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MOLECULAR TOXICOLOGY

Munich Oktoberfest experience: remarkable impact of sex and age in ethanol intoxication

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Abstract Approximately 5,000 of 6 million annual visitors of the Oktoberfest in Munich have to undergo medical treatment. Patients with alcohol intoxication without trauma or further complications are all treated in a specialized medical camp. We studied these patients in order to identify risk factors and to assess the relevance of the Glasgow Coma Score (GCS) and of ethanol blood concentrations for patient management. In 2004 totally 405 patients suffering from ethanol intoxication without trauma were treated in the medical camp. A complete set of the following data was obtained from all 405 patients: GCS, ethanol blood concentration, age, sex, blood pressure (mean, systolic and diastolic), body temperature, heart rate, blood sugar, GOT, γ-GT, and CK. A multivariate logistic regression model was applied to identify risk factors predicting patients at increased risk of hospitalization. Low GCS ($\leq$8 vs. >8, OR: 4.18, CI: 1.96–8.65) low age (20–29 vs. $\geq$30 years, OR: 2.35, CI: 1.05–5.65) and male gender (male vs. female, OR: 3.58, CI: 1.36–9.34) independently predicted patients that had to be hospitalized. All other parameters including ethanol blood concentrations were not explanatory. Patients with GCS $\leq$ 8 ($n = 66$) had a lower median blood pressure ($P = 0.0312$) and showed a smaller increase in blood pressure during the observation period compared to patients with GCS > 8 ($P < 0.001$), suggesting that this subgroup may require longer recovery periods. Men aged 20–29 years were at highest risk for hospital admission. Increased risk could not be explained by higher ethanol blood concentrations in this subgroup. Importantly, GCS < 6 does not justify endotracheal intubation in ethanol

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intoxicated patients, when further complications, such as trauma, can be excluded.

Keywords Ethanol intoxication · Glasgow coma score · Hospitalization · Endotracheal intubation · Acute alcohol intoxication

Introduction

In 2004 approximately 6 million individuals visited the Oktoberfest in Munich. About 5,000 of the visitors had to undergo medical treatment for different reasons. Patients with alcohol intoxication without trauma or obvious complications ($n = 405$) were treated in a specialized medical camp. These are good conditions to study risk factors in acute alcohol intoxication. One of the common problems physicians have to face is the decision whether an intoxicated patient has to be hospitalized. Often this decision has to be made under time pressure. Therefore, identification of risk factors would be helpful. In addition, we asked, whether the Glasgow Coma Score (GCS) and blood ethanol concentrations may be relevant in patient management. Two previous studies suggested that both parameters may be of only limited relevance (Sperry et al. 2006; Frey et al. 1976). However, one study (Sperry et al. 2006) has been performed in ethanol intoxicated patients with additional traumatic brain injury, which complicates evaluation of the consequences of ethanol alone. The second study (Frey et al. 1976) includes severely alcohol intoxicated patients. However, only a relatively small number of individuals has been enrolled. Therefore, the present study including a relatively large cohort of individuals suffering exclusively from alcohol intoxication, offers excellent conditions for identification of risk factors and optimization of patient management. A similar study has not been published before.

We observed a clear association of the risk of confinement to hospital with age and gender. Surprisingly, young men aged 20–29 years were at highest risk of hospitalization, which at first glance seems to be in contrast to the general opinion that women become intoxicated more quickly than men.

Materials and methods

Patients

A total of 405 patients suffering from alcohol intoxication without trauma or further obvious complications were admitted to the medical camp. All patients were visitors of the Munich Oktoberfest in 2004 and gave written consent to joining the study at discharge from the medical camp. Exclusion criteria were (1) trauma, (2) lack of alcoholisation, (3) complications requiring emergency measures. Patients data, including age and gender, were documented using a standardized documentation sheet. During a physical examination the Glasgow Coma Score (GCS) was determined at admission to and at discharge from the medical camp. All patients received an intravenous infusion of either 500 ml Ringer-Lactate solution or 10% glucose solution. The decision for either Ringer-Lactate or glucose infusion was made according to the result of the blood glucose determination, whereby patients with $\leq$100 mg/dl received glucose solution and patients with >100 mg/dl received Ringer-Lactate. All infusions were warmed up to 37°C in order to prevent hypothermia. Blood pressure (mean, systolic and diastolic), heart rate, body temperature, respiratory rate, blood glucose, oxygen saturation and acid-base balance were regularly checked. During their stay in the medical camp the decision had to be made whether hospitalization was necessary. This decision was exclusively made by experienced emergency physicians and was primarily based on evaluation of the neurological status. Ethanol blood concentration, blood sugar, GOT, γ-GT, bilirubin, CK and urea have been determined according to published standard assays (Micke et al. 2003; Brulport et al. 2007).

Statistical analysis

Statistical analysis was performed using SAS/STAT, version 9.1 software (2004). To identify relevant parameters of influence on the risk of hospitalization (model finding) a multivariate logistic regression model was used. Eight possible parameters of influence were included, whereby all parameters were determined at admission to the medical camp: gender (male versus female), age, GCS, systolic and diastolic blood pressure, temperature, heart rate, and blood ethanol concentration. Age was categorized into three groups in a first analysis: 10–19, 20–29 and >30 years. In a second analysis five groups were included into the model: 10–19, 20–29, 30–39, 40–49, >50 years. GCS was dichotomized into >8 versus $\leq$8. Systolic blood pressure was dichotomized at the 25% percentile: $\leq$100 versus >100 mmHg. Similarly diastolic blood pressure was dichotomized at the 25% percentile: $\leq$50 versus >50 mmHg. Temperature was dichotomized at the 25% percentile: $\leq$34.9 versus >34.9°C. Heart rate was dichotomized at the 75% percentile: $\geq$98 versus <98 beats per minute. Blood ethanol concentration was categorized into five groups: <1, 1–1.49, 1.5–1.99, 2–2.49, $\geq$2.5 g/L. To evaluate the influence of these parameters a backward stepwise selection using the Wald test with a P value 0.05 as exclusion criterion (Tanner et al. 2006; Schmidt et al. 2007). Stepwise forward selection was used in order to confirm the result with a P value of 0.05

of the score chi-square statistic as inclusion criterion. Furthermore, the P value of the Wald chi square statistic is given for each Maximum-Likelihood estimate of the model parameters (Mohrmann et al. 2005). Odds ratios were calculated as the ratios between the odds of patients that had to be hospitalized versus patients that could be discharged from the medical camp. Models were compared using the Akaike information criterion (AIC). To evaluate the appropriateness of the model the Hosmer and Lemeshow (2000) goodness-of-fit test was performed. Furthermore, we examined the ROC curve. The influence of single subjects on the estimation of the regression parameters was assessed according to Pregibon (1981). Differences in blood pressure, temperature and heart rate at admission to and at discharge from the medical camp have been visualized by box plots. The horizontal line in the middle of a box shows the median of the sample. The edges of a box mark the 25th and 75th percentiles. The whiskers show the range of values that fall within 1.5 box-lengths. Values >1.5 box-lengths from the 25th or 75th percentiles are marked by a dot. Possible differences between the data at admission and at discharge were analyzed by the two-sided Wilcoxon signed rank test. The Wilcoxon rank sum test was applied to determine differences between women and men as well as between GCS ≤ 8 and GCS > 8 with respect to ethanol concentrations, blood pressure and other variables. Two-sided tests were performed if not indicated otherwise. Quartiles, minimal and maximal values, are given for continuous variables. Spearman's rank correlation coefficient and the related test as well as scatterplots were used to examine correlations between GCS, ethanol concentrations and other factors. Percentages of men and women in different age classes were compared using the chi-square test. Additionally crude odds ratios and 95% confidence intervals were computed.

Results

Description of the intoxicated cohort

Approximately 5,000 visitors of the Oktoberfest in 2004 had to undergo medical treatment for different reasons. Those with alcohol intoxications without trauma or obvious complications ($n = 405$) were treated in a specialized medical camp as described under "Patients and Methods". The GCS, blood pressure (mean, systolic and diastolic), body temperature and heart rate have been determined at admission and at discharge from the medical camp (Table 1). GCS, blood pressure (mean, systolic as well as diastolic) and body temperature increased during the observation period in the medical camp ($P < 0.001$, Wilcoxon signed rank test). In contrast, heart rate decreased between admission and discharge ($P < 0.001$, Wilcoxon signed rank test).

Table 1 Patients characteristics

Parameter	Median	25–75% percentiles
Glasgow Coma Score (GCS)[a]		
at admission to the camp	12.0	10.0–13.0[b]
at discharge from the camp	15.0	15.0–15.0[c]
second contact 2–3 months later	15.0	15.0–15.0[d]
Blood pressure at admission (mmHg)[a]		
Systolic	110.0	100.0–125.0
Diastolic	70.0	60.0–80.0
Mean	83.3	73.3–93.3
Blood pressure at discharge (mmHg)[a]		
Systolic	120.0	110.0–134.0
Diastolic	72.0	63.0–80.0
Mean	88.7	80.0–99.2
Body temperature (°C)[a]		
At admission to the camp	35.0	34.9–36.1
At discharge from the camp	36.3	35.9–36.7
Heart rate (beats per min)[a]		
At admission to the camp	84.0	72.0–98.0
At discharge from the camp	76.0	67.0–90.0
Blood sugar (mg/dl)	92.0	78–108
GOT (µmol/L)	0.56	0.45–0.77
γ-GT (µmol/L)	0.39	0.26–0.65
Bilirubin (mg/dL)	0.67	0.56–0.81
CK (µmol/L)	1.84	1.26–2.80
Creatinine (µmol/L)	89.0	78.0–102.0
Urea (mg/dL)	61.0	47.0–72.0
Blood ethanol concentration (g/L)	2.09	1.61–2.50
Age (years)	24	20–34[e]
Observation period (time between admission and discharge) (h)	2.42	2.17–2.78

In 2004 totally 405 visitors of the Munich Oktoberfest suffering from ethanol intoxication without trauma or additional complications were treated in a specialized medical camp. 121 patients (29.9%) were women and 284 (70.1%) were men

[a] $P < 0.001$ comparing the difference between admission and discharge from the medical camp (Wilcoxon signed rank test, two-sided test)

[b] Minimum–maximum: 3–15

[c] Minimum–maximum: 7–15

[d] Minimum–maximum: 15–15

[e] Minimum–maximum: 14–82

Blood sugar, GOT, γ-GT, bilirubin, CK and urea remained in the normal range in the intoxicated cohort (Table 1). Median ethanol blood concentrations were 2.09 g/L. 7, 15, 25, 22, and 31% of the patients had blood ethanol concentrations <1, 1.00–1.49, 1.50–1.99, 2.00–2.49 and ≥2.5 g/L. Median blood concentrations did not differ significantly between women and men ($P = 0.421$, Wilcoxon rank sum test). Similarly, no significant difference in GCS

at admission was obtained between both sexes ($P = 0.307$, U test for unpaired data).

Predictive factors for hospitalization and prognosis

One of the major goals of this study was to analyze whether the risk for hospitalization can be predicted by the parameters determined at admission to the medical camp. Of the 405 patients confined to the medical camp because of alcohol intoxication, 43 had to be hospitalized. In order to identify possible risk factors eight parameters were included into a logistic regression model (Table 2a). Backward selection resulted in three parameters that were accepted as explanatory. The association between GCS and risk of hospitalization (OR: 3.92, CI: 1.93–7.96) was not surprising, since GCS is one of the parameters for decision-making. In contrast, the strong association with gender was unexpected. Men had a strongly increased risk of hospitalization compared to women (OR: 3.72, CI: 1.40–9.89). A second surprising result was a strong association with age. Individuals aged 20–29 years had a higher risk compared to individuals aged ≥30 years (OR: 2.42, CI: 1.10–5.32) as well as compared with individuals aged ≤19 years (OR: 3.00, CI: 1.16–7.81) (Table 2a). All other parameters (Table 2b) were not accepted as explanatory.

The strong influence of GCS was not surprising, since low GCS was one of the criteria for confinement. Therefore, we performed an additional regression analysis omitting GCS from the model (Supplemental Table 1A). However, this did not alter the result, since age and gender remained the only parameters included into the model. In order to systematically analyze the influence of age we separately included age groups 10–19, 20–29, 30–39 and 40–49 and ≥50 years into the model (Supplemental Table 1B). Obviously, individuals aged 20–29 years were at highest risk for hospitalization.

All 405 patients recovered from ethanol intoxication without complications. No endotracheal intubations were performed on any of the 405 patients including the 43 hospitalized individuals. The median time between admission and discharge from the medical camp was 2:25 h (2:10–2:47 h, 25–75% percentiles). All hospitalized patients were discharged without complications by the latest 2 days after confinement.

Remarkable differences in cohort composition concerning age and gender

In the previous paragraph we have identified risk factors for hospitalization which is relevant for the emergency physician. Next we analyzed the composition of the cohort confined to the medical camp, since identification of individuals at increased risk of ethanol intoxication may be relevant for prevention. A first and obvious risk factor for confinement to the medical camp was male gender. Only 29.9% of the 405 intoxicated patients were women. In addition, young age was of relevance. Individuals aged 20–29 years were clearly overrepresented in the intoxicated cohort compared to all other age groups (OR: 5.5, CI: 2.69–11.18). Similarly, individuals younger than 30 years were overrepresented compared to individuals ≥30 years (OR: 4.13, CI: 2.29–7.44). It should be considered that these odds ratios have been obtained by comparison of age groups in the intoxicated cohort ($n = 405$) with the respective age groups in the total population in Germany in 2004 as a reference population (Supplemental Table 2). There-

Table 2 Logistic regression model predicting the risk of hospitalization of 405 individuals suffering from ethanol intoxication

Parameter	Odds ratio (OR)	95% Confidence interval of OR	P value of the Wald test
A. Explanatory factors accepted by the logistic regression model			
Glasgow Coma Score (≤8 versus >8)[a]	3.92	1.93–7.96	0.0002
Gender (male versus female)	3.72	1.40–9.89	0.0084
Age (20–29 versus ≤19 years)	3.00	1.16–7.81	0.0187[b]
Age (20–29 versus ≥30 years)	2.42	1.10–5.32	
B. All other parameters analyzed were not regarded as explanatory by the model			
Heart rate (≥98 versus <98 beats)[a]			0.6909
Body temperature (≤34.9 versus >34.9°C)[a]			0.5483
Diastolic blood pressure (≤50 versus >50 mmHg)[a]			0.3396
Blood ethanol concentration (<1, 1–1.49, 1.5–1.9, 2–2.49, ≥2.5 g/L)[a]			0.3294
Systolic blood pressure (≤100 versus >100 mmHg)[a]			0.0872

AIC = 252 (final model), (AIC = 276, intercept only). Hosmer and Lemeshow goodness-of-fit test confirms the adequacy of the model ($P = 0.3748$). Forward selection yields the same results

[a] Parameters were determined at admission to the medical camp

[b] Wald test for the variable 'age' with three groups (≤19, 20–29, ≥30 years)

fore, considering our reference group, the above mentioned odds ratios indicate the risk of visiting the Oktoberfest and consuming so much alcohol that confinement to the medical camp was necessary. We could not use the total visitors to the Oktoberfest as a reference group, because no reliable data on age and gender of this cohort is available.

A striking difference was observed between women and men when individuals ≥50 years were considered. Women aged ≥50 were clearly underrepresented in the intoxicated cohort compared to men ≥50 years (OR: 2.97, CI: 1.19–8.80). This difference is additionally illustrated by the total numbers, since only 6 out of 44 individuals aged ≥50 years were women. The chi-square test was applied to systematically compare the percentage of women and men in different age classes (Supplemental Table 3). Women ≥40 years were underrepresented compared to men ($P = 0.0158$). Similarly women ≥50 as well as ≥60 years ($P = 0.0138$ and $P = 0.0158$, respectively) were underrepresented. In contrast, no significant difference between women and men was obtained for individuals younger than 40 years.

In conclusion, young individuals aged 20–29 years are at highest risk of alcohol intoxication and confinement to the medical camp. In contrast, women older than 50 years are clearly underrepresented in the cohort of intoxicated individuals.

Association of Glasgow Coma Score (GCS) with clinical parameters

The median GCS at admission of the 405 patients was 12 (10–13, 25–75% percentiles; 3–15, minimum–maximum; $n = 405$). 66 patients (16.3%) had a GCS smaller or equal to eight (frequency distribution: Supplemental Figure 1). At discharge from the medical camp the mean GCS increased to 15 (15–15, 25–75% percentiles; 7–15, minimum–maximum). The median time period between admission and discharge was 2:25 h. At a second contact 2–3 months after discharge from the medical camp all patients had a GCS of 15. The median GCS values were similar between women and men (Supplemental Figure 2) and were not associated with the patients age (Supplemental Figure 3) and with blood ethanol concentrations (Supplemental Figure 4). Similarly, no correlation between GCS and blood ethanol concentrations was obtained using the Spearman correlation test (correlation coefficient: −0.019; $P = 0.698$).

At admission to the medical camp the cohort of ethanol intoxicated patients showed a decreased blood pressure compared to the respective data at discharge ($P < 0.001$; Wilcoxon signed rank test). In addition, patients with a GCS ≤ 8 had slightly decreased blood pressure compared to patients with GCS > 8 (Fig. 1, $P = 0.0312$). Interestingly, the GCS was associated with recovery of blood pressure. Patients with a GCS > 8 showed an increase in mean blood pressure from 92.5 mmHg (90.9–94.2, 95% CI) to 98.2 mmHg (96.8–99.7, 95% CI) during approximately 2:25 h, the median time period between admission and discharge from the medical camp (Fig. 1, $P < 0.001$, Wilcoxon singed rank test). In contrast, blood pressure did not significantly increase for patients with a GCS ≤ 8 (Fig. 1b, $P = 0.1122$). Values for mean blood pressure were 87.7 mmHg (84.2–91.1, 95% CI) at admission and 89.8 mmHg (86.6–93.1, 95% CI) at discharge. Obviously, the GCS defines a group of patients who require more time to recover from decreased blood pressure.

Similar to blood pressure also body temperature increased between admission and discharge (Fig. 1; $P < 0.001$). However, body temperature recovered independently from GCS. Heart frequency decreased between admission and discharge ($P < 0.001$), which also occurred independently from GCS (Fig. 1).

No association of ethanol blood concentrations with clinical parameters

Ethanol blood concentrations did not correlate with any of the determined clinical parameters, including GCS, blood pressure, body temperature, heart frequency, GOT, γGT as well as CK (Supplemental Figure 5).

Discussion

The Munich Oktoberfest: ideal for studying ethanol intoxication and improving patient management

The Munich Oktoberfest offers a unique possibility to study large cohorts of patients with ethanol intoxication and to optimize patient management. An advantage of the Oktoberfest Medical Care System is that all individuals with alcohol intoxication without trauma or other obvious complications are treated in a specialized medical camp. All patients treated in this camp in 2004 ($n = 405$) have been analysed in the present study. We were predominantly interested in two questions of practical relevance: (1) Are there risk factors for hospital admission. When an intoxicated individual has been admitted to the medical camp the physician has to decide, whether hospital confinement is necessary or not. Therefore, availability of risk factors would be of relevance for the emergency physician. (2) Are there risk factors for confinement to the medical camp. Individuals at increased risk tend to consume too much alcohol, finally leading to confinement. Identification of subpopulations at increased risk may be relevant for prevention.

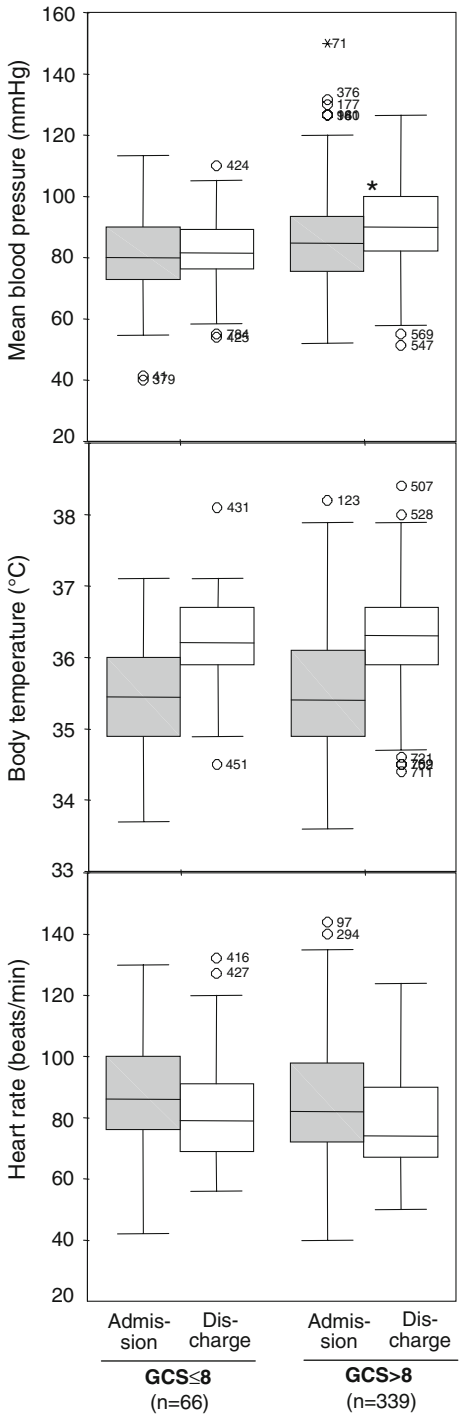

Fig. 1 Mean blood pressure, body temperature and heart rate of 405 alcohol intoxicated individuals at admission and at discharge from the medical camp. Individuals with a Glasgow Coma Score (GCS) ≤ 8 and >8 were analyzed separately

Identification of independent risk factors for hospital admission: GCS, age and gender

Age, gender and GCS are independent risk factors for hospital admission. These parameters were clearly associated with the physician's decision whether a patient from the medical camp has to be hospitalized or may be discharged. In our cohort hospital admission was necessary for 43 of 405 patients. Therefore, we applied a multiple regression model in order to identify independent predictors of hospital admission. Interestingly, gender and age were strong independent predictors. Surprisingly, men were at higher risk of hospitalization than women. (OR: 3.58, CI 1.37–9.34). This is unexpected and in contrast to the general view that men are less susceptible to alcohol than women. Further analysis identified individuals aged 20–29 years as a high risk group compared to older patients (OR: 2.42; CI: 1.10–5.32). In conclusion, 20–29 years old men are at highest risk of being confined to hospital. This observation can not be explained by higher blood ethanol concentrations in the subgroup of young men. In contrast, men aged 20–29 years had lower blood ethanol concentrations (median: 2.14 g/L) compared to men aged 30–39 years (median: 2.40 g/L; $P = 0.0317$, one-sided Wilcoxon rank sum test test) or compared to men aged 40–49 years (median: 2.38; $P = 0.3319$, one-sided Wilcoxon rank sum test test). Blood ethanol concentrations of young men (20–29 years) did also not differ significantly from that of young women, aged 20–29 (median: 2.13 g/L, $P = 0.7937$ Wilcoxon rank sum test). Therefore the mechanism responsible for the increased risk of young men can not be identified from our set of data. We can not exclude a higher biological susceptibility to ethanol toxicity of men aged 20–30, although this would be in contrast to the well known general robustness of this subpopulation. In our opinion, a plausible explanation might be that young individuals, especially young men, tend to ignore their individual critical limits of ethanol intoxication. Peer pressure and lack of experience may be responsible for this behaviour.

GCS was a major risk factor for hospital admission (OR: 3.92, CI: 1.93–7.96). This is trivial, since GCS already is established as one of physician's factors for decision-making. During a second contact 2–3 months after discharge GCS had amounted to normal levels of 15.

Risk factors for alcohol intoxication: male gender and young age

Analyzing risk factors for confinement to the medical camp we identified male gender and young age (20–29 years) as highly significant predictive factors. Interestingly, these are the same risk factors as those for hospital confinement. This would fit the explanation that especially young men tend to ignore their limits and drink so heavily that they not only had to be transported to the medical camp but also had to be confined to hospital. In conclusion, individuals aged 20–29 years, especially men, are the optimal target group for preventive measures.

The opposite scenario was observed for woman older than 50 years. This subgroup was clearly underrepresented in the cohort of intoxicated individuals (OR: 0.34, CI: 0.11–0.84). A plausible explanation for this observation may be that women older than 50 years behave more sensible and respect their limits concerning ethanol consumption.

Some patients need more time to "sober up"

The median time between admission and discharge from the medical camp was 2:25 h (2:10–2:47 h, 25–75% percentiles). For most patients this seems to be sufficient since during this period we observed a strong increase in GCS (Supplemental Figure 1), an increase in blood pressure and a normalization of body temperature (Fig. 1). Nevertheless, low GCS at admission to the medical camp identifies a subgroup of patients requiring more time to "sober up". Patients with a GCS ≤ 8 had a lower blood pressure at admission to the camp compared to patients with higher GCS. During a median recovery period of 2:25 h blood pressure normalized in patients with GCS > 8 but not yet in patients with GCS ≤ 8. This observation suggests that longer recovery periods may be justified for patients with GCS ≤ 8.

GCS ≤ 6 does not necessarily justify endotracheal intubation

One of the general rules in intensive medicine is that a GCS < 8 may justify endotracheal intubation (Winchell and Hoyt 1997). The situation may be different, when alcohol intoxication is the only reason of the decrease in GCS. In our cohort 22 patients had a GCS ≤ 6, of whom nine patients had to be hospitalized. Eight patients even had a GCS ≤ 4 of whom four had to be hospitalized. However, no endotracheal intubation was performed and all patients could be discharged without complications. In conclusion, our results show that a GCS ≤ 6 does not necessarily justify endotracheal intubation, when the decrease in GCS is exclusively caused by alcohol intoxication.

Blood ethanol concentrations are not a criterion for the degree of intoxication

In 1976 a study with severely alcohol intoxicated patients came to the conclusion that blood alcohol levels are not a criterion for the degree of intoxication (Frey et al. 1976). At a first glance this may be surprising. However, our data confirm the results of Frey and colleagues. Blood alcohol concentration did not correlate with GCS, or with blood pressure, or any of the determined clinical parameters. Importantly, blood alcohol concentrations were not associated with the risk of hospitalization. Similarly, blood alcohol concentrations did not predict GCS in a cohort of ethanol intoxicated patients with traumatic brain injury (Sperry et al. 2006). In conclusion, mean GCS was decreased in our ethanol intoxicated cohort, but ethanol concentrations did not correlate with the severity of intoxication. This may be explained by large interindividual differences in ethanol susceptibility that do not allow establishment of clear dose-response relationships in a population.

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