Title: HALOTHANE DECREASES ALBUMIN SYNTHESIS

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INTRODUCTION

Since a major function of the liver is synthesis of export proteins, we have examined the effect of clinically relevant levels of halothane on 1) albumin and transferrin synthesis by the isolated perfused rat liver, and 2) albumin synthesis in the intact rat.

METHODS

Liver perfusion: Livers were perfused ex situ for 4.25 hours with a heterologous mixture consisting of rat erythrocytes washed twice with 0.9% saline and heparinized rabbit plasma (Hct 25-29%). Control perfusions were exposed to O_2/CO_2 (95/5) while halothane perfusions were treated with 1.5% halothane (equivalent to 1.35 MAC) in O_2/CO_2. Albumin and transferrin production by the liver were measured by linear regression of accumulated values, expressed as mgh^{-1} per 300 g rat. Results in the control and halothane treated groups were compared by Student's t test.

In vivo studies: Albumin synthesis in intact rats was measured by the (^{14}C)carbonate method of McFarlane (1). Four groups of rats were studied: Group I, lightly anesthetized with ether for less than 5 minutes, immediate measurement; Group II, anesthetized with halothane (0.90 to 1.35 MAC) for one hour followed by measurement; Group III, anesthetized with halothane for one hour, measurement 24 hours later; Group IV, anesthetized with halothane for one hour then anesthetized with halothane 24 hours later for 30 minutes followed by measurement. Anesthetized rats (Groups II-IV) were not intubated but were ventilated by a mask technique shown to maintain pH and ABG in the normal range. The albumin synthetic rate, in mg/hour/300g rat, was calculated for animals in each treatment group. Control and treatment groups were compared by one way analysis of variance and the Student-Neuman-Keuls multiple comparison procedure.

RESULTS

Liver perfusions: Halothane perfusate and bile flow rates did not differ significantly from control values, nor did urea production.

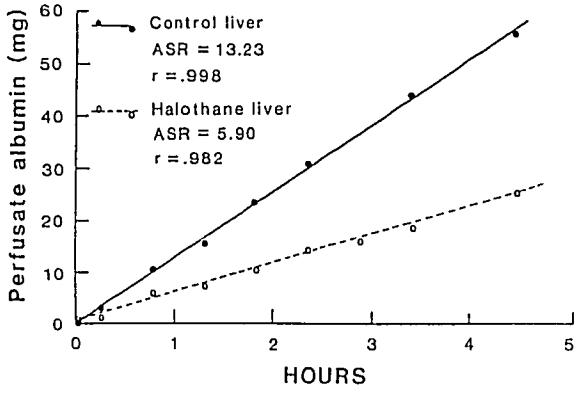

Figure 1 shows plots of the albumin synthetic rate (ASR) by representative control and halothane treated livers. A constant rate of production was found throughout the course of each perfusion. Similarly, transferrin was synthesized at a constant rate. However, the overall rate of synthesis of each of these export proteins was significantly depressed by halothane exposure.

Table 1 shows the mean and standard error for albumin and transferrin synthesis by control and halothane-treated rat livers. Halothane reduced albumin synthesis by about 40% and transferrin synthesis by nearly 50%.

Table 1

Group	(n)	Protein Synthesis (mg/hr per 300g rat) Albumin	Transferrin
Control	(6)	12.42 ± 1.15	4.35 ± 0.74
Halothane	(5)	7.10 ± 0.73*	2.40 ± 0.17**

* differs from control ($p<0.01$)
** differs from control ($p<0.02$)

In vivo studies: Table 2 shows the mean and standard error for the albumin synthetic rate in each treatment group. The mean rate of Group IV, animals anesthetized twice with halothane, differs significantly from the means of all other groups.

Table 2

Group (n)	Treatment	Time of Measurement*	Synthetic Rate (mg/h/300g rat)
I (14)	No halothane	Immediate	14.07 ± 0.76**
II (6)	Halothane x 1	Immediate	11.00 ± 1.29***
III (6)	Halothane x 1	24 h	11.81 ± 1.42***
IV (8)	Halothane x 2	24.5h	7.07 ± 1.06

* After initial anesthesia
** Differs from Group IV, $p<0.01$
***Differs from Group IV, $p<0.05$

CONCLUSION

In isolated perfused livers, halothane depression of protein synthesis appeared early and remained constant. Significant depression of albumin synthesis did not occur in intact rats either immediately or 24 hours after one exposure, but marked depression (50%) followed a second, short exposure. These results, taken together, suggest an early effect due to halothane itself, rather than its metabolites, which requires induction to become manifest in the intact animal.

REFERENCES

1. McFarlane AS: Measurement of synthetic rates of liver-produced plasma proteins. Biochem J 89:277, 1963

Supported by the South African Medical Research Council and the Study Center for Anesthesia Toxicology, Vanderbilt University.