2. Study on Circulation and Gas Metabolism in the Liver under Low Oxygen Inhalation in Human Subjects

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Hypoxemia arises in various grades due to respiratory or cardiac insufficiency. Accordingly, the knowledge of the patho-physiological phenomena of the body which occur in response to the hypoxemia is helpful for clinicians.

For more than 10 years, Prof. Hara and co-workers have investigated the systemic and visceral circulations and metabolisms in induced hypoxemia by the venous catheterization method, and many reports have been published. The problems concerning the circulation and metabolism of the liver in the resting state and under induced hypoxemia were published previously by Ohbayashi and Takasu. Here their abstracts will be presented with further discussion at this symposium.

METHODS AND SUBJECTS

Each patient was subjected to the venous catheterization; the arterial blood was obtained from the femoral artery and the venous blood was drawn through the catheter. The hepatic blood flow was estimated by the B.S.P. method of Bradley and, at the same time, various parameters of the blood circulation and gas metabolism in the liver were measured, e.g. hepatic venous wedge pressure, splanchic oxygen consumption. After a course of measurement during a resting state was over and another course of measurement (of the hepatic blood circulation and hepatic gas metabolism) was made during the 15-20th minute after introduction of the hypoxemia test, which was performed by Levy's method with 10% oxygen gas. The cardiac output was measured by Fick's direct method in the resting state and at the 20th minute of the hypoxemia test.

Subjects examined were 28 cases in total and they consisted of 5 groups.

Group I: Normal subjects (6 cases).
Group II: Patients with pulmonary tuberculosis who were scheduled to be operated on for surgical treatment (10 cases). This group consisted of 2 subgroups; subgroup A represents those who gave no abnormal liver function test, and subgroup B represented those who gave slightly abnormal liver function tests.
Group III: Convalescent patients with acute hepatitis (4 cases). This group covered the stage of the disease between the 37th and 114th day after the onset of the disease; liver function tests and liver biopsy findings were nearly normal in all cases.
Group IV: Chronic hepatitis (4 cases). This group covered the stage of the disease between the 4th and 21st month since the onset of acute hepatitis; liver biopsy revealed the degeneration of hepatic cells, round cells infiltration and slight fibrosis.
Group V: Cirrhosis of the liver (4 cases). This group represented those in whom signs of hepatic insufficiency (ascites, jaundice etc.) have subsided to a considerable extent.

RESULTS

The observed effect of hypoxemia was as follows.

1) Systemic circulation and gas metabolism:

The observed response was nearly the same in all groups with regard to the artery blood pressure, cardiac output, arterial blood O₂ contents and total O₂ consumption of the body. The arterial blood pressure was reduced by about 15% and the cardiac output was either unchanged or slightly reduced; the arterial blood O₂ content was reduced by 30-40% and the total O₂ consumption was slightly reduced (by about 20%).

2) Hepatic venous wedge pressure:

This was measured in 2 normal subjects and 7 cases with liver diseases (Group III and IV). It was increased by 18% in normal subjects and increased by 28% in patients with liver disease.

![Fig. 1. Change in Estimated Hepatic Blood Flow due to 10% O₂ Inhalation](image-url)
(3) Estimated hepatic blood flow (Fig. 1):
It was increased markedly in Group I, by +68%; it was also increased in Group II, by +31%; within this group the hepatic blood flow was different between the 2 subgroups, the increase being marked in subgroup A (+50%) but nil in subgroup B. It was increased slightly on the average in Group IV, but decreased in 3 of 4 cases. Furthermore, the hepatic blood flow was decreased in Group III (−26%) and V (−30%).

(4) Splanchnic oxygen extraction (Hepatic arterial-venous O₂ difference) (Fig. 2):

![Fig. 2. Change in Splanchnic O₂ Extraction and Its Ratio due to 10% O₂ Inhalation](image)

The splanchnic O₂ extraction was either unchanged or slightly increased in Group I. Responses were different within Group II; it was decreased by −26% in subgroup A but increased by +32% in subgroup B. It was increased in the other three groups, especially in Group III where it was increased by +70%.

(5) Splanchnic oxygen consumption (Fig. 3):

![Fig. 3. Change in Splanchnic O₂ Consumption due to 10% O₂ Inhalation](image)

This was increased markedly in Group I by +80%. On the other hand, it was increased only to a slight extent in Group II, III and IV; there were even cases of obvious decrease in some of Group II. In cases of Group V it was generally decreased to some extent.

**DISCUSSION AND CONCLUSIONS**

(1) The hepatic blood flow during the induced hypoxemia was markedly increased in normal subjects and pulmonary tuberculosis patients without hepatic dysfunction. However, it was scarcely increased in patients with pulmonary tuberculosis with hepatic dysfunction, and decreased reversely in patients with liver disease. Then, distinct decreases were seen in convalescent stage of acute hepatitis and cirrhosis of the liver.

The change of the hepatic blood flow rate was not parallel with that of systemic circulation, e.g. the arterial blood pressure or the cardiac output. Accordingly, it was considered that the change of the hepatic blood flow in response to the induced hypoxemia depended on the change in the hepato-portal vascular system. Therefore, the marked increase in the hepatic blood flow was presumably due to an active dilatation of the hepatic blood vessel. That the hepatic blood flow was not increased but even decreased can be explained as being due to the absence of such a dilatation of the hepatic vessel. Since there was a more distinct rise in the hepatic venous wedge pressure, in spite of a decrease in the hepatic blood flow in hepatitis patients, one might also postulate that the portal system was congested under acute induced hypoxemia in the liver diseases.

(2) The splanchnic oxygen extraction in the acute induced hypoxemia was slightly increased in about two-thirds of all cases, regardless of the marked lowering of the arterial oxygen saturation.

(3) The splanchnic oxygen consumption was markedly increased in normal subjects, but in hepatic patients the splanchnic oxygen consumption was not increased so much; particularly in the cases with cirrhosis of the liver even a distinct decrease in the splanchnic oxygen consumption was seen. In pulmonary tuberculosis patients including those with normal hepatic
function, the splanchnic oxygen consumption was only slightly increased almost equally with hepatitis patients. These findings seem to suggest that the cases of subgroup A of pulmonary tuberculosis have had latent disturbances of the hepatic function which were not detected with routine tests.

Then, observing the splanchnic oxygen consumption in relation to the hepatic blood flow and the splanchnic oxygen extraction, it was as follows. The splanchnic oxygen consumption under induced hypoxemia was remarkably increased from the range of 30–50 cc/min./m² at rest to the range of 65–85 cc/min./m² owing to marked increase of hepatic blood flow and slight increase of splanchnic oxygen extraction in normal subjects (Fig. 4). On the other hand, in patients with pulmonary tuberculosis or liver disease, the splanchnic oxygen consumption at rest was almost equal to the one in normal subjects, but in the majority of them, it did not reach the range of normal subjects during the induced hypoxemia (Fig. 5). From this viewpoint, it was considered that the healthy liver performed well the regulation of the metabolism in response to the oxygen insufficiency, while the liver with disturbed function was deficient in such a metabolic compensation; particularly this was nil in the cirrhotic liver.

REFERENCES

3. Metabolic Effects of Hypoxia and Hypercapnia on the Liver Related with Hepatic Circulation†

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As an alternative and a preliminary study of the behavior of hepatic circulation and metabolism especially that of carbohydrates during respiratory insufficiency, investigations of these functions during hypoxemia of arterial oxygen saturations of 65–55%, induced by 10% O₂ inhalation were carried out. This induced condition is not identical with, but is closely related to that of acute clinical respiratory insufficiency.

Methods and Materials
A total of 30 subjects (group I: healthy controls, group IIA: pulmonary tuberculosis without hepatic dysfunction, group IIB: pulmonary tuberculosis with hepatic dysfunction, group III: recovery phase of acute hepatitis, group IV: chronic hepatitis, group V: hepatic cirrhosis) were studied.

10% O₂ was administered by the Levy’s method and necessary blood samples were obtained before and 15–20 minutes after the beginning of the hypoxemia by hepatic vein catheterization to determine the hepatic circulation and metabolism.

On the other hand, as a fundamental experiment the effect of hypoxemia on the methyleneblue reducing ability of tissue (liver, heart, brain and kidney) was studied by having mice breath 5 and 10% O₂ and a mixture containing 5% O₂ + 5% CO₂.

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