SHORT COMMUNICATION

GASTRIC RESPONSES TO FLUPENTHIXOL, A NEW THIOXANTHENE DERIVATIV IN RATS

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Summary: Flupenthixol, a new thioxanthene derivative, was studied for its effects on gastric secretion and gastric ulcers in rats. The compound diminished the volume of gastric secretion, decreased total acid output and protected the glandular gastric mucosa. The observations may be of clinical significance.

Key words : Flupenthixol, pylorus-ligation, gastric ulcer, gastric secretion

INTRODUCTION

Tricyclic antidepressants (3) and monoamine oxidase inhibitors (4) have been shown t possess gastric antisecretory activity in rats. The possibilitiy that thioxanthene derivatives ma have similar action has led to the study of the effects of flupenthixol, introduced as antidepres ant (9), on gastric secretion and gastric ulcers in rats.

MATERIALS AND METHODS

For the study the method of Skoryna and Webster (11) was employed. Albino rat (Haffkine Strain) of either sex with body weight ranging from 120-180 g were used. Th animals were housed in individual cages having specially designed grid floor to preven coprophagy and were deprived of food but allowed water ad libitum. Twenty fou hr later pylorus ligation, with care not to occlude any blood vessels, and cardia ligation, sparing the vagi, were performed under ether anaesthesia. Flupenthixo dissolved in distilled water was given subcutaneously immediately after the surgica procedure. Five hr later the stomachs were removed under ether anaesthesia. The gastri contents were collected, volume and pH determined. The total acidity of the gastric content was determined by titration with 0.01 N-NaoH using phenolphthalein as an idicator and ex pressed in mEq/L of total acids. The total acid output in μ Eq/5 hr was calculated. Th stomachs were cut open along the greater curvature and examined for mucosal ulcers in th glandular portion. The scoring from 1-5 for the severity of the lesions was done accordin to the method of Adami, Marrazzi-Uberti and Turba (1). The results were compared with th control animals which received equivalent amount of 0.9% saline after surgical procedure, a described for drug treated rats.

RESULTS AND DISCUSSION

The effects of flupenthixol on gastric secretion and gastric ulcers after 5 hr of pyloric and cardiac ligation are summarized in Table I. Flupenthixol produced a statistically significant

Table I: Gastric anti-secretory and anti-ulcer activity of Flupenthixol in rats.

Drug mg/kg S.C.	*No. of animals*	*Weight g ± S.E.*	*Vol. /100g ml ±S.E.*	*pH±S.E.*	*Total acidity m Eq/L±S.E.*	*Total acid output μ Eq/5 hr ±S.E.*	*Mean ulcer score*	*Percent ulcer protection.*
Control	10	153.0±7.8	0.75±0.028	3.7±0.36	68.0±8.0	54.0±6.6	2.0	—
1.0	8	138.0±15.0	0.57±0.08*	3.0±0.4	68.0±14.6	45.0±15.0	0.32	84.0
3.0	12	179.0±10.0	0.38±0.04**	3.8±0.55	75.0±13.7	33.0±5.9*	0.48	76.0
10.0	14	146.0±9.0	0.41±0.12*	3.8±0.37	67.0±11.4	36.0±5.3*	1.3	35.0

*P<0.05 **P<0.001

decrease in the volume of gastric secretion and total acid output and protected the rats against mucosal lesions. These effects were however not dose dependent. The pH did not change significantly. The development of ulcers was apparently prevented by the drug and this could be correlated with the decrease in the acid output brought about by the drug. Antonsen(2), Debnath *et al.* (5) and Sharma *et al.* (10) have also reported a close correlation between the total acid output and the extent of ulceration of the gastric mucosa in Shay rats. Here it is worth noting that although flupenthixol has been shown to possess anti-inflammatory activity in rats (6), it did not produce gastric lesions in pylorus-ligated rats, rather it had a protective action. The protective action was surprisingly more marked with 1 and 3 *mg/kg* doses than with 10 *mg/kg* dose. These observations may be of clinical interest as steroid (7) as well as non-steroid (8) anti-inflammatory agents are known to produce or aggravate gastric ulcers in humans. The mechanism of antisecretory and anti-ulcer effect remains to be elucidated.

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