

Endoscopic evaluation of gastric mucosa after oral administration of ibuprofen in dogs

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ABSTRACT

Experiments were carried out on 3 groups of dogs in order to evaluate changes in gastric mucosa after oral administration of therapeutic and toxic doses of ibuprofen at the Centre for Advanced Studies in Clinical Medicine and Therapeutics, Madras Veterinary College, Chennai, India. Clinical examination of animals, routine blood profile and endoscopic evaluation of gastric mucosa were carried out on day 5 and day 8 of the experiment. All group II dogs administered with therapeutic doses of ibuprofen evidenced severe congestion of the mucosa on day 5, and small, bleeding ulcers on day 8, upon endoscopic examination. All dogs in group III showed severe signs of haemorrhage on day 5. It was concluded that dogs were more sensitive to ibuprofen than human beings and that it should be used judiciously in animals.

Key words: dog, ibuprofen, toxicity, endoscopy

Introduction

The large group of agents known collectively as non-steroidal anti-inflammatory drugs (NS AIDs) are used in man and animals because of their antipyretic, anti-inflammatory and analgesic effects (FLOWER et al., 1985). The mechanism of action of these drugs is to inhibit the synthesis of

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prostaglandins, which are the prime mediators of the inflammatory process. Side-effects included gastroduodenal ulceration and haemorrhage, which can lead to severe blood loss or gastrointestinal perforation. Side-effects of ibuprofen in human beings have been well documented (CARSON et al., 1987). Published studies in veterinary literature are predominantly case reports. The purpose of this study was to compare the effects on gastric mucosa produced by oral administration of the reported therapeutic, as well as toxic dosages of ibuprofen in dogs.

Materials and methods

Eighteen adult mongrel dogs in an age range of from 14 to 16 months and with a mean body mass of 14.6 kg were used. The laboratory-conditioned dogs were given a complete physical examination and found to be in good health. In all dogs, complete blood count, serum biochemical profile: and faecal examinations were made and found to be normal. Dogs were fed daily with 250 g of beef with rice and given water *ad libitum*.

Experimental design: Group I (6 animals) - control; Group II (6 animals) - Ibugesic liquid® 15 mg/kg orally 3 times daily; Group III (6 animals) - Ibugesic liquid® 90 mg/kg orally 3 times daily. Endoscopy was performed on day 5 and day 8 of the experiment with the aid of Olympus OES - P20 Fiberoptic gastroscope.

Results

Clinical signs reported in Group II dogs on day 5 included vomiting, melena, varying degrees of lethargy, and weakness. In Group III dogs, all the above signs were severe, with pallor of the mucous membranes and haemetemesis. In the serum biochemical profile, lowered plasma protein and elevated levels of blood urea nitrogen were noticed. On endoscopy, all dogs in Group II displayed congestion of the gastric mucosa and haemorrhage. Two dogs in Group III had a small, bleeding ulcer in the pyloric antral region.

By the end of day 8 clinical signs had worsened to the point where there was severe anaemia, melena vomiting mixed with blood, pale mucous membranes and weakness. Mean PCV was 20.3%, mean RBC count was 3.84×10^6 cells/ml., and mean haemoglobin concentration was 6.8 g/dl.

RBC indices were within normal range, indicating that the anaemia was normocytic and normochromic (Table 1). A highly significant difference ($P<0.01$) was noticed between different groups in haemoglobin concentration. Highly significant differences were also noted in the packed cell volume and total erythrocyte count between Group I and Group II, and between Group I and Group III. A significant difference between Group II and Group III was noticed in packed cell volume and total erythrocyte count. A highly significant difference was noticed in MCV and MCHC values between Group I and Group III, and a significant difference between Group I and Group II. No significant differences were found in MCHC values among groups.

Results of serum biochemical analysis revealed a low level of total protein (4.2 - 4.6 g/dl) and elevated levels of blood urea nitrogen in two dogs in Group III. On endoscopy, all dogs had a coffee-coloured fluid in the stomach, indicating haemorrhage, in addition to the small, raw, bleeding ulcers seen in the gastric mucosa. One dog in Group III was noted as having a perforated ulcer in the pyloric region. The animals were sacrificed on day 8 and the lesions were confirmed at necropsy.

Table 1. Mean \pm SE values of haemogram in three groups of dogs

Blood parameters	Group I	Group II	Group III
Haemoglobin (g %)	11.53 \pm 0.45 ^{ab}	6.8 + 0.44 ^{ac}	6.08 \pm 0.21 ^{bc}
Packed cell volume	36.67 \pm 1.90 ^{ab}	20.32 \pm 1.41 ^{af}	17.97 \pm 0.94 ^{bf}
RBC ($\times 10^6$ ml)	6.06 \pm 0.22 ^{ab}	3.84 \pm 0.15 ^{af}	3.53 \pm 0.12 ^{bf}
MCV (fl)	57.26 \pm 3.22 ^{db}	52.83 \pm 3.23 ^d	48.99 \pm 4.45 ^{bd}
MCH (Pg)	19.05 \pm 0.75 ^{db}	17.71 \pm 0.84 ^d	17.18 \pm 0.57 ^b
MCHC (%)	33.30 \pm 1.15	33.63 \pm 2.75	33.90 \pm 1.14

The mean superscribed with letter(s) a, b (or) c differ significantly ($P\leq 0.01$) between 1 and 2, 1 and 3 (or) 2 and 3, respectively. The mean superscribed with letter(s) d, e (or) f differ significantly ($P\leq 0.05$) between 1 and 2, 1 and 3 (or) 2 and 3, respectively.

Discussion

Non-steroidal non salicylatic anti-inflammatory agents are used extensively in human beings, having a lower frequency of adverse effects than salicylates (ROUDEBUSH and MORSE, 1981). Gastro-intestinal ulceration is the most common toxic effect of non-steroidal anti inflammatory drugs in dogs (ROMATOWSKI, 1984). One of the agents - ibuprofen - is widely used and available in many over-the-counter preparations. DAEHLER (1990) stated that perforating gastric ulceration is associated with non salicylates, non-steroidal anti in-flammatory agents in dogs.

The toxic effects of ibuprofen in dogs are believed to be caused by slow drug elimination leading to persistently high blood concentration (ROMATOWSKI, 1984). An additional factor contributing to toxicity of ibuprofen is hypoalbuminemia. Albumin acts as a catalyst, binding with the predominantly negatively charged non-steroidal anti inflammatory agents. In dogs with low albumin concentrations, the unbound fraction of the non-steroidal drug may increase substantially (DAEHLER, 1990). The unbound molecules are potentially active and an increase in adverse reactions may be anticipated (FOWLER, 1987).

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ADMAS et al. (1969) reported that even when adverse clinical signs were not evident in dogs treated with low doses of ibuprofen, intestinal inflammation and gastric ulceration were observed on necropsy. SCHERAL and FREY (1987) stated that on the basis of pharmacokinetic data, it was recommended that commercial ibuprofen be given twice daily.

It is concluded that dogs are more sensitive than human beings to the adverse gastro intestinal effects of ibuprofen, and that it should therefore be used judiciously.

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SAŽETAK

Istraživanja su provedena s ciljem da se utvrde promjene na sluznici želuca u pasa nakon primjene terapijskih i toksičnih doza ibuprofena. Tako su petog i osmog dana nakon primjene provedene kliničke, hematološke i endoskopske pretrage pasa. U pasa je endoskopijom utvrđena jača kongestija sluznice petog te manje krvareći vrijedovi osmoga dana nakon primjene terapijskih doza ibuprofena. Primjenom toksičnih doza prouzrokovalo se jače krvarenje sluznice već petoga dana. Na osnovi istraživanja autori zaključuju da su psi osjetljiviji na ibuprofen u odnosu na čovjeka te da se taj lijek može primjenjivati samo uz najveći oprez.

Ključne riječi: pas, ibuprofen, toksičnost, endoskopija
