THE EFFECT OF ENTERAL OXYGEN ADMINISTRATION ON THE HEPATIC CIRCULATION DURING HALOTHANE ANAESTHESIA: CLINICAL OBSERVATIONS

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SUMMARY

A study of the estimated hepatic blood flow (EHBF) using a colloidal gold technique in 28 patients undergoing saphenous vein stripping, showed that the EHBF decreased to 68% of its initial value during the period of halothane anaesthesia and operation. When enteral oxygen was added EHBF increased to 82% of its initial value. An investigation in 14 other patients undergoing upper abdominal operations showed that enteral oxygen administration caused the oxygen saturation of the portal blood to increase from 55 ± 7.2% (mean ± SEM) to 80 ± 6.2% and, by producing a concomitant decrease in portal pressure, led to a reduction in the portocaval pressure gradient from 74 ± 12.5 to 38 ± 8.7 mm H2O. It is suggested that the oxygen content of the portal blood per se influences the tone of hepatic presinusoidal sphincters. It is concluded that enteral oxygen administration may minimize disturbances in the hepatic circulation occurring during halothane anaesthesia and surgical operations.

Halothane anaesthesia is known to produce a decrease in total hepatic blood flow in man (Epstein et al., 1965; Cooperman, 1972). In the cat, it has been shown to increase the portocaval pressure gradient and to reduce the level of the oxygen saturation in the portal blood (Gelman, 1970). Previous experimental work on rats and cats showed that the administration of enteral oxygen during halothane anaesthesia led to an increase in the portal blood flow and also to an increase in Po2 in the liver tissue. The present investigation was undertaken to determine if enteral oxygen administration could similarly correct the disturbances induced in the hepatic circulation in man during halothane anaesthesia, and if so, to elucidate the mechanisms involved.

METHODS

In the first series of clinical observations, total hepatic blood flow was measured in 28 patients undergoing ligation and stripping of the saphenous vein under halothane anaesthesia. The total hepatic blood flow was studied using a radioactive colloid gold technique. This method was developed by Dobson and Jones (1952) and thereafter used successfully in many experimental and clinical studies (Playoust, McRae and Boden, 1959; Restrepo et al., 1960; Levy et al., 1961; Smith et al., 1966). A collimator radioactivity counter was placed over the liver externally and changes in counting rate following the i.v. injection of 2-3 μCi of 198Au were recorded. This activity was plotted as a logarithm against time. Since the liver uptake curve of this colloid behaves as the reciprocal of the blood disappearance curve, measurement of its liver uptake was preferred for the following two reasons: (1) this measurement does not record the extra-hepatic colloid accumulation which may be increased by the reduction in the total hepatic blood flow, known to result from anaesthesia and surgical trauma; (2) it permits the use of a smaller dose of radioactive colloid.

The half-time of the fast component of the liver uptake curve (T1/2) was determined from the graph recorded on semilogarithmic paper. The uptake constant K was calculated from T1/2 by means of the formula:

\[ K = \frac{\ln 2}{T_{1/2}} = \frac{0.693}{T_{1/2}}. \]

The estimated hepatic blood flow (EHBF) was obtained by multiplying K by the blood volume. The latter was calculated from the plasma volume and the venous haematocrit. The plasma volume was determined by a standard dye dilution method (Evans Blue—T-1824 10–12 mg) after completion of all the measurements of EHBF.
The determinations of EHBF were made at the following times:
(1) on the day before operation;
(2) during operation, for which the anaesthetic comprised a mixture of 60-65% nitrous oxide and 0.5-1.0% halothane in oxygen. The patients were ventilated artificially and muscle relaxation was obtained by the use of tubocurarine 0.5 mg/kg body weight;
(3) during enteral oxygen administration, which was given via a nasogastric tube at a rate of 0.5-1.0 litre/min of oxygen. Excess oxygen escaped without difficulty from the stomach past the nasogastric tube, into the oesophagus and through the mouth. Enteral oxygen was administered to 20 of the 28 patients, and eight served as controls. The third measurement in the control group was performed at the end of the operation.

In a second series of clinical observations on 14 patients undergoing upper abdominal operations, measurements of the oxygen saturation of blood in both the portal vein and the inferior vena cava were made together with the pressure changes which occurred in these vessels.

A standard anaesthetic technique was employed. After induction of anaesthesia with thiopentone and administration of suxamethonium, endotracheal intubation was performed and the patients were ventilated artificially with halothane 0.5-1.0% in nitrous oxide in oxygen, muscular relaxation again being obtained with tubocurarine. The umbilical vein was exposed in the abdominal wall and, after the passage of a bougie, was cannulated with a polyethylene catheter which was advanced to a branch of the portal vein. A second cannula was inserted into the inferior vena cava via the saphenous vein in the groin and advanced until its tip lay at the junction of the hepatic veins and the inferior vena cava.

Before the peritoneal cavity was opened, measurements of caval and portal vein pressures and oxygen saturations were made. These were recorded both before and after enteral oxygen administration. In this second series of patients oxygen was given through a nasogastric tube at a flow rate of 0.5-1.0 litre/min, as in the first group.

Informed consent was obtained from all 42 patients before performing the various procedures and measurements outlined above.

The data were analysed statistically in the same manner as that described in the previous study on animals (Gelman, 1975). In the second group of 14 patients, the correlation coefficient between oxygen saturations of the portal blood and the portocaval pressure gradients was calculated also.

### RESULTS

In the first series of 28 patients, undergoing saphenous vein stripping, EHBF decreased to 68% of the initial value during the period of anaesthesia and operation (table I). When enteral oxygen was given, EHBF increased to 82% of the initial value.

In the second series, of 14 patients, enteral oxygen administration before laparotomy caused the oxygen saturation of the portal blood to increase from $55 \pm 7.2\%$ to $80 \pm 6.2\%$ (mean $\pm$ SEM) and, by producing a decrease in portal vein pressure, caused a reduction in the portocaval pressure gradient from $74 \pm 12.5$ to $38 \pm 8.7$ mm H$_2$O; these changes were statistically significant ($P<0.05$) when evaluated by

| Table I. Changes in estimated hepatic blood flow (EHBF) values during ligation and stripping of saphenous vein under halothane anaesthesia and enteral oxygen administration (mean values $\pm$ SEM) |
|---|---|---|
| Indices of blood flow | Experimental group (20 patients) | Control group (8 patients) |
| | Halothane anaesthesia | Halothane anaesthesia |
| | Before operation | Before enteral oxygen | During enteral oxygen | Before operation | During operation | End of operation |
| The uptake constant $K$ (min$^{-1}$) | $0.394 \pm 0.028$† | $0.269 \pm 0.018*$† | $0.322 \pm 0.021*$‡ | $0.382 \pm 0.022$† | $0.267 \pm 0.021*$ | $0.252 \pm 0.017*$ |
| EHBF (ml/min) | $1970 \pm 13.9$† | $1345 \pm 91*$† | $1610 \pm 105*$‡ | $1895 \pm 128$† | $1325 \pm 102*$ | $1255 \pm 98*$ |
| Total hepatic blood flow as % of initial value | 100 | 68 | 82 | 100 | 70 | 66 |

* Significant difference ($P<0.05$) between these values and the initial data, according to Wilcoxon's test.
† Significant difference ($P<0.05$) between these values and the values during the third period of observation, according to Wilcoxon's test.
‡ Significant difference ($P<0.05$) between these values and the corresponding ones in the control group, according to Student $t$ test.
The results of this study refute the assumption expressed by Poupa (1959) in his comprehensive monograph on enteral oxygen administration, that oxygen, given in this manner, does not affect portal or hepatic blood flow.

In our previous work in animals (Gelman, 1975) the increase in the total hepatic blood flow observed during enteral oxygen administration was a result of an absolute increase in the portal fraction. Although differential measurements of the hepatic blood flow fractions were not made in our investigations in the human subjects, it is tempting to assume that, as in the cat, the significant increase observed in the total hepatic blood flow in man also resulted from an increase in the portal fraction.

The decrease in the portocaval pressure gradient observed during enteral oxygen administration—a measurement which reflects portal vascular resistance—is presumed to result from a diminution in the tone of the presinusoidal inlet sphincter. That an increase in portal blood oxygen saturation should produce a decrease in the vascular resistance in the liver would seem to be a paradox. In other vascular trees, an increase in the partial pressure of oxygen produces an increase in the vascular resistance: in an isolated limb artery in vitro (Carrier, Walker and Guyton, 1964), in the dog's leg (Ross et al., 1962) and in the brain (Kety and Schmidt, 1948). However, one should consider the complexity and differences in the blood supply to the liver.

From a teleological point of view, one might propose that maintenance of a high oxygen tension in the sinusoidal blood would be necessary for the liver cell. One may postulate, therefore, that in those situations where the portal blood oxygen tension is reduced, the tone of the inlet sphincter increases. This would limit the flow of deoxygenated blood into the sinusoids, and allow a greater proportion of the sinusoidal blood supply to be derived from the hepatic artery with a higher oxygen tension. Conversely, when the portal blood oxygen tension increases, the inlet sphincter tone would decrease thus allowing a greater proportion of oxygen-rich portal blood to perfuse the sinusoids. Such a regulatory mechanism in the hepatic circulation would help to maintain an optimal oxygen tension in the sinusoidal blood in the presence of a reduction in hepatic blood flow or portal oxygen content.

Pilipenko (1967) reported an improvement in liver function tests in some liver diseases after enteral oxygen administration. It is possible that these beneficial effects resulted not only from the increased amount of oxygen delivered to the liver cell, but also from the concomitant increase in hepatic blood flow. The role of enteral oxygen administration in liver disorders is of interest and deserves further investigation. It should be borne in mind that an artificial increase in the hepatic blood flow during anaesthesia may result in the exposure of the organ to a greater total dose of anaesthetic agent. However, any adverse effect that halothane may have on the liver would not appear to be dose dependent.

The failure, in our study, to produce any significant increase in oxygen saturation in inferior vena caval blood would indicate the inefficacy of enteral oxygen in the treatment of general hypoxia (Cooper, Smith and Pask, 1960; Coxon, 1960; James et al., 1963; Silva-Moreno, 1964; Awad, Brassard and Caron, 1970).

The results of our study suggest that the technique of enteral oxygen administration should be evaluated further as a means of minimizing the disturbances in the liver circulation which are known to occur during anaesthesia and surgery. It is possible that this technique may have an application in patients with pre-existing impairment of liver function.

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References

Observations cliniques.


Effet de la administration entérale d’oxygène sur la circulation hépatique pendant l’anesthésie par l’halothane: observations cliniques.

RESUMEN

Un estudio del flujo de sangre hepática calculada (EHBF) usando una técnica de oro coloidal en 28 pacientes sometidos a una remoción de la vena safena mostró que el EHBFR diminuía al 68% de su valor inicial durante el período de anestesia de halotano y operación. Cuando se añadió oxígeno enteral, el EHBFR aumentó al 82% de su valor inicial. Una investigación en otros 14 pacientes sometidos a operaciones abdominales superiores mostró que la administración de oxígeno enteral producía la saturación de oxígeno de la sangre portal hasta aumentar del 55 ± 7,2% (media ± SEM) al 80 ± 6,2% y, al producir un descenso accesorio en la presión portal, llevó a una reducción en la pendiente del de la presión portal a 74 ± 12,5 a 38 ± 8,7 mm H2O. Se sugiere que el contenido de oxígeno de la sangre portal influencia, por sí mismo, el tono de los esfínteres pre-sinusoidales hepáticos. Se llega a la conclusión de que la administración de oxígeno enteral puede minimizar los desórdenes de la circulación hepática que se producen durante la anestesia de halotano y las operaciones quirúrgicas.