DENEYSEL ARAŞTIRMALAR - EXPERIMENTAL RESEARCH

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

BİL. İO ENTER!K ANASTOMOZUN MİDE PARYETAL HÜCRE KÜTLESİ VE PROSTAGIANDİN E, BENZERİ AKTİVİTEYE ETKİSİ

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SUMMARY

After ligation of the common bile duct, cholecystojejwwstomy was performed in fifteen guinea pigs as a model of internal biliary diversion. Sham operalion was done in twelve quinea pigs to sen>e as the control group. After a follow up period which changed between 17 to 21 days the parietal cell mass increased significantly while prostaglandin Ei like activity in the stomach showed a marked decrease in the biliary diversion group compared with the control group (p<0.05). Also PGEz like activity in the stomach, in both groups were matched, as a response to stress. It was observed that PGEo 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.

KtyVVords: Biliary diversion, Parietal cell mass. Prostaglandin (PG)U? like activity

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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 kitlesinin önemli ölçüde arttığı, midedeki prostaglandin Ez benzeri aktivitenin ise önemli derecede azaldığı görüldü (p < 0.05). Her iki grupta da midedeki PGEı benzeri aklivite, strese cevap olarak da karşılaştırıldı. Stress uygulamasını takiben her iki grupla da PGE2 benzeri aktivitenin birbirine yakın düzeylere indiği görüldü (p>0.05). Biliyer diversiyon grubundaki bütün kobaylarda, mıtllipl karaciğer apseleri, perikolanjit ve karaciğer fonksiyonlarında bozulma gözlendi.

Anahtar Kelimeler: Biliyer diversiyon, Parietal hücre kitlesi, Prostaglandin (PG)E: ben/eri aktivite

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It has been known since experiments of Exalto in 1911 and, Mann and Willianson in 1923 that pancreatobiliary diversion to a lower segment of intestine or biliary diversion alone (either internal or external) increases the susceplibility 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 bilary 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 tha alkalinizing effect of bile, but later

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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).

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

This experiment was designed do 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 Surgicial Research Unit of Deparment of Hacettepe, on 37 female guinea gigs weighing 270 to 510 g (mean: 340 g).The animals were dividedeinto 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 introperitoneally.

After a median laparatomy, a cholecystojejunostomy 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 commo bile duct was disccted without ligation and the gallbledder manipulated. After closure of the abdominall 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 (Ai and A2) (Fig. 1). The seven guinea pigs in group Ai were reoperated immediately. Their stomachs were removed and the posterior wall was used to count parietal cell mass and the anterior wall was stored at -20°C, later to be used for prostaglandin E2 like activity determination.

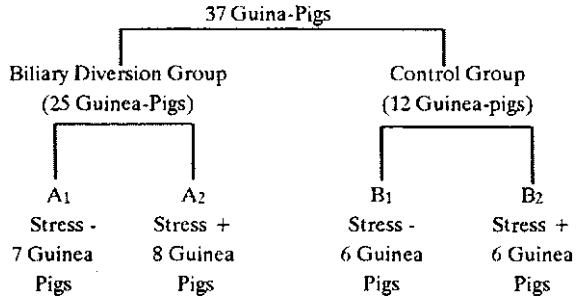


Figure 1. Schematic representation of group.

For parietal cell count sections from the gastric wall were taken as shown in Fig. 2 and stined with H.E. under a high power field (x640) of light microscope the number of parietal cells in each representative sections of the areas A,B and C were counted in four fields and the average cound was calculated (Fig. 2). Liver biopsies and blood samples were also taken during the laparatomy. The response of the stomach to cold and restraint stress was evaluated in eight guinea pigs (Group A2, Fig. 1) by immobilizing them at +4°C for 5-6 hours.

The 12 guinea pigs in the control group were also divided into two group's (Bi and B2) and treated similarly as the biliary diversion group.

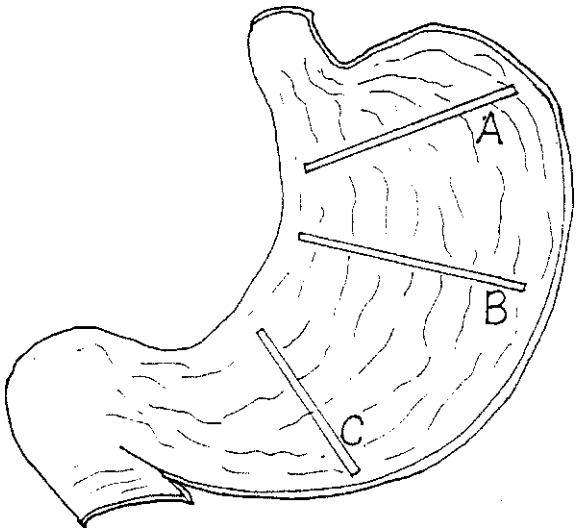


Figure 2. Zones of stomach from where different sections are made.

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 miscoscopically 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 arc shown in Table 1, Figure 3. The parietal cell mass increase d 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 arc shown below. A marked increase in parietal cell number can be seen in the biliary diversion group (Figures 4 and 5).

Praglandin E2 Like Activity in the Stomach

PGE2 like activity levels for all groups arc 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 scrum 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)

A = Fundus		B = Corpus		C = Antrum	
Bil.Div.Gr.	Control Gr.	Bil.Div.Gr.	Control Gr.	Bil.Div.Gr.	Control Gr.
20	35	40	30	35	25
55	40	45	35	25	30
70 ,	45	35	35	20	25
65	50	35	40	30	35
60	40	40	30	30	25
65	45	45	35	35	20
65	40	35	35	30	25
65	45	30	35	30	20
60	50	35	25	50	30
55	55	45	30	35	25
60	40	40	35	35	20
55	45	40	30	30	25
60		45		30	
55		40		25	
50		40		30	
Mean 60.66	40.83	39.33	32.91	29.33	20.83
S.B. 1.53	1.60	1.18	1.14	1.72	1.30

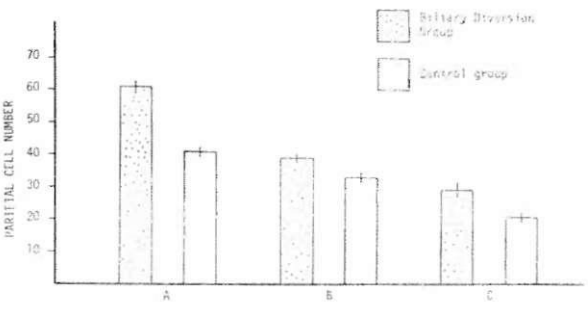


Figure 3. The number of parietal cells in different zones (A,B,C) of the stomach.

because of the wide diversity of the obtained results no statistical analysis and interpretation could be made so they arc not mentioned here.

So, we were unable to demons!rale the gastric hypersecretion seen after biliary diversion but were able to demonstrate the increase in the parietal cell mass, which Ihcorectically should accompany (his 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 ct 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

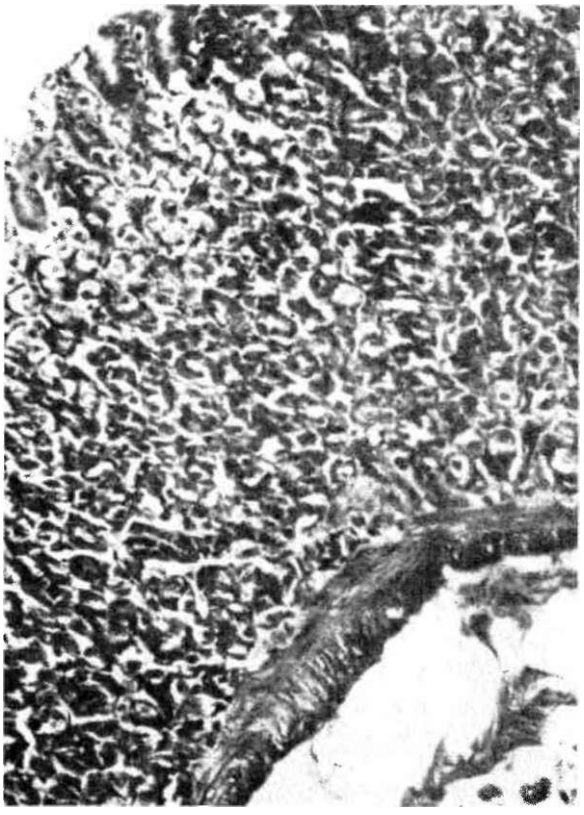
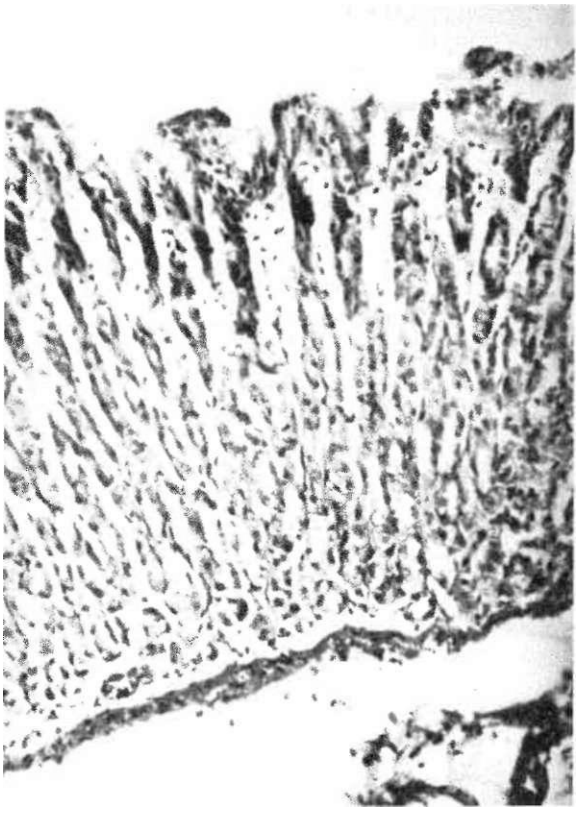


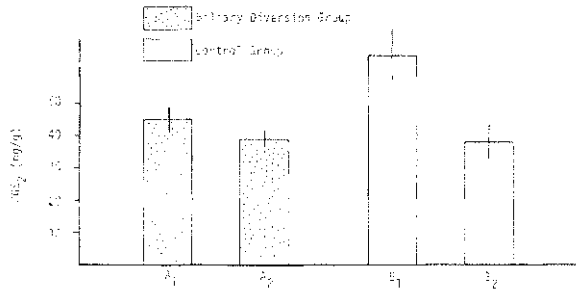
Figure 4. A Field from the gastric mucosa (/one B) of a guinea-pig from the bilary diversion group (I Mi. X46U).



ligureS. A Field from the gastric mucosa {/one H) of a guinea-pig from the control group (I1.H. X230).

Table 2. PGE2 Like activity (material) ng/g stomach

	Bil.Div.Group		Control Group
	51.7		30.3
Ai Group	37.0	Bi Group	67.0
(Stress -)	25.0	(Stress -)	60.2
	44.6		72.0
	50.4		73.8
	47.7		86.9
	60.6		
Mean	45.28		65.03
S. Fi.	4.34		7.85
	43.9		36.2
	48.0		27.9
A2 Group	37.6	B2 Group	51.2
(Stress +)	33.1	(Stress +)	36.5
	47.3		24.0
	34.3		54.2
	33.1		
	32.1		
Mean	38.67		38.33
s. e.	2.37		4.98



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

the control group after stress aflication, contrary to what might be cxpcctcd.

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 incidance seen 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.

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