COMPARATIVE GASTRIC ULCEROGENIC EFFECTS OF NAPROXIN, FENOPROFEN AND RECTIFIED SPIRIT IN ALBINO RAT

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ABSTRACT:

A study of comparative ulcerogenicity of naproxen, fenoprofen and rectified spirit was conducted under dissecting as well as laboratory microscope. Different parameters of mucus barrier disruption were studied in detail and a statistical comparison was made between the three drugs used. It was found that under dissecting microscope the difference was non-significant but under light microscope naproxen was maximally ulcerogenic followed by rectified spirit and fenoprofen was least ulcerogenic.

INTRODUCTION:

Peptic ulcer is a conglomerate of heterogenic disorders, which manifests itself as break in (he Gastrointestinal (GIT) mucosa. Originally all ulcers in the GIT were believed to be caused by aggressive action of hydrochloric acid and pepsin in the mucosa, and thus they became known as peptic ulcers. This may not be the only cause, there may be lack or defect in the mucosal layer[1].

The Naproxen and Fenoprofen are phenyl propionic acid derivatives, which have anti-inflammatory analgesic and anti-pyretic effect[2]. The rectified spirit is 90% alcohol[3] It has got few therapeutic uses, but it is used as cheap beverage. It is also depressant of the central nervous system[4]. This study was designed to observe the morphological changes in the gastric mucosa by localizing the site of lesion under dissecting microscope. Then detailed morphological study with the help of light microscope was done to assess the changes in the epithelium and the gastric glands with reference to various secretory cells.

MATERIALS AND METHODS:

This study was performed in the Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi. Two non-steroidal anti-inflammatory drugs (NSAID) used in the study were administered in 1% gum acacia in distilled water by oral intubation in a volume of 1 ml. per 100 grams' body weight. The doses were 7.1 grams per kilogram body weight for Naproxen and 32.3 grams per kilogram body weight for Fenoprofen \ The Rectified spirit was administered in a dose of 0.5 ml. per 100 grams' body weight*.

A total of 30 animals used in this study were divided into two groups. Control and Experimental, having 15 animals each with a weight range of 200 to 350 grams. These animals were kept on fasting for 24 hours. Water however was available to them freely. The animals were sacrificed six hours after the treatment.

(1) Control Group: They received gum acacia in the same volume as used for ulcerogenic agent.
(2) Experimental Group: These animals received ulcerogenic agents only.

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The stomach was examined under the dissecting microscope for estimation of median erosion score according to the arbitrary scale of Bonta. Each erosion was given score as given in this table:

Approximate Diameter of Ulcer/Erosion in mm.	Score
Less than 1	0.5
1-2	1.0
2-3	2.0
3-4	4.0
More than 4	8.0
Perforation	12.0

The cumulative score of one group was divided by the number of animals in each group and expressed as median erosion score.

After tissue treatment 6µ thick sections were taken and stained with hacmatoxylene and Eosin (H&E) and Periodic Acid Schiffs reagent (PAS) staining technique.

The mucosal thickness was measured on 10X objective and 8X ocular with the help of an ocular micrometer. The height of surface mucous cells, mucous neck cells and Chief cells were noted under oil emersion. The number of these cells were recorded in a strip covering in a whole field measuring 150pi in width extending from the surface uptil base of the gastric gland. Three such fields were counted in this manner and average count was calculated for each specimen.

RESULTS:

The results of this study are given in tables I to X.

TABLE-I
MEDIAN EROSION SCORE

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	0	0	0
EXPERIMENTAL	4.6±0.97	3.50±0.44	4.10±0.42

Statistical Comparison between Naproxen and Fenoprofen $p < 0.05$
Naproxen and Rectified Spirit $p < 0.05$ Fenoprofen and Rectified Spirit $p < 0.05$

TABLE - II
MEAN MUCOSAL THICKNESS (µm) OF THE STOMACH

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	532±29.77	515±33.18	548±29.39
EXPERIMENTAL	386±14.8	400.8± 17.7	373.6±11.14

Statistical Comparison between Naproxen and Fenoprofen $p<0.001$ Naproxen and Rectified Spirit $p<0.001$ Fenoprofen and Rectified Spirit $p<0.001$

TABLE - III
MEAN SURFACE MUCOUS CELL COUNT

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	51.20±3.52	50.60±3.13	52.60±3.82
EXPERIMENTAL	27.13±1.82	31.13±1.43	28.59±1.56

Statistical Comparison between
Naproxen and Fenoprofen $p<0.001$
Naproxen and Rectified Spirit $p<0.01$
Fenoprofen and Rectified Spirit $p<0.001$

TABLE - IV
MEAN MUCOUS NECK CELL COUNT

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	29.14±3.09	27.80±2.78	28.20±2.96
EXPERIMENTAL	18.66±0.60	24.99±2.45	24.46±2.89

Statistical Comparison between
Naproxen and Fenoprofen $p < 0.001$ Naproxen and Rectified Spirit $p < 0.001$ Fenoprofen and Rectified Spirit p: Non significant

TABLE - V
MEAN PARIETAL CELL COUNT

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	54.00±3.97	51.20±3.39	55.80 ± 2.84
EXPERIMENTAL	59.26±3.54	74.19±5.36	70.19±3.47

Statistical Comparison between
Naproxen and Fenoprofen $p<0.001$ Naproxen and Rectified Spirit $p<0.001$ Fenoprofen and Rectified Spirit $p<0.001$

TABLE-VI
MEAN CHIEF CELL COUNT

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	81.20±6.89	80.40±5.38	77.00 ±6.13
EXPERIMENTAL	55.19 ± 0.80	75.46±2.54	76.06±4.54

Statistical Comparison between
Naproxen and Fenoprofen $p<0.001$ Naproxen and Rectified Spirit $p<0.001$
Fenoprofen and Rectified Spirit p Non Significant

TABLE-VII
MEAN HEIGHT (µm) OF SURFACE MUCOUS CELLS

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	12.48 ± 0.72	12.55 ± 0.74	12.35±0.57
EXPERIMENTAL	8.09 ± 0.25	12.32 ± 0.38	10.68±0.67

Statistical Comparison between Naproxen and Fenoprofen p<0.001 Naproxen and Rectified Spirit p<0.001 Fenoprofen and Rectified Spirit p<0.01

TABLE-VIII
MEAN HEIGHT (µm) OF MUCOUS NECK CELLS

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	8.88 ± 0.30	8.89 ± 0.24	9.05 ± 0.25
EXPERIMENTAL	9.50 ± 0.37	9.78 ± 0.22	8.90 ± 0.42

Statistical Comparison between Naproxen and Fenoprofen p<0.05 Naproxen and Rectified Spirit p<0.001 Fenoprofen and Rectified Spirit p<0.001

TABLE-IX
MEAN SIZE (µm) OF THE PARIETAL CELLS

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
LCONTROL	12.50 ± 0.26	12.36±0.29	12.20±0.33
EXPERIMENTAL	11.72±0.17	11.53±0.26	12.26±0.26

Statistical Comparison between Naproxen and Fenoprofen p: Non Significant Naproxen and Rectified Spirit p <0.05 Fenoprofen and Rectified Spirit p <0.05

MEAN HEIGHT (µm) OF THE CHIEF CELLS

GROUPS	NAPROXEN	FENOPROFEN	RECTIFIED SPIRIT
CONTROL	8.20 ± 0.33	8.45±0.27	8.13±0.27
EXPERIMENTAL	8.88 ± 0.24	8.88±0.29	9.07±0.25

Statistical Comparison between
Naproxen and Fenoprofen p: Non Significant Naproxen
and Rectified Spirit p: Non Significant Fenoprofen and
Rectified Spirit p: Non Significant

DISCUSSION

The propionic acid represents the largest chemical class of NSA1D. Several of them are being used widely. This paper discusses the observations made on Naproxen and Fenoprofen from this group. The rectified spirit used, as a cheap beverage among poor was also included to make a comparison between drugs and commonly used beverage also. Our results show significant parameters of mucous barrier disruption with all the three ulcerogenic agents used as compared to the control.

Naproxen shows most significant ulcerogenicity among the three. It is evident from the significantly more erosion score, mucous cell and parietal cell changes. Our results are in agreement with the observations of AU: Orlicz et al.[8]. They had performed a histological study in rat support the clinical observation of mucosal destruction like ulcerous niche and upper gastrointestinal hemorrhage. But AU: Fung et al[9]. had shown in their histological analysis in dogs that there were non-significant changes observed under light microscope but moderate effect was observed under electron microscope. This is probably because the rat is less tolerant of NS AID than the dogs. The other reason is that they have taken the biopsies after 0. 1. 2 and 3 hours but we have sacrificed the

animals after 6 hours. Therefore, our time is almost double as compared to their time period. This finding is in agreement with the findings of AU: Fujee et al[11]. They observed highly significant gastric damage in rats after 6 hours' treatment with fenoprofen although this drug is less ulcerogenic in our study as compare to the Naproxen.

We conclude that all the three drugs used produce changes in the gastric mucosa with the most damage produced by the naproxen followed by rectified spirit and the fenoprofen. Most NSAID inhibit prostaglandin cyclooxygenase activity, which results in a prostaglandin deficiency at tissue level that is responsible for the gastric damage.

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