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Hepatic oxygen delivery-consumption relationship during anesthesia and hypoxemia in dogs

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The liver has been considered to be more resistant to hypoxemia than the brain, heart, or kidneys. This is chiefly because hepatic oxygen delivery (HDO_2) is more than adequate to meet hepatic oxygen consumption (HVO_2), approximately five times, at the steady state. Therefore, even though hypoxemia is induced, the liver can compensate for the decrease in HDO_2 by elevating the oxygen extraction ratio to the maximal level. HDO_2, however, tends to be suppressed by inhalational anesthesia which usually decreases hepatic blood flow, and once hypoxemia develops due to decreased hepatic blood flow during inhalational anesthesia, the liver will not be able to compensate for the decrease in the HDO_2. This can result in suppression of the HVO_2 to the critical point below which hepatic energy metabolism will be occasionally disturbed.

This study was designed to determine the critical HDO_2 level during halothane anesthesia compared with thiamylal anesthesia as a control. Another aim of this study was to measure oxygen metabolism in the liver during hypoxemia, since hepatic oxygen metabolism could be impaired by a decrease of HVO_2 below the critical HDO_2.

Twenty-nine mongrel dogs were used in the study. Anesthesia was induced with ketamine 50 mg, i.m. and thiamylal 15 $mg \cdot kg^{-1}$ i.v. Under controlled ventilation with pancuronium, maintaining $Paco_2$ at 30–40 mmHg, animals were anesthetized with N_2-O_2-1.5 MAC halothane or N_2-O_2-thiamylal 30 $mg \cdot kg^{-1} \cdot h^{-1}$ i.v. Following laparotomy, the inspired oxygen concentration was gradually reduced from 21% to 15%, 12%, 10%, 8%, and 6%, which was achieved by mixing air and nitrogen, and maintained for 30 min at each fraction of inspired oxygen (Fio_2) concentration during halothane or thiamylal anesthesia. At each period, hepatic arterial blood flow (HABF) and portal venous blood flow (PVBF) were assessed by electromagnetic flowmetry, and cardiac output was measured by the thermodilution technique. Blood gas tension was analyzed in arterial, portal venous, and hepatic venous blood obtained through the catheters placed in the each vessel. HDO_2 and HVO_2 were calculated by the following formulae [1].

$$HDO_2 = CaO_2 \times HABF + CpvO_2 \times PVBF$$

$$HVO_2 = (CaO_2 - ChvO_2) \times HABF + (CpvO_2 - ChvO_2) \times PVBF$$

In these formulae, CaO_2, $CpvO_2$, and $ChvO_2$ represent the oxygen contents in the arterial, portal venous, and hepatic venous blood, respectively. The arterial ketone body ratio (AKBR, acetoacetate/β-hydroxybutyrate) was measured at each Fio_2 as an indicator of hepatic energy charge [2].

Logarithmic correlation equations between HDO_2 and HVO_2 in the both anesthesia groups were calculated from HDO_2 and HVO_2 at each Fio_2. Figure 1 depicts the correlation equation curves of the two anesthetic groups: $y = 1.01 + 1.23 \cdot \ln X$ ($r = 0.89$, $P < 0.01$) for the thiamylal group and $y = -0.76 + 1.76 \cdot \ln X$ ($r = 0.89$, $P < 0.01$) for the halothane group. The critical HDO_2 point, below which a small decrease in HDO_2 results in a larger drop in HVO_2, corresponds with the shoulder of the linear regression curve. This critical HDO_2 on the halothane curve shifted down and to the right, approaching the point (HDO_2 = 6.85 ml $O_2 \cdot min^{-1} \cdot 100\ g^{-1}$, HVO_2 = 2.63 ml $O_2 \cdot min^{-1} \cdot$

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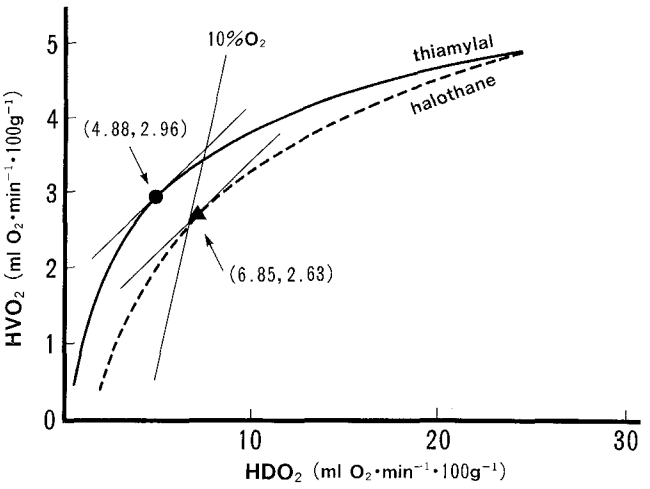

Fig. 1. Hepatic oxygen delivery-consumption relationship curves of halothane (*dashed line*) and thiamylal (*solid line*) anesthesia. The halothane anesthesia curve shifts down and to the right with progression of hypoxemia. HDO_2, hepatic oxygen delivery; HVO_2, hepatic oxygen consumption

100 g^{-1}), whereas it was well maintained on the thiamylal curve at the point (4.88, 2.96). This critical HDO_2 appeared at an Fio_2 well below 0.1 on the thiamylal curve, but it appeared at an Fio_2 above 0.1 on the halothane curve.

In the present study, halothane anesthesia decreased both HDO_2 and HVO_2 more prominently than thiobarbiturate at equivalent Fio_2, and the regression curve of halothane was below that of thiamylal at all Fio_2. Moreover, the difference between the two curves was widened as hypoxemia progressed. Thiamylal maintained HVO_2 better against depression of HDO_2 by means of elevating the oxygen uptake ratio, unless HDO_2 shifted below the critical HDO_2 which was 4.88 ml $O_2 \cdot min^{-1} \cdot 100\ g^{-1}$. On the other hand, halothane could not maintain HVO_2 at any HDO_2 below 6.85 ml $O_2 \cdot min^{-1} \cdot 100\ g^{-1}$ which was the critical HDO_2 of halothane. The present study also indicates that the minimum requirement of HVO_2 for the liver to survive would be between 2.6 and 3.0 ml $O_2 \cdot min^{-1} \cdot 100\ g^{-1}$. The AKBR was more significantly suppressed in the halothane group than in the thiamylal group at all hypoxic Fio_2 levels, and particularly at $Fio_2 = 0.08$ the AKBR decreased to 0.3 in the halothane group whereas it was 0.6 in the thiamylal group. An AKBR below 0.4 for more than 48 h has been reported to be fatal in postoperative patients [2]. Nagano et al. [3] reported that halothane decreased hepatic oxygen demand but not always proportionally to the decrease in oxygen delivery. Also, some in vitro studies support our supposition that halothane decreases hepatic oxygen consumption, resulting in impairment of electron transport and mitochondrial energy production [4,5].

In conclusion, further decrease in HVO_2 with halothane anesthesia and a concomitant depletion of hepatic energy charge does not seem to provide any protection against hepatic oxygen deprivation but suggests that HVO_2 is reduced in cases of extremely poor HDO_2, and this decrease of HVO_2 can be life-threatening.

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