"ENTEROTOXIC EFFECTS OF INDOMETHACIN, NIMESULIDE AND CELECOXIB IN FOREGUT AND MIDGUT OF ALBINO RATS"

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CONTENT

SUMMARY & CONCLUSION

The gastrointestinal tract (GIT) is the main target of NSAIDs toxicity. It is the most common drug-induced toxicity that can be fatal. Worldover 35 million people consume these drugs on a daily basis. Conservative calculation estimates that approximately 1, 07,000 patients are hospitalized annually for non-steroidal anti-inflammatory drug (NSAIDs) related gastrointestinal complications, and at least 16,500 NSAIDs related deaths occur each year. According to prospective data from Arthritis Rheumatism, and Ageing Medical Information System (ARAMIS), 13 of every 1,000 patients with rheumatoid arthritis who take NSAIDs for one year have a serious gastrointestinal complication. Therefore, the objective of the present study was to compare the effects of three different NSAIDs-Indomethacin, Nimesulide and Celecoxib on the foregut & midgut of albino rats. 48 albino rats were taken for the studies which were divided into 3 groups. Each group comprised of 16 rats out of which 4 were taken as control and remaining 12 as experimental group. The experimental group was further subdivided into three subgroups of 4 rats each.

Each experimental subgroup was subjected to the administration of a particular drug in a dose of 10 mg/kg of the body weight per day for a period of 1, 2 and 3 weeks respectively, while the controls were administered the vehicle (distilled water).

After administration of the drugs, the tissues were collected from oesophagus, cardiac part of stomach, duodenum, jejunum, ileum and colon (proximal part). The tissues were fixed in formalin, processed and tissue blocks were made in paraffin wax. 3–5μ thick sections were cut and stained with haematoxylin and eosin. The sections were examined under low and high power (magnification) and selected slides were photographed. Microscopic changes in the form of hypertrophy and hyperplasia were noted in response to injuries caused on mucosa of oesophagus and cardiac part of the stomach by NSAIDs.

The cellular hyperplasia was considered as an initiating and promotional event to protect the epithelial lining of the above two regions of the GIT. Increase in the thickness of epithelium was seen in all the subgroups of Celecoxib but there were decrease in the thickness of epithelium at the end of 2nd week treated subgroup with Indomethacin and 3rd week treated subgroup with Nimesulide. The decreased in the thickness probably indicated that the rate of multiplication or regeneration of the epithelium was far less than the effects of destruction of epithelium caused by both groups. This may be due to selective COX-2 inhibitors. It indicated that Celecoxib causes mild, Indomethacin severe while Nimesulide causes moderate injures to the epithelium. In the cardiac part of

stomach also an increase in the thickness of epithelium was noted in cases of Indomethacin and Nimesulide treated sub groups. However, the Celecoxib treated subgroups showed a decrease in the thickness of epithelium.

In the duodenum an increase in the height of villi was noted but height of villi in the Jejunum and Ileum was seen to decrease. It was observed that the increase in the height was maximum with Indomethacin and less with Nimesulide and Celecoxib. It is thus suggested that the selective COX-2 inhibitors show a very favorable gastrointestinal safety profile. There is a widespread feeling that a new era is beginning with COX-2 inhibitors in the treatment of rheumatic conditions. The only foreseen drawbacks are that these drugs may be associated with a new side effect, although earlier results have not shown this to be the case. However, perhaps the selective COX-2 inhibitors will be equally associated with some of the side effects of conventional NSAIDs, such as relapse of inflammatory bowel disease, contributing to appendicitis in the elderly and causing an aggressive form of diverticulitis [46]. Their possible contribution to delayed ulcer healing and some forms of inflammation [47] needs further assessment.