Evaluation of gastro protective activity of Fish Oil (Omega-3 Fatty Acids) against experimentally induced acute gastric ulceration in Rats

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ABSTRACT

Fish oils contain the omega-3-fatty acids eicosapentaenoic acid and docosahexaenoic acid precursors of certain eicosanoids that are known to have a wide range of clinical use. The present study was conducted to evaluate the anti ulcer activity of fish oil in HCl-ethanol induced acute ulcer model. The animals were divided into five groups with six rats in each group. Ranitidine (30mg/kg/orally) used as a standard and Fish oil 5% v/w and 10% v/w used as a test-I & II, other group was administered normal diet for 30days. On the 31st day ulcers was induced by administration of HCl and then stomach was removed from rats observed under magnified lance to count ulcer index. 10% v/w and ranitidine pretreated groups showed significant gastro protective activity compared with HCl treated group. In the physical observation of HCl treated gastric mucosa showed extensive lesions compared with other groups. The above study observations proved Fish oil (omega-3-fatty acids) have antiulcer activity but there is requirement of further pre-clinical and clinical studies to support and increase the use of fish oil in the treatment of various pathological conditions.

KEYWORDS: Docosahexaenoic acid, Eicosapentaenoic acid, Fish oil, HCl, Omega-3-fatty acid, Ulcer index

INTRODUCTION

Peptic ulcer disease (PUD) encompassing gastric and duodenal ulcer is the most Prevalent gastrointestinal disorder. The pathophysiology of PUD involves an imbalance between offensive (acid, pepsin and H. pylori) and defensive factors (mucin, prostaglandin, bicarbonate, nitric oxide and growth factors) [1]. Currently there are different classes of drugs likes proton pump inhibitors, H2 receptor blockers, anti-
cholinergics, antacids, ulcer protective are available for treatment of peptic ulcer but all the drugs have side effects and limitations [2]. Some psychological conditions like anxiety, stress, surgical shock, burns and trauma also stimulate gastric acid secretion and leads to ulcer [3]. Free radicals, oxidants, physical, chemical factors are also involved in the pathogenesis of PUD [4]. A number of drugs are used in the treatment of ulcers but its clinical evaluation shows the incidence of relapses, side effects with interaction of other drugs[5]. To overcome all these drawbacks herbal medicine is preferred. This herbal medicine deals with plant and plant products, extracts in treating diseases and these medicines are consider safer and no side effects [6]. The epidemiological studies in the early 1970s Bang and Dyerberg advanced the hypothesis that long chain unsaturated Omega-3 fatty acids present in the fishes and other marine animals which the Eskimos consumed produced beneficial effects on IHD [7]. This fish oil have cardio-protective activity [8], hypolipidemic [9], anti-cancer [10], anti-depressant [11], anti-inflammatory activity. Fish oil can also be used in the treatment of rheumatoid arthritis, inflammatory bowel syndrome, stimulation of immune system [12], treatment of schizophrenia [13], nutrition and gastrointestinal disorders. The present study undertaken to determine the antiulcer potential of the Fish oil using experimental gastric ulcer model namely HCL/ethanol induced in comparison with ranitidine as a standard drug.

MATERIALS AND METHODS

Chemicals
Soft gelatin capsule of fish oil containing (Eicosapentaenoic acid (EPA)- 180mg, Docosahexaenoic acid (DHA)- 120mg/ capsule) form (E - Merck pharmaceuticals), Ranitidine 150mg (Glaxosmith Pharmaceuticals), Ketamine (Ketalar-Parkes and Davis).

Experimental Animals
Albino Wistar male rats of 150-200g were used for the study. Animals were housed in well ventilated room (temperature 23± 2°C, humidity 65-70% and 12h light/dark cycle) [14] in central animal house (Raja Muthiah Medical college and hospital, Annamalai University). Animals were fed with standard pellet diet and water ad libitum [15]. Ethical clearance was taken from the institutional Animal Ethical Committee (Register No.160/1999/CPCSEA, Annamalai University, Annamalai Nagar, India) and the approved experimental design no. (proposal No632, dated 18/03/2009).

Study center
The study was undertaken at Central Animal House, Raja Muthiah Medical College and Hospital, Annamalai University.

Study design
The rats were divided into five groups of 6each. Group I Normal control (Normal diet). Group II - Experimental control-(Hcl 1.5 ml/ oral/1 day Normal diet). Group III - Standard (Ranitidine 30mg/kg/orally) Group IV - Test- I (Fish oil 5% (v/w)/ kg/ orally) Group V -Test-II (Fish oil 10% (v/w)/kg/orally)

All the drugs were administered orally once daily for 30 days. The Animals in all the groups were fed with standard pellet diet and water ad libitum during the experimental period. Ranitidine was suspended in 1% Carboxymethyl cellulose [16]. The fish oil and Ranitidine was administrated by oral intra-gastric route.

Induction of acute ulcer
After 30 days, animals in all the groups except group I were deprived of solid food for 24 hours with water ad libitum. They were housed in cages with wide mesh wire bottoms to prevent coprophagy. Following the method of Okabe with slight modifications, 1.5 ml of HCL -ethanol mixture (0.15M of HCL in 70% v/v ethanol) was given orally for the induction of acute gastric mucosal damage [17]. At the end of the experimental period i.e. on 31st day, the rats were sacrificed one hour after the administration of HCL- ethanol mixture, by cervical dislocation (under I.M Ketamine ) [18]. The stomach was excised and the extent of gastric mucosal damage was determined by measuring each lesion in mm along its greater length. The ulcers in this model were localized in the glandular portion of stomach mucosa. Tracing paper was placed over the stomach and outline of the stomach and the areas of erosions

of ulceration were traced on it for determining ulcer index [19].
Ulcer index = 10/X [Where X = Total mucosal area/ Total ulcerated area]

Statistical analysis
Data are reported as MEAN±SEM and were analysed by S.P.S.S (16.0) version software. One way ANOVA followed multiple comparison (Dunnet t) used to obtain statistical significant P<0.05 [20].

RESULTS
The ulcer index which measures the extent of gastric mucosal damage was significantly high in HCl - ethanol treated group compared with other groups. But pretreatment with Ranitidine and 10% fish oil significantly reduced ulcer index. Less significant difference was observed with 5% fish oil treated group with other groups (Table-1).

In the physical observation normal diet treated group showed normal gastric mucosa (Figure-1) but HCl treated group stomach showed extensive gastric mucosal damage lesion appear as blackish red hemorrhagic patches in transverse bands parallel to long axis of the stomach (Figure-2). Ranitidine administered group rats showed almost normal gastric mucosa with less hemorrhagic spots (Figure-3) and 10% fish oil administered group rat gastric mucosa showing almost normal gastric mucosa with small hemorrhagic spots (Figure-4).

Table 1: Effect of Fish oil on HCl induced acute gastric ulcers

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose/Route/No. of days</th>
<th>Ulcer Index (MEAN±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-I</td>
<td>Normal diet/ oral/ 30days</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td>(Normal control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-II</td>
<td>HCl 1.5 ml/ oral/ 1 day</td>
<td>26.71±1.61</td>
</tr>
<tr>
<td>(Experimental Control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-III</td>
<td>Ranitidine 30mg/kg/orally/30days</td>
<td>1.73±0.51*</td>
</tr>
<tr>
<td>(Standard)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-IV</td>
<td>Fish oil 5%/v/w/orally/30days</td>
<td>17.71±0.24*,†</td>
</tr>
<tr>
<td>(Test- I)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-V</td>
<td>Fish oil 10%/v/w/orally/30days</td>
<td>1.95±0.31*</td>
</tr>
<tr>
<td>(Test-II)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(* P<0.05 significant compared group-II with other groups,
†P<0.05 significant compared group-III with group-IV)
DISCUSSION

According to previous studies, in most of the cases the etiology of the ulcers was due to increase in the activity of aggressive factors and decrease in the activity of protective endogenous defense mechanisms. Agents that increase the activity of factors like HCl, bile acids, drugs like aspirin, hormonal neuronal and decrease the activity of factors are mucous formation, bicarbonate and prostaglandin synthesis leads to ulcer formation. Robert introduced the concept of gastric cyto-protective, a property by which prior
administration of non-secretory dose of a prostaglandin would protect the rat stomach against damaging effect of various agents. There are so many models to induce ulcers among that HCl-ethanol mixture model is very commonly used to induce experimental ulcers in animals. In this study we studied the effect of fish oil on HCl induced gastric ulcer. The results obtained from this study showed fish oil to have great mucosal protection action. Pretreatment with fish oil reduced the ulcer index level compared with HCl treated group. In this study 10% of fish oil showed most gastro protective effect than 5% fish oil treated group. The efficacy of fish oil was compared with Ranitidine group. 10% fish oil treated group showed results same like standard Ranitidine according to the old hypothesis acid secretion was thought to be the single cause of ulcer formation and reduction in acid secretion was thought to be the major approach towards therapy. Now, treatment of ulcer mainly targets to increase the defensive system along with lowering of acid secretion. Numerous epidemiological, clinical interventional and laboratory studies, worldwide have shown that fish oil containing omega-3 fatty acids provide protective effects mainly through its antioxidant defense mechanism. In the present study also, fish oil had proved its cyto-protective action in gastric mucosa of rats against HCl-ethanol induced damage by its antioxidant mechanism. Hence fish oil has antiulcer activity. Thus the present study offers a conclusive evidence that diet supplemented with deep sea fatty fish or fish oil can protect against gastric lesions induced by various noxious agents. Further studies on fish oil are needed to evaluate its action on gastric acid secretion, mucus secretion and chronic models of ulceration.

REFERENCES


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