THE EFFECTS OF LYSOPHOSPHATIDYLCHOLINE ON THE RAT GASTRIC MUCOSA AT ACID AND NEUTRAL $_{p}H$

R.S. Newbery, G.P. Martin, N.C. Turner, C. Marriott, Department of Pharmacy, Brighton Polytechnic, Moulsecoomb, Brighton BN2 4GJ

Duodenogastric reflux is thought to be a major predisposing factor in the pathophysiology of gastric ulceration. In support of this hypothesis many investigations have been carried out to demonstrate the toxicity of topically applied bile salts to the gastric epithelium. Research into the effects of other biliary compounds on the stomach has in comparison been sparse, despite the observation of Johnson & McDermott (1974) that significantly higher concentrations of lysophosphatidylcholine (LPC) were present in the gastric aspirates of ulcer patients compared to control subjects. Moreover LPC has been shown to be as severely damaging as bile salts when directly applied to the gastric mucosa (Davenport 1970; Orchard et al 1977). These latter studies however were carried out at neutral pH whereas the pH of the stomach rarely rises above pH 3 for prolonged periods. The object of this study was therefore to assess the significance of pH upon the gastric epithelial toxicity of LPC.

An ex vivo gastric chamber technique was employed as described by Mersereau & Hinchey (1973). Following surgery the stomachs of male Wistar rats (450-600g) were bathed for 30 minutes with saline to allow recovery before experimentation. The subsequent three 1 hour periods were designated periods I, II and III during which the stomachs were exposed to one of the following five regimes:

	Control A	Control B	1	2	3
Period I	ATS	ATS	ATS	ATS	ATS
Period II	ATS	NTS	ATS + 5mM LPC	ATS + 20mM LPC	NTS + 5mM LPC
Period III	ATS	ATS	ATS + 5mM LPC	ATS + 20mM LPC	ATS + 5mM LPC

Acid test solution (ATS) contains 100 mM HCl, 54 mM NaCl, PEG 5 g/l + ^{14}C PEG 10 μCi l^{-1}. Neutral test solution (NTS) contains 100 mM mannitol, 34 mM NaCl, 20 mM Tris buffer, PEG 5 g l^{-1} + ^{14}C PEG 10 μCi l^{-1} at pH 7.4. All bathing solutions were replaced every 15 minutes and the NaCl concentration was altered accordingly to maintain osmotic balance when LPC was present.

5 mm LPC in acid solution causes an increase in H^+ ion flux and a decrease in potential difference, both significant ($p < 0.05$) when compared to controls using a two-tailed Mann-Whitney U-test. Application of acidified 20 mM LPC also causes significant increases in H^+, Na^+ and K^+ ion fluxes and a decrease in potential difference ($p < 0.05$). Visible damage to the mucosa was observed at both LPC concentrations with greater severity at 20 mM. LPC toxicity in acid solution was less than that reported in previous studies. Treatment with 5 mM LPC in pH 7.4 Tris buffer for 1 hour followed by a further hour of LPC in ATS is considerably more damaging than exposure to 5 mM LPC in acid solution for 2 hours. A comparison revealed significant increases in H^+ and Na^+ ion fluxes and changes in potential difference and volume of the bathing solution ($p < 0.05$).

We conclude that LPC is acutely damaging to the gastric epithelium at both acid and neutral pH although barrier disruption is greatly enhanced at the higher pH. The lower pK_a of LPC lies between the pH values at which experiments were conducted suggesting that the state of ionization may be of importance in determining epithelial toxicity. These results demonstrate transient changes of pH following duodenogastric reflux to be of major importance in determining the ulcerogenic potential of LPC in the stomach.

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