Effect of Bilioenteric Anastomosis op the Parietal Cell Mass and Prostaglandin E₂ Like Activity in the Stomach in Guinea-Pigs

**SUMMARY**

After ligation of the common bile duct, cholecystojejunostomy was performed in fifteen guinea pigs as a model of internal biliary diversion. Sham operation was done in twelve guinea pigs to serve as the control group. After a follow up period which changed between 17 to 21 days the parietal cell mass increased significantly while prostaglandin E₂ like activity in the stomach showed a marked decrease in the biliary diversion group compared with the control group (p<0.05). Also PGE₂ like activity in the stomach, in both groups were matched, as a response to stress. It was observed that PGE₂ like activity in both groups fell down to a similar level after stress testing (p<0.05). Multiple liver abscesses, pericholangitis and derangement of liver function tests were observed in all of the animals in the biliary diversion group.

**Keywords:** Biliary diversion, Parietal cell mass, Prostaglandin (PG)E₂ like activity

**ÖZET**

Bir internal biliyer diversiyon modeli olarak 75 kobayda, koledok kanalının bağlanmasını takiben kolesistojejunostomi yapıldı. Kontrol grubu olarak kullanılmak üzere 12 kobayda da sham ameliyatı yapıldı. 17-21 günlük bir takip süresi sonunda, biliyer diversiyon grubunda, kontrol grubuna nazaran, parietal hücre kiltesinin önemli ölçüde arttığı, midedeki prostaglandin E₂ benzeri aktivitenin ise önemli derecede azaldığı görüldü (p<0.05). Her iki grupta da midedeki PGE₂ benzeri aktivite, strese cevap olarak da karşılaştırdı. Stress uygulamasını takiben her iki grupda da PGE₂ benzeri aktivitenin birbireye yakın düzeylere indiği görüldü (p>0.05). Biliyer diversiyon grubundaki bütün kobaylarda, multipl karaciğer apseleri, perikolanjit ve karaciğer fonksiyonlarında bozulma gözlemdi.

**Anahtar Kelimeler:** Biliyer diversiyon, Parietal hücre kiltesi, Prostaglandin (PG)E₂ ben/eri aktivite

It has been known since experiments of Exalto in 1911 and, Mann and Williamson in 1923 that pancreatobiliary diversion to a lower segment of intestine or biliary diversion alone (either internal or external) increases the susceptibility to peptic ulcer, acute gastric mucosal lesions and gastrointestinal bleeding (1-3,5,7,8,11-14,16). It was also noted that hepatic abscesses, microscopic pericholangitis and derangement of liver function tests were frequent findings after experimental biliary diversion, in addition to peptic ulcer (2,3,7-9).

Initially it was proposed that the ulcers seen after biliary diversion were due to depriving the duodenum of the alkalizing effect of bile, but later
it was observed that gastric acid secretion increased after biliary diversion, (4,5) and search has been directed to find out the cause of this hypersecretion. Various factors have been proposed, including increased histamine secretion from the small intestine, or inability of the functionally deranged liver to destroy the histamine from small intestine, malabsorption of fatty acids which resulted in decreased inhibition of gastric secretory hormones from the intestine, but none of them has been proved as a definite cause of gastric hypersecretion (4,6,9,10,15,16).

Prostaglandins, especially of the E and F type, which are found in the gastrointestinal tract are known to inhibit gastric secretion, have cytoprotective and ulcer healing properties (17,18).

This experiment was designed to determine whether the same stimulus that caused gastric hypersecretion, also resulted in an increase of the parietal cell mass; the stomach to stress after biliary diversion.

**METHOD**

The study was performed at the Surgical Research Unit of Department of Hacettepe, on 37 female guinea pigs weighing 270 to 510 g (mean: 340 g). The animals were divided into two groups

A) Biliary diversion group (25 guinea pigs) and B) Control group (12 guinea pigs).

All of the animals were anesthetized with 25 mg/kg nembutal sodium (Nembutal) injected intraperitoneally.

After a median laparotomy, a choledochotomy with one layer 6-0 prolene sutures and ligation of the common bile duct in the supraduodenal area was performed in the biliary diversion group. In the control group the common bile duct was dissected without ligation and the gallbladder manipulated. After closure of the abdominal ligation and the gallbladder manipulated. After closure of the abdominal wall the animals were followed for a period of 17 to 21 days. 10 guinea pigs were excluded from the study in the biliary drainage group because of death secondary to peritonitis, liver abscess, and anastomotic leakage.

At the end of the follow-up period (17-21 days) 15 guinea pigs in the biliary diversion group were divided into two groups (A1 and A2) (Fig. 1). The seven guinea pigs in group A1 were reoperated im-

![Figure 1. Schematic representation of group.](image)

![Figure 2. Zones of stomach from where different sections are made.](image)
In all of the groups PGE2 like activity was measured by bioassay method (19,20). The results were evaluated with Mann-Whitney U test.

RESULTS

No macroscopic lesion including ulceration, and erosion was found on the gastric or duodenal mucosa both in the biliary diversion and the control groups either with or without stress. Livers of the animals in the biliary diversion group had multiple abscesses, and pericholangitis microscopically, Livers were normal both macroscopically and microscopically in the control group. No statistical difference was found between alkaline phosphatase levels of the biliary diversion and control group but SGOT and SGPT levels were markedly raised (2 to 3 fold) in the biliary diversion group compared with the control group (p < 0.05).

Parietal Cell Mass

The average number of parietal cells in a high power field of light microscope (x640) representative of the zones labeled A, B, and C are shown in Table 1, Figure 3. The parietal cell mass increased significantly in the biliary diversion group, in all zones (p< 0.05).

Two comparative photographs of the same zone of stomach, one from the biliary diversion, the other from the control group are shown below. A marked increase in parietal cell number can be seen in the biliary diversion group (Figures 4 and 5).

Prostaglandin E2 Like Activity in the Stomach

PGE2 like activity levels for all groups are shown in Table 2 (Figure 6). As can be seen, PGE2 like activity in the stomach decreases significantly after biliary diversion (p<0.05) but this difference disappears after the application of stress to both groups (p>0.05), since the magnitude of the decrease in the control group is greater than the decrease in the biliary diversion group.

DISCUSSION

It has been demonstrated by various authors up till now that gastric acid secretion increases, and a liability to peptic ulceration occurs after biliary diversion. The more distal is the biliary diversion on the small intestine, the more is the liability to peptic ulceration.

Also it has been shown by different authors that a chronic humoral stimulus that causes gastric hypersecretion (such as repeated injections of histamine to guinea pigs) also increases the parietal cell mass (22).

Considering these previous findings, gastric acid secretion and serum gastrin levels (as the possible cause of this hypersecretion) were measured both in the biliary diversion and control groups. But

Table 1. Average parietal cell Number per high power field (X640)

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<tr>
<th></th>
<th>A = Fundus</th>
<th>B = Corpus</th>
<th>C = Antrum</th>
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<td>35</td>
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<td>60</td>
<td>40</td>
<td>45</td>
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<tr>
<td>Mean</td>
<td>40.83</td>
<td>39.33</td>
<td>32.91</td>
</tr>
<tr>
<td>S.B.</td>
<td>1.53</td>
<td>1.18</td>
<td>1.14</td>
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because of the wide diversity of the obtained results no statistical analysis and interpretation could be made so they are not mentioned here.

So, we were unable to demonstrate the gastric hypersecretion seen after biliary diversion but were able to demonstrate the increase in the parietal cell mass, which theoretically should accompany this hypersecretion.

The number of parietal cells in three representative zones of the gastric mucosa (A, B and C) were found to be increased to a statistically significant level in the biliary diversion group, compared with the sham operated group. This increase may be related to a chronic humoral stimulus, which both causes gastric hypersecretion and functional hyperplasia of the parietal cells, although this humoral agent hasn’t been clearly defined yet. Nielsen et al (15). Have shown that strum gastrin levels in clinical cases increase after biliary diversion and also Orloff et al. Have slated that they have isolated a hormone responsible for the intestinal phase gastric secretion (21).

To see whether there is any difference with respect to stress endurance between the biliary diversion and control groups, the second phase of the experiment was designed.

Prostaglandin E₂ like activity in the stomach showed a marked decrease in the biliary diversion group which may be related to the decreased duodenal alkalinization. Restraint and cold stress did not decrease it further than the level reached in

Figure 3. The number of parietal cells in different zones (A, B, C) of the stomach.

Figure 4. A Field from the gastric mucosa (zone B) of a guinea-pig from the biliary diversion group (1 M. X46U).

Figure 5. A Field from the gastric mucosa (zone H) of a guinea-pig from the control group (1 L. H. X230).
Table 2. PGE2 Like activity (material) ng/g stomach

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<thead>
<tr>
<th>Bil.Div.Group</th>
<th>Control Group</th>
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<td>51.7</td>
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<td>37.0</td>
<td>67.0</td>
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<tr>
<td>25.0</td>
<td>60.2</td>
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<tr>
<td>44.6</td>
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<td>50.4</td>
<td>73.8</td>
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<tr>
<td>47.7</td>
<td>86.9</td>
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<td>60.6</td>
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Mean 45.28  S. E. 4.34

Sekil 6. PGE2 levels in biliary diversion and control groups as a response to stress.

the control group after stress affiliation, contrary to what might be expected.

After stress application the difference between Prostaglandin E2 like activity disappears, since they both decrease to the same level.

Multiple liver abscesses, pericholangitis were observed in all of the animals after biliary diversion. Although such a high incidence of cholangitis and liver abscess is not seen in clinical cases; a high incidence has been reported from experimental biliary diversions, especially in dogs (2). These pathologic findings can be attributed to differences between the species. We do not believe that this complication has developed secondary to inadequate biliary drainage because the alkaline phosphatase did not demonstrate any elevation.

The fact that no ulcers or erosions were found on the gastric and duodenal mucosa may be the result of insufficiently short period of follow up or the result of species difference.

The inability to inactivate histamine and other hormones of intestinal origin, because of poor or subclinicals deranged liver function, may be responsible or at least partly responsible from the increased peptic ulcer incidence observed after biliary diversion.

The increase in parietal cell mass and the decrease in PGE2 like activity in the stomach may be responsible for the increased gastric acid secretion and the high peptic ulcer incidence observed after biliary diversion although the stimulus for these changes has not been elucidated completely yet.

REFERENCES


