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Original Article

Effect of Vitamin E on Indomethacin Induced Gastropathy in Mice

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Abstract

Background:To evaluate the effect of indomethacin on gastric mucosa of mice and to study the effect of Vitamin E on Indomethacin treated gastric mucosa.

Methods: In this experimental study 48 adult male mice were randomly divided into four groups ,comprising of 12 mice each. Group A was labelled as the control group. Evion 400mg/kg was given to group B. Indocid 25mg/kg was administered to group C. Combination of Indocid and Evion (25mg/kg & 400 mg/kg respectively) was given to group D. Dose was administered for three days to 6 mice of each group and for eight days to other 6 mice. Their body weights at the beginning and end of experiment were noted. Stomach was dissected, washed and fixed. The histological parameters observed were epithelial integrity and haemorrhage.

Results: In group A and B findings were normal. Weight of animals in group C was significantly decreased as compared to group D (p-value<0.05). Disturbed integrity of gastric mucosa and haemorrhages were seen in group C.

Conclusion: Indomethacin produced gastric ulcers were decreased by giving Vitamin E in mice.

Keywords: Peptic Ulcer Disease (PUD), Vitamin E, Gastric mucosa, Indomethacin

Introduction

Peptic ulcer disease is characterized by ulcers and sores in lining of stomach or duodenum.[1] Gastric mucosal defence constitutes a layer of mucus, bicarbonate, proteins and prostaglandins and hinders back diffusion of pepsin and acid.[2]

Indomethacin (NSAID) is a drug having analgesic and antipyretic activity.[3] Indomethacin induced gastric mucosal lesions are associated with decreased prostaglandins.[4] Indomethacin directly kills gastric epithelial cells by interacting with them. It reduces mucus and bicarbonate secretion which helps in protecting the epithelium. Mucus and bicarbonate secretion is stimulated and gastric acid secretion is inhibited by prostaglandins.[5] Mucosal defence is impaired by reduction in prostaglandin and mucus secretion and increased secretion of acid resulting in production of ulcer.[6]

Vitamin E is a lipid soluble antioxidant having anti-inflammatory effects.[7] Vitamin E elevates the synthesis and secretion of prostaglandins by activating enzymes.[8]

Materials and Methods

This animal interventional study was conducted in King Edward Medical University, Lahore. Duration of experiment was 23 days. Experimental animals Swiss albino mice were obtained from Veterinary Research Institute, Lahore and were shifted to Post Graduate Medical Institute Lahore. Forty eight adult male mice were randomly divided into four groups A,B ,C and D comprising of 12 mice each. These four groups were subdivided into subgroups A1, A2, B1, B2, C1, C2, D1 and D2 having six mice each. Cages were labelled as A, B, C and D according to groups of mice. 25mg/kg body weight of Indocid was given each day. Ground powder of one capsule of Indocid was mixed with 2ml of distilled water to make a stock solution. 400mg/kg body weight of Vitamin E was given each day. One capsule of Evion was mixed with 2ml of corn oil to prepare stock solution. Feeding tube was used to administer Evion and Indocid suspension. Daily dose of Indocid and Evion was calculated as :Dose (in ml) = 0.002 x Wt (Wt = weight of the animal in gm)

Group A was labelled as the control group. Evion 400mg/kg was administered to Group B. Indocid 25mg/kg and combination of Indocid and Evion (25mg/kg & 400 mg/kg) was given to Group C and Group D respectively. A1, B1, C1 and D1 were given dose for 3 days and A2, B2, C2 and D2 for 8 days. The body weight of each animal was recorded at the start of experiment by digital balance in order to calculate the dose. It was recorded daily till the end of experiment before they were sacrificed.

After 24 hours of last dose the animals were sacrificed. Incision was made along the lesser curvature of

stomach. Stomach was washed with normal saline. Stomach from different subgroups were fixed in 10% formalin in pre-labeled containers. Body of stomach was separated from pylorus by cutting transversally into two halves. For microscopic study 2X4 mm measuring strips were separated from pyloric region and histological parameters were studied. Gastric epithelium was observed under 4X as well as 10X to look for its integrity. Haemorrhages were observed in experimental groups at magnification of 10X and 40X objectives.

Results

Mean weight of the animals at the end of study was slightly increased in A, B and D groups but it was significantly reduced in subgroups C1 and C2. The mean body weight of C1 in start of experiment was 25.83±3.81gm whereas at the end it was 22.07±1.87gm. Mean weight in C2 at the start was 24.16±1.72gm and 21.42±1.77gm at the end of experiment (Fig 1).

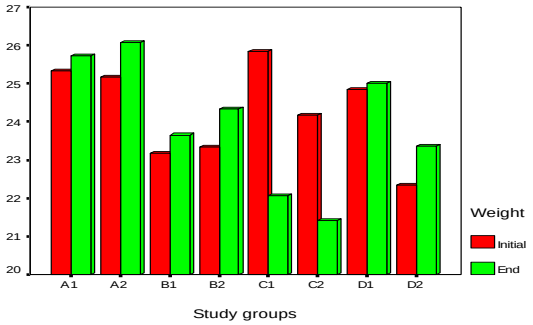

Fig. 1: Comparison of weight of mice (beginning vs. end) in study groups.

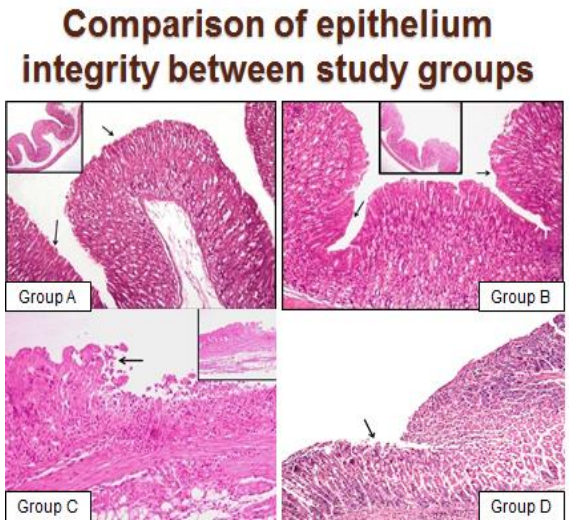

Figure 2. A photomicrograph of pyloric part of stomach showing epithelium in study groups. (H&E stains, Magnification 100X)
Group A. Intact epithelium;Group B. Intact epithelium;Group C. Disrupted EpitheliumGroup D. Disrupted epithelium

Colour page

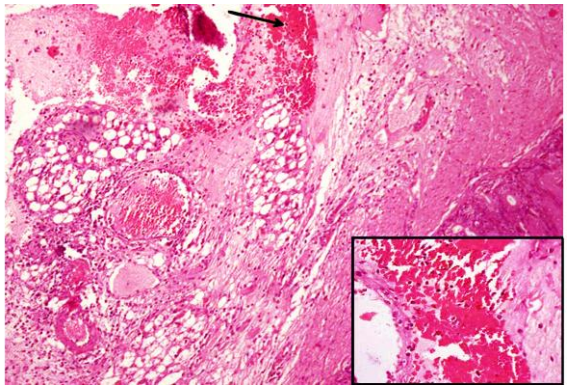

Figure 3: A Photomicrograph of stomach pylorus showing haemorrhage in group C (H&E stain, Magnification 900X):Black arrow: Serosal haemorrhage

Slight increase in weight was seen in group D with the exception of 2 animals in each subgroup D1 and D2 (Fig.1).Mean weight at the start in subgroup D1 was 24.83±2.92gm and at the end it was 25.02±2.98gm. In D2 the mean weight at start was 22.33±1.75gm while at the time of sacrifice it was 23.37±1.49gm (Fig.1)

In histological studies epithelial integrity was intact in all mice in subgroups A1, A2, B1, and B2 (Fig. 2). Epithelium was disrupted in all subjects of C1 and C2. Denuded mucosa was also seen in the lumen (Fig. 2). Intact epithelium was observed in 4 subjects of D1 and D2 each but was disrupted in 2 subjects of D1 and D2 each (Fig. 2).Haemorrhage was seen in only one specimen of C1 and C2 each (Fig. 3)

Discussion

Indomethacin produces gastric ulcers in humans and animals.[9] Supplementation of diet with Evion enhances the gastric mucosal barrier.[10] The reduction in weight of mice with Indomethacin is consistent with the findings carried out by Elahi et al in 2009.[11] Koch et al also noted weight loss with indomethacin in their study.[12] A study carried out in 2011 showed that Vitamin E treated animals had a consistent increase in body weights. Mean body weights in vitamin E group at end of experiment were statistically higher ($p < 0.05$) compared to the values obtained at the beginning.[13] Histological examination revealed that epithelial integrity was disrupted in experimental group given Indomethacin while it was intact in most of group given Evion along with Indomethacin. Vitamin E increased the levels of mucus phospholipids in the epithelium.[14] It was suggested that Indomethacin caused desquamation of the epithelial cells along with the disarrangement of mucosal layer of stomach.[15]

This study is in accordance with a study carried out in 2006 which suggested that Indomethacin produced gastric lesions by inhibiting prostaglandin biosynthesis and increasing acid secretion.[16] It was also concluded in a study, that Indomethacin damages the cell membranes of epithelial, parietal and endothelial cells.[17] These findings were similar to previous studies suggesting that vitamin E intake strengthen the gastric mucosal barrier and decrease the lipid peroxidation in membranes.[18]

There was serosal haemorrhage in one case each in C1 and C2 subgroups (Figure 3). Present finding did not coincide with the findings of Park and Chang who reported haemorrhage in the lamina propria.[19] Damage to mitochondria at the site of local or systemic concentrations of Indomethacin resulted in mucosal integrity, ulceration and haemorrhage.[20]

Conclusion.

1.Indomethacin administration not only caused mean decrease in weight of animals, there was also disruption of epithelial integrity. Serosal haemorrhage was also observed in one case.

2.The present study manifest protective outcome of vitamin E on gastric mucosal injury by increasing secretion of prostaglandins.

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