# EFFECT OF AUTONOMIC DRUGS ON THE STRESS INDUCED ACUTE GASTRIC ULCERATION IN RAT

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**Summary:** Stress ulcers were induced by subjecting rats to forced immobilisation and cold (4° to 7 °C) for 4 hrs. The nature of drugs which afford varying degrees of protection against such ulceration, bring out the complexity of the factors involved in the study of pathogenesis of acute gastric ulceration due to stress.

**Key words :** stress restraint acute gastric ulceration

## INTRODUCTION

Acute gastric ulceration and haemorrchage are common in a variety of clinical situations. The pathogenesis of these ulcerations is not clearly understood (2). Involvement of sympathetic nervous system in the pathogenesis of acute gastric ulceration has been reported (2,4,5.). The object of the present work was to study the effect of some autonomic drugs in prevention of stress induced acute gastric ulceration.

## MATERIALS AND METHODS

Albino rats of either sex weighing between 150 to 300 *gm* were included in this study. Animals were fasted for 24 hrs prior to the experiment. Only tap water was provided as libitum during this period. Animals were subjected to restraint and cold stress as reported by Senay and Levine (3).

Animals were immobilised by placing them individually in small, wide-mouthed glass bottles which provided adequate accommodation but did not allow any movement. These bottles were kept at 4° to 7°C in the refrigerator for 4 hrs.

Animals were sacrificed after 4 hrs by a blow on the head and by cutting both the carotid arteries. Abdominal cavity was opened and the stomach was quickly removed. It was opened along the greater curvature. The mucosa was washed with normal saline at room temp. and was inspected for the presence of ulceration and haemorrhage with the help of a magnifying glass.

Lesions were defined as erosions of the gastric mucosa at least 1 mm in diameter, the edges of which were sharply demarcated and their bases were red or black. Groups of animals were treated with one of the following drugs 30 min before exposure to stress. Reserpine was given 24 hrs before exposure to stress. Drugs used were adrenaline tartrate (1 and 10 $\mu g/kg$), atropine

salfate (1 *mg* and 10 *mg/kg*), ephedrine hydrochloride (1 *mg/kg*), carbachol (1 *mg/kg*), physostigmine salicylate (0.1 *mg/kg*), tolazoline hydrochloride (10 *mg/kg*), propranolol hydrochloride (5 *mg* and 10 *mg/kg*), reserpine (1 *mg/kg*), tyramine (1 *mg/kg*).

All the drugs were administered by intraperitoneal injection. Doses are mentioned in terms of salts.

## RESULTS

It was observed that 83.3% of rats subjected to cold and restraint for 4 hrs developed acute gastric ulceration and sometimes haemorrhage (Fig. 1). Acute gastric ulceration was observed in the glandular portion only. Perforation of the stomach was not observed in any of the animals.

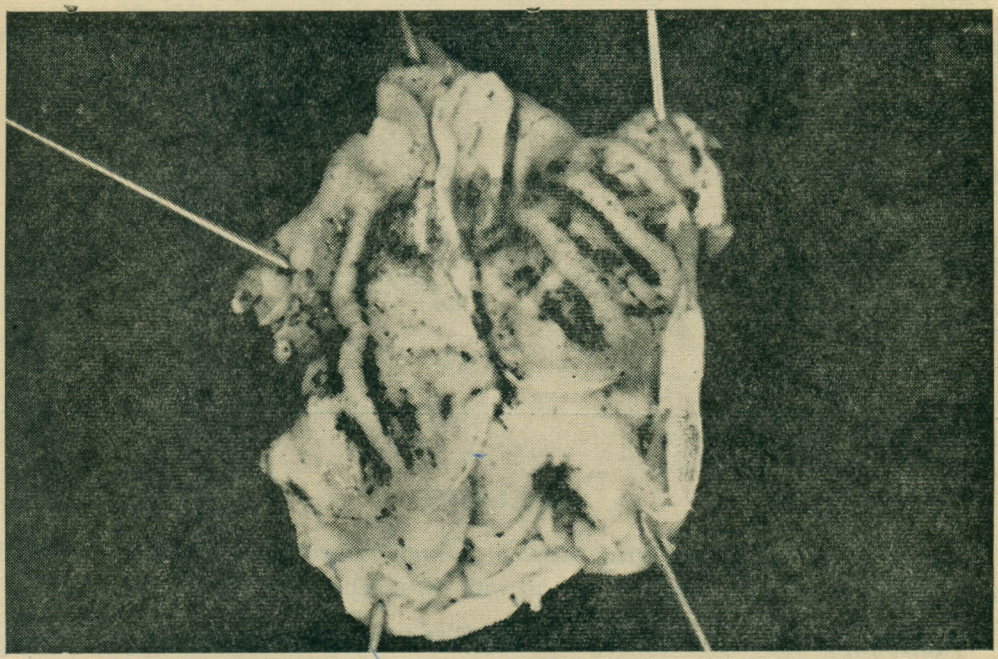

Fig. 1: Showing stress induced acute gastric ulceration in grandular part of the stomach.

Of the various drugs used, reserpine, tolazoline, propranolol, ephedrine, tyramine and atropine afforded varying degrees of protection against restraint and cold induced gastric ulceration. Consolidated results are shown in Table I.

Propranolol in 5 *mg/kg* dose did not afford any protection, but in a dose of 10 *mg/kg*, showed adequate protection.

Carbachol, physostigmine and adrenaline did not show any protective action against stress induced gastric ulceration.

TABLE I : Showing the effect of drugs on stress induced ulceration.

| *Sr. No.* | *Treatment* | *No. of rats used* | *No. of rats showing U+H* | *Percentage* |
|---|---|---|---|---|
| 1. | Control | 60 | 50 | 83.3 |
| 2. | Atropine Sulphate 1 *mg./kg* | 20 | 3 | 15.0 |
| 3. | Atropine Sulphate 10 *mg/kg* | 10 | 1 | 10.0 |
| 4. | Carbachol 1 *mg/kg* | 10 | 10 | 100.0 |
| 5. | Physostigmine Salicylate 0.1 *mg/kg* | 10 | 10 | 100.0 |
| 6. | Adrenaline Tartrate 10 *mg/kg* | 20 | 16 | 80.0 |
| 7. | Reserpine 1 *mg/kg* | 5 | 0 | 0.0 |
| 8. | Propranolol Hydrochloride 10 *mg/kg* | 10 | 2 | 20.0 |
| 9. | Tolazoline Hydrochloride 10 *mg/kg* | 10 | 2 | 20.0 |
| 10. | Ephedrine Hydrochloride 1 *mg/kg* | 10 | 0 | 0.0 |
| 11. | Tyramine 1 *mg/kg* | 10 | 0 | 0.0 |

U+H = Ulceration and Haemorrhage.

## DISCUSSION

The results show that synergism between restraint and cold is quite effective in producing acute gastric ulceration and are in agreement with those reported by Senay and Levine (3).

Reserpine, a well known ulcerogenic drug, which depletes the catecholamine stores in the body, effectively prevented acute stress induced ulcers. This paradoxical action may be purely due to its tranquillising action. Similarly, the alpha-adrenergic receptor blocking agent (Tolazoline) and beta-adrenergic receptor blocking agent, (propranolol 10 *mg/kg*) also afforded considerable degree of protection against stress induced ulceration. These results indicate the possible involvement of the sympathetic nervous system in the pathogenesis of stress induced acute gastric ulceration, and are in agreement with those of Djahanguiri *et al.*(2). Propranolol in smaller doses (5 *mg/kg*) however was quite ineffective. The indirectly acting sympathomimetic amines like ephedrine and tyramine also exhibited the protective action against stress induced ulceration. Their mode of action is not clear from this study, and may be related to a purely local vasoconstrictor action.

Atropine produced well marked protection against the stress induced ulceration, as indicated by our results and Brodie and Hanson (1). The fact that atropine afforded a significant degree of protection while carbachol and physostigmine were ineffective against the stress induced gastric ulceration, also substantiate the involvement of cholinergic mechanisms in the pathogenesis of the stress induced ulceration.

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