INHIBITION OF MAST CELL POPULATION BY L-GLUTAMINE IN ASPIRIN-INDUCED ULCERATION IN RAT STOMACH

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Summary: The effects of an amino acid L-glutamine on aspirin-induced gastric lesions as well as on the mast cell population were studied in rats. L-glutamine had a pronounced inhibitory effect on gastric lesions produced by oral aspirin administration. Aspirin-induced increase in the mast cell population of the stomach was also prevented. Parenteral administration of aspirin did not produce any significant damage to the gastric mucosa.

Key words: aspirin, gastric ulcer, L-glutamine, mast cell

INTRODUCTION

The mast cells are an important source of histamine in the body and they occur in the submucosal as also between the muscular layers of the stomach (19). The exact mechanism of aspirin-induced gastric lesions is not known. It has been reported by various authors that aspirin produces gastric mucosal damage both in man and animals (4,5,6,20). In a preliminary communication, we have demonstrated that aspirin-induced gastric lesions in rats can be controlled effectively by oral administration of L-glutamine ten min before aspirin treatment (13), but the mechanism of this protection is not clear. The present investigation was undertaken to elucidate the role of mast cells in the aetiopathogenesis of aspirin-induced gastric lesions. Such studies may throw some light on the mechanism of inhibition of aspirin-induced gastric lesions by L-glutamine.

MATERIALS AND METHODS

Male albino rats weighing 120-160 g were used in four groups. The rats were fasted for 18 hr before use but were allowed free access to water. Both aspirin and L-glutamine were suspended in 1% carboxy methyl cellulose (CMC) and were given orally, through a stomach tube. The rats of group I (control) received only 1% CMC and those of group II received aspirin at a dose of 100 mg/kg. The animals of group III received L-glutamine (1 gm/kg), ten min prior to the administration of aspirin. The rats of group IV received aspirin (100 mg/kg.ip suspended in CMC. The drugs were diluted in such a fashion that the volume of CMC administered never exceeded 2 ml per rat. Four hr after aspirin administration during which time food and water had been withheld all the animals were killed by decapitation. The stomachs were removed, slightly distended oesophageal junction for fixation the stomachs were opened along was kept for histological examination stained with 0.1% toluidine blue.

For the determination of the ulcer index, the remaining portions of the stomach were expressed in terms of the total damage and degranulated mast cells.

Simultaneously the ulcer index of the remaining portions of the stomach was determined by a haemorrhage index (20x) with a square grid and the number of rats treated with the drugs was noted. Neither developed any gastric lesions when compared to animals in the control group.

Effect of L-glutamine on aspirin-induced gastric lesions and haemorrhages were determined at a dose of 1 gm/kg largely pre-aspirin (aspirin alone) was 52.87±12.27 (percent respectively. Following pre-treatment of rats by L-glutamine, the above groups, the percent degranulated mast cells were 47.9% and 47.6% respectively.

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were removed, slightly distended for 10 min by instillation of 1% formalin solution through the esophageal junction for fixation of the inner and outer layers of the gastric wall. Subsequently the stomachs were opened along the greater curvature and a portion of the glandular stomach was kept for histological examination. For visualization of mast cells the sections (10 μm) were stained with 0.1% toluidine blue solution (10).

For the determination of the mast cell counts in the stomach wall, three sections were made from each stomach and in each slide, eight fields were counted. The total number of cells and the relative percentage of intact and degranulated cells obtained in eight fields of three different sections was noted and the mean was determined. The counting was performed under a light microscope at a magnification of 400 with an optical micrometer and the results were expressed in terms of the total number of cells per mm² area and the percentage of intact and degranulated mast cells.

Simultaneously the ulcer index of the rats in four different groups was determined with the remaining portions of the glandular stomach according to the method of Okabe et al. (12). To determine the ulcer index, the length of the lesions was measured under a dissecting microscope (20x) with a square grid and the lengths (mm) were summed to give index for each rat. A number of rats treated with different doses of L-glutamine suspended in 1% CMC alone neither developed any gastric mucosal damage nor any deviation in the number of mast cells as compared to animals in the control group (unpublished observations).

RESULTS

Effect of L-glutamine on aspirin-induced lesions in rat stomach:

The results are summarized in Table I. As a result of aspirin administration, mucosal lesions and haemorrhages were observed in the glandular portion of stomach. L-glutamine at a dose of 1g/kg largely prevented these lesions (13). The ulcer index for animals in group II (aspirin alone) was 52.87±12.78 mm and that for the animals in group III (L-glutamine prior to aspirin) was 14.9±2.78 mm. Thus, L-glutamine produced 71.82% inhibition of the aspirin-induced gastric lesions in rats. A small number of lesions (ulcer index 15.7±4.1 mm) was observed in rats of group IV (aspirin 100 mg/kg, ip).

Effect of L-glutamine on the mast cell count of aspirin-induced ulcerated rat stomach wall:

The mast cell count of the stomach wall in the control animals was 26.2±1.5/mm² of which 43.9% were degranulated. Following the administration of aspirin, the mast cell count increased to 47.3±1.47/mm² of which about 80.35% of the cells were degranulated. In the above groups, the percentages of intact mast cells were 56.08±1.12 and 19.63±2.21 respectively. Following pretreatment with L-glutamine the mast cell count of the aspirin treated stomach was within normal limits (26.7±1.51/mm²); the percentages of intact and degranulated cells were 47.65±0.98 and 52.33±1.2 respectively. After ip aspirin the number
of cells/mm² area of the stomach was 30.7 ± 2.1 and the percentages of the intact and degranulated cells were 46.3 ± 2.23 and 53.69 ± 2.25 respectively (Table I).

Table I: Ulcer index and mast cell population of stomach in different groups of rats treated with aspirin.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ulcer index (mm±SD)</th>
<th>Mean* mast cell count (per mm²±SD)</th>
<th>Mean* percentage of degranulated cells (±SD)</th>
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<tr>
<td></td>
<td></td>
<td>intact</td>
<td>degranulated</td>
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<tr>
<td>I Vehicle only (n=9)</td>
<td>26.2 ± 1.5</td>
<td>56.08 ± 1.12</td>
<td>43.91 ± 1.3</td>
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<tr>
<td>II Aspirin (100 mg/kg, orally) (n=14)</td>
<td>52.87 ± 12.78</td>
<td>47.3 ± 1.47</td>
<td>19.63 ± 2.21</td>
</tr>
<tr>
<td>III L-glutamine (1 g/kg, orally) + Aspirin (100 mg/kg, orally) (n=14)</td>
<td>14.9 ± 2.78</td>
<td>26.7 ± 1.51</td>
<td>47.65 ± 0.98</td>
</tr>
<tr>
<td>IV Aspirin (100 mg/kg, ip) (n=8)</td>
<td>15.7 ± 4.1</td>
<td>30.7 ± 2.1</td>
<td>46.3 ± 2.23</td>
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</table>

P values: II : III < 0.01 II : IV < 0.2 I : II < 0.01 I : III < 0.001 I : IV < 0.01 I : III < 0.2 II : III < 0.01 I : IV < 0.001 I : IV < 0.001 II : III < 0.001

*Means of 6–9 observations.

DISCUSSION

L-glutamine (1 g/kg orally) administered prior to aspirin (100 mg/kg orally) inhibited gastric ulceration in rats. Furthermore, there was a rise in the number of mast cells and the proportion of degranulated cells in the rat stomach following aspirin treatment. The cellular changes were prevented by the prior administration of L-glutamine. Several authors have tried to produce gastric damage after sc (1), iv (3) and ip (2,11) administration of aspirin but in all these cases the gastric damage was not marked as was observed following oral administration. In our study too, ip aspirin was much less damaging both in terms of ulcer index and mast cell changes.

It is well known that the mast cells are responsible for the liberation of histamine to stimulate the oxyntic cells and finally through neural and endocrinal mechanisms there is an increased secretion of acid (6,17). Recently it has been established by Heap and Kiernan (8) that the basal secretion of acid is partially controlled by the level of circulating histamine, deriv-
The intact and degranulated rats treated with aspirin.

<table>
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<th>Mean*</th>
<th>degranulated</th>
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<tr>
<td></td>
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<tr>
<td>12</td>
<td>43.91±1.3</td>
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<tr>
<td>1</td>
<td>80.35±1.05</td>
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<tr>
<td>2</td>
<td>52.33±1.2</td>
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<tr>
<td>23</td>
<td>53.69±2.25</td>
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<th>I : II &lt; 0.001</th>
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<td>2</td>
<td>II : III &lt; 0.001</td>
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<td>1</td>
<td>I : IV &lt; 0.2</td>
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In the present investigation the percentage of degranulated mast cells in the stomach was significantly increased by aspirin, indicating that more histamine presumably was available for release in the aspirin treated animals. This may be an important factor responsible for the production of gastric changes following aspirin treatment. L-glutamine afforded almost complete protection. The rise in the mast cell count in the aspirin-treated rat stomach had some relationship with the ulcer index. Presumably, L-glutamine prevented the aspirin-induced changes in the gastric mucosa by inhibiting the liberation of histamine-like substances from the mast cells in the stomach wall.

ACKNOWLEDGEMENTS

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REFERENCES

Cadmium Induced Reproduction Changes

Summary: 1- Cadmium-induced single low dose administration liver glycogen levels were elevated sugar was at a low level. 3-7 days were conspicuous. 4- In contrast increased plasma cholesterol to translate these observations

Key words: cadmium chorine serum chol

The toxicity of cadmium is well known to have an abdominal pains and myalgia gastrointestinal processes including testicular (19, 20, 21) and accelerated

Cadmium is one of the most toxic elements known to man. Since the cadmium whether any disturbance of liver function disturbance of liver function to fifty five days period was the administration of cadmium or

Male adult langurs of weighed, numbered and maintained large canines and the patches on the rump have been considered wheat chapatty (unleaved broths) were provided with water ad

Cadmium chloride in a dose of 1.5 mg/kg body weight was administered intraperitoneally. On day 30 and 50 of


