Activity of brush border membrane enzymes in proximal jejunum of portal hypertensive rats

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Purpose. Malabsorption accompanies portal hypertension, especially when associated with chronic liver disease. The development of portal hypertension is accompanied by significant alterations in the splanchnic microcirculation. In this study, the effect of extrahepatic and intrahepatic portal hypertension on brush border membrane enzymes was estimated.

Methods. Portal hypertension was induced in rats by partial portal vein ligation (PPVL) (n = 6) and common bile duct ligation (CBDL) (n = 6), and the activity of sucrase, lactase, alkaline phosphatase, and leucine aminopeptidase (LAP) in the intestinal homogenate was measured.

Results. Intrasplenic pulp pressure (ISPP) (in cm of saline) was found to be elevated in PPVL (21.3 ± 1.47) and CBDL animals (21.5 ± 1.79) as compared with findings in their respective sham-operated controls (12.74 ± 0.86, 11.83 ± 1.04). Only sucrase and LAP activity was significantly elevated (P < 0.05) in the PPVL group. No changes were observed in the CBDL group.

Conclusion. Only sucrase and LAP activities were increased in PPVL rats.

Key words: experimental portal hypertension, brush border membrane enzymes, lactase, sucrase, alkaline phosphatase, leucine aminopeptidase

Chronic portal hypertension has been shown to be associated with marked alterations in the gastrointestinal microcirculation, gastric mucosa, and small intestinal transit.1–6 Gastrointestinal tract involvement in portal hypertension includes the formation of esophageal varices, gastropathy,7,8 enteropathy,9 and colopathy.10 Nagral and coworkers11 reported congestive jejuno-pathy in 84% of portal hypertensive patients. Congestive jejuno-pathy was defined by the presence of ectatic capillaries and venules in the villi, with an increase in the number of vessels. Our own observations revealed clubbing and blunting of villi, in addition to vascular congestion in the jejunum.8 The effect of these changes in gastrointestinal morphology on function is not clearly established. Thus, although malnutrition is commonly observed in patients with chronic liver disease,6,12 only some alterations in absorptive function have been described in vivo.13–17 More recently, Hayashi and coworkers18 demonstrated sugar malabsorption in rats with suprahepatic portal hypertension, although Romiti et al.19 could demonstrate only fat malabsorption in cirrhotic patients. An earlier study had shown decreased activity of alkaline phosphatase, aminopeptidase, acid phosphatase, and succinic dehydrogenase in carbon tetrachloride-induced experimental cirrhosis in rats.20 In the present study, we made an attempt to measure the activity of brush border membrane enzymes and to compare this activity in extrahepatic and intrahepatic portal hypertension models.

Wistar rats of either sex, weighing 125–200 g, were used for the study. Extrahepatic portal hypertension was produced by partial portal vein ligation (PPVL),21 and intrahepatic portal hypertension was produced by common bile duct ligation (CBDL).22 In both groups, portal hypertension was confirmed by the measurement of intrasplenic pulp pressure.23 Sham-operated animals were used as controls for both groups. Animals were killed 25–28 days after PPVL and 18 days after CBDL, and the small intestine was removed, washed with saline, and stored at −20°C. A homogenate of the intestines was prepared, and the biochemical parameters studied. The activities of sucrase and lactase were determined by measuring d-glucose liberated from the respective sugar, using the glucose oxidase peroxidase method.24 Alkaline phosphatase was measured by the
specific activity of brush border enzymes in PPVL and CBDL groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Alkaline phosphatase (µmol/min per mg protein)</th>
<th>Sucrase (µmol/min per mg protein)</th>
<th>Lactase (µmol/min per mg protein)</th>
<th>Leucine aminopeptidase (µmol/min per mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPVL (n = 6)</td>
<td>0.116 ± 0.06</td>
<td>0.067 ± 0.028*</td>
<td>0.005 ± 0.003</td>
<td>0.034 ± 0.015*</td>
</tr>
<tr>
<td>Control (n = 5)</td>
<td>0.090 ± 0.06</td>
<td>0.035 ± 0.01*</td>
<td>0.0022 ± 0.0004</td>
<td>0.019 ± 0.003*</td>
</tr>
<tr>
<td>CBDL (n = 5)</td>
<td>0.247 ± 0.08</td>
<td>0.046 ± 0.014</td>
<td>0.007 ± 0.001</td>
<td>0.025 ± 0.007</td>
</tr>
<tr>
<td>Control (n = 6)</td>
<td>0.195 ± 0.14</td>
<td>0.035 ± 0.022</td>
<td>0.004 ± 0.003</td>
<td>0.019 ± 0.011</td>
</tr>
</tbody>
</table>

*P < 0.05

Note, in the CBDL group, enzyme estimations were done in five of the six animals that underwent surgery.

PPVL, partial portal vein ligation; CBDL, common bile duct ligation

A significant decrease in the activity of intestinal membrane enzymes in CCl₄-induced cirrhosis in rats, contrary to our observations. The difference in the activity of the enzymes measured, except for sucrase and leucine aminopeptidase, which showed a minor alteration in the levels of brush border membrane vesicles in PPVL rats, with no change in CBDL rats. The elevated sucrase and leucine aminopeptidase levels in PPVL rats as compared with findings in CBDL rats are not related to the severity of congestion of the jejunum, as ISPP was comparable in the two groups. Manevska, in an earlier report, had shown a decrease in the activity of intestinal membrane enzymes in CCl₄-induced cirrhosis in rats, contrary to our observations. This difference could have arisen because, although we had produced portal hypertension secondary to CBDL, our animals had not developed cirrhosis (data not shown) at the time they were killed. It is possible that, had cirrhosis developed, we may have demonstrated a similar trend. On the contrary, we found that the membrane enzymes were elevated in PPVL rats. It appears that the difference in results obtained for PPVL and CBDL rats could be attributed to the different models used. In addition, CBDL animals were administered trimethoprim—sulfamethoxazole for 5 days prior to surgery, were killed nearly 1 week earlier than the PPVL rats, and were fed supplemental Bengal gram (cicer arietenum). Although unlikely, we cannot dismiss these factors as an explanation for the observed differences on the basis of the present observations.

In another study, Said et al. measured LAP activity as a marker enzyme in mucosal homogenates and brush border membrane vesicles in PPVL rats, and showed no difference between the experimental and sham-operated rats. However, in our study, PPVL rats showed elevated LAP and sucrase activity in whole intestinal homogenate. This difference may be attributed to the duration of portal hypertension, (as they had killed their animals at 14 days), and to differences in the material used for the measurement of enzyme activities.

Finally, it appears premature to postulate a unifying hypothesis for these observations; more detailed studies are needed. In conclusion, our results demonstrate only a minor alteration in the levels of brush border membrane enzymes in extrahepatic portal hypertensive rats.

References