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Alcohol Elimination Rate After Inhalation of Oxitol(2-Ethoxyethanol)

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Summary. A 39-year-old man, accused of driving a car under the influence of ethanol, claimed that the use of an oxitol-containing floor lacquer prior to the drive might have enhanced the concentration of ethanol. Since oxitol has a higher affinity to alcohol dehydrogenase than ethanol, interaction could not be excluded primarily. With the client's informed consent 104 g of ethanol was given orally in a chamber at exposure to 0 ppm and 316 ppm oxitol, respectively. No difference in the elimination rate of ethanol was found. After combined exposure to oxitol and ethanol a decrease of the neutrophilocytes and the thrombocytes was found, as well as an increase of the serum creatine kinase. After exposure solely to ethanol, there were no abnormal blood sample changes.

Key words: Oxitol, alcohol elimination rate, granulocytopenia – 2-Ethoxyethanol, inhalation

Zusammenfassung. Ein 39jähriger Mann, angeklagt des Führens eines Kraftfahrzeugs unter Alkoholeinfluß, behauptete, daß die Arbeit mit einem Oxitolenthaltenden Fußbodenlack vor der Fahrt die Blutalkoholkonzentration erhöht habe. Da Oxitol eine höhere Affinität zur Alkoholdehydrogenase als Äthanol hat, konnte primär eine Wechselwirkung nicht ausgeschlossen werden. Mit Einwilligung des Probanden wurden ihm in zwei Versuchen 104 g Äthanol per os in einer Kammer mit und ohne Oxitoldämpfe (316 ppm) verabreicht. Es wurde kein Unterschied in der Ausscheidungsrate des Äthanols gefunden. Bei Äthanolgabe in Oxitolatmosphäre wurde ein Abfall von Neutrophilen und Thrombocyten sowie ein Anstieg der Serum-Kreatinkinase

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beobachtet. Bei alleiniger Äthanolapplikation zeigten sich keine Veränderungen der Blutwerte.

Schlüsselwörter: Oxitol, Alkoholeliminationsrate, Granulozytopenie – 2-Ethoxyethanol, Inhalation

A 39-year-old man was stopped at 00.15 a.m. by the police for driving of a car under the supposed influence of ethanol, because he did not signal when turning left. A breath test was positive. A blood test withdrawn at 01.55 a.m. revealed 0.154 p.c. ethanol (mean value of two analyses showing 0.147 p.c. and 0.161 p.c., respectively). In Denmark, for legal purposes, 0.010 p. c. is deducted from the mean value of two analyses for ethanol, resulting in a "minimal value", which is the one used by the court. The "minimal value" for the subject was thus 0.144 p.c. ethanol. He was charged for driving under the influence, as the Danish legal limits are 0.08 and 0.12 p.c., respectively. The subject claimed that he, on the day of the driving, had been lacquering a floor and this might be responsible for the high blood alcohol level. The lacquer contained 20% oxitol, 13% aromatic hydrocarbons, and 0.4% methanol. The used thinner contained 27% aromatic hydrocarbons and 5% oxitol. All included he had used between 10 and 20 l of these products. The room was unventilated, and the temperature had been between 25 and 35° C. The room was 4 m high, the floor was 10×15 m.

Before appearing at the court his counsel asked the clinic of occupational medicine whether the vapors from the lacquer might interfere with the elimination rate of ethanol.

Ethanol is metabolized almost exclusively in the liver, catalyzed by the unspecific enzyme alcohol dehydrogenase (ADH) [8]. Inhibition of ADH can slow down the rate of ethanol elimination. Ingestion of chloral hydrate can inhibit the metabolism of ethanol in man. This effect is caused by the metabolite trichloroethanol [6]. Oxitol is also an alcohol and is metabolized in vitro by human liver ADH. Furthermore, oxitol has a Michaelis constant value which is approximately half that of the Michaelis constant for ethanol [1], and a twofold greater affinity of oxitol than of ethanol to ADH is thus expected from the ratio between the Michaelis constants. We therefore decided to examine whether any interaction between oxitol and ethanol could be demonstrated in man in a chamber exposition experiment.

The rate of ethanol elimination determined on different days in the same individual varies little. Therefore, studies of the effect of drugs or other agents on ethanol metabolism are best designed by using each individual as his own control rather than by comparison of two groups of subjects [5].

Material and Methods

The person examined was the accused. The physical examination at the clinic prior to the experiment revealed no physical abnormalities, except that this liver was palpable one finger under the curvature. The person stated that he had been drinking 10 beers a day during the last

15 years. The following analyses were normal: hemoglobin, erythrocyte and differential count, thrombocyte count, alcaline phosphatase, alanine aminotransferase, lactate dehydrogenase, serum creatine kinase, serum creatinine and urine for analysis for glucosis, blood, and albumen.

On the experimental days, the client was requested to present with an empty stomach. Before every exposure his ventricle was aspirated, and urine was collected for analysis of glucosis and drugs to eliminate the possibilities of other impacts on the rate of ethanol elimination. The subject was not informed in advance whether or not he was to be exposed to oxitol. The subject remained in the chamber from 9.00 a.m. to 2.35 p.m. On the 1st day he was not exposed to oxitol. On the 2nd day he was exposed to oxitol by a technique described by Stokholm and Cohr [7]. The mean concentration was 316 ppm except during a period of 20 min of the exposure, when the concentration increased to 3,500 ppm and again dropped to the 316 ppm level. From 9.00–9.45 a.m. he was given 104 g of ethanol diluted with water. He was working an ergometer cycle from 9.00 to 10.10 to shorten the time necessary to obtain equilibrium of ethanol. Later on he worked the cycle from 11.15–11.30 a.m. During the rest of the experimental period he was sitting at a table. A standardized light meal was given at 11.30 a.m. and 0.45 p.m. Blood samples for ethanol analysis were drawn at 1-h intervals. The procedures were identical for the 2 days, and the client was under observation during the whole experimental period.

Blood samples for analysis of leukocyte and differential count, thrombocyte and serum creatine kinase were taken in the morning before the exposure, and were repeated the following mornings.

Results

The elimination of blood ethanol with and without exposure to oxitol is shown in Table 1. No differences in the elimination rates were observed. There was no difference in the regression coefficients for the 2 days ($P > 0.10$).

His stomach was found empty when aspirated. Neither glucosis nor drugs were found in the urine collected in the mornings before the exposure.

The hematological and enzymatical findings are shown in Table 2. On the day following the combined exposure to ethanol and oxitol a decrease in thrombocytes and neutrophil granulocytes as well as an increase in serum creatine kinase were found. The measured values were outside the reference interval. The changes were normalized 3 days later. On the day following the exposure to alcohol only no changes were found.

Table 1. Elimination rate of ethanol without exposure/ during exposure to oxitol

Day 1 No exposure to oxitol		Day 2 Exposure to oxitol 316 ppm	
Time	% ethanol	Time	% ethanol
11.40 a.m.	0.128	11.40 a.m.	0.125
0.40 p.m.	0.104	0.40 p.m.	0.097
1.40 p.m.	0.077	1.40 p.m.	0.072
2.35 p.m.	0.051	2.35 p.m.	0.050

Table 2. Hematological and enzymatical changes after exposure to ethanol alone and to ethanol and oxitol

Analysis performed (reference interval)	Day 1 Ethanol alone	Day 2 Ethanol and oxitol	Day 3	Day 6	Day 10
Leukocyte count mia/l (3.0–8.5)	8.8	12.0	7.6	14.0	9.0
% neutrophil segmented granulocytes (42%–79%)	47%	49%	29%	62%	44%
Thrombocytes mia/l (160–400)	258	348	30	289	246
S-creatine kinase U/l (15–110)	43	38	111	52	—

Discussion

Drugs or unabsorbed alcohol could be ruled out as factors interfering with elimination. Fructose is known to increase the elimination rate of ethanol [4]. A possible intake of, e.g., a large amount of honey could be ruled out since no glucosis was found in the urine. The rate of alcohol elimination thus appeared to be influenced only by the factors controlled in the exposure chamber.

The person claimed that, when exposed to 316 ppm oxitol, he was more troubled by irritation of the respiratory tract than when lacquering the floor. Upon lacquering the floor the exposure had probably been below 316 ppm oxitol. The mean chamber exposure exceeded the threshold limit value threefold.

No influence of oxitol was found in the elimination rate of ethanol.

We had chosen to examine only for oxitol because this solvent has a greater affinity to alcohol dehydrogenase than ethanol. Other components of the lacquer have not been examined.

As for hematologic and enzymatic changes, a decrease was found in thrombocytes and neutrophil granulocytes and an increase in serum creatine kinase after the combined exposure to ethanol and oxitol. Normal values of these variables were found after the exposure to ethanol alone. However, thrombocytopenia is seen from hours to weeks after intake of large quanta of alcohol [3], and increased serum creatine kinase has been reported after intake of alcohol [2]. Exposure to oxitol alone was not performed.

Whether the changes observed were induced by the ethanol alone or by the combination of ethanol and oxitol cannot be answered by this study. The person was asked if he had done anything unusual including drinking large quantities of ethanol the evening after the combined exposure to oxitol and ethanol, but he claimed that this was not the case.

Conclusion

Thus, an acute exposure to oxitol at 316 ppm during light physical activity did not influence the elimination rate of ethanol in this experiment. The neutrophil

granulocytes and thrombocytes decreased and the serum creatine kinase increased after combined exposure to ethanol and oxitol. The explanation of these findings could not be pointed out with certainty. The clinic answered the counsel in accordance with the experiment findings that no evidence was found that oxitol did influence the elimination rate of ethanol in the case concerned.

The client was convicted for driving under the influence of ethanol according to the law.

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