Isoflurane and Hepatic Oxygenation

FATAL HEPATIC INJURY directly related to anesthesia is a rare event. However, varying degrees of postoperative hepatic dysfunction are observed relatively often after operations. Although the precise mechanism for hepatic dysfunction after anesthesia has not been demonstrated, there is considerable evidence that liver hypoxia plays a significant role in the multifactorial etiology of postoperative liver dysfunction. Thus, the article by Conzen et al. in this issue of Anesthesiology, which describes effects of isoflurane on hepatic oxygenation, is of considerable interest. The study demonstrated that isoflurane, when administered to dogs receiving a background narcotic infusion, produced progressive decreases in mean arterial pressure, hepatic surface oxygen tension, and hepatic venous PO₂, whereas splanchnic oxygen consumption remained unchanged. Together, these results suggest that the liver could be at risk for cellular hypoxia during isoflurane anesthesia.

However, these results should be interpreted in light of several factors. First, the effects of isoflurane on splanchnic circulation and oxygenation were obtained in the presence of a background narcotic, piritramid, and the results were compared with those obtained during piritramid administration only. The effects of piritramid on splanchnic circulation have not been studied extensively, but it has been demonstrated that other narcotics cause substantial alterations in the splanchnic circulation. For example, a relatively small dose of morphine, 0.2 mg·kg⁻¹, increased splanchnic blood flow by 19% in humans. An earlier study in monkeys revealed that morphine, 2 mg·kg⁻¹, resulted in a 23% increase in both portal and hepatic arterial blood flows. In dogs, morphine, 1 mg·kg⁻¹, led to a 55% increase in mesenteric blood flow, whereas doses of 3 mg·kg⁻¹ were associated with a 40% reduction in flow. A similar biphasic dose response to morphine was observed during experiments with an isolated canine intestinal loop preparation: small doses of morphine produced vasodilation of the intestinal vasculature, whereas larger doses led to vasoconstriction. The reasons for these disparate responses may be related to the balance of dose-dependent effects of morphine on histamine and/or catecholamine turnover. Other narcotics also influence the splanchnic circulation. For example, fentanyl induced a dose-related vasodilation in an isolated intestinal loop preparation. In the study by Conzen et al., the contribution of hepatic arterial flow to the total hepatic blood flow in the control group was rather small, less than 10% of total hepatic flow, whereas this value is usually 25–30% in dogs. Alfentanil appears to decrease hepatic arterial blood flow when administered to dogs receiving halothane anesthesia. Does piritramid similarly decrease hepatic arterial blood flow? Is such a decrease a reflection of the usual reciprocal relationship between hepatic arterial blood flow and portal blood flow? This study does not answer these questions, but it is evident that the reported changes in hepatic circulation and oxygenation must be attributed not only to isoflurane, but also to a complex interaction between isoflurane and piritramid.

Perhaps the story is even more complicated because laparotomy has also been shown to induce hepatic circulatory changes. The factors responsible for these changes have not been identified, but might include direct manipulation of the viscera and/or a general stress response accompanied by altered concentrations of vaso-
active substances, including catecholamines, renin-angiotensin, vasopressin, etc., that may act on the splanchnic circulation. Conzen et al. avoided laparotomy but performed a thoracotomy and manipulated the surface of the liver through an incision in the diaphragm, maneuvers that may have produced subsequent disturbances in splanchnic circulation.

It is interesting to note that hepatic arterial blood flow did not change significantly during their experiments even when mean arterial pressure decreased by 44%. It appears that isoflurane alone tends to increase hepatic arterial blood flow, whereas the combination of surgical stress plus isoflurane usually decreases or does not change hepatic arterial blood flow. The direct measurement of tissue oxygen tension by multwire surface electrodes represents the application of state-of-the-art investigative techniques to anesthetic problems, and these experienced investigators are experts with this method. However, the measurement of PO2 on the surface of the liver may not characterize hepatic oxygenation in the whole liver. The surface of the liver may represent hepatic arterial blood flow more than the combination of hepatic arterial blood flow and portal blood flow. In both pigs and rats, measurements of liver surface blood flow tended primarily to reflect hepatic arterial flow, thus underestimating the contribution of portal venous flow to the total hepatic blood flow. Furthermore, there is anatomic evidence that the liver capsule contains a dense arterial network. These findings, combined with the observation that the general pattern of the PO2 histograms for the liver surface is similar to that in tissues that receive inflow from arterial blood only, suggest that oxygen tension data for the liver surface may not represent those for the whole organ. It is, therefore, unfortunate that some measure of global hepatic function was not performed to quantify influences on the entire organ.

What are the clinical implications of this study? The study confirms some previous observations that even relatively severe arterial hypotension induced by isoflurane is usually well compensated by an increase in hepatic oxygen extraction. Unaltered splanchnic oxygen consumption observed in this study only partially supports this view; oxygen uptake in the liver per se was not determined, and it is conceivable that oxygen uptake in the liver and preportal tissues responded differently. Common sense still dictates that severe arterial hypotension should be avoided because it may result in inadequate circulation not only to the liver and splanchnic viscera, but to other organs as well. Is isoflurane better for the liver than other anesthetics? Conzen et al. did not attempt to answer this question. Comparison of this study with other available data suggests that isoflurane might be preferable to other inhalation anesthetics, because the hepatic circulation appears to be better maintained during isoflurane anesthesia. However, it appears that the definitive answer to this important question lies in future studies.

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References