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VARIATION OF TFAA IN LIVER CELLS AFTER AN INHALATION OF HALOTHANE

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Trifluoroacetic acid (TFAA) which is the final metabolic substance of halothane, is discharged in urine. Its peak is around 10 hours after inhalation of halothane. The mechanism of this retardation of discharge may be attributed to the circulation of TFAA in intestines and the liver or to metabolism of halothane deposited on fatty tissues after inhalation of halothane. We previously discussed the possibility of the former. In the present work, we performed the experiment which examined the possibility of the latter.

Experimental method

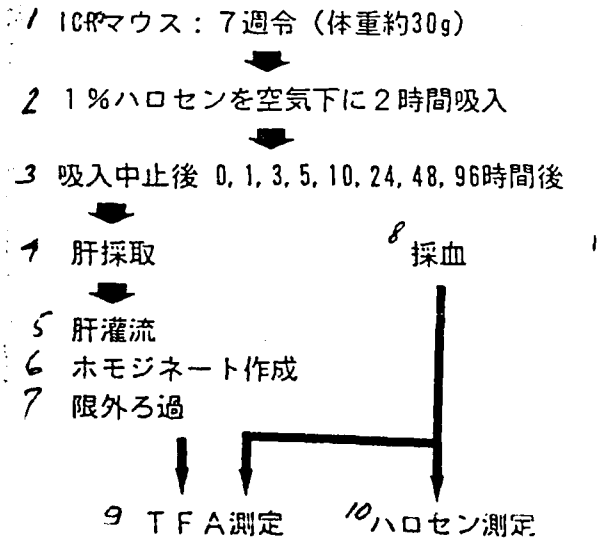
ICR mice (weight about 30 g) which were seven weeks old, inhaled 1% halothane in the air for two hours. After two hours of inhalation, we dissected them at 0, 1, 3, 10, 24, 48 and 96 hours and recovered their livers and collected blood samples from their hearts. The livers were cleaned by biological saline solution and homogenated by distilled water. The resulting homogenated liver was ultra filtered to yielding liver cells. We determined TFAA concentration liver cells and blood by ion-chromatography. Further, halothane concentration in blood was determined by the equilibrium method using gas chromatography. The value of TFAA was expressed by mean ±SD, its inspection was done by the student t-test. When the risk rate is less than 5%, we regarded it as significant. We also determined the distribution volume and half value period of halothane concentration applying a two compartment model.

Results

We did not detect any TFAA in liver cells and blood samples of mice which did not inhale halothane. In Figure 2, we show variations of TFAA concentration in liver cells. The TFAA concentration increased up to five hours after the end of inhalation. The significance was 5% right after and three hours after the end of the inhalation and 1% after five hours at the end of the inhalation, respectively. Figure 3 shows variations of TFAA concentrations in blood. The TFAA concentration became maximum five hours after the end of inhalation. It displays a very similar trend to that in liver cells. Figure 4 depicts variation of halothane concentration in blood. The halothane concentration was highest at the end of inhalation and we did not detect any trace of halothane 10 hours after the end of inhalation. The distribution volume of organs whose blood stream flow is very large like the liver was about 90.7 times larger than those organs whose blood flow is slow like fatty tissues. Further, the half value period was 10.7 min. and 99.5 min. for high speed blood flow organs and low speed blood flow organs, respectively.

Figure 1. Experimental method

1--ICR mouse: 7 weeks old (wt. about 30g); 2--inhalation of 1% halothane in the air for 2 hrs; 3--0.1, 3.5, 10, 24, 48, 96 hrs after the end of inhalation; 4--liver taken out; 5--liver cleaned; 6--homogenate was prepared; 7--ultra filtration; 8--blood sample taken; 9--TFAA measurement; 10--halothane measurement



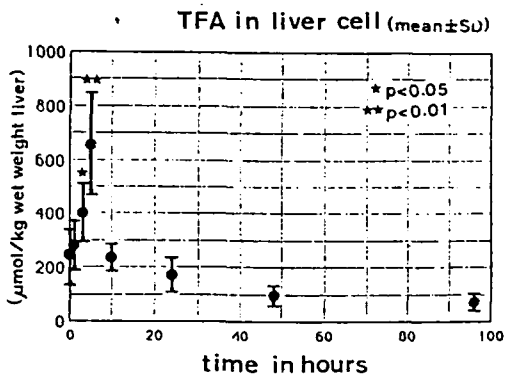


Figure 2

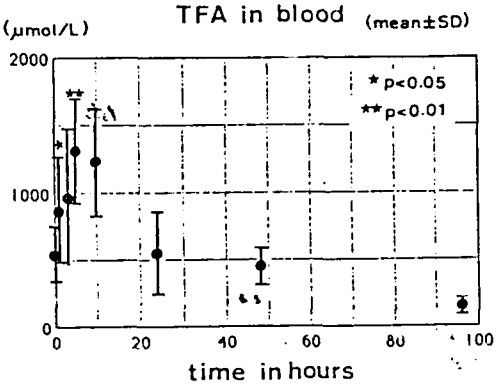


Figure 3

Discussion

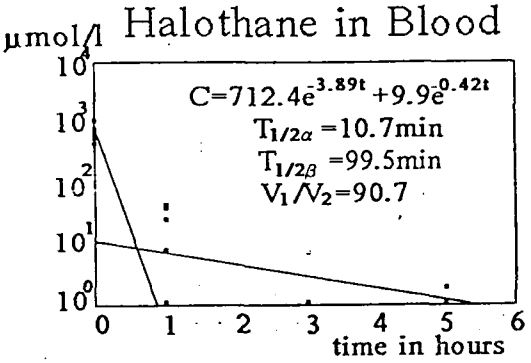


Figure 4

The increase in TFAA after the inhalation of halothane is due to the production of TFAA in the liver. The retardation of discharge in the urine is attributed to the fact that halothane deposited on fatty tissues is metabolized continuously after the inhalation of halothane. Since the TFAA level in the blood varies very similarly with that in the liver, TFAA may be considered to easily pass through liver cell membranes. The distribution volume and half value period for the organs whose blood flow speed is fast were about 90.7 times larger and about 1/9 smaller than those for the organs whose blood flow speed is slow.

References

[1] G. Okita, et al.: Effect of inhaled halothane concentration on the discharge of trifluoroacetic acid (TFAA). Masui to Sosei, 19: 39-42, 1983

[2] K. Sakai, et al.: Effect of fatty tissues at Monmyaku area on metabolic degradation of halothane. Masui to Sosei, 22: 65-69, 1986

[3] H. Kinoshita, et al.: Effect of trifluoroacetic acid (TFAA) Masui to Sosei, 24: 53-55, 1988