ANTIULCER ACTIVITY OF AGNITUNDIRASA AND ITS COMPARISON WITH CIMETIDINE IN SHAY RAT

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ABSTRACT:Agnitundirasa was tested for antigastric ulcer activity in shay rat model. Oral dose of 10 mg/kg reduced the ulceration in shay rat. With 20mg/kg dose the ulceration was completely absent. The antigastric ulcer activity of agnitundirasa (20 mg/kg) was found to be equal to the effect produced by cimetidine (20 mg/kg). The reduction in gastric acidity was more with cimetidine and the reduction in peptic activity was more with agnitundirasa.

Introduction

The exact mechanism of gastric ulcer (also known as peptic ulcer) for mation is not yet clearly known even-though several factors are known to cause peptic ulcer1. Many groups of drugs are used in the treatment of peptic ulcer in allopathy. But majority of them do not cure the disease and give only temporary relief from the gastric pain. Drugs like cimetidine and ranitidine are claimed to heal the ulcers and are used in the treatment of benign gastric ulcer and duodenal ulcer2. According to Ayurvedic physicians ulcer formation is due to improper digestion of food and agnitundirasa pills are claimed to cure peptic ulcers by way of improving digestion. But there is no scientific proof to support such claim. Vaidya Yoga Ratnavali’ a formulary of Ayurvedic medicines contains a monograph on agnitundi vati’ and it is stated to be useful in loss of appetite, indigestion, dysentery and diarrhoea3. Ayurvedic formulations are relatively cheaper. They are also claimed to be less toxic. Hence the present study was conducted to test the antiulcer activity of agitundirasa and compare it with cimetidine in experimental ulcer model.

Materials and Methods

Agnitundirasa pills of a company that are used by the local Ayurvedic physician are purchased. The composition of each pill is as follows. Two salts, 5.4mg; three myrobalans, 5.4 mg each; mercury sulphur,aconite, sodium bicarb, yavakshar, plumbago, carum, ajmoda, cuminum, embelia, ginger, piper longum, piper nigrun, 1.8 mg each; nuxvomica, 32.5mg. the total weight of each pill is nearly 65.0 mg. the ingredients of the pill are nearly same as that described in Agnitundi vati of vaidya Yoga Ratnavali. Cimetidine and the contents of the pill were usspended in 1% carboxymethylcellulose (CMC) separately when required. Topfer’s reagent of Centron Research Laboratories, Bombay was used.

Studies in Shay rat

Albino rats of either sex supplied by B.N. Ghosh & co., Calcutta were used in our studies. Rats weighing more than 150 g were fasted for 72 hrs and those weighing less than 150 g were fasted for 48hrs4. The rats were allowed to take were ad libitum. Care was taken to avoid coprophagy. Phylorus ligation was
done under ether anaesthesia \(^4,5\). Drugs were administered soon after pylorus ligation orally. The control animals received 1% CMC suspension. One group received cimetidine 20 mg/kg in 1% CMC. Two pairs of animals received agnitundirasa in doses of 10 and 20 mg/kg body weight. There more animals were treated with 20 mg/kg agnitundirasa. The animals were maintained without food and water for 24 hours after pylorus ligation and were killed by spinal traction. The abdomen was opened, the oesophagus end of the stomach was also ligated and the stomach was isolated with its contents intact. The greater curvature of the stomach was cut longitudinally and the gastric juice was collected into a beaker. The mucosa was washed with 1 ml of distilled water and the washings were also collected into the beaker. Distilled water 9 ml was added to this and centrifuged. The volume of the supernatant was measured and aliquots were taken for analysis of the following parameters. The stomach mucosa was observed for ulcers after washing with a gentle stream of tap water.

Total acidity

A volume of 2 ml diluted gastric juice was titrated with 0.01 N sodium hydroxide run from a micro burette using phenolphthalein as indicator and the acidity was expressed as mg HCl/100 g body weight of the rat.

Free acidity

It is determined in a similar manner using Topfer’s reagent as indicator any sodium hydroxide was run until canary yellow colour was observed.

Peptic activity

The method of Lowry et al (1951) was used and the activity was expressed as µ mol Tyrosine/100 g body weight\(^6\).

Ulcer index

The method of Anderson and Soman (1965) was used for scoring the ulcer index\(^7\). For more than 30 ulcers or large areas of ulcers with confluence or impending perforation a score of 5+ was given by us. Haemorrhagic spots or pits were counted as ulcers.

Results

Cimetidine reduced the volume of gastric juice secreted. It significantly reduced the total acidity and free acidity. It also reduced the peptic activity. Agnitundirasa did not decrease the volume of gastric juice secreted. With 10 mg/kg dose of agnitundirasa the acidity, peptic activity and ulcer index were reduced. As this dose did not inhibit ulcer formation completely it was not tested on more animals. With 20 mg/kg dose the peptic activity was still reduced and the ulceration was completely inhibited. The reduction in acidity and peptic activity produced by 20 mg/kg agnitundirasa were statistically significant. All these results are shown in the table. The effect of the treatments were expressed as percentage of the control and are shown in the figure.
Discussion

The dose effect relationship of cimetidine on total acidity, free acidity, peptic activity and ulcer index was studied and only the results of 20 mg/kg dose were presented here as the anticulcer activity was found to be good with this dose. Several reports are found in the literature explaining the mechanism of antiulcer action of cimetidine. Black and his associates (1972) postulated that its H2 receptor blockade activity is responsible for its antiulcer activity\(^8\). Cimetidine antagonized pentagastrin, histamine and carbachol induced hyperacidity in gastric fistula rats\(^9\). It protects experimental animals from gastric ulceration induced by stress, pyloric ligation, aspirin and related compounds\(^10\). It antagonized the ulcerogenic activity of aspirin, oxyphenylbutazone and indomethacin. It enhanced PEG2 synthesis in rat\(^11\) and also reversed the indomethacin inhibited PEG2 synthesis\(^12\). From these studies it appears that cimetidine reduces gastric acidity and ulceration by reduced cholinergic activity, reduced histaminergic mechanism by H\(_2\) receptor blockade and by enhancement of prostaglandin synthesis.

TABLE 1: Effect of Agnitundirasa and Cimetidine in Shay Rat.

| Treatment            | VGJ | TA         | FA       | PA            | UI         |
|----------------------|-----|------------|----------|---------------|------------|
| Vehicle‡‡ (Control)  | 3.12| 14.38±1.76 | 2.81±0.33| 1821.60±160.34| 4.2±0.37   |
| Agnitundirasa 10 mg/kg‡ | 7.53| 0.88       | 1390.80  | 2.0+          |
| 20 mg/kg ‡‡          | 31.0| 7.84*±1.15 | 0.99**±0.41| 1097.54**±89.81| ----     |
| Cimetidine 20 mg/kg‡‡ | 1.50| 2.80***±0.18| 0.34***±0.17| 1465.18±157.53 | ----     |

VGJ : Volume of gastric juice (ml); TA: Total acidity;
FA : Free acidity (TA and FA HC 1/100 g body weight);
PA : Peptic activity (µ mol tyrosine/100 g body weight;
UI : Ulcer index; --- : No ulcer;
‡ : Average of 2 experiments; ‡‡: Average of 5 experiments;
* : P< 0.05; **: P<0.01; ***: P<0.001
Agnitundirasa does not seem to interfere with the secretion of gastric juice as it did not reduce the volume of gastric juice secreted. It may be inhibiting ulcer formation by way of reducing acidity and peptic activity of the gastric juice secreted (table and figure). The presence of sodium bicarbonate and two other salts (details not given) may be responsible for the reduced acidity. The presence of mercury may be partly responsible as mercuric acetate is reported to decrease acid secretion\textsuperscript{13}. The ingredients like ginger, piper longum, piper nigrum, cuminum are known for their carminative activity. Myrobalans which contain tannic acid exhibit astringent action. The major ingredient of the formulation is nuxvomica. It is known for its bitter action on secretory activity. Studies are in progress to find out the role of these carminatives, astringents and bitters in the prevention of peptic ulcer formation. Contrary to the popular belief of improving digestion, agnitundirasa was found to reduce peptic activity and acidity with 20 mg/kg dose and inhibit peptic ulcers in shay rat. Its ulcer inhibiting activity is very significant and was equal to the activity produced by 20 mg/kg dose of cimetidine in shay rat.
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