THE EFFECT OF BILE ON THE GASTRIC MUCOSAL BARRIER IN THE PRESENCE AND AFTER BLOCKADE OF NORMAL GASTRIC ACIDITY

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Abstract

Induced physiologic changes in the gastric mucosa was investigated both in the presence of normal gastric acidity and after parietal cell vagotomy (PCV), in dogs. Cholecystogastrostomy and common bile duct ligation was,performed in eleven and PCV was added to this procedure in five dogs. During histopathological examination, 70 days after the procedure, both groups proved to have superficial gastritis. The most prominent changes occurred at the anastomotic site and at the gastric antrum. Bile had broken down the gastric mucosal barrier and the Na+ flux roughly paralleled the H + back diffusion. Potassium had taken part in the bi-directional movement of ions in the gastric mucosa, as well as the sodium flux, and in the late phase it accompanied the action of sodium ions. The destruction of the K+ - H + pump, possibly located in the plasma membrane, may be the responsible mechanism of thisflux (JPMA39: 231, 1989).

INRODUCTION

Bile destructs the gastric mucosal barrier. Disruption of this barrier is believed to have occurred when there is an increase in the net flux of hydrogen ions into the mucosa, accompanied with a net flux of sodium ions into the lumen[1]. An intact layer of gastric surface epithelial cells is critical for the maintenance of gastric mucosal cytoprotection[2]. These cells produce an alkaline secretion rich in sodium, are semipermeable to hydrogen ions and are protected from injury by a mucus layer. When irritants such as bile, aspirin, lysolecithine, urea or ethanol are introduced in the stomach; a hydrogen ion loss from the lumen is detected, in addition to an increase in luininal sodium. A fall in gastric transmucosal electrical potential differen-ce, changes in gastric mucosal blood flow, histamin secretion into the gastric juice and to the venous blood flow of the stomach and an increase in the luminal pepsin content is also detected. [3-6] In this study, the effect of bile on the gastric mucosa was examined in the presence and after blockade of normal gastric acidity. A chronic model was chosen to simulate the effects of bile on the apatomically intact normal stomach.

MATERIAL AND METHODS

Eleven Mongrel dogs, weighting approxImately 14 Kgs. each were allocated into two groups. The animals were fasted for 16 hours and were anesthetized with sodium pentobarbital 20 mg/Kg. The abdomen was entered through an upper midline incision. The stomach was clamped both at the cardioesophageal junction and at the pylorus with two noncrushing intestinal clamps. After cannulation of the splenic vein, a gastrotomy was performed four centimeters proximal to the pylorus on the anterior surface of the stomach and gastricjuice samples were taken for pH measurements. Follow ing irrigation of the stomach with 100 nil of 160 mEq/L HCL, splenic venous blood and gastric juice samples were obtained at 1,15 and 30 minutes for Na+, K+ and H3 determinations. Mucosal biopsies

were taken from the gastric antrum and corpus. A cholecystogastrostomy was constructed between the fundus of the gall bladder and the existing gastrotomy. The structures of the hepatoduodenal ligament, except for the portal vein and the hepatic artery were doubly ligated in order to achieve total biliary diversion into the stomach. Five animals received an additional parietal cell vagotomy and served as Group IL Ringers lactate in 5%dextrose was infused through an antecubital vein throughout the experiment and the day following surgery. The animals were allowed to eat and drink freely starting the second postoperative thy. The animals in both groups were reoperated 70 days after the experiment. The same protocol described above was repeated after the pylorus and cardioesophageal junction was clamped. The ani mals were sacrifled after total gastrectomy at the end of the second operation. The mucosal spedmens obtained at the first operation and the stomach removed after the second operation were sent for histopathological examination and were examined with 4,16,40 and 100 magnifications under light microscope, after they were stained with hemotoxylene. For H3 determinations, 2 ml. blood was drawn into heparinised tubes over 0.5 trichloracetic add and was centrifugated at 3000 rpm.s. 0.5 ml. of the supernatant was placed into scintillation vials containing 10 ml. of Bray's solution. H3 was assessed with a Packard tricanal liquid scintillation counter and the results were recorded as cpm/ml. Sodium and potassium ion determinations were made photometrically. All values were subjected to a Student's 't' test for statistical significance.

RESULTS

The normal structure of the stomach was observed in mucosal biopsies taken during the construction of cholecystogastrostomy, in which the surface epithelium presented a slightly folded configuration and the nonnal cell populationwas present in the Ianiina propria (Figure 1).

Figure 1. Normal gastric mucosa of the dog, preceding cholecysto- gastrostomy (CG) .H.E.x110.

Histopathological studies performed 70 days later revealed superficial gastritis in all specimens. This superficial gastritis was characterised with proliferation of the surface epithelium, cystic dilatation of the glands, increase in the inflammatory cell count in the lamina propria and lymphoid byperplasia (Figure 2).

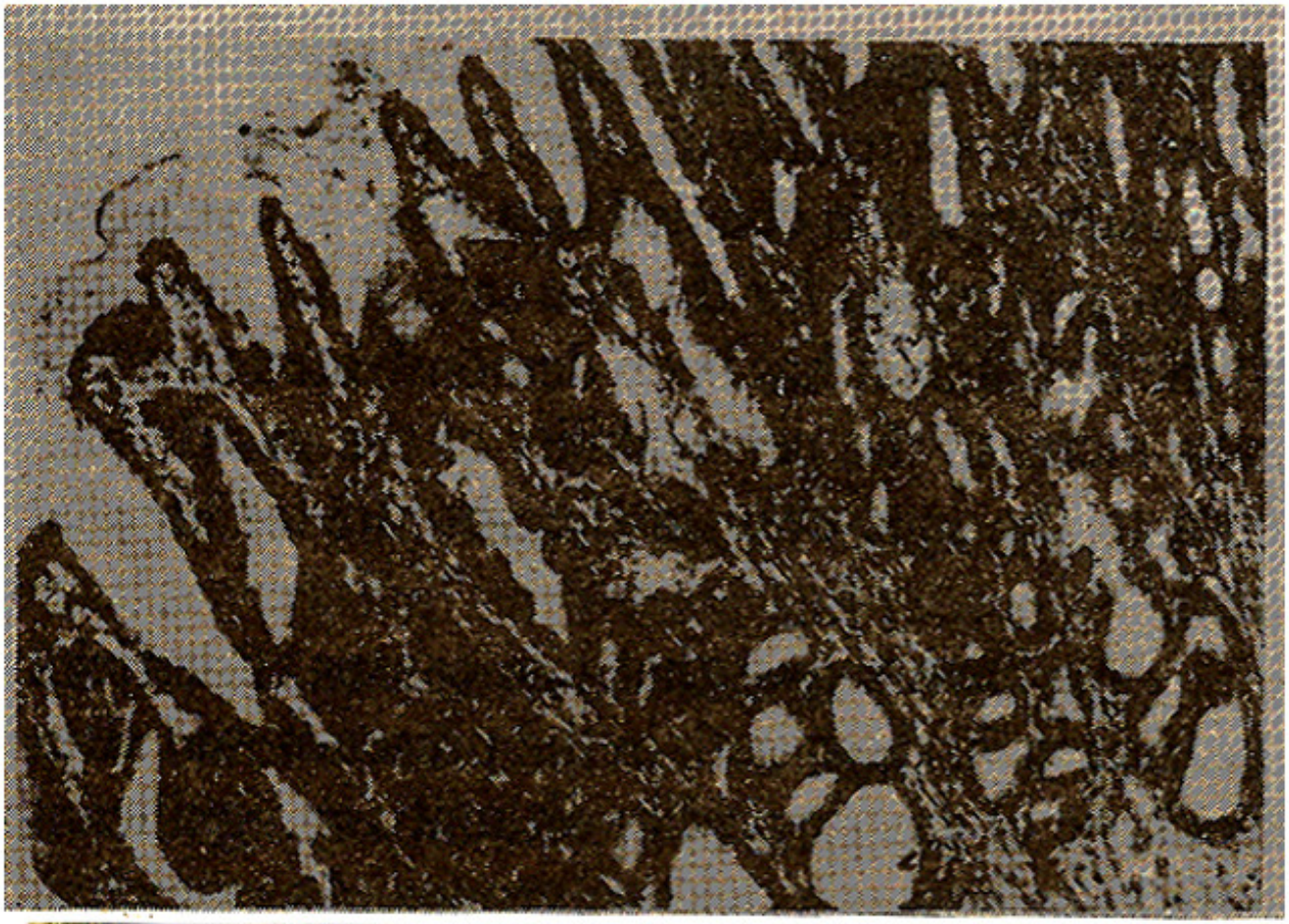

Figure 2. Superficial gastritis 70 days after CG.H.E.x110.

The most prominent findings were at the anastomotic site and at the gastric antrum. The mean pH value in Group I was gastrostomy (CG) (Pc 0.01). In Group II, where a parietal cell vagotomy (PCV) was added to CG, the mean pH value was found to be 2.02± 0.39 initially and 5.10±1.11 seventy days after the procedure (pc 0.01). Preoperative and postoperative H3 values in Group I is demonstrated in Figure 3.

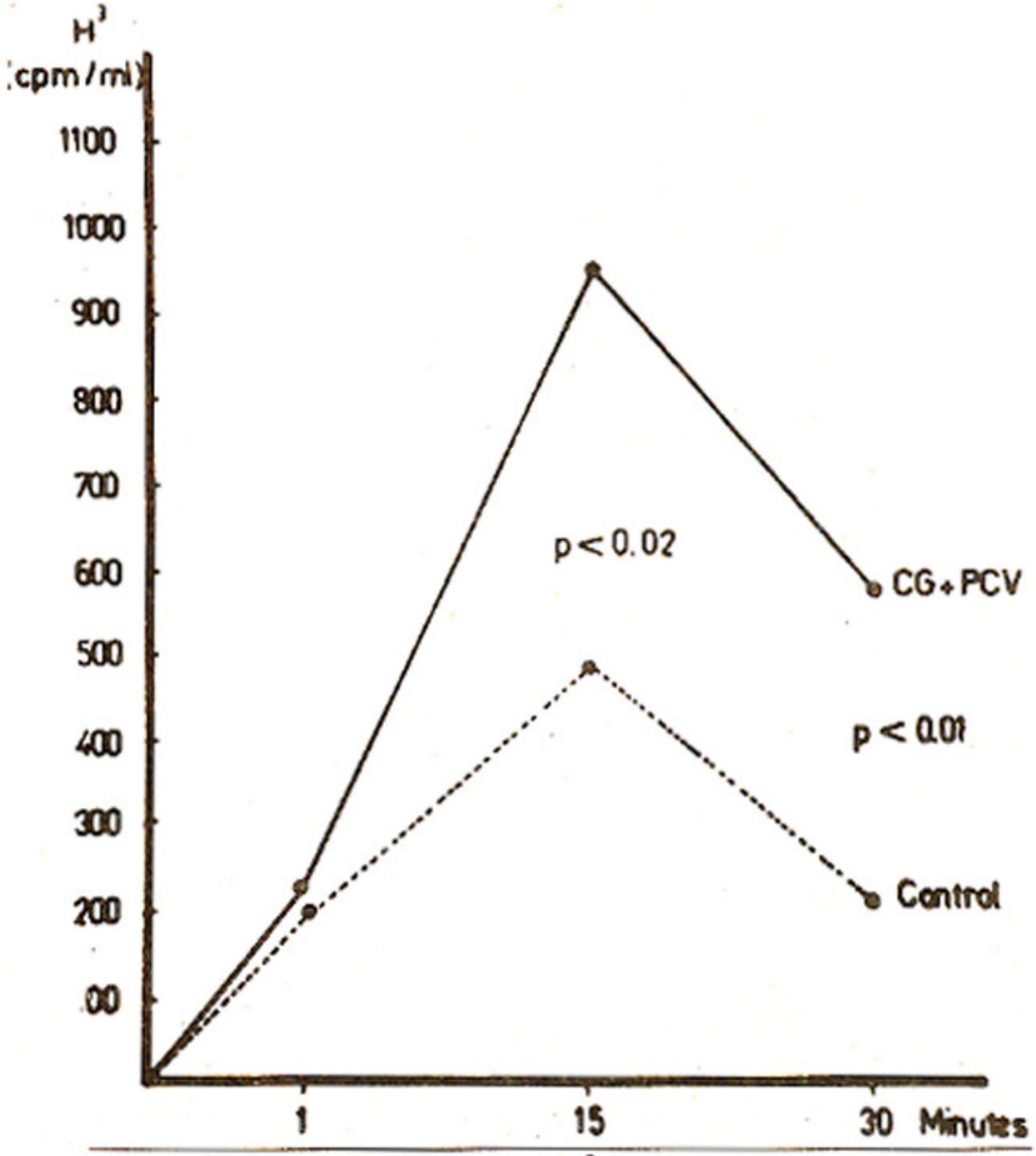

Figure 4. The change in H^3 in Group II, after CG and parietal cell vagotomy (PCV).

The difference between the first and second values was found statistically significant at 15 (p c 0.01) and 30 minutes (Pc 0.05). In Group II (Figure 4)

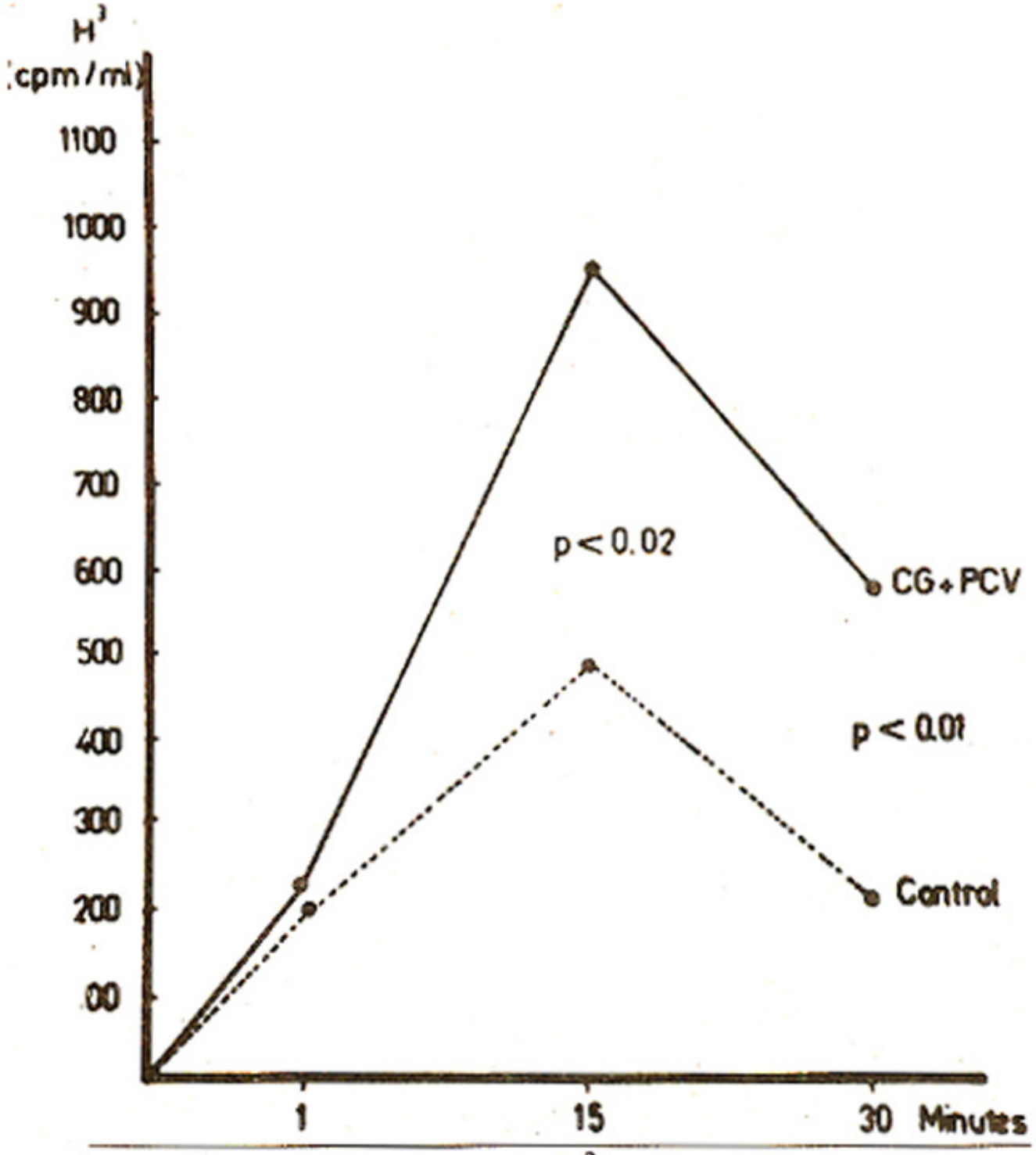

Figure 4. The change in H^3 in Group II, after CG and parietal cell vagotomy (PCV).

no significant difference was found between the H3 values at 1 minute. However, at 15 and 30 minutes the difference was found to be statistically, significant (Pc 0.02 and Pc 0.01, respectively). The gastric juice Na + concentrations before and after CG in Group us shown in Figure 5.

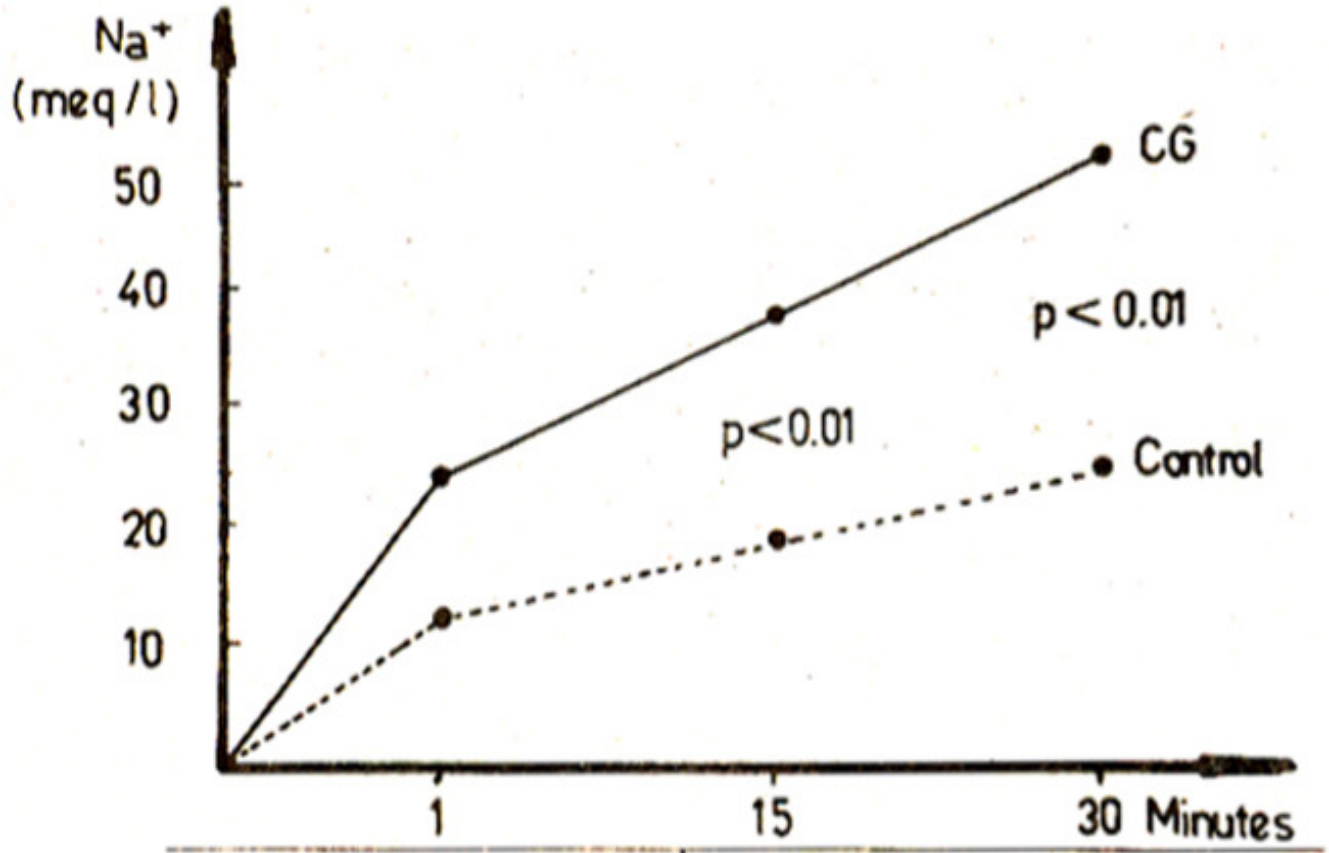

Figure 5. Gastric juice Na^+ concentration in Group I. (CG: Cholecysto- gastrostomy, CG + PCV:Cholecystogastrostomy and parietal cell vagotomy).

The difference was found statistically significant at 15 and 30 minutes (P< 0.01). Similarly the difference between the first second values in Group II was found significant at 1 (P <0.05), 15 (P<0.01) and 30 minutes (P<0.01) (Figure 6).

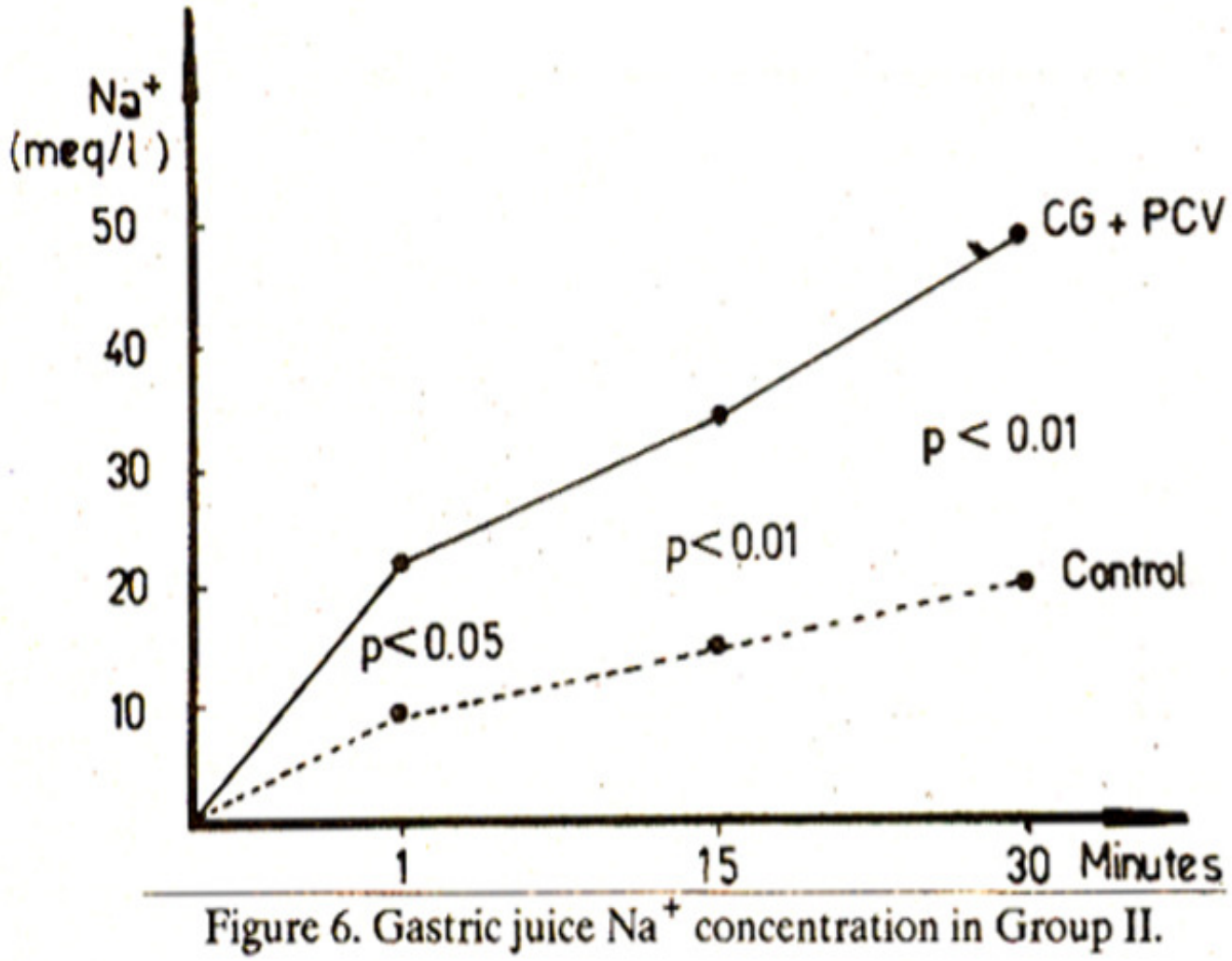

Figure 6. Gastric juice Na^+ concentration in Group II.

There was statistically significant difference between the gastric juice K+ concentrations before and after CG at 15 ($P<0.05$) and 30 minutes ($P<0.01$) (Figure 7).

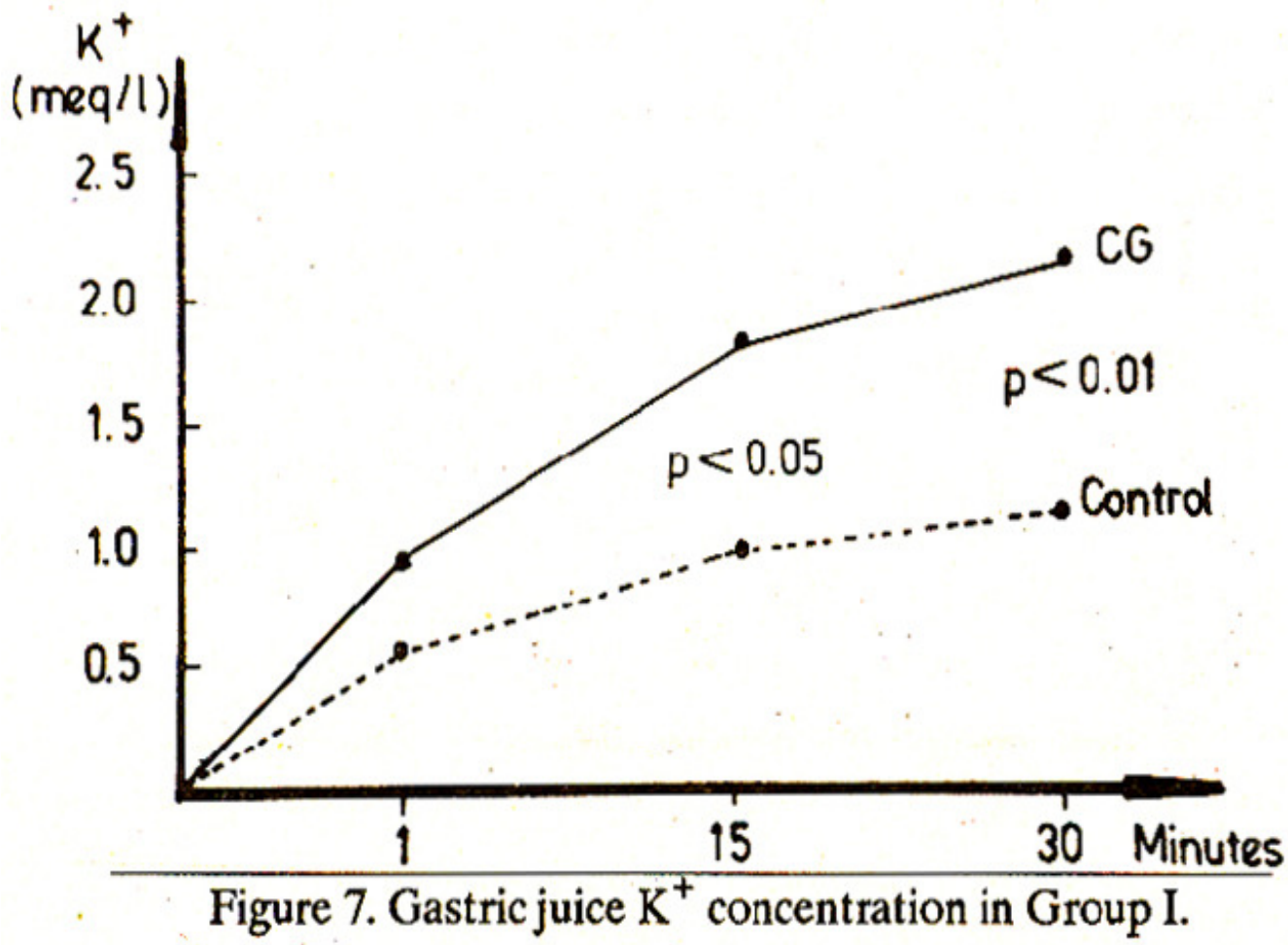

Figure 7. Gastric juice K^+ concentration in Group I.

In Group II the difference was statisfically significant only at the 30th minute (P<0.02) (Figure 8).

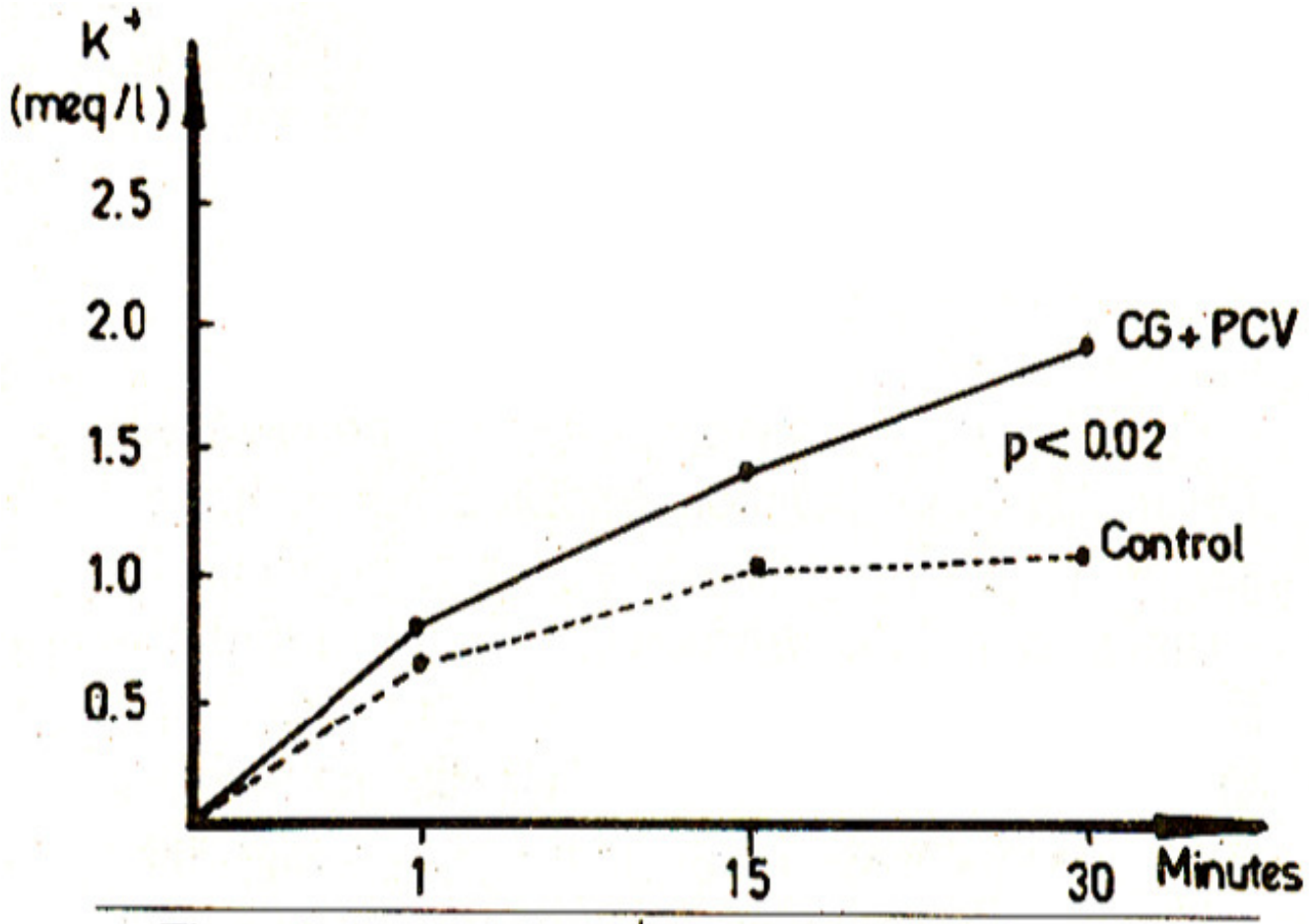

Figure 8. Gastric juice K^+ concentration in Group II.

DISCUSSION

Intestinal contents or bile causes superficial gastritis in the stomach. Lawson showed that bile causes gastritis at the gastric antrum and at the site of gastrointestinal anastomosis after 100 days[7]. Published data claim that the gastric mucosal barrier has some properties in common with the erythrocyte membrane[8]. It permits limited concentrations of H+ to diffuse passively from the lumen into the tissue and Na+ and water in the reverse direction. [9-11] Like other irritants such as ethanol and aspirin; bile salts cause injury in the stomach characterised with this ion exchange. The mechanism by which bile salts disrupt the gastric mucosal barrier is obscure. One possibility is that bile salts enter the mucosa before causing cellular injury. In support of this idea, Davenport has shown that taurocholate is absorbed from canine gastric pouches[8]. A second possibility is that gastric mucosal damage is mediated through the detergent action of intraluminal bile salts. Two major constituents of mucosal membranes are phospholipid and 'cholesterol, which are both readily dissolved by bile salt micelles[1]. Although it is claimed that there is a demand for an acid milieu for' the bile salts to be injurious to the stomach, it has been demonstrated that bile salts increase the permeability of the gastric mucosa to the ions even in the absence of luminal acid[12,13]. We have shown that bile causes superficial gastritis in 70 days, 'both in the presence and after blockade of gastric acidity without any significant difference between the two groups. As expected, the most prominent changes occurred at the anas tomotic site an4 at the gastric antrum. Our preparation has led to establishment of bile reflux gastritis much sooner than reported

previously. H^+ back diffusion, which exhibits a functional measure to the damage of the gastric mucosal barrier, has been assessed with the help of H^3. H^3 back diffusion did not reveal any significant difference at the beginning in both groups but, began to rise afterwards and remained elevated and then decreased after 15 minutes. The decrease in the H^3 back diffusion after the peak at 15 minutes can be explainedby the decrease of H^3 in the gastric lumen since, H^+ back diffusion has been demonstrated to be directly related to the availability of H^+ within the gastric lumen. [4,14] Luminal Na^+ concentrations after bile refiux gastritis showed a steady increase in both groups starting from the first minute. Luniinal K concentrations were found significantly higher at 15 and 30 minutes in Group I and at 30 minutes in Group II. Thus, it has been proved that there is no linear correlation between the action of Na^+ and H^+ back diffusion. The increase in luminal K^+ concentrations can be explained with anatomic damage to the gastric mucosa. It is possible that the C — H^+ pump located at the plasma membrane of the parietal cell maybe damaged by the bile salts and the luminal C may be increased due to this process. Parietal cell vagotomy proved to be ineffective in providing a more alkaline milieu in the stomach in this study. This can be attributed to the very high pH of the bile that is diverted into the stomach in both groups. When the results of this experimental study are evaluated from the clinical point of view, surgical procedures which lead to bile reflux in the stomach need to be reevaluated.

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