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EFFECTS OF THE DICLOFENAC SODIUM (NSAID) ON GOBLET CELLS IN CAECAL MUCOSA OF ALBINO RATS.

1. **IMTIAZ ALI WAGGAN**
2. **NAHEED KHAN**
3. **DUR MUHAMMAD SHAIKH**
4. **ABDUL LATIF JOKHIO**

1. ***Associate Professor***
   Department of Anatomy
   DOW MEDICAL COLLEGE
   D.U.H.S. KARACHI – 74200.
   E-mail: i.waggan @ duhs.edu.pk
2. ***Assistant Professor***
   Department of Anatomy
   DOW MEDICAL COLLEGE
   D.U.H.S. KARACHI – 74200.
3. ***Assistant Professor***
   Department of Pathology
   SINDH MEDICAL COLLEGE
   D.U.H.S. KARACHI
4. ***Sr. Lecturer***
   Department of Anatomy
   CHANDKA MEDICAL COLLEGE
   SHAHEED MUHTARMA
   BENAZEER BHUTTO
   MEDICAL UNIVERSITY
   (SMBBMU) LARKANA

Correspondence:
1. **DR.IMTIAZ ALI WAGGAN**
   Associate Professor
   DEPARTMENT OF ANATOMY
   DOW MEDICAL COLLEGE
   D.U.H.S. KARACHI – 74200.
   E-mail: i.waggan @ duhs.edu.pk

ABSTRACT

OBJECT: *To evaluate the effects of diclofenac sodium (NSAID) on Caecal Goblet cells of albino rats.*
DESIGN: *An animal study carried on experimental albino rats.*
SETTING: *An animal study carried out in the Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi.*
METHOD: *Diclofenac sodium was administered to male albino Rats at a dose of 2 mg/kg body weight orally once daily for two weeks. These animals were sacrificed, Caeca were identified and removed, opened along mesenteric border, fixed in alcoholic formalin, Embedded in paraplast, 4 um thick sections were cut on rotary microtome, stained with periodic acid Schiff's (PAS) reagent. The histomorphological Features of caecal mucosa were compared with those in the control animals.*
RESULTS: *The study revealed that diclofenac sodium addimis-tration produced depleted intracytoplasmic mucin Content in goblet cells in caecal mucosa of albino Rats.*
CONCLUSION: *The results suggest that diclofenac sodium causes Severe caecal mucosal damage in albino rats.*

KEY WORDS: Diclofenac sodium, Caecum, Goblet cells, Albino rat.

INTRODUCTION

Diclofenac is an anti-inflammatory agent approved for several uses in the United States as a sodium or potassium salt. It is a benzene acetic acid derivatives, designated chemically as 2-[2, 6—dichloroophenyl amino benzene acetic acid] mono-sodium or mono-potassium salts. It is a faintly yellowish white to light beige virtually odorless, slightly hygroscopic crystalline powder. It is recommended for the long term treatment in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and for short term treatment in renal colic, acute gout, acute musculoskeletal injury, acute painful shoulder, Postoperative pain, migraine, and dysmenorrhoea. In addition, an ophthalmic solution after cataract extraction[1].
Although the drug diclofenac sodium is contraindicated in patients who have Experienced asthma, urticaria or other allergic type reactions, GIT disturbances, hepatic Insufficiency, renal impairment, and pregnancy[2]. But quacks are liberally using the drug Unchecked in general clinical practice in our population, which may be prohibited by the Government under rules.
This study was done to evaluate the effects of diclofenac sodium (NSAID) on caecal goblet cells of albino rats.

MATERIALS AND METHODS

Eighty albino rats were used in this study, which were obtained from Animal House of Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi. All were male, 20 weeks of age, weighing 180—200 grams, looking active and healthy.
These animals were housed in the experimental room of Animal House maintained onbalanced laboratory diet and water ad libitum with 12 hours light and dark cycle.
Eighty animals were divided into two equal groups; A and B, each comprising of 40 animals.

- Group- A animals were given diclofenac sodium (developed in Novartis Pharma Pakistan Ltd) at a therapeutic dose of 2 mg/kg body weight orally Once daily for 2 weeks [3].
- Group -B animals used as control and were given normal saline (equal volume of dose given to group- A) orally once daily for 2 weeks.

All the rats were sacrificed on day-15 of the experiment by giving deep ether Anesthesia and were operated to obtain their caeca, which were fixed in alcoholic Formalin, embedded in paraplast and 4 um thick sections were cut on rotary microtome. These sections were stained with PAS reagent. The histomorhpological features of caeca in both groups were observed with respect to mucigen content in goblet cells. The amount of mucigen present in the form of granules in the surface and intestinal Glands were studied. In this connection, three considerations were made, the number of mucigen granules, and intensity of the staining reactions.

After screening all the slides of mucigen contents of all the surface and Crypt cells was arbitrarily divided in to five degrees, recorded in + (scanty), ++ (slight), +++ (moderate), ++++ (marked), and +++++ (heavy).

RESULTS

General Observations

The animals in group- A looked slow and weak during last 2-3 days of Experimental period. They appeared lethargic, their response to stimuli was Sluggish and food intake was decreased as compared to animals of group- B.

Microscopic Observations

Under laboratory microscope the animals of group -A showed epithelial mucous Secreting cells in mucosa disrupted and exfoliated at places with moderate degree of pyknotic nuclei. Inflammatory exudates including numerous lymphocytes, plasma cells and neutrophils and the mucigen contents in goblet cells on the surface and crypts was Scanty to negligible was observed in almost all of the animals, as shown in Figure -1.

The animals of group- B served as a control and appeared healthy and normal with no sign of ill health. They showed normal activities throughout the Experimental period, responded quickly to stimuli and their food intake was normal.

On microscopy, intact histological structure without any change in caecal mucosa was observed, as shown in Figure-2.

DISCUSSION

The present study was designed to observe the morphological effects of diclofenac sodium (NSAID) on goblet cells present in caecal mucosa of albino rats.

The diclofenac sodium administered in a normal therapeutic dose of 2 mg/kg body weight, once daily orally for 2 weeks [3] produced exfoliation and depletion of

FIGURE-1:

Photomicrograph of 4 um thick paraplast section of caecal mucosa stained with PAS in diclofenac sodium treated (group-A) albino rat, showing depleted intracytoplasmic mucin content in goblet cells at the erosion/ulcer area under high power objective,x416.

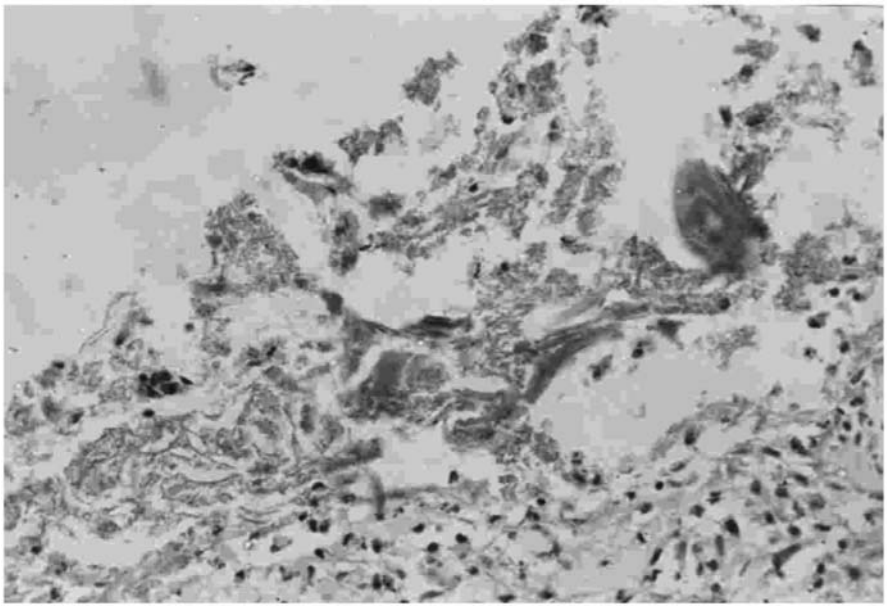
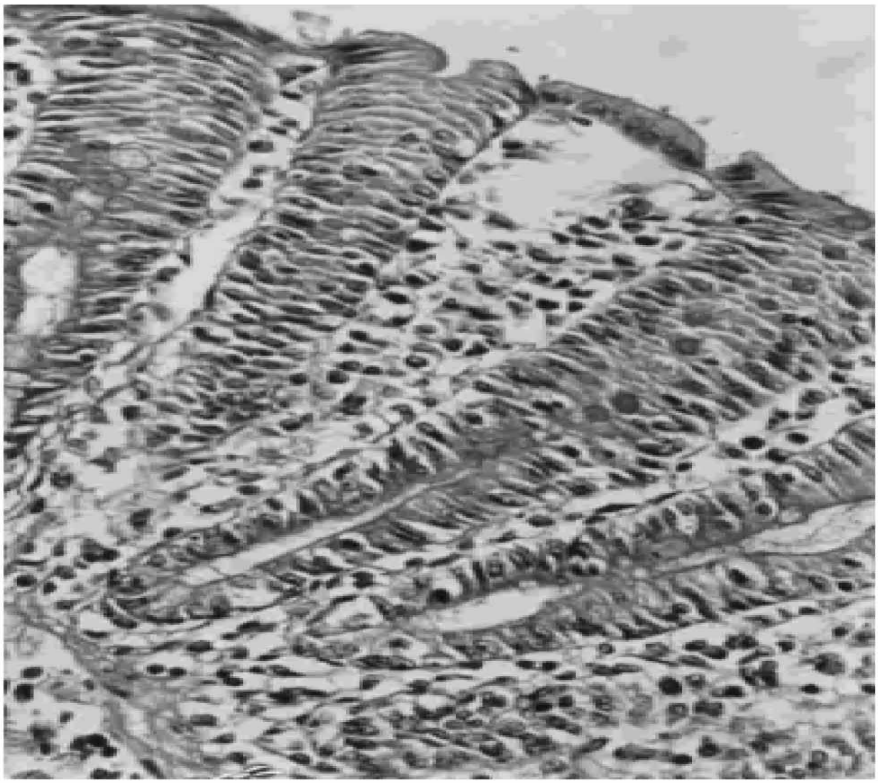


FIGURE-2:

Photomicrograph of 4 um thick paraplast section of caecal mucosa Stained with PAS in control (group-B) albino rat, showing normal intracytoplasmic mucin content in goblet cells under high power Objective, x416.



epithelial cells of caecal mucosa.

After treatment with diclofenac sodium (NSAID) in animals of group-A, general behavior changed to ill, sluggish and decreased food intake which may be attributed to unwanted effects of diclofenac sodium toxicity. In this context our results are in agreement with Gabriel et al[4], Bjarnason et al[5], and graham et al[6] who stated that administration of diclofenac sodium was associated with increased gastrointestinal toxicity include mild dyspepsia or cachexia as well as more serious gastrointestinal reactions such as ulceration, bleeding, perforation and other events leading to hospitalization or death.

On microscopic examination of caecum revealed decreased mucosal thickness with decreased total epithelial cell count per unit area and changes in cytoplasm, i.e. decreased mucin contents. These changes are in conformity with the Studies by Van-kolfshoten[7], Kaufman8, Graham et al[6], and Manocha[3]. In those studies the investigators found common mucosal lesions, i.e. erosions and ulcers found in stomach, small and large intestines except caecum.

A highly significant decrease in mucosal thickness was observed which may be attributed to the injurious effect caused by diclofenac sodium (NSAID) which might have resulted into onset of the demolition with extensive exfoliation of surface epithelial cells and ulceration, mucosal lining of caecum showed necrosis which according to Kumar et al[9] resulted most commonly from sudden severe ischemia due to irreversible injury to cells.

Inflammatory necrosis associated with intake of NSAID along with marked infiltration of lymphocytes, plasma cells, apoptotic, pyknotic, flattened cells, and neutrophils were noticed in lamina propria as well as within epithelium. Our findings are in agreement with Kumar et al[9] and Lee[10] who found that the presence of apoptotic bodies especially in the colonic crypts might indicative to exposure in particular to NSAID therapy. Apoptosis was found to be a conspicuous feature in cases of colitis related beyond reasonable doubt to the administration of diclofenac sodium. Apoptotic bodies were present in substantial number in colitis associated with diclofenac sodium.

The mechanisms by which drugs bring about apoptotic changes are far from clear. In NSAID associated colitis, cryptal apoptosis have been frequently accompanied by other histological abnormalities, more notably an increase in lymphocytes in lamina propria as well as increase in intraepithelial lymphocytes mainly in crypts themselves. In some instances there has been evidence of more acute crypt damage with incipient or even frank crypt abscess formation.In the case of NSAID associated lesions, however, apoptosis has been accompanied by inflammatory changes and in particular by a focal increase in intraepithelial lymphocytes in the crypts and may well be immunologically mediated[10].

The mucin contents in goblet cells become depleted and observed scanty to slight on PAS stained sections. Our results are in complete agreement with Lee[10] who found that the crypts showed substantial goblet cell depletion with diclofenac sodium. The inflammatory changes in which both plasma cells and lymphocytes participation were accompanied by more severe reaction and even crypt dissolution.

CONCLUSION

These results suggest that diclofenac sodium causes severe caecal mucosal damage in albino rats.

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