SHORT COMMUNICATION

GASTRIC RESPONSES TO FLUPENTHIXOL, A NEW THIOXANTHENE DERIVATIVE
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 to possess gastric antisecretory activity in rats. The possibility that thioxanthene derivatives may have similar action has led to the study of the effects of flupenthixol, introduced as antidepressant (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 rats (Haffkine Strain) of either sex with body weight ranging from 120-180 g were used. The animals were housed in individual cages having specially designed grid floor to prevent coprophagy and were deprived of food but allowed water ad libitum. Twenty four hr later pylorus ligation, with care not to occlude any blood vessels, and cardiac ligation, sparing the vagi, were performed under ether anaesthesia. Flupenthixol dissolved in distilled water was given subcutaneously immediately after the surgical procedure. Five hr later the stomachs were removed under ether anaesthesia. Flupenthixol was determined by titration with 0.01 N-NaOH using phenolphthalein as an indicator and expressed in mEq/L of total acids. The total acid output in µ Eq/5 hr was calculated. The stomachs were cut open along the greater curvature and examined for mucosal ulcers in the glandular portion. The scoring from 1-5 for the severity of the lesions was done according to the method of Adami, Marrazzi-Uberti and Turba (1). The results were compared with the control animals which received equivalent amount of 0.9 % saline after surgical procedure as described for drug treated rats.

<table>
<thead>
<tr>
<th>Drug mg/kg S.C.</th>
<th>No. of animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
</tr>
<tr>
<td>1.0</td>
<td>8</td>
</tr>
<tr>
<td>3.0</td>
<td>12</td>
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<tr>
<td>10.0</td>
<td>14</td>
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The results showed a significant decrease in the volume of gastric mucosal lesions. This may be correlated with the decrease in the total acid output of the stomachs

The authors gratefully acknowledge the generous supply of flupenthixol from the Sandoz Pharmaceutical Corporation.
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 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.

ACKNOWLEDGEMENTS

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REFERENCES


LETTER TO THE EDITORS

PRESSOR RESPONSE

Sir,

A volume/dose relationship of saline 9% Nacl administered between 5-7.5 kg anesthetized rats intraperitoneally (Fig.1). The pressor response is not new, however the changes in blood pressure has not been mentioned.

The pressor response is seen in the segment adjacent to the injection site. The pressor response is not new, however the changes in blood pressure has not been mentioned.