury [16]; however, they may be affected by many factors, including acute or chronic alcohol consumption. In addition, alcohol consumption is often observed in patients involved in traffic accidents, which is one of the major causes of liver injury. Our study found a significant correlation between BAC and both AST and ALT in ED patients. BAC has an effect on the elevation of serum AST and ALT levels. However, the association between BAC and the elevation of AST and ALT levels was strongest when the BAC was higher than 50 mg/dL. Even so, the elevation in AST and ALT levels caused by alcohol is not that significant and the increase in BAC may only sometimes cause an elevation in AST and ALT levels, which may not have relevance in the clinical setting. Therefore, when patients are found to have an elevation of AST and ALT levels, the influence of alcohol should not be the first consideration.

Few studies have investigated the relationship between AST and ALT levels and BAC in acute alcohol consumption patients. In a baseline survey in Denmark, 905 people (aged 30–50 years) were studied and the prevalence of abnormal liver-derived enzymes was examined. Liver-derived enzymes were found to be associated with a moderate self-reported alcohol consumption adjusted for body mass index and smoking [17]. In our study, we found that although elevation of BAC after acute alcohol consumption did not dramatically increase the level of hepatic enzymes, there was a significant positive association between these variables. In general, alcohol drinking results in a moderate elevation of serum AST and ALT levels (74±93 IU/L and 49±71 IU/L, respectively, in our study). When alcohol consumption is less, with a BAC of below 50 mg/dL (which is the legal intoxication level in many countries), the influence of serum AST and ALT levels is even lower.

Previous studies have reported that AST and ALT have a surprisingly weak or non-existent relationship with alcohol consumption [10,18,19]; however, these results were almost always derived from a blood test in routine follow-up. Although the correlation between alcohol consumption and AST/ALT was also weak in our study, we found a significant correlation between BAC and hepatic enzymes levels. This result indicates that BAC and hepatic enzymes are related to each other but this is not necessarily a linear correlation. This difference may result from the different patient groups being studied and differences in patient numbers. Our patients with an identifiable BAC were mainly ED patients who had just consumed alcohol and their blood samples were drawn shortly after they had arrived at the ED. In contrast, previous studies have generally used self-reported questionnaires to report the amount of alcohol consumption, which might not reveal a correlation between BAC and hepatic enzymes. Nevertheless, the low correlation coefficients obtained in our study suggest that the influence of alcohol should not be the first consideration if an elevation in AST and ALT levels is detected in clinical practice during the management of ED patients.

Gamma-glutamyltransferase is a liver enzyme that has also been used as a marker of alcohol consumption [20–22]. However, this biomarker was not available in our study because it was not measured routinely in the emergency setting of our hospital. The lack of this parameter is a limitation to the analysis of our results. In addition, an AST-to-ALT ratio greater than 2 suggests that alcohol is the etiology, but only 35.1% of our patients' ratios were greater than 2. However, our patients were collected from an emergency setting, which may have different results. Our study is the first to survey the AST/ALT ratio in the acute stage of alcohol consumption. The implications of these findings warrant further investigation and suggest that an elevation of AST and ALT levels with an AST-to-ALT ratio greater than 2 cannot be referred to as alcohol hepatitis in patients with acute alcohol consumption in an ED setting.

Our study showed that 79.2% of the intoxicated patients were male, and female patients were significantly younger than males. We also found that men had significantly higher AST and ALT levels and BACs than women, and that there was an age difference in alcohol consumption between the sexes.

As a retrospective study, this study has several potential limitations. First, it is a single-institution study, and therefore may only reflect local patient characteristics. Nevertheless, our patients included all "random" patients at an ED of an urban hospital in a large city, and thus do not represent any particular population. As with most retrospective reviews, unmeasured or unknown confounding variables may have been responsible for the effects seen and the subsequent conclusions. In addition, throughout the study period, the alcohol testing was usually performed selectively.

Although this may have resulted in selection bias, it would not have affected the calculation of BAC and hepatic enzymes. Moreover, we did not include in our protocol serum assays for the markers of hepatitis B virus and hepatitis C virus. Although some patients enrolled in this study might have had chronic hepatitis or fatty liver, we already excluded patients who had a medical history of hepatitis, and those known to have chronic alcohol consumption. We believe that this missing information is not likely to confound our results. Furthermore, without an acute episode, serum AST and ALT levels are not usually increased in the carriers of hepatic virus (23,24). Another limitation of our study is that we took a one-time measurement of blood alcohol and compared this with hepatic enzyme elevation, which typically is a more chronic process. Finally, there are other factors such as obesity, serum triglyceride levels, history of alcohol consumption, and alcohol dehydrogenase that can affect the serum level of alcohol; however, it is not easy to obtain this information in an ED setting. Therefore, we only presented the epidemiological relationship between BAC and hepatic enzymes in this analysis. Further studies should focus on the relationship between the serial blood sampling of BAC and serum AST and ALT levels or use liver biopsy to establish a possible relationship between alcohol consumption and liver damage to confirm the potential relationship. The influence and pathophysiology of BAC when it is over 50 mg/dL should also be further studied.

In conclusion, alcohol intoxication affects serum AST and ALT levels in patients when their BAC is above 50 mg/dL. However, the association between increased levels of hepatic enzymes and alcohol consumption is not strong. Higher levels of alcohol consumption above this value may only cause a limited increase in hepatic enzymes. Therefore, when patients visit the ED and are found to have an elevated AST/ALT, even when intoxicated by alcohol, the influence of alcohol on these enzymes is relatively small, and other causes of liver injuries should be investigated.

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