Thiamin Depletion after Ethanol and Acetaldehyde Administration to Rabbits

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Summary The role of thiamin in the catabolism of ethanol and acetaldehyde has been investigated. When thiamin and subsequently ethanol were administered orally to rabbits, the thiamin concentration in blood increased slightly during the first 3 h and then decreased gradually. After 12 h, it became lower than the value before thiamin administration. Finally, it reached the lowest value after 24 h and then increased slowly to revert to normal in 72 h. It is suggested that thiamin participates in the catabolic pathway of ethanol. An oral administration of pyrazole, an inhibitor of alcohol dehydrogenase, followed by ethanol to rabbits caused a delay in ethanol elimination from blood. When acetaldehyde was injected intravenously to rabbits, thiamin concentration and the transketolase activity in blood decreased gradually and after 12 h the thiamin level reached its lowest value, then increased slowly and normalized in 72 h. Thus, it could be postulated that the decrease in thiamin after an acute ethanol ingestion linked greatly to the acetaldehyde catabolism.

Key Words thiamin, ethanol, acetaldehyde, transketolase

There are ample documentations which indicate that the nutritional status of thiamin is closely linked to alcohol ingestion (1–8). In our previous study (9), we clarified that the acute ethanol ingestion in the rabbit produced a rapid decrease in blood thiamin levels and the transketolase activity [EC 2.7.1.1] in erythrocytes and an increase in thiamin pyrophosphate (TPP) effect in erythrocytes. The decrease in blood thiamin after the ethanol ingestion was much greater than after an isocaloric glucose administration. Recently, we also clarified that the activity of hepatic microsomal ethanol oxidizing system (MEOS) was significantly decreased in thiamin deficient rats as compared with control rats. In vitro addition of thiamin or thiamin pyrophosphate caused the restoration of the decreased MEOS activity and this effect was dependent on the concentration of thiamin in rat liver microsomal fractions (10). These facts suggest that thiamin is partly involved in the oxidation of ethanol. The present study has been conducted to clarify the effect of thiamin on

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other metabolic and catabolic pathways of ethanol.

MATERIALS AND METHODS

_Treatment of animals._ Male rabbits, _Oryctolagus cuniculus_ var. _domesticus_, weighing about 2.5–3.0 kg were used throughout the experiments. Each rabbit was fasted for 24 h after each treatment and from the second day of the experiment, a restricted diet (100 g/day) of commercial rabbit chow (Oriental Co., Japan, thiamin concentration: 0.8 mg/100 g) was fed to every rabbit during the experimental period.

1) _Effect of simultaneous administration of thiamin and ethanol to rabbits._ Immediately after oral administration of thiamin (0.5 mg/kg body weight), ethanol (4 g/kg) was administered orally with a stomach tube to rabbits. As a control, ethanol was replaced with water. Blood samples were collected from a vena praeauricularis.

2) _Effect of pyrazole on ethanol administered rabbits._ One mmol/kg body weight of pyrazole, an inhibitor of alcohol dehydrogenase [EC 1.1.1.1] and 4 g/kg of ethanol were applied successively to rabbits orally by stomach tube. As a control for the ethanol determination, rabbits fed ethanol without administration of pyrazole were used.

3) _Effect of acetaldehyde administration._ Acetaldehyde (20 mg/kg body weight) was intravenously injected slowly (spending 5 min) and then blood samples were collected.

_Analytical procedures._ The concentrations of ethanol and thiamin in blood and the activity of transketolase in erythrocytes were measured by the the methods described in the previous paper (9). Acetaldehyde was measured by the gas chromatographic method of Wartburg and Ris (11).

RESULTS

1) _Effect of simultaneous administration of thiamin and ethanol to rabbits_

Rabbits fed thiamin and ethanol were noticed to be quite intoxicated and nystagmus was observed from 15 min to 3 h after the ethanol ingestion. Figure 1 shows the thiamin and ethanol concentrations in blood of the rabbits fed with thiamin and ethanol (solid lines) and the thiamin concentration in blood of the thiamin administered rabbits (broken line). Ethanol in the blood of the thiamin and ethanol administered rabbits increased rapidly and reached a maximum in 1–3 h, then decreased. The thiamin concentration in blood of the same rabbits increased slightly till 3 h after the administration and then decreased gradually. After 24 h, the thiamin concentration reached its lowest value, then increased slowly and reverted to normal in 72 h. In control rabbits (administered thiamin and water), the blood thiamin level rose rapidly to the highest value 2 h after the thiamin administration; then it decreased to the normal value gradually. The transketolase activity in erythrocytes, no significant change was observed in both groups.

Fig. 1. Thiamin and ethanol concentrations in blood after administration of thiamin and ethanol or thiamin alone to rabbits. The values represent the average and standard error of 5 experiments.

Fig. 2. Ethanol concentration in blood of rabbits after administrations of pyrazole plus ethanol or ethanol alone. The values represent the average and standard error of 5 experiments.

2) Effect of pyrazole on ethanol fed rabbits
The ethanol concentration in blood of rabbits administered pyrazole plus...
3) Effect of acetaldehyde administration

Acetaldehyde and thiamin concentrations in blood were measured in acetaldehyde administered rabbits as shown in Fig. 3. Acetaldehyde in blood increased...
temporarily and decreased rapidly. The thiamin concentration in blood was reduced gradually and after 12 h it reached its lowest value, then increased slowly and almost normalized in 48 h. The transketolase activity in erythrocytes decreased in parallel with the blood thiamin level in acetaldehyde injected rabbits (Fig. 4).

**DISCUSSION**

In the previous study (9), we administered a dose of 13 ml/kg body weight of 30% ethanol (about 1/3 of LD₅₀) to rabbits and found that the thiamin concentration decreased gradually in proportion to the decrease in elevated ethanol concentration in blood. A similar phenomenon was observed in an experiment on human subjects (12). The present study indicates that the simultaneous administration of thiamin with ethanol increases thiamin concentration at first, but this value tends to decrease coincidently with the decrease of blood ethanol and then becomes lower than that before thiamin administration (Fig. 1). Several studies (6, 13, 14) suggested that the absorption of thiamin from the gastrointestinal tract was impaired by the effect of ethanol. However, it is not convincible that the present findings were merely due to the inhibition of thiamin absorption. A significant decrease in thiamin below the non-administered level at the time of ethanol elimination indicates the involvement of thiamin in the catabolic pathways of ethanol. As the nystagmus and ethanol depletion curve in blood of rabbits fed ethanol and thiamin were similar to those in rabbits fed ethanol without thiamin administration (9), it can be concluded that the administration of thiamin may not have an influence either on the blood ethanol concentration or on prevention of nystagmus in the ethanol administered rabbits. Centerwall and Criqui (15) claimed that the fortification of alcoholic beverage with thiamin was economically advantageous for preventing the Wernicke-Korsakoff syndrome as compared with the cost of treatments of this disease. However, the present study casts a question on the efficacy of this plan.

Administration of pyrazole, an inhibitor of alcohol dehydrogenase, retarded the elimination of ethanol from blood (Fig. 2), but no significant change was observed in blood thiamin levels between rabbits fed ethanol and pyrazole, and those fed pyrazole and glucose (data not shown). Although Abe et al. (8) clarified that the alcohol dehydrogenase activity in the liver decreased in thiamin-deficient and ethanol administered rats, the involvement of thiamin in this enzyme could be negligible.

It is worthy to note that acetaldehyde, a key intermediate in the ethanol catabolism, caused a decrease in the thiamin level and transketolase activity in blood in a similar manner as the case of ethanol administration (Figs. 3 and 4). It is postulated that a decrease in thiamin concentration after an acute ethanol administration can be attributed to the acetaldehyde catabolism.

From previous evidence that is summarized in the Introduction, together with the observations reported in this paper, it seems likely that thiamin participates in
various stages of the catabolic pathways of ethanol. Further studies may confirm these relationships.

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REFERENCES


