Histological Study on the Possible Protective Effect of Co-enzyme Q10, Evening Primrose and Esmoprazole on Indomethacin Induced Gastric Ulcer in Adult Male Albino Rats

Thesis

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Summary

Current treatment of gastric ulcer is associated with several side-effects, which emphasizes the need for new therapeutic modalities. It is believed that the therapeutic outcome of Coenzyme Q10 and Primerose can be more effective than traditional lines of treatment.

This work aimed to study the protective effect of Coenzyme Q10 and Primerose in comparison to Esomeprazole on Indomethacin- induced gastric mucosal damage in adult male albino rats, monitored by histological, immunohistochemical and morphometric methods.

This study was carried out on forty eight adult male albino rats, weighing 180-220 g. They were divided as follows:

Group I (Control group): included eight rats, this group were subdivided into the following equal subgroups:

- **Subgroup Ia:** two rats without intervention.

- **Subgroup Ib:** two rats received 0.5 ml gum acacia dissolved in distilled water (solvent of indomethacin) orally using an oral gastric tube on the 2nd day of experiment (corresponding to groups II& IV).

- **Subgroup Ic:** two rats were injected with 0.5 ml olive oil (solvent of CoQ10) intraperitoneally and on the 2nd day received in addition 0.5 ml gum acacia as in subgroup Ib (corresponding to group III).

- **Subgroup Id:** two rats received 0.5 ml distilled water (solvent of esomeprazole) orally via gastric tube and on the 2nd day received in addition 0.5 ml gum acacia (corresponding to group V).

Rats were sacrificed at the same time of the corresponding experimental groups.

received single **Group II (Indomethacin group):** included eight rats which ● oral dose of 50 mg/kg of INDO dissolved in gum acacia on the 2nd day of experiment.

Group III (coenzyme Q10 and indomethacin group): included eight rats ● which were injected intraperitoneally with coenzyme Q10 (dissolved in olive oil) in a daily dose 10mg/kg for 2 consecutive days, then INDO was given on the 2nd day 1 hour after CoQ10.

Group IV (Primrose and indomethacin group): included eight rats which ● of 10g/kg were injected with evening primrose intraperitoneally in a daily dose for 2 consecutive days, then INDO was given on the 2nd day 1 hour after EP.

: This group was **)Group V (Esomeprazole and indomethacin group●** :rats each subdivided into 2 subgroups 8

mg/kg/day of esomeprazole **Subgroup Va (low dose):** eight rats received 5- (dissolved in distilled water) orally using a gastric tube for 2 consecutive days, then INDO was given on the 2nd day 1 hour after ESP.

mg/kg/day of **Subgroup Vb (high dose):** eight rats received 20- esomeprazole (dissolved in distilled water) orally using a gastric tube for 2 consecutive days, then INDO was given on the 2nd day 1 hour after ESP.

Rats were deprived of food but had free access to water 24 hours before ulcer induction. Gastric ulceration was induced by giving the rats indomethacin. After six hours of ulcer induction, rats were anesthetized and stomach of each group was dissected, washed by saline and cut along the greater curvature and examined grossly and cleansed gently with normal saline. Specimens were processed then subjected to H&E and PAS stains and immunohistochemical staining using Anti-Caspase-3and Anti-PCNA antibody.

Morphometric measurements were done to measure the mean area % of PAS positive reaction and Anti-Caspase-3and Anti-PCNA antibody positive reaction. The results were then statistically analyzed.

Gastric ulcer induced by indomethacin administration caused significant increase in the ulcer index as compared with the control rats. A significant decrease in the ulcer index in all treatment groups as compared with INDO group was observed.

Regarding the antioxidant status, there was a significant increase in MDA level in INDO group when compared with other groups.

In H&E stained fundic sections of INDO group, showed multiple deep erosions. The surface columnar mucus-secreting cells were lost. There were extravasation of RBCs and distorted architecture of fundic glands. Mononuclear inflammatory cellular infiltration was noticed with congested blood vessels. There were apoptotic changes in parietal cells. The basal parts of the fundic glands also showed apoptotic chief cells.

The PAS stained sections revealed a significant decrease in area % of PAS reaction in INDO group as compared with the other groups. Loss of PAS reaction from the surface cells with its presence in the neck part of the gastric glands was revealed. There was a significant increase in area % of Caspase immunoreaction in INDO group as compared with all other groups. There was a significant decrease in area % of PCNA expression in INDO group as compared with the control group.

Sections of the CoQ10+INDO group showed restoration of the normal architecture of the fundic mucosa with erosions in few areas .Some parietal cells were with normal appearance, others were with vacuolated cytoplasm and eccentric pyknotic nuclei. There were extravasated RBCs in the lamina propria. There was widening of some glands. Restored organization of bases of fundic glands was observed with some necrotic areas in between.

A significant increase in area % of PAS reaction in CoQ10+INDO group when compared with INDO group was revealed. A significant decrease in area % of caspase immunoreaction and a significant increase in area % of PCNA expression in CoQ10+INDO group as compared with INDO group were revealed.

Sections of the EP+INDO group showed restoration of the normal architecture of fundic mucosa. The fundic pits showed slight widening. Areas of erosion were also noticed with congested blood vessels. Bases of the glands were restored with some parietal cells showed vacuolated cytoplasm. A significant increase in area % of PAS reaction in EP+INDO group as compared with INDO group was also revealed. A significant decrease in area % of caspase immunoreaction and a significant increase in area % of PCNA expression in EP+INDO group as compared with INDO group were observed.

In ESP(a)+INDO group, examination of H&E fundic sections showed restored architecture of gastric mucosa with marked widening of the fundic glands and some areas with erosions. Mononuclear inflammatory cell infiltration was seen in lamina propria. Most parietal cells and chief cells showed vacuolated cytoplasm and small darkly stained nuclei. A significant increase in area % of PAS reaction in ESP(a)+INDO group when compared with INDO group was revealed.

In ESP(b)+INDO group, examination of H&E fundic sections showed normal architecture of fundic mucosa. The fundic pits showed slight widening. Many parietal cells showed vacuolated cytoplasm and small dark nuclei. Bases of most of the gland were restored with normal appearance of chief cells and parietal cells. A significant increase in area % of PAS reaction in ESP(b)+INDO group when compared with INDO group was revealed. A significant decrease in area % of caspase immunoreactions and a significant increase in area % of PCNA

expression in ESP(b)+INDO group as compared with INDO group were observed.