

within normal limits in pylorus ligated albino rats (10). It has also been observed by us that while bilateral adrenalectomy fails to prevent the fall in gastric tissue histamine concentration in animals under acute stress (7), parenteral injection of Betamethasone over a period of twelve days brings down gastric tissue histamine concentration to a very low level (14).

The present experiment was planned to study the late effect of bilateral adrenalectomy or subdiaphragmatic vagotomy on gastric tissue histamine concentration in albino rats.

MATERIALS AND METHODS

Animals : 42 healthy albino rats of either sex obtained from Sarabhai Research Centre, weighing 110–180 g, housed in separate cages were divided into five groups.

Experimental procedures: The animals in different groups were fasted for 24 hours; only water was allowed. The first group served as control. The animals under this group were sacrificed after the period of fasting by a blow on head and section of carotid arteries; their stomachs were removed, cleaned and processed for extraction of histamine and bioassay. The second and third groups of animals were subjected to mock subdiaphragmatic vagotomy and subdiaphragmatic vagotomy respectively. They were left in their respective cages and were carefully maintained for a period of 14 days by allowing food and water *ad libitum*. These animals were sacrificed on the fifteenth day, their stomachs removed and processed as in the first group for extraction and bioassay of histamine. The fourth and fifth groups of animals were operated for mock bilateral adrenalectomy and bilateral adrenalectomy respectively. While the animals in the fourth group were allowed food and water *ad libitum* following the operation, the animals in the fifth group received food and 0.9% saline. The animals were carefully maintained for a period of 14 days in their respective cages and on the fifteenth day of operation, they were sacrificed and their stomachs removed and processed as in the first group for extraction and bioassay of histamine. Extraction of gastric tissue histamine and its bioassay: After weighing the stomachs, they were cut into fine pieces in 2 ml per gram of N hydrochloric acid and ground up with a little previously cleaned and dried sand in a mortar. 10 ml of distilled water per gram of tissue was added during grinding. The extract was put in a flask and boiled for a minute. Just before assaying it was centrifuged and the supernatant neutralised with N NaOH and made upto a given volume (5). Histamine content was estimated by following a standard biological assay method. Each histamine estimation was carried out by using terminal portion of ileum of a 24-hour fasted medium

sized guinea pig in a thermostatic organ bath, temperature of which was kept constant at 37°C. Atropinized Tyrode's solution was used as bath fluid. The presence of histamine in the stomach extract was confirmed by mepyramine maleate with a dose of 0.2 ml 2.5x10⁻⁶M. Three point assay was performed following a fixed time schedule. Histamine concentration was calculated and expressed in micrograms per gram of tissue.

RESULTS

Gastric tissue histamine concentration in $\mu\text{g/g}$ of tissue under different experimental situations have been presented in histogram (Fig. 1). It can be seen that neither of the experimental situations of mock subdiaphragmatic vagotomy, subdiaphragmatic vagotomy or mock bilateral adrenalectomy could bring any significant change in gastric tissue histamine concentration in course of 14 days in comparison to the control level of 12.73 $\mu\text{g/g}$ of tissue.

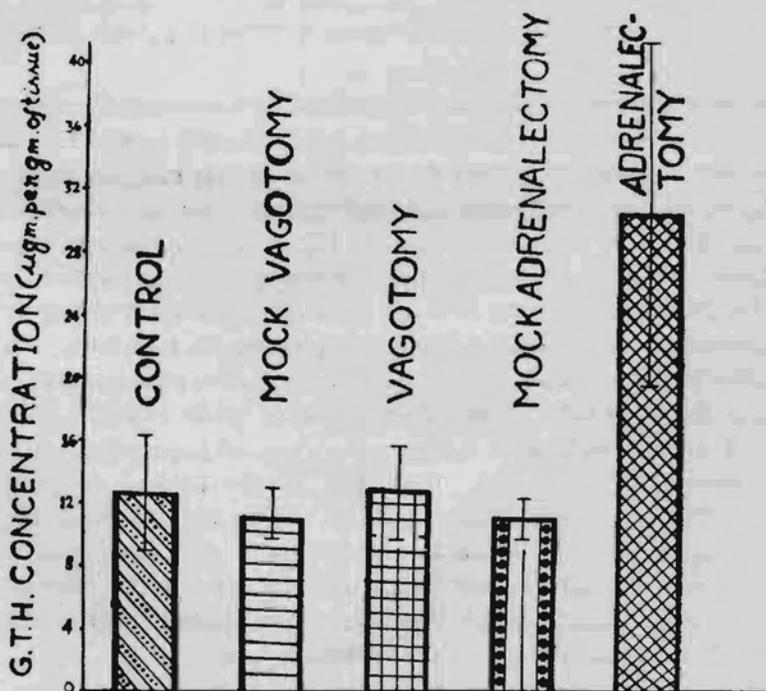


Fig. 1 : Histogram showing G.T.H. concentration in albino rats, 14 days after subdiaphragmatic vagotomy and bilateral adrenalectomy.

On the other hand, following bilateral adrenalectomy, gastric tissue histamine concentration went upto two and half times of the basal level during the period of 14 days, thus indicating that following bilateral adrenalectomy, possibly a rise in synthesis and storage of histamine took place in the stomach wall of albino rats.

DISCUSSION

Stimulation of oxyntic cells by histamine as a mediator for the secretagogue action of vagal discharge has been suggested (3). Metiamide, a H_2 receptor blocker has been shown to block the vagal response of gastric secretion (2). We have reported earlier that overactivity of vagus nerves in stress decreases the mast cell population possibly by releasing histamine from mast cells and thereby making them unstainable (13). Subsequent findings have confirmed this view as it has been observed that stimulation of vagal fibres leads to reduction of gastric tissue histamine concentration, the reduction being more with increased duration of stimulation (9). It has been further observed that subdiaphragmatic vagotomy when associated with pylorus ligation could prevent the fall in gastric tissue histamine concentration due to stress of pylorus ligation alone (18).

Since vagal stimulation releases histamine from stomach wall and subdiaphragmatic vagotomy under acute experimental situation preserves the normal histamine content of gastric tissue and in view of the fact that a rise in gastric mucosal mast cell population has been shown to occur following subdiaphragmatic vagotomy within 7 days in rats with or without stress of pylorus ligation (12,13), it is reasonable to expect an increase in gastric tissue histamine concentration following subdiaphragmatic vagotomy. But the result of the present experiment does not show any significant change in gastric tissue histamine concentration, 14 days after subdiaphragmatic vagotomy. It is likely that immediately after vagotomy as histamine releasing influence of vagus is removed, histamine stays bound to the mast cells, makes them stainable while normal turnover of mast cell continues which explains why there is increase in mast cell population in the gastric mucosa 7 days after subdiaphragmatic vagotomy. But, as the present result shows that the gastric tissue histamine concentration remains within normal limits 14 days after subdiaphragmatic vagotomy as in mock subdiaphragmatic vagotomy group, it appears that a tissue level adjustment takes place following subdiaphragmatic vagotomy in course of 14 days which brings gastric tissue histamine concentration back within normal limits. The nature of this adjustment needs to be investigated.

On the other hand, the result shows that following a period of 14 days after bilateral adrenalectomy gastric tissue histamine concentration went upto two and half

times to that of normal value. Our earlier observations (19, 20) show that bilateral adrenalectomy over a period of 5-15 days leads to an increase in gastric mucosal mast cell population while daily injection of Betamethasone over a period of 5 days decreases their number. Since mast cells are one of the probable sites for histamine synthesis in rat stomach, it is quite logical to think that gastric tissue histamine concentration would be more following bilateral adrenalectomy and less following injection of Betamethasone.

Earlier, we had demonstrated (14) that gastric tissue histamine concentration is reduced to a great extent following injection of Betamethasone daily over a period of 12 days. The result of the present experiment clearly demonstrates that adrenals have a long term influence in controlling the gastric tissue histamine concentration. In view of the observations (4,15) that histamine release from mast cells depends on level of extracellular glucose, Na^+ and H^+ concentration and also on the integrity of the cell metabolism and since the above changes are bound to develop following removal of adrenals, the rise in gastric tissue histamine concentration in the present experiment following bilateral adrenalectomy could be due to absence or release of histamine from the gastric wall and its accumulation thereby. But it seems improbable that such enormous rise (30.84 against the control value of 12.73 $\mu\text{g/g}$ of tissue) in gastric tissue histamine concentration can be explained simply by removal of adrenal's histamine releasing effect on cells; possibly the later effect is also associated with increase in synthesis of histamine in gastric wall.

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