Pharmacology Biochemistry & Behavior, Vol. 18, Suppl. 1, pp. 139–140, 1983. © Ankho International. Printed in the U.S.A.

Blood Ethanol and Acetaldehyde Levels in Japanese Alcoholics and Controls

SHOJI HARADA,* DHARAM P. AGARWAL,† H. WERNER GOEDDE† AND SATOSHI TAKAGI‡

*Institute of Community Medicine, University of Tsukuba, Japan
†Institute of Human Genetics, University of Hamburg, F. R. Germany
‡and National Hospital of Alcoholics, Kurihama, Japan

HARADA, S., D. P. AGARWAL, H. W. GOEDDE AND S. TAKAGI. *Blood ethanol and acetaldehyde levels in Japanese alcoholics and controls.* PHARMACOL BIOCHEM BEHAV **18:** Suppl. 1, 139–140, 1983.—Aldehyde dehydrogenase (ALDH) isozyme I deficiency in hair root samples from 105 healthy individuals and 72 alcoholics was determined using isoelectric focusing. From these individuals, 12 male alcoholics (2 with ALDH isozyme I deficiency and 10 normal) and 45 healthy controls (18 with ALDH isozyme I deficiency and 27 normal) were investigated for their blood ethanol and acetaldehyde levels by gas chromatography after an acute dose of alcohol (0.5 g ethanol/kg body wt.). Peak blood ethanol values of about 10 mmol/l were attained after 1 hour both in alcoholics and normal controls irrespective of their ALDH type. There was no significant difference in the blood ethanol level during the 5 hr post-drinking period in both the groups. Peak blood acetaldehyde concentration was significantly higher in healthy controls and alcoholics deficient in ALDH isozyme I after alcohol drinking (about 30 μmmol/l) than in individuals with normal ALDH isozyme I (3 μmmol/l). However, no significant difference in blood acetaldehyde was observed between alcoholics and controls.

Aldehyde dehydrogenase isozyme deficiency Blood ethanol and acetaldehyde levels Gas chromatography Alcoholism

HIGHER blood acetaldehyde levels after alcohol drinking have been reported in alcoholics and their relatives compared to control subjects [4,9]. Persons who show facial flushing and other vasomotor symptoms after moderate alcohol intake also have higher blood acetaldehyde concentrations than non-flushers [6]. Japanese subjects found deficient in isozyme I of aldehyde dehydrogenase (ALDH EC 1.2.1.3) also had higher blood acetaldehyde levels than normal individuals [3]. However, due to various methodological complications involved in the determination of blood acetaldehyde, the reported values are controversial [2]. Recent modifications of the deproteinization step minimize the artefactual formation of acetaldehyde from ethanol and its enzymatic oxidation [1, 5, 7, 10, 11].

In the present study, we report on the blood ethanol and acetaldehyde levels after alcohol drinking in Japanese alcoholics and controls. The results are discussed in context of aldehyde dehydrogenase isozyme I deficiency and flushing among these subjects.

METHODS

Twelve Japanese male alcoholics (2 deficient in ALDH isozyme I and 10 normals) and 45 healthy controls were investigated for their blood ethanol and acetaldehyde levels by the method of Mizoi and Eriksson [7] after an acute dose of alcohol. Subjects drank whiskey (0.5 g ethanol/kg body wt.) diluted with water before breakfast. Two ml of blood was taken from an anticubital vein every 30 min for a 5 hr period. One ml of whole blood was immediately transferred into a 10 ml glass tube and mixed with 4 ml of physiological saline containing 6% perchloric acid. The tubes were closed with a rubber stopper. After centrifugation at 5,000 g for 5 min in the cold, 1 ml supernatant was transferred into a 10 ml vial and tightly closed with a rubber stopper and an aluminium cap. The vials were incubated at 60°C for 30 min in a head space sampler. Ethanol and acetaldehyde concentrations were measured by gas chromatography using a flame ionization detector (Perkin Elmer). Chromosorb 101 was employed as the carrier medium in a 3×1500 mm column. All analyses were carried out in duplicate.

RESULTS AND DISCUSSION

Ethanol levels in alcoholics and control subjects after alcohol intake are shown in Fig. 1. Peak blood ethanol values were attained after about 1 hr both in alcoholics and controls (mean value, 10 mmol/l). There was no significant difference in the blood ethanol level during the 5 hr period in both the groups.

Acetaldehyde levels in the blood of alcoholic and control subjects with or without ALDH isozyme I deficiency are shown in Fig. 2. Peak blood acetaldehyde concentrations were significantly higher in healthy controls and alcoholics deficient in ALDH isozyme I (flushing types) after alcohol drinking (mean value, 30 μmol/l). The peak blood acetaldehyde and steady-state blood acetaldehyde levels in non-flushing healthy controls and alcoholics were very low (mean

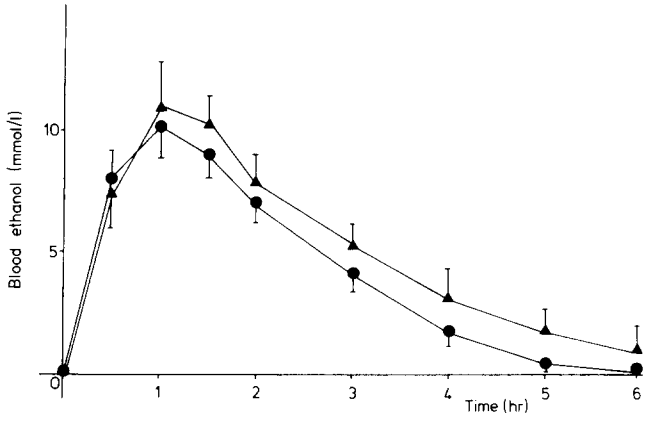

FIG. 1. Blood ethanol levels in healthy controls (▲−▲) and alcoholics (●−●) after alcohol drinking.

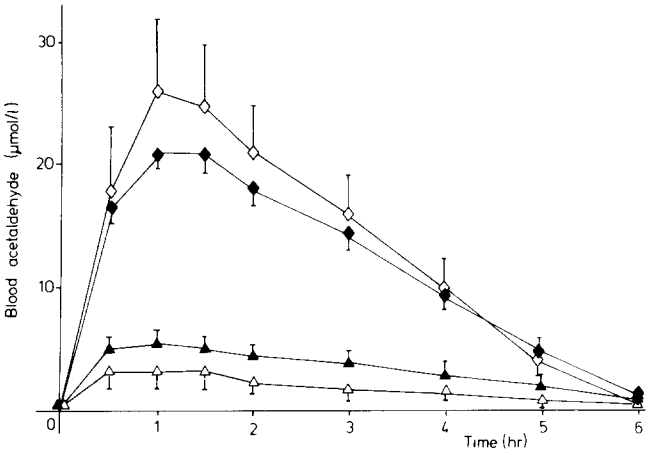

FIG. 2. Blood acetaldehyde levels in controls and alcoholics after alcohol drinking. Healthy controls: Deficient-ALDH; ◇−◇); Normal ALDH ◆−◆. Alcoholics: Deficient-ALDH; △−△; Normal ALDH ▲−▲.

value, 5 and 3 μmol/l). It seems therefore, that previous reports showing higher blood acetaldehyde levels in alcoholics [9] might be due to the artefactual formation of acetaldehyde during the handling and processing of the blood samples. Interindividual differences in the artefactual formation of acetaldehyde may also contribute to the differences in mean blood acetaldehyde levels between different groups of subjects. Nevertheless, it is likely that chronic alcoholics with hepatic damage may show elevated blood acetaldehyde levels [2]. A recent study in baboons showed that chronic ethanol feeding increased plasma free acetaldehyde levels and was negatively correlated with liver ALDH activity [8].

REFERENCES

1. Christensen, J. M., H. Angelo and J. Knop. Determination of acetaldehyde in human blood by a gas chromatographic method with negligible artefactual acetaldehyde formation. *Clin Chim Acta* **116:** 389–395, 1981.
2. Eriksson, C. J. P. Problems and pitfalls in acetaldehyde determination. *Alcoholism* **4:** 22–29, 1980.
3. Harada, S., D. P. Agarwal, H. W. Goedde. Aldehyde dehydrogenase deficiency as cause of facial flushing reactions to alcohol in Japanese. *Lancet* **2:** 982, 1981.
4. Korsten, M. A., S. Matzusaki, L. Feinman and C. S. Lieber. High blood acetaldehyde levels after ethanol administration. Difference between alcoholic and non-alcoholic subjects. *N Engl J Med* **292:** 386–389, 1975.
5. Lindros, K. O. and C. J. P. Eriksson. Artefactual acetaldehyde formation during human blood perchlorate deproteinization. *Subst Alcohol Actions/Misuse* **2:** 341–347, 1981.
6. Mizoi, Y., I. Ijiri, J. Tatsuno, T. Kijima, S. Fujiwara, J. Adachi and S. Hishida. Relationship between facial flushing and blood acetaldehyde levels after alcohol intake. *Pharmacol Biochem Behav* **10:** 303–311, 1979.
7. Mizoi, Y. and C. J. P. Eriksson. General discussion. Titisee-Symposium on Alcohol Metabolism in Humans and Its Enzymes. Titisee, Germany, January 21–24, 1982.
8. Pikkarainen, P. H., E. R. Gordon, M. E. Lebsack and C. S. Lieber. Determinants of plasma free acetaldehyde levels during the oxidation of ethanol: effects of chronic ethanol feeding. *Biochem Pharmacol* **30:** 799–802, 1981.
9. Schuckit, M. A. and V. Rayses. Ethanol ingestion: Differences in blood acetaldehyde concentrations in relatives of alcoholics and controls. *Science* **203:** 54–55, 1979.
10. Stowell, A. R. An improved method for the determination of acetaldehyde in human blood with minimal ethanol interference. *Clin Chim Acta* **98:** 201–205, 1979.
11. Wartburg, J.-P. and M. M. Ris. Determination of acetaldehyde in human blood. *Experientia* **35:** 1682–1683, 1979.