Research Article

Gastric antiulcer activity of melatonin and its potentiation by pyridoxine in pylorus ligated rats

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Abstract

Aim: To study the gastric antiulcer activity of melatonin and its potentiation by pyridoxine in pylorus ligated rats. **Methods:** Eighteen healthy albino rats were divided into three groups of six each. Group A received normal saline, Group B received melatonin (15mg/kg/day) and Group C was given melatonin and Pyridoxine (0.3mg/kg/day). Drug treatment was continued orally for 2 wks and at the end animals were starved for 36 hours. pylorus ligation was carried out under ether anesthesia. After 18 hours of pylorus ligation, all the animals were sacrificed and their stomachs were removed. **Results:** The volume of secretion, PH and ulcer index was noted in all the three groups. Melatonin showed reduction in acid secretion, ulcer index and rise in PH and its effect was potentiated by pyridoxine. **Conclusion:** It appears that the anti ulcer activity of melatonin may be due to its anti-oxidant property. The protective effect of melatonin has been further potentiated by pyridoxine, which may enhance the synthesis of endogenous melatonin.
Keywords: Melatonin pyridoxine ulcer index pylorus ligation.

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INTRODUCTION

Peptic ulcer disease is a major health problem with multifactorial etiology. The development of gastric ulcer occurs with acid and the breakdown of mucosal defense. Local mechanisms implicated in mucosal defense are mucousal alkaline secretion, mucosal hydrophilicity, rapid epithelial cell renewal, rich mucosal blood flow, mucosal sulphydryls, and increased resistance of gland cells in deep mucosa to acid and peptic activity[1]. Endogenous antioxidants are now being utilized to combat acute stress[2]. Melatonin, a neurohormone is a potent endogenous antioxidant[3]. It promotes the formation of reduced glutathione, which is the major antioxidant in the GIT mucosa[4]. The present study was undertaken to evaluate the anti ulcer activity of melatonin against acute gastric ulcers induced by pyloric ligation. It was also aimed to find out whether pyridoxine, a co enzyme in the synthesis of endogenous melatonin, potentiates the anti ulcer activity of melatonin[5].

MATERIALS AND METHODS

Wistar strain albino rats of either sex weighing 200-250 gms were kept in the department animal house at room temperature (25^0-30^0 c) and were fed on regular laboratory diet (standard pellet diet) with water ad libitum. Eighteen rats were divided into three groups six in each. Group A (n=6) served as control and was given normal saline. Group B (n=6) was given melatonin (15mg/kg/day) and Group C (n=6) was treated with both melatonin and pyridoxine (0.3 mg/kg/day) All the drugs were given orally. The treatment was continued for a period of 36 hrs and kept in raised mesh bottomed cages to avoid coprophagy. Pyloric ligation was performed for all the rats as described by shay *et al*[6]. Under ether anesthesia, the abdomen was opened by a small midline incision below the xiphoid process. The pyloric portion of the stomach was identified, slightly lifted out and ligated, avoiding traction to the blood supply. The stomach was then replaced carefully and the abdominal wall closed by

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interrupted sutures. Animals were deprived of both food and water during the post-operative period and were sacrificed at the end of eighteen hours after the operation. The stomach was dissected out as a whole by passing a ligature at the esophageal end. The stomach was separated from the surrounding tissues and brought out as a whole along with its contents. The contents were subjected to centrifugation (3000 rpm-for 10mts)and then analyzed for volume, PH and ulcer index. The PH was estimated using Indi krome PH strips (glaxo India ltd) with PH ranges of 2-4.5and 5-8.5 with a difference in range of0.5. Ulcer index was calculated by the following formula.

$$\text{Ulcer index} = \frac{10}{x}$$

$$\text{Where } x = \frac{\text{Total mucosal area}}{\text{Total ulcerated area}}$$

For the estimation of ulcer index the stomach was cut open along the greater curvature and the inner surface was examined for ulceration with the help of a simple dissecting microscope. Usually circular lesions were observed but sometime linear lesion were seen.

Statistical Analysis

The result were analyzed using one way ANOVA with Duncan's multiple range test and values are mean ± SE(Table I).

RESULTS

Table 1: Effect of melatonin and melatonin + pyridoxine combination on volume, PH, and ulcer index in pylorus ligated rats

Group	Treatment	Volue(ml)	Ph range	Ulcer index
A	Normal saline	7.68 ± 0.069	1.87 ± 0.41	0.51 ± 0.03
B	Melatonin	5.16 ± 0.184$^{(a)}$	3.13 ± 0.08$^{(a)}$	0.17 ± 0.01$^{(a)}$
C	Melatonin+pyridoxine	4.1 ± 0.07$^{(a,b)}$	3.99 ± 0.07$^{(a,b)}$	0.03 ± 0.01$^{(a,b)}$
One way ANOVA	F 1280.52 1545.16 1198.17 P < 0.001 < 0.001 < 0.001			

Values are mean ± SE, N = 6 in each group, $p^a < 0.001$ as compared to control (Duncan's multiple range test), $p^b < 0.001$ as compared to group B (Duncan's multiple range test)

The average volume of gastric acid secretion in the melatonin group was 5.16 ml which is a significant reduction from the control group. Similarly the average PH is 3.13 and ulcer index was 0.17 in the melatonin group. The rise in PH and the reduction in ulcer index were also significantly changed from the control group .When melatonin and pyridoxine were combined there was further significant reduction in gastric volume (4.10 ml) significant rise in PH and ulcer index was also very much reduced. Pretreatment with melatonin for two weeks produced significant anti ulcer effect. The effect of melatonin was further potentiated by simultaneous administration of pyridoxine. (Table I).

DISCUSSION

The etiology of peptic ulcer is unknown in most of the cases, yet it is generally accepted that it results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms[7]. To regain the balance, different therapeutic agents are used to inhibit the gastric acid secretion or to boost the mucosal defense mechanisms by increasing mucus production, stabilizing the surface epithelial cell or interfering with the prostaglandin synthesis[8.] The causes of gastric ulcer after pyloric ligation are believed to be due to stress induced increase in gastric HCL secretion and stasis of acid. According to Shay *et al*, the volume of secretion is an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid. A role for reactive oxygen metabolites, free radicals and nitric oxide has been suggested in the pathogenesis of gastric ulcer[9,10]. In previous studies the neurohormone melatonin by virtue of its anti-oxidant properties has been shown to protect the liver against oxidative damage. Hence the similar anti-oxidant property of melatonin could be the reason for the observed significant reduction in the gastric acid secretion and ulcer index and also the rise in PH. Pyridoxine, a co-factor in the synthesis of endogenous melatonin potentiated the free radical scavenging property of melatonin. In conclusion it appears that melatonin may have a significant gastric ulcer protective effect and the combination of melatonin and pyridoxine may be utilized either as monotherapy or as adjuvant to the existing conventional therapy like H_2 antagonists and proton pump inhibitors.

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