MUCOSAL INJURY: THE COMBINED EFFECTS OF LYSOPHOSPHATIDYLCHOLINE AND SODIUM TAURODEOXYCHOLATE ON THE RAT STOMACH

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

Phospholipids particularly phosphatidylcholine (PC) have been demonstrated to have a protective role in mitigating gastric damage induced by topical agents including bile salts. Within the duodenum, PC undergoes hydrolysis by pancreatic phospholipase A_2 (PPA) to yield lysophosphatidylcholine (LPC). Whereas one previous study has shown that LPC reduces bile salt induced gastric injury (Clémençon 1981), Martin & Marriott (1981) suggest a potentiation of damage at some bile salt concentrations. LPC alone is acutely damaging to the gastric mucosa although the degree of mucosal toxicity is pH dependent. The purpose of this investigation therefore is to define the role of LPC in alkaline biliary reflux, where luminal pH may be a determinant of the severity of ulceration.

Experiments were conducted upon male Wistar rats using an ex vivo gastric chamber technique, bathing solutions being replaced every 15 minutes. For the first hour (period I control), the stomach was exposed to acid test solution (ATS) containing 100 mM HCl, 54 mM NaCl, PEG 5 g l^{-1} and [^{14}C] PEG 10 µCi l^{-1}. For the subsequent two 1 hour periods (periods II and III) one of four protocols was employed: A) ATS in periods II and III, B) neutral test solution (NTS) in period II followed by ATS in period III, C) ATS containing 5 mM LPC + 5 mM sodium taurodeoxycholate (STDC) in periods II + III, or D) NTS containing 5 mM LPC + 5 mM STDC in period II followed by ATS containing 5 mM LPC + 5 mM STDC in period III. NTS at pH 7.4 comprised 100 mM mannitol, 34 mM NaCl, 20 mM Tris buffer, PEG 5 g l^{-1} and [^{14}C] PEG 10 µCi l^{-1}.

LPC and STDC, contained in either ATS or NTS are damaging to the gastric mucosa causing significant increases in ion fluxes when compared to controls (Mann-Whitney U test). Also, when LPC + STDC is applied in NTS followed by treatment in ATS there is a significant decrease in potential difference (PD).

Table 1

	Group C		Group D	
	Period II	Period III	Period II	Period III
ΔH^+ (µEq)	-24.5 ±3.7	-32.2±3.9	-	-62.3 ±5.5*
ΔNa^+ (µEq)	25.2 ±2.9*	27.9±3.7	12.4 ±2.01	45.1 ±2.5*
ΔK^+ (µEq)	1.63±0.12	1.7±0.1	1.25±0.15	2.7 ±0.16*
ΔPD (mV)	1.4 ±0.9	2.6±0.6	4.7 ±0.7	5.6 ±1.1*

Values are expressed as mean changes per 15 mins ± SEM
* Denotes a significant difference between groups C and D ($p < 0.05$)

Subsequent visual assessment confirms that greater ulcerative damage was present in rats from group D compared to group C. These results indicate that an equimolar concentration of LPC and STDC is more damaging when applied initially in NTS than in ATS provided the mucosa is placed under subsequent acid load. Comparison of results from a 2 hour treatment with ATS containing LPC and STDC with those reported for STDC alone (Newbery et al 1984) indicate that LPC has little effect on overall bile salt toxicity. Although mean ion fluxes are generally less than those obtained for STDC alone no significant differences could be shown except an approximate 35% reduction in K^+ flux ($p < 0.05$). This study demonstrates that unlike PC, LPC has little effect on bile salt induced gastric injury at acid pH and suggests that the activity of PPA to be of importance in determining the toxicity of bile salts in reflux related ulcer disease. Moreover the magnitude and duration of rise in gastric pH following alkaline reflux may be of considerable significance in determining ultimate topical irritancy.

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