Does increased gastric mucus play a role in the ulcer-protecting effects of zinc sulphate?

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Summary. Zinc sulphate pretreatment i.p. produces dose-related reductions in stress ulcer incidence in pylorus-occluded rats. The associated increases in gastric wall mucus, in stressed and nonstressed animals, suggest that a similar effect may contribute to its ulcer-reducing ability in man.

Reduced gastric mucus production is thought to play a part in stress ulcer formation[1,2]. Since zinc pretreatment has been found to reduce the incidence of gastric ulcers produced by stress in rats[3], the present study was undertaken to examine the possibility that the ulcer-protecting action of zinc may have been due to an effect on the gastric mucus.

Methods. Male Sprague-Dawley rats (150–200 g), prepared for pylorus occlusion[4], were given 1 i.p. injection of zinc sulphate ($ZnSO_4 \cdot 7H_2O$; May & Baker Ltd) 22, 44 or 88 mg/kg (expressed as the salt, including its water of crystallisation) 48 h before use. Zinc sulphate was dissolved in 0.9% NaCl w/v (saline). Similar volumes of saline (1 ml/kg) were given by the same route to the controls. Following pretreatment injections, the animals were then starved for 48 h but allowed free access only to 8% sucrose in 0.2% NaCl w/v which was removed 1 h before experiments.

The pylorus was occluded at the start of the experiment. Rats subjected to stress were put into individual close-fitting tubular restraint cages of wire mesh and exposed to 4 °C; control animals were returned to their starvation cages at room temperature (23 ± 1 °C). All were killed after a period of 2 h, and accumulated gastric secretion collected for measurements of volume and total acidity[4]. Following examination of the gastric mucosa for lesions[5], the mucus in the stomach wall was measured[6]. The difference between the stomach weights before and after 15-min-immersion in acetylcysteine (Sigma), representing the amount of mucus removed, was expressed as a percentage of the original stomach weight. The data were analysed using Student's t-test or the χ^2 test.

Results. All nonstressed groups showed a low incidence of lesions, appearing only as occasional mucosal petechiae (table, a). Stress produced a high incidence of lesions, mainly haemorrhagic ulcers, in the saline-pretreated controls (table, b). Increasing doses of zinc sulphate progressively lowered stress ulcer incidence, significant with 44 mg/kg ($p<0.05$) and 88 mg/kg ($p<0.01$). All the lesions were confined to the gastric glandular mucosa.

Gastric secretory volume tended to be reduced by zinc sulphate pretreatment in nonstressed rats, significant with 88 mg/kg ($p<0.05$; table, a). Stress-reduced gastric secretory volume, in saline-pretreated animals ($p<0.05$; table, b), was even lower with zinc sulphate pretreatment ($p<0.02$ with 44 mg/kg; $p<0.001$ with 88 mg/kg). The total acid output in nonstressed rats was also reduced by zinc sulphate ($p<0.05$ with 44 mg/kg; $p<0.01$ with 88 mg/kg; table, a). As observed with the secretory volume, stress also reduced total acid output in the saline-pretreated controls ($p<0.01$; table, b), but no further reductions were seen in the stressed rats pretreated with zinc sulphate.

The mucus content of the stomach wall of nonstressed animals tended to increase with zinc sulphate treatment, reaching significance with 88 mg/kg ($p<0.001$; table, a). Stress markedly lowered stomach wall mucus in the saline-pretreated rats ($p<0.01$; table, b), but zinc sulphate reversed the stress-induced change ($p<0.05$ with 44 mg/kg; $p<0.001$ with 88 mg/kg).

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Effects of zinc sulphate pretreatment on gastric lesions, gastric secretion and stomach wall mucus in stressed pylorus-occluded rats

Pretreatment (i.p.)	Dose (mg/kg)	No. of rats used	No. of rats with glandular lesions	Gastric secretory volume (ml/100 g b. wt/h)	Total acid (μEq HCl/ 100 g b. wt/h)	Mucus in stomach wall (% original wet wt of stomach)
a) Nonstressed groups						
Saline	1 ml/kg	17	3 (18%)	0.94 ± 0.09	45.22 ± 4.12	8.12 ± 0.67
Zinc sulphate	22	14	2 (14%)	0.85 ± 0.08	37.94 ± 7.15	8.35 ± 0.64
Zinc sulphate	44	16	2 (13%)	0.77 ± 0.13	32.77 ± 4.62[a]	9.11 ± 0.65
Zinc sulphate	88	17	3 (18%)	0.70 ± 0.08[a]	25.81 ± 5.30[c]	11.12 ± 0.62[d]
b) Stressed groups						
Saline	1 ml/kg	14	13 (93%)[g]	0.68 ± 0.08[e]	27.13 ± 3.76[g]	5.50 ± 0.39[g]
Zinc sulphate	22	16	12 (75%)[g]	0.62 ± 0.07[e]	30.53 ± 4.34	6.42 ± 0.37[f]
Zinc sulphate	44	16	10 (63%)[a,g]	0.42 ± 0.05[b,f]	25.68 ± 4.18	6.75 ± 0.43[a,g]
Zinc sulphate	88	18	7 (39%)[c]	0.36 ± 0.04[d,h]	25.56 ± 3.79	8.50 ± 0.70[d,g]

The values shown are means ± SEM. [a]$p < 0.05$, [b]$p < 0.02$, [c]$p < 0.01$, [d]$p < 0.001$; compared with its own saline-pretreated control. [e]$p < 0.05$, [f]$p < 0.02$, [g]$p < 0.01$, [h]$p < 0.001$; compared with its corresponding nonstressed group.

Discussion. The ability of zinc sulphate pretreatment to produce dose-related decreases in the incidence of stress-induced gastric lesions, as well as the gastric secretory volume and total acid output in nonstressed or in stressed rats, confirms previous observations and conclusions[3]. However, the associated dose-related changes in stomach wall mucus suggest a relationship between gastric wall mucus and stress ulcer protection by zinc sulphate. Since the adopted method[6] measures mucus in the superficial secretory layer of the gastric mucosa, it is reasonable to deduce that an increase in mucus adhering to the gastric mucosa would provide greater protection against the acidity and peptic activity of gastric juice[2]. The high incidence of stress ulcers associated with a significant decrease in gastric wall mucus, and the reversal of these parameters by zinc sulphate do indeed support this deduction.

Zinc sulphate has already been shown to reduce the severity of gastric ulcers in man[7-9]; thus it is conceivable that its mucus-increasing effect could contribute to increased mucosal resistance to ulceration. The present observations indicate an action on the stomach following absorption from a parenteral site of administration, whereas clinical investigations[7-9], using the oral route, only suggest this possibility. It is unlikely that zinc sulphate produces its effects through a toxic action[10, 11].

The mechanism through which zinc sulphate exerts its mucus-increasing effect is unclear, but 3 possibilities may be speculated upon; inhibition of gastric histamine release[10] may increase mucus formation[2], the sulphate moiety of the preparation may influence chondroitin sulphate synthesis[2, 12], or zinc itself may stimulate mucus formation.

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Chemical protection of mouse spermatocytes against gamma-rays with 2-mercaptopropionylglycine

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Summary. The radiosensitivity of primary spermatocytes in pachytene stage was estimated by counting the number of spermatids in the testes of control and MPG-treated mouse after exposure to 500, 1000 and 1500 R of Co^{60} gamma-rays. For this purpose, control and MPG-treated mice were killed 5 days after irradiation and countings of spermatids was made in stages I and II of the tubules. It has been observed that, although there was a death of primary spermatocytes in irradiated MPG-protected groups, quantitatively significant protection was afforded by this drug at all the 3 dose-levels studied.

Since the radioprotective properties of MEA[1] and AET[2] became known, many studies have been carried out to study the effect of sulfhydryl compounds in modifying radiation injury, especially in the mammalian germ cells. In 1953, Kaplan and Lyon[3], published their first report on experiments in which 2-mercaptoethylamine (MEA) was used in an attempt to protect the hereditary material against ionizing radiation. But the later works in this field were mainly concerned with clarifying the ability of different substances to prevent radiation-induced changes in the individual's reproductive mechanisms rather than concentrating on the purely genetic consequences of irradiation. However, recently, many unsuccessful attempts have been made at chemical protection from radiation related to genetic damages[4, 5]. Leonard and Deknudt[6] have presented evidence that some radioprotective agents, administered simultaneously, gave a favourable effect with regard to translocation resulting from spermatogonial X-irradiation in the mouse. A combination of ATP-AET-serotonin had provided highly significant efficiency in protecting the mouse spermatogonia against 300 R of X-rays[7]. Most of the study up to date used chemical protectors (cysteine, cysteamine and AET) to modify injury in mammalian germ cells against X-rays. Present study deals with the radioprotective action of MPG on the primary spermatocytes of mouse testes against various doses of gamma-rays.

Material and methods. Swiss albino male mice from an inbred colony, 6–8 weeks old, and weighing about 24 g, were used in the experiments. 3 sets of experiments were conducted, each using a different irradiation dose. Each set contained an experimental (MPG-treated) and a control group with equal number of animals. The experimental animals in each set were injected with 20 mg/kg b.wt of MPG (2-mercaptopropionylglycine received from Santen Pharmaceutical, Osaka, Japan, dissolved in distilled water with PH adjusted to 6.4 with 0.1 N NaOH before use) i.p. and the control group received an equal volume of distilled water in the same manner. After treatment, the animals of the 3 sets were exposed to a Co^{60} gamma-source to give a total dose of 500, 1000 and 1500 R respectively at the dose rate of 25 R/min. 3 mice of each treatment (control and drug-treated) were killed at 5 days after post-irradiation, and testes were removed. The testes of each mouse was fixed in Bouin's fluid and 6 μm sections were stained with Harris hematoxylin-eosin and PAS-hematoxylin for qualitative and quantitative studies respectively. Number of spermatids were counted in I and II stage, in carefully selected median cross-sections of the tubules from each mouse testes. Spermatids were counted only if the greater part of the nucleus was included in the sections (intensity of staining and presence

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