IN VITRO STUDIES ON MECHANISM FOR CONCENTRATING FUNCTION OF GALLBLADDER

Hirotune IGIMI, M.D.*, Tatsuo HAMADA, M.D.** and Hidehiko SHIMURA, M.D. *

The First Department of Surgery, School of Medicine, Fukuoka University, Fukuoka, 814 Japan *
The First Department of Surgery, Faculty of Medicine, Kyushu University, Fukuoka, 813 Japan **

Summary

The mechanism for concentrating function of gallbladder was studied in vitro, turning and attention to changes in the gallbladder bile composition, especially a marked increase of Na⁺ and a marked decrease of Cl⁻ in the the concentrating process of hepatic bile to gallbladder one. The following results were obtained by the present investigations: 1) bile acids present in bile regulate the rate of Na⁺ and Cl⁻ transport; 2) the epithelial membrane of the gallbladder can be regarded as being a simple semi-permeable membrane.

Key Words: electrolyte transport, water transport, bile acid concentration of bile, gallbladder-bile.

Introduction

The gallbladder is known as the organ which concentrates the hepatic bile to the gallbladder one. Although many works have been done on the mechanism for concentrating function of the gallbladder, the proposal by Diamond¹-⁵, where an active transport of NaC1 would first take place, resulting in a passive transport of water, has been generally accepted.

It has been known that an intracystic pressure is always positive, being determined by the factors comprising the secretion pressure of hepatic bile, the antagonistic pressure of the Oddi sphincter and the antagonistic pressure of the gallbladder muscle. Thus, the authors would propose that the intracystic pressure is one of the factor participating in the absorption of water through the gallbladder epithelium.

Observing the composition of gallbladder bile, it is found that there is a great difference between two representative electrolytes, Na⁺ and Cl⁻. That is to say, the levels of Na⁺ and Cl⁻ in the hepatic bile are similar to those in the serum, but in the gallbladder bile a marked decrease of Cl⁻ level is noted despite a marked increase of Na⁺ level, as shown in Table 1. These suggest that Na⁺ and Cl⁻ may not always be transported in a coupling form. However, few reports have given attention to elucidate the mechanism for concentrating function to the gallbladder.

The pH of the gallbladder bile is approximately the same as or slightly lower than that of the hepatic bile and serum which are approximately neutral⁶. Neutrality or slight acidity of the gallbladder bile despite a marked decrease of Cl⁻ level suggests that the hepatic bile must be concentrated to the gallbladder one, maintaining electrolytes balance. The above facts may not be explained without assuming the presence of anions corresponding to Na⁺ other than Cl⁻ in the bile. These anions would be originated from bile acids,
Table 1. Composition of human bile

<table>
<thead>
<tr>
<th></th>
<th>Gallbladder bile</th>
<th>Hepatic bile</th>
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<tbody>
<tr>
<td>Total bile acids (mg/ml)</td>
<td>43.3 – 121.6</td>
<td>3.1 – 21.9</td>
</tr>
<tr>
<td>Inorganic substances (mEq/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cl⁻</td>
<td>18.6 ± 4.7</td>
<td>77 – 127</td>
</tr>
<tr>
<td>Na⁺</td>
<td>248.6 ± 15.2</td>
<td>122 – 164</td>
</tr>
<tr>
<td>K⁺</td>
<td>15.7 ± 1.0</td>
<td>3.2 – 9.7</td>
</tr>
</tbody>
</table>

From the analyses of Jensen, Aubertin & Tayeau (4), Sakai (5), Hirose (6) and Radvin, Johnston, Austin & Riegel (7).

Taking into consideration that the content of other low molecular anions such as HCO₃⁻, CO₃⁻, and SO₄⁻ are very small in the bile. Provided that the bile acids would not be permeable freely into the epithelial membrane and thus regulate the rate of low molecular ions, the difference between Na⁺ and Cl⁻ content could be elucidated.

If the bile would be concentrated according to the above assumptions, the mechanism for concentrating function of the gallbladder could be simple and the gallbladder bile could be easily produced from the hepatic one using in vitro model system. To verify this, the present experiments were carried out.

Materials and Methods

1) In vitro dialysis across visking membrane

*Canine gallbladder bile:* Healthy mongrel dogs were fasted for 18 hours and laparotomized to aspirate bile samples from the gallbladder. In the aspiration, care was taken to avoid contamination by blood. The bile samples (pH 7.2) were stored in a refrigerator at -20°C until tested.

*Model gallbladder bile:* This solution was prepared by dissolving NaCl (Wako Pure Chemical Industries, Ltd., Osaka) and sodium cholate (Nakarai Chemicals, Ltd., Kyoto), which is selected as a representative bile salt, in deionized water (pH 8.2). The level of Na⁺, Cl⁻ and cholic acid in the solution corresponded to that of Na⁺, Cl⁻ and total bile acids (T.B.A.) present in the canine gallbladder bile, respectively.

*Na⁺ and Cl⁻ solution:* NaHCO₃ (Wako Pure Chemical, Ltd.) and NaCl were dissolved in deionized water (pH 8.2). The level of Na⁺ and Cl⁻ corresponded to that present in the canine gallbladder bile.

Visking tube (Pore size 24 Å; Union Carbide Corp.) was used as a semipermeable membrane and attached to (C) of the diffusion apparatus to make compartment (A) and (B), as shown in Fig. 1. To prevent water transport due to osmotic gradient, (A) was made as a blind