STUDIES ON GALACTOSE TOLERANCE TEST IN PATIENTS WITH LIVER DISEASE

Saburo Kikuchi, Katsumoto Kato, Osamu Shiga, Takahiko Oya, and Madoka Ito

2nd Department of Internal Medicine, Nagoya University School of Medicine
(Director: Associate Prof. Saburo Kikuchi)

ABSTRACT

Oral galactose tolerance tests were performed on 56 patients with liver disease, 31 with diabetes mellitus and 17 normal subjects. Intravenous galactose tolerance tests were done on 25 liver disease, 6 diabetes mellitus and 6 normal subjects. Each liver disease was histologically confirmed by needle biopsy under laparoscopy. Serum galactose and glucose were measured gaschromatographically. Oral galactose tolerance test is useful for the diagnosis of liver cirrhosis and chronic hepatitis, but metabolic disorder of galactose can be found in diabetics. Therefore abnormalities in oral galactose tolerance test do not necessarily mean the existence of hepatic damage. There exists a relatively good correlation between the degree of abnormal oral galactose tolerance test and the level of serum $\gamma$-globulin, cholinesterase and ICG disappearance rate. As for intravenous galactose tolerance test, half life is a useful index as well as oral galactose tolerance test. But it can be concluded that oral galactose tolerance test is superior to intravenous galactose tolerance test from the point of view of technical simplicity and the burden to patients.

INTRODUCTION

Galactose tolerance test has long been described as a liver function test based on carbohydrate metabolism. The test is, however, not in general use because of the difficulty of galactose determination in the blood.

Studying pentose metabolism in our laboratory, we found that the disappearance time of xylitol, administered orally, in the blood was longer in patients with liver disease than in normal subjects. It would be interesting to study galactose metabolism in cases of liver disease since monosaccharides such as galactose which can be specifically metabolized in the liver would be an excellent indicator of liver injury.

Sweely et al. and Wells et al. reported gaschromatographic separation of monosaccharides. We employed this method in the galactose tolerance test and found that the method was very satisfactory for the determination of blood glucose and galactose. The results indicate that the galactose tolerance
test is useful for the diagnosis of liver disease and that diabetics has abnormal galactose tolerance test without liver injury.

**METHOD**

A 1 : 20 Somogyi filtrate of each serum was analyzed chromatographically for glucose and galactose according to the method of Sweely. Sorbitol was used as internal standard.

As shown in Fig. 1, there was an excellent quantitative separation of galactose, glucose and sorbitol.

![Fig. 1. Separation of galactose and glucose by gaschromatography.](image)

After an overnight fast, blood was drawn from the cubital vein and 30 g of galactose in 300 ml warm water were given orally. Blood was then drawn every 30 min. for 2 hours. 10 mg/100 ml NaF were added to the blood to prevent glycolysis.

Intravenous galactose tolerance test was performed by the method of Tengstrom and his coworkers. After an overnight fast, 350 mg/kg galactose in 30% solution (KABI) were injected rapidly within 3 min. Venous blood was then drawn every 10 min. for 60 min.

**MATERIALS**

Oral galactose tolerance tests were performed on 104 subjects including 8 cases of acute hepatitis, 26 chronic hepatitis (active form), 22 liver cirrhosis, 31 diabetes mellitus and 17 normal subjects.

Intravenous galactose tolerance tests were done on 7 cases of acute hepatitis, 8 chronic hepatitis (active form), 10 liver cirrhosis, 6 diabetes mellitus and 6 normal subjects. Each liver disease was histologically confirmed by needle biopsy under laparoscopy.

**RESULTS**

Fig. 2, shows the means of serum galactose concentration at each interval of the oral galactose tolerance test. Serum galactose concentration in normal
subjects was 17 mg/100 ml at the end of 30 min. after oral galactose administration and 5 mg/100 ml at 60 min. after oral galactose. Peak serum galactose concentration was reached 60 min. after oral galactose administration in liver disease patients. The highest concentration was obtained in cases of liver cirrhosis. While serum galactose disappeared 60 min. after oral administration in normal subjects, it did not disappear till 120 min. after oral administration in liver disease patients. The mean concentration at 60 min. after oral administration in normal subjects and liver disease patients were significantly different.

In diabetics, there was a peak serum galactose concentration 60 min. after oral administration. The time course of galactose concentration in diabetics was between that of normal subjects and of liver disease patients.

The sum of serum galactose levels of every 30 min. for 2 hours was expressed as $\sum$Galactose. $\sum$Galactose was quite high in the liver disease group in contrast to the control and it was the highest in the cirrhosis group. There was also a significant difference between $\sum$Galactose in liver cirrhosis and chronic hepatitis (Fig. 3).

![Graph showing serum galactose level course after the oral administration of galactose (30 g).](image1)

While liver disease patients had greater urinary excretion of galactose for 3 hours after oral administration (5% of total load) than normal subjects (1% of total load), it is concluded that the diagnostic value of serum

![Graph showing $\sum$Galactose in patients with various diseases compared with the normal subject (oral galactose tolerance test).](image2)
galactose determination is higher than that of urine galactose determination.

There was a good correlation between serum galactose concentration 60 min. after oral administration and the levels of serum γ-globulin, cholinesterase, alkali-phosphatase and ICG disappearance rate. There was, however, no correlation between the galactose concentration and the levels of serum transaminase and BSP excretion.

It should be noted that some patients who had normal routine liver function tests had abnormal galactose tolerance test. Two of these patients had recurrence. Galactose tolerance test is useful for evaluating the prognosis of acute hepatitis. Some patients with chronic inactive hepatitis had abnormal galactose tolerance test without any abnormality in other liver function tests. Further studies are necessary to establish the usefulness of this test.

All cases of diabetes reported in the present paper had no history of jaundice and had no abnormalities in routine liver function tests. Many diabetics, however, had abnormal galactose tolerance test. Fig. 4, shows the change in blood glucose level after galactose administration. While there was almost no change in blood glucose level in normal subjects, there was a striking increase in diabetics and a moderate increase in cases of liver disease. It is possible that diabetics have secondary metabolic disturbance of galactose, since galactose is metabolized via the conversion to glucose. Therefore, an abnormal galactose tolerance test cannot be attributed necessarily to hepatic
disorders. It seems likely that abnormal galactose tolerance test results from metabolic disorder of glucose.

Fig. 5 shows half life of serum galactose after intravenous galactose administration; 24.4 ± 7.7 min. in liver cirrhosis, 21.3 ± 10.9 min. in acute hepatitis, 13.3 ± 2.6 min. in chronic active hepatitis and 9.4 ± 0.9 min. in normal subjects. There was a significant difference between the means for normal subjects and the groups with liver disease. Since serum galactose level 50 min. after intravenous injection is a good index as well as the half life, the determination of the former alone is recommended in order to simplify the procedure (Fig. 6).

![Graph showing half life of serum galactose after intravenous galactose administration.](image)

**Fig. 6.** Serum galactose level 50 minutes after the injection (intravenous galactose tolerance test).

![Graph showing relationship between LGala (oral test) and T_{1/2} (intravenous test).](image)

**Fig. 7.** Relationship between \( \Sigma \text{Gala.} \) (oral test) and \( T_{1/2} \) (intravenous test).

\[ r = 0.784 \quad p < 0.001 \quad (n = 20) \]

Half life is apparently a good index for differential diagnosis, but as shown in Fig. 7 there was a good correlation between the half life of galactose after i.v. administration and \( \Sigma \text{Galactose.} \) Oral administration is more practical than i.v. administration.

**CONCLUSION**

Galactose tolerance test was performed on patient with liver disease and diabetes mellitus. Serum galactose was measured chromatographically.

1) Oral galactose tolerance test is useful for the diagnosis of liver disease. It enables the differential diagnosis of liver cirrhosis and chronic hepatitis.
2) Urinary excretion of galactose for 3 hours after oral galactose administration generally increases in patients with liver disease, but it has less diagnostic value than the alteration in serum galactose concentration.

3) Abnormalities in oral galactose tolerance test do not necessarily mean the existence of hepatic damage, as metabolic disorder of galactose can be found in diabetics.

4) There is relatively good correlation between the degree of abnormal oral galactose tolerance test, and the level of serum \( \gamma \)-globulin, cholinesterase and ICG disappearance rate.

5) There are some cases of acute hepatitis in the recovery stage, having an abnormality in galactose tolerance test without having any other abnormal liver function tests. Galactose tolerance test is valuable for evaluating the prognosis of such cases.

6) As for intravenous galactose tolerance test, half life is a useful index as well as oral galactose tolerance test. It can be concluded that oral galactose tolerance test is superior to intravenous galactose tolerance test from the point of view of the technical simplicity and the burden to patients.

REFERENCES


