Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

Research Paper

COMPARITIVE STUDY OF ANTI ULCER EFFECT OF ALOE VERA, OMEPRAZOLE AND RABEPRAZOLE IN ASPIRIN INDUCED PEPETIC ULCERS IN GUINEA PIGS.

Venitary Science

KEYWORDS : Aloe vera, peptic ulcer, Aspirin, Omeprazole, Rabeprazole, PPIs (Proton pump inhibitors), g.i.t. (gastro intestinal tract)

Dr. ASHUTOSH KUMAR SINGH — Gold Field Institute Of Medical Sciences & Research. (Asst.Prof., Department of Pharmacology) Village. Chhainsa, Ballabhgarh, Faridabad-121004

B. KAVITHA — Gold Field Institute Of Medical Sciences & Research. (tutor, Department of Pharmacology) Village. Chhainsa, Ballabhgarh, Faridabad-121004

ABSTRACT

Comparitive study of anti-ulcer effect of Aloe vera, Omeprazole and rabeprazole in Aspirin induced peptic ulcers in guinea pigs. SUB TITLE: To study and compare the anti ulcer effect of Aloe Vera, Omeprazole and Rabeprazole in Aspirin induced peptic ulcers in Guinea pig. SUMMARY: This study was performed to compare the Anti-ulcer effects of Aloe vera, Omeprazole & Rabeprazole on Aspirin induced peptic ulcers in Guinea pigs of either sex weighing between 400 – 600 gm were randomly allotted into four groups with six animals each. Aspirin 200 mg/kg- body weight was administered orally and kept fasting for 6 h. A. vera powder was mixed with gum acacia, the solution was administered orally through the oral gavage to guinea pigs in the dose of 200 mg/kg. Omeprazole 3.5mg/Kg, Rabeprazole 2.5-mg/kg body weight was administered orally as a standard drug for present study. At the end of the study, ulcer index were studied. The significance of difference between means of control and treated groups were determined by one- way analysis of variance (ANOVA) test.

INTRODUCTION

Peptic ulcer disease is a common worldwide problem[2]. Peptic ulcer is a chronic disease. Peptic ulcer occurs in that part of the g.i.t. which is exposed to gastric acid and pepsin. It results probably due to an imbalance between the aggressiae(acid, pepsin, bile and H. pylori) and the defensiae(gastric mucus and bicarbonate secretion,prostaglandins, nitric oxide, innate resistance of the mucosalcells)factors1.Taking notice of the increase in peptic ulcer, particularly in India and other developing countries, the aim of drug therapy in peptic ulcer is to afford symptomatic relief of abdominal pain and neutralization of excess acid and to promote healing of ulcers and to prevent its recurrence. Apart from dietary manipulation, bed rest and prohibition of smoking, many drugs are now in use for the treatment and prevention of peptic ulcer but PPI's (Omeprazole, lansoprazole,pantoprazole, rabeprazole are first line drugs. The present study was undertaken to compare the Anti ulcer effect of PPIs and Aloe vera.

Materials & methods:

Guinea pigs of either sex weighing between 400-600gm were used for the study. The study was performed in the Department of Pharmacology after obtaining approval from institutional Animal Ethics commiittee. Animals were randomly allotted into four groups with six animals each. First group was taken as Aspirin induced peptic ulcer group, second group was taken as Aspirin+Aloe vera, third group was Aspirin+Omeprazole, Fourth group was Aspirin+Rabeprazole. Guinea pigs were administered Aspirin 200mg/Kg orally and fasted for 6hrs. Aloe vera powder was mixed with gum acacia and diluted with distilled water. The prepared solution was administered 20mg/Kg orally through the gavage to guinea pigs.(Subramanian et al., 2007). Omeprazole was used in dose of 2.5-mg/kg body weight, i.e. 1.25 mg to each guinea pig of 3rd group. Rabeprazole was used in the dose of 2.5-mg/kg body weight, i.e. 1.25 mg to each guinea pig of 4th group **(Veterinary pharmacology & Toxicology, 2nd edition).** First Aspirin 200 mg/kg- body weight was administered orally and kept fasting for 6 h. To each group of animals required dose of drugs was given orally in the empty stomach in the morning daily (7:00- 8:00 am) for 7 days continuously. Drugs were administered in the stomach of animals through syringe, as the guinea pig's soft palate is continuous with the base of the tongue with only a small opening known as palatal ostium. This makes passage of a feeding needle very difficult. On the 7th day, all animal of each group were sacrificed by stunning, abdomen was opened in midline and stomach with duodenum was removed. The stomach and duodenum were cut through greater curvature and it was washed with physiological saline. Inner surface of stomach and duodenum were examined for ulcers.

Ulcer Index:

After administration of drugs, ulcers of various size and shapes accompanied by intense hyperaemia and edema were counted, and the ulcerative index (UI) in mm was calculated as:

UI= (n lesion I) + (n lesion II) X2 + (n lesion III) X3

Where, **I** = presence of edema, hyperemia and single, submucosal punctiform hemorrhages (petechiae)

II = presence of submucosal, hemorrhagic lesions with small erosions

III = presence of deep ulcer with erosions and invasive lesions **(Szelenyl and Thiemer, 1978).**

Statistical analysis: Data were expressed as mean ± SEM. Statistical analysis was done using ANOVA test.

RESULTS: The gastric ulcer control group presented with features of ulceration. On gross examination, serosal surface of stomach showed marked indurations, dilated blood vessels, ecchymosis and hemorrhagic sites (Fig.No.1). Mucosal surface presented with features of severe degree of hyperemia, congestion and large number of pin point ulcers of varying sizes with central clots and features of perforation in the stomach. The ulcer index U.I ± SEM were calculated for each group of animals.U.I±SEM for Aspirin group is24±0.69, it is reduced to 18.33±0.56 with Aloe vera, to 16.33±0.63 with Omeprazole and to 13.16±0.80 with Rabeprazole. Gross features were depicted in these photographs .

Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

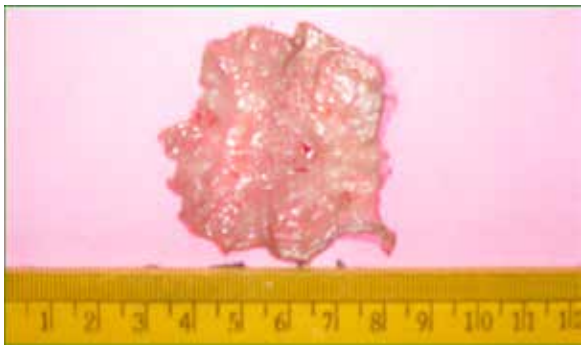


Fig.No. 1 – Photograph showing Aspirin induced ulcers in Guineapigstomach.

Fig. No. 2- Photograph showing Aloe vera treated Guinea pig stomach.

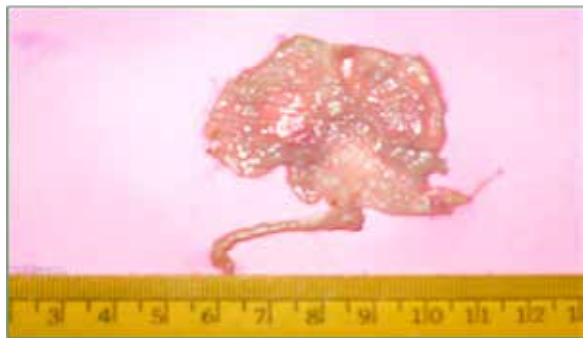


Fig. No. 3- Photograph showing Omeprazole treated Guinea pig stomach.

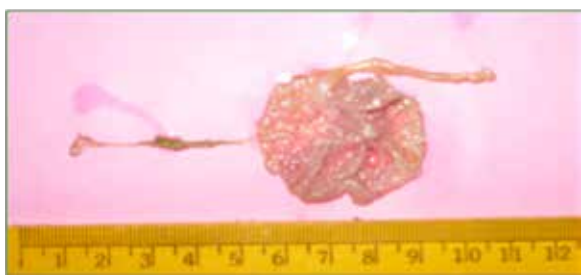


Fig. No. 4- Photograph showing Rabeprazole treated Guinea pig stomach.

Table. 1: Ulcer index of guinea pigs measured for 4 groups

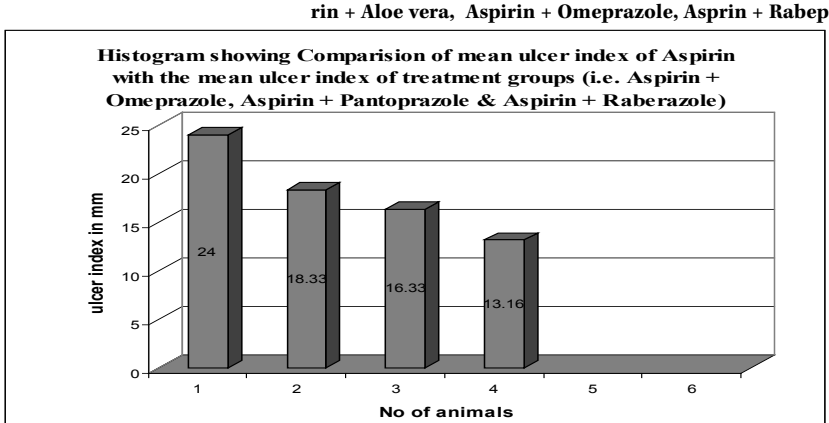
Ulcer index(m.m) for	Guineapig 1	Guineapig 2	Guineapig 3	guineapig 4	Guineapig 5	Guineapig 6	Mean(M)
Group-1	23	20	28	25	21	27	24
Group-2	19	16	18	20	19	18	18.33
Group-3	16	17	14	16	18	17	16.33
Group-4	15	13	16	11	15	13	13.16

Table.2: Mean (M), standard deviation (S.D), Standard Error (S.E), Probability (p) value for 4groups

GROUP	Dose Mg/kg	S.D	Ulcer-index ± SEM	p value
1 (Aspirin)	200mg/Kg	1.70	24±0.69	<0.05(significance)
2 (Aspirin + Aloe vera)	200mg/kg + 20mg/kg	1.36	18.33±0.56	<0.05(significance)
3 (Aspirin + Omeprazole)	200mg/kg + 3.5mg/kg	1.54	16.33±0.63	<0.05(significance)
4 (Aspirin + Rabeprazole)	200mg/kg + 2.5mg/kg	1.97	13.16±0.80	<0.05(significance)

By using one-way ANOVA D.f. = 3.10
F = 26.01 ,
p = <0.05, *so the result is considered to be significant.*

Table. 3 : Histogram showing comparison of Mean ulcer index of Aspirin with the mean ulcer index of treatment groups (Aspirin + Aloe vera, Aspirin + Omeprazole, Asprin + Rabeprazole)



DISCUSSION:

The primary objective of the work was to undertake the study of well known anti-ulcer drugs already used therapeutically and a herbal drug - Aloe vera to prevent or minimize the ulcerogenic effect of aspirin. The result shows that aspirin is capable of producing gastric ulcerations. The dose used to produce these ulcers was very high as it was intended to produce ulcers in all animals. The anti-ulcer drugs omeprazole, rabeprazole and Aloe vera succeeded in giving significant protection in animals when they were used simultaneously with aspirin.

Normally ulcers do not occur in the stomach even through the two substances, acid and pepsin, which are potential aggressive forces capable of damaging the mucosa, are always associated with normal physiology of stomach. So the gastric mucosa must have some inbuilt protecting mechanisms, which prevent ulcer formation and this protecting mechanism must be somewhat disturbed before ulcer is formed. Once the mucosa is damaged and ulcer is formed, it is maintained by acid and pepsin.

According to **Flenstom and Turnbery(1984),** the basic cause of peptic ulcer is imbalance between the rate of acid and pepsin secretion in gastric juice and degree of protection afforded by the gastro-duodenal mucosal barrier. The mucous cells of gastric lining secrete viscid and adherent mucus and the very tight intercellular junction of gastric epithelial cells constitute the gastric mucosal barrier. **Graham (1986), Jaszewky (1990) and Kurata (1990)** have reported that this gastric mucosal barrier is disrupted by ingestion of aspirin. **Grossman (1961)** has shown that faecal blood loss can occur after parenteral administration of aspirin in man.

Peirson et al (1961) showed that the quantity of blood loss is dose dependent and is also related to frequency of drugs administration. Aspirin inhibits prostaglandin synthesis by an action on enzyme prostaglandin synthetase. Prostaglandin exerts a cytoprotective effect on gastric mucosa **(Guth et al, 1979).** Prostagladin depresses gastric secretion and produce gastric mucosal vasodilatation. Inhibition of prostaglandin synthesis could result in vaso-constriction leading to ischemic damage with ulcerations.**Warren and Marshall (1983)** have pointed out that in more than 75% of patients suffering from duodenal ulcer, there is a significant association between gastritis due to campylobacter pylori and duodenal ulcer.

The main targets of medical therapy of peptic ulcer are relief of pain, promotion of ulcer healing and prevention of ulcer recurrence. This work is also done to evaluate the prophylactic efficacy of anti-ulcer drugs; omeprazole, pantoprazole and rabeprazole. All these drugs are suppose to reduce gastric secretion, which will contribute in prevention of ulcer formation. **Howberg CJ et al (1986)** has suggested that inhibition of acid secretion is the best strategy to reduce gastric mucosal damage and bleeding.Omeprazole is the first anti-secretary drug studied in a clinical trail to produce a sustained reduction of gastric acidity for 24 hours after a single dose.

Lindsberg et al (1987) have studied the inhibitory action of omeprazole on acid secretion and found that it markedly inhibits both basal and stimulated gastric acid secretion. **Massino Claar G et al (1998)** concluded in their clinical trial that both standard and high dose of Omeprazole are equally safe and effective regiments for the treatment of NSAID induced gastrointestinal ulcers when anti- inflammatory treatment is not discontinued.**Miner P (2005)** is one of his articles depicted that Rabeprazole is a newer generation proton- pump inhibitor that suppresses the gastric proton pump and acid secretion more rapidly than dose omeprazole, lansoprazole or pantoprazole.

The antiulcer activity of *A. vera* is due to its anti-inflammatory (Robert et al., 1979), cytoprotective (Mahattanadul, 1995), healing (Teradaira et al., 1993) anti oxidant activity and mucus stimulatory effects (Visuthipanich, 1988). *A. vera* has anti-inflammatory effects of leukocyte-endothelium interaction in the gastric microcirculation of *H. pylori* infected rats (Prabjone et al., 2006). The observation that *A. vera* extract inhibits acid secretion may be due to the presence of lectins in the plant (Blitz et al., 1963). Lectins are proteins/glycoproteins which are capable of recognizing and binding to carbohydrate moieties (Bardocz et al., 1995). It has been shown that lectins inhibit aminopyrine uptake by parietal cells (Healey et al., 1998). Thus, the ability of the extract to inhibit gastric acid output maybe as a result of direct action on the acid producing cells. Administration of *A. vera* enhance mucous resistance and resulted in decrease of ulcer index and ulcerated surface. *Aloe buettneri* extract increased gastric mucus production (Kossi et al., 2011).

The cytoprotective action of *A. vera* may be due to its active ingredients like tannins, saponins and flavonoids (Rajasekaran et al., 2005a). The proton pump inhibitor, omeprazole is having a mechanism of action on the development of acute ulcers and accelerate the healing of preexisting ulcers appears to be mainly due to it's potent and long lasting antisecretory activities (Osamu, 1984). This study suggest that *A. vera* possess cytoprotective effects and acid reducing effects like omeprazole.

CONCLUSION: The main aim of this experimental work was to compare the prophylactic efficacy of Aloe vera, Omeprazole and Rabeprazole when used concurrently with aspirin. Therefore, to the second, third, and forth groups of animals these drugs were used respectively along with aspirin. The dose of all drugs were given on the basis of body weight of the animals. To the second group animals, Aloe vera significantly reduced the ulcerogenic effect of Aspirin and the ulcer-index was reduced to 18.33mm as compared to Aspirin used alone. *A. vera* showed statistically significant anti-ulcer activity comparable to standard drug. Therefore, the results were suggestive of anti ulcerogenic activity of *A. vera*. However, the cellular mechanisms for these actions remain to be established. To the third group of animals, omeprazole significantly reduced the ulcerogenic effect of aspirin. The ulcer-index was reduced to 16.33mm as compared to aspirin used alone. To the fourth group of animals, Rabeprazole significantly reduced the ulcerogenic activity of aspirin. The ulcer index was 13.16mm as compared to aspirin used alone The ulcer-index with rabeprazole is also lesser than that of Aloe vera & omeprazole. The mean ulcer indexes of three drugs are formed to be statistically significant (P value is < 0.05).

Finally, it can be concluded that herbal drug Aloe vera and proton pump inhibitors-Omeprazole and Rabeprazole has prevented the ulcerogenic effect of aspirin effectively, although, not completely. The treated ulcer-index was slightly more with Alo vera than Omeprazole and least with Rabeprazole.

Volume : 3 | Issue : 10 | October 2014 • ISSN No 2277 - 8179

REFERENCE

Szelenyl and Thiemer. Distention ulcer as a model for testing of drugs for ulcerogenic side effects. Arch Toxicology 1978, 41 : 99-105. | | Graham DY, Smith JL and Dobbs SM. Gastric adaptation occurs with aspirin administration in man Dig. Sci, 1983, 28:1-6. | Grossman MI. A new look at peptic ulcer. Ann. Inern. Med. 1976,84: 57. | Goodman and Gillman. 10th edition, 2001, pp-698. | Lanas A, Sekar NC, Hirschowitz Bl. Objective evidence of aspirin use both in ulcer and on ulcer upper and lower Gl bleeding. | Massinro Clear G, Monaco S, Delrecho Blanco E, Capursol, Fussillo M, Annibale B. Omeprazole 20 or 40 mg daily for healing gastro-duodenal ulcers in patients receiving NSAIDs, Aliment pharmacol Ther, 1998 May, 12 (5) : 463-8 | Rang HP and Dale MM. proton pump inhibitors (Omeprazole) pharmacology 2nd ed. (1991) chapter 19 | Rodenck PJ, Wilkis HC, Meade TW. The gastro-intestinal toxicity of aspirin ; an overview of randomized control trials. British journal of clinical pharmacology 1993, 35 : 219-226. | Blitz J, Smith J, Gerard J (1963). Aloe vera gel in peptic ulcer therapy: preliminary report. J. Am. Osteopathic Asso., 62: 731-735. | Yagi A, Shibata S, Nishioka I, Iwadare S, Ishida Y (1982). Cardiac stimulant action of constituents of Aloe saponaria. J Pharm Sci., 71: 739-741. | Kossi M, Kwashie E, Amégnona A, Kodjo A, Aklikokou MG (2011). Gastro protective Effect of Hydro alcoholic Extract of Aloe buettneri. IJPR, 10(1): 69-74. | Scheiman JM. NSAID : cytoprotection and gastro-intestinal injury. Gastroenterol Clin North Am 1996, 25 : 279. | Schoen RT, Vender RJ. Mechanism of NSAIDs induced gastric damage. Am J Med 1989, 86 : 449. | | Warren JR and Marshal RJ. Unidentified curved bacillion gastric epithelium in active chronic gastric. Lancet, 1983, I : 1273-5. | Vani Prasad. Veterinary pharmacology & Toxicology , 2nd edition, 2001. |