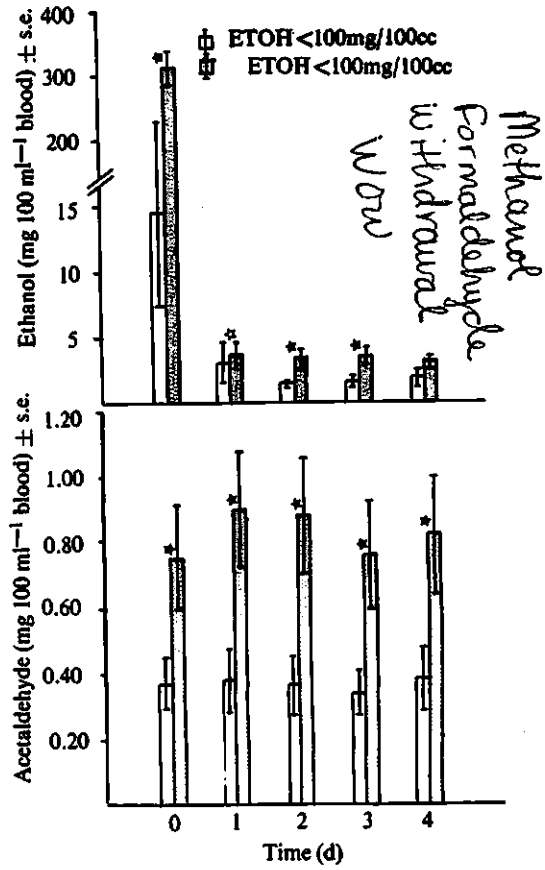
G. Magrinat



Methanol Formaldehyde Withdrawal WOW

abstract

Very Important!, formaldehyde?

Ethanol and Methanol Metabolites in Alcohol Withdrawal

THE twenty-one subjects participating in this study were serial admissions to the St Louis Detoxification Center during the period of December 2–21, 1971. Their ages ranged from 29 to 72 yr and they comprised twenty males and one female. A blood sample (10 ml) was obtained from the patient on admission, when a symptom intensity rating evaluation was carried out[1,2]. Blood concentrations of ethanol, methanol, acetaldehyde and formaldehyde-formate were determined by gas-liquid chromatography[3,4]. This procedure was repeated on four consecutive days (total of five samples), after which the patient was discharged from the Center.

All participating subjects received chlordiazepoxide, flurazepam and a high potency vitamin B complex and C in a fixed schedule[5,6].

About one-half of the subjects had initial blood levels of ethanol of less than 100 mg/100 ml, while those of the remainder were well above 100 mg/100 ml. We therefore arbitrarily selected a blood level of ethanol of 100 mg/100 ml as the criterion for categorizing the patients into two groups—a low-alcohol group and a high-alcohol group. Students *t*-test or the *t*-test for the difference of matched pairs was used for the statistical evaluation of the data[7].

The mean admission blood alcohol level of the low-alcohol group was 14.4 mg/100 ml (s.e. ±7.1) while that of the high-alcohol group was 309 mg/100 ml (±27.2). The blood ethanol levels for both groups over the 5-d observation period (Fig. 1) rapidly returned towards a non-alcoholic level, although on days 1 and 2 they were still significantly higher in the high-alcohol group.

Blood acetaldehyde concentrations over the 5 withdrawal days for the two groups are shown in Fig. 1. The high-alcohol group acetaldehyde blood level was significantly higher on admission day (0.747 ± 0.162 mg/100 ml) than it was in the low-alcohol group (0.378 ± 0.080 mg/100 ml). This large and statistically significant difference between the two groups endured for the 5 d of hospital confinement. These blood

Fig. 1 Upper: Blood ethanol levels and standard errors in high-alcohol (N=12) and low-alcohol (N=9) separated groups during alcohol withdrawal. ★: $P \leq 0.05$ between groups on common measurement day; ☆: $P \leq 0.05$ between each group on different measurement days. Lower: Blood acetaldehyde levels and standard errors as above.

acetaldehyde concentrations, particularly for the high-alcohol group, are considerably higher than those reported in a laboratory controlled alcohol intake-withdrawal study[8]. But, as suggested from that study and supported by some of our laboratory observations, the 5–10-fold increased blood acetaldehyde concentrations in our patients could be a reflexion of the content of impurities contained in the alcoholic beverages consumed by our patients when "on the street".

The blood methanol concentration (Fig. 2) also exhibited marked differences between the two groups. There was a highly significant elevation of methanol in the admission sample for the high-alcohol group (1.54 ± 0.27 mg/100 ml) which was also apparent on day 1 (0.17 ± 0.08 mg/100 ml).

The formaldehyde-formic acid blood concentrations for the high-alcohol group were higher on admission and for each of the 4 observation days (Fig. 2). Peak level (5.58 ± 1.18 mg/100 ml) achieving significance was reached on the third observation day, and this significant elevation over the formaldehyde-formic acid blood concentration in the low-alcohol group (1.20 ± 0.17 mg/100 ml) was still observed on the fourth observation day. To our knowledge, this formaldehyde–formic acid response has not been reported before from this type of clinical population.

Both the high- and the low-alcohol groups exhibited high (abnormal) total scores in the intensity of withdrawal symptoms rating scores obtained on the admission day evaluation (Fig. 3). Subsequent daily behavioural evaluations showed that the rating scores for total withdrawal symptoms of the low-alcohol group rapidly returned towards normal, the total scores on all days being significantly lower than the admission score. In the high-alcohol group, the abnormal behaviour was greatest on this first observation day and then gradually returned towards normal levels. Examination of the peak scores for each of the ten factors revealed that only eating and sleeping disturbance

differed significantly between the high- and low-alcohol groups, the more deviant scores belonging to the high-alcohol group. In all cases, however, the high-alcohol group had statistically significant elevations in blood concentrations of ethanol, methanol and their metabolites and also showed total disrupted withdrawal signs and symptoms significantly greater than those of the low-alcohol groups.

Separating the twenty-one subjects participating in this study into high- and low-alcohol groups resulted in the emergence of a number of interesting differences between the two groups. The delayed and marked elevation in blood concentrations of the methanol metabolites, formaldehyde-formate, does support the hypothesis that the oxidative enzyme systems induced by chronic alcohol consumption will shift to metabolize methanol when ethanol is abruptly withdrawn. This would be expected and is consistent with the concept of competitive inhibition for the common enzyme systems for methanol and ethanol metabolism. Increased availability of the common enzyme systems shortly after abrupt ethanol withdrawal was thus associated with a marked decrease in methanol blood level and a delayed and marked elevation in the blood concentration of the methanol metabolites, formaldehyde-formate. We speculate that a critical accumulation of these methanol metabolites may be the primary factor which results in the expression of withdrawals.

These changes in formaldehyde–formate levels, together with the observed high and sustained acetaldehyde blood levels (high-alcohol group) implicated the impurities contained in the alcoholic beverages consumed by the "street alcoholics" before admission. The much higher blood acetaldehyde levels reported for "street alcoholics" used in this study compared with levels obtained from alcoholics in a controlled laboratory indicates that caution must be exercised in the interpretation, extrapolation or application of the results obtained in the artificial setting to what is happening in the "real world". This consideration as well as the many speculations and questions raised will be examined further in subsequent studies.

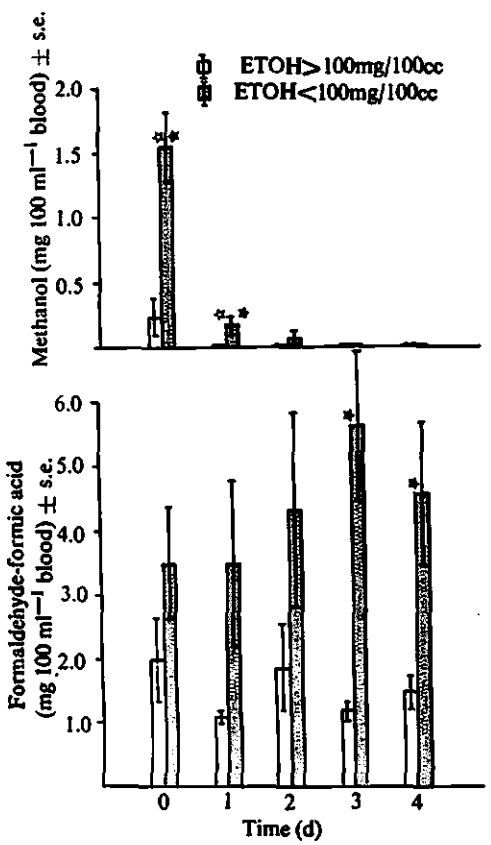


Fig. 2 Upper: Blood methanol levels and standard errors in high-alcohol (N=12) and low-alcohol (N=9) separated groups during alcohol withdrawal. ★: $P \leq 0.05$ between groups on common measurement day. ☆: $P \leq 0.05$ between each group on different measurement days. Lower: Blood formaldehyde–formic acid levels and standard errors as above.

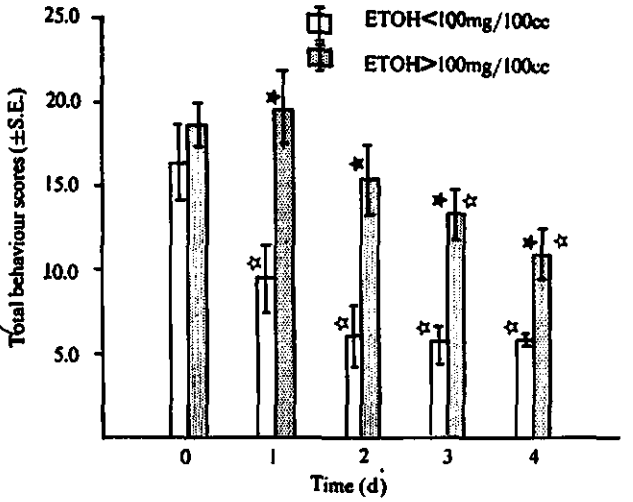


Fig. 3 Severity of behavioural disruption scores for high-alcohol (N=12) and low-alcohol (N=9) separated groups during alcohol withdrawal. ★: $P \leq 0.05$ between groups on common measurement days; ☆: $P \leq 0.05$ between each group on different measurement days.

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