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Research Article

CLINICO-HAEMATOLOGICAL CHANGES AFTER LONG TERM ADMINISTRATION OF NSAIDS

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ABSTRACT

Twenty four healthy mongrel dogs of 1-2 years of age were equally divided in to four groups. Group A was kept as control group, while dogs of groups B, C and D were treated with aspirin @ 100 mg/kg b. wt orally, ibuprofen @ 10 mg/kg b. wt orally and nimesulide @ 05 mg/kg b. wt orally, respectively. All these drugs were administered once daily for 10 days. Blood was collected from all dogs on 11th day for haematological parameters. The clinical signs recorded were vomition, diarrhoea, depression, dehydration and anorexia in aspirin and ibuprofen treated groups. The drugs tested did not produce any significant changes in total erythrocyte count, total leukocyte count, differential leukocyte count, total plasma protein, platelet count and erythrocyte indices when compared to the control group. A significant reduction in haemoglobin concentration and PCV % was recorded in the aspirin treated group. The clotting time was significantly reduced in the ibuprofen treated group, while it increased in aspirin treated group. There was an increase in respiration and pulse rates in aspirin treated group. Thus it can be concluded that the administration of nimesulide did not reveal any untoward significant effect in dogs.

Key words: Aspirin, ibuprofen, nimesulide.

Inflammation, pain and pyrexia are the most important symptoms of altered homeostasis of living organisms. Inflammation is the reaction of vascularized living tissue to local injury and consists of many interdependent cellular and humoral events, which serves to destroy, dilute or isolate the injurious agent and repair the damaged tissues. Many of the non- steroidal anti-inflammatory drugs have been reported to act on acute and chronic inflammatory conditions (Abramson and Weissmann, 1989). Non- steroidal anti-inflammatory drugs are heterogeneous group of compounds, often chemically unrelated, which nevertheless share certain therapeutic actions and side effects.

Aspirin is the prototype of non steroidal anti-inflammatory drugs (NSAIDs) and hence these compounds are often referred to as aspirin like drugs. Aspirin is a salicylic acid derivative and is still the most widely prescribed analgesic and anti-inflammatory agent. It might cause gastro duodenal ulcers in dogs (Cosenza, 1984). Ibuprofen is a propionic acid derivative and has analgesic, antipyretic and anti-inflammatory properties (Satoskar and Bhandarkar, 1991). Nimesulide chemically is a 4-nitro-2-phenoxy-methane sulfonide. Rossi *et al*. (1991) reported that flubiprofen and nimesulide possessed marked anti-inflammatory, analgesic and antipyretic activities. Nimesulide is not a cyclooxygenase inhibitor in gastric tissue and neither induced gastric lesions nor affected renal function (Magni, 1993).

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MATERIALS AND METHODS

Experimental Design: To evaluate the clinico-haematological changes after long term administration of anti-inflammatory drugs, 24 healthy mongrel dogs of 1-2 years of age were divided in to four groups Groups- A to D). Group A was kept as control group, while dogs in groups B, C and D were treated with aspirin @ 100 mg/kg b. wt orally, ibuprofen @ 10 mg/kg b. wt orally and nimesulide @ 05 mg/kg b. wt orally, respectively. All these drugs were administered once daily for 10 days. All the dogs were dewormed by administrating praziquantel 50 mg, pyrantel embonate 144 mg and febantel 150 mg containing deworming tab/ 10 kg body weight. After seven days of deworming the experimental dogs were vaccinated against rabies by injecting anti-rabies vaccine. An acclimatization period of 21 days was allowed, following anti-rabies vaccine, under normal feeding and management conditions by keeping them in cages prior to starting the experimental work.

Haematological Studies: To study the effect of long term administration of NSAIDs on haematological parameters, blood was collected from dogs of all groups, after 10 days of drug administration. The haematological

parameters such as total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), total plasma protein, platelet count, erythrocyte indices (MCV, MCH, MCHC), haemoglobin (Hb) concentration, packed cell volume (PCV) and clotting time were studied as per the standard method of Jain (1986). The data were statistically analysed (Snedecor and Cochran, 1967).

Studies on Clinical Observations: To study the effect of NSAIDs on clinical parameters, the dogs of all groups were observed daily and rectal temperature, pulse and respiration rate were monitored daily. Dogs of all groups were observed daily for other clinical symptoms viz. dullness, depression, anorexia, vomiting, diarrhoea etc.

RESULTS AND DISCUSSION

A significant reduction in Hb concentration and PCV (Table 1) was recorded in the aspirin treated group (group B). However, other drugs did not produce any significant change in the Hb concentration and PCV. Decreased PCV values in group B suggested reduction in the size of erythrocytes and hence microcytic anaemia, while decrease in the Hb concentration suggested hypochromic anaemia (Jain 1986). The reduction in PCV and Hb concentration may be a consequence of diffuse capillary bleeding following long term administration of aspirin. The findings of this experiment are in agreement with the findings of Cosenza (1984), Velenkar *et al.* (1999) and Sharma (2002).

The clotting time was significantly reduced in dogs treated with ibuprofen, whereas it was significantly increased in the aspirin treated dogs. Aspirin is known to selectively and irreversibly inhibit the cyclo-oxygenase activity of platelets (Adoms, 2001). Therefore, it reduces platelet aggregation and increase the clotting time. Aspirin is therefore used therapeutically in the prophylaxis of diseases associated with accelerated platelet aggregation i.e. coronary artery disease and post-operative deep vein thombrosis (Patrono, 1994). TEC, TLC, DLC, thrombocyte count, MCV, MCH and MCHC concentrations were in the normal range and did not differ much among groups at all days of observations (data not shown).

There was no major effect of different drugs on rectal temperature which varied between 101- 102°F in all groups at all days of observations. In the present investigation, the aspirin also increased the respiration rate and pulse rate (Table 2). The increase in respiration rate might be due to acid-base imbalance. The increased pulse rate in aspirin treated group may be due to increased circulating plasma volume and cardiac output (Sharma, 2002). The clinical response to NSAIDs was also systemically recorded. All the drugs barring nimesulide evoked significant changes. The clinical signs recorded were vomition, anorexia, lethargy, depression, diarrhoea and dehydration. These findings may be attributed to effect of NSAIDs on gastro-intestinal mucosa. Local irritation by the orally administered drugs might have induced a back diffusion of acids into the gastric mucosa. This in turn might have induced tissue inhibition of biosynthesis of prostaglandins, which serve as local cytoprotective agent. Similar observation was previously recorded by Cosenza (1984).

The result of the present investigation suggests that treatment of dogs with nimesulide did not produce any untoward effect on the haematological and clinical parameters. Therefore, nimesulide can be regarded as the safest drug in the treatment of anti-inflammatory condition.

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Table 1
Effect of chronic administration of NSAIDs on certain haematological parameters in dogs

Group No.	Treatment	Hb (gm/dl)	PCV (%)	Plasma protein conc. (gm/dl)	Clotting time (min)
A	Control	9.40±0.35	30.53±0.95	7.70±0.63	1.16±0.04
B	Aspirin	8.40**±0.30	27.90**± 0.90	7.75±0.43	1.55**±0.10
C	Ibuprofen	9.60±0.17	31.00±1.07	7.25±0.33	0.95**±0.01
D	Nimesulide	9.73±0.20	31.50±1.10	7.68±0.78	1.10±0.04

Number of animal in each group = 6 ** Statistical significance at $p < 0.01$ in relation to control (CRD)

Table 2
Effect of chronic administration of NSAIDs on pulse and respiration rate from 1st to 10th day

Days	Pulse rate in Group				Respiration rate in Group			
	A (Control)	B (Aspirin)	C (Ibuprofen)	D (Nimesulide)	A (Control)	B (Aspirin)	C (Ibuprofen)	D (Nimesulide)
1	100.00±1.50	106.80**±1.08	101.95±1.10	100.23±1.10	26.02±1.05	30.80**±0.68	27.00±1.10	27.23±0.50
2	99.50±1.15	107.84**±1.15	98.00±1.05	100.00±1.20	25.80±1.15	31.10**±0.55	26.89±1.32	26.50±0.79
3	97.55±0.90	109.95**±2.18	96.92±1.22	97.95±1.05	27.55±1.25	31.95**±0.58	28.92±0.77	28.20±0.95
4	96.88±0.78	110.00**±1.47	97.00±1.16	96.80±1.30	28.00±0.98	32.00**±0.67	28.10±0.86	28.18±0.70
5	96.20±1.05	113.05**±1.97	96.05±1.10	97.30±1.12	28.20±0.65	33.05**±0.77	28.05±0.70	27.65±0.62
6	96.00±1.56	113.95**±1.18	95.55±1.25	96.95±1.05	27.60±0.56	32.95**±0.88	27.55±1.25	26.95±0.99
7	95.55±1.60	114.02**±1.36	95.15±1.18	96.05±1.20	28.55±0.59	32.95**±0.88	28.15±0.78	27.55±1.00
8	95.01±1.98	112.00**±1.15	94.80±1.20	95.02±1.35	28.01±0.63	33.80**±0.55	27.80±0.99	27.92±1.05
9	95.50±2.10	111.95**±1.80	95.02±1.05	96.02±1.20	28.00±0.40	33.95**±0.80	28.20±0.95	28.10±0.95
10	94.56±1.85	111.67**±1.75	94.80±1.10	95.10±1.25	28.46±0.55	35.67**±0.75	28.80±1.10	28.02±1.25

Number of animal in each group = 6 ** Statistical significance at $p < 0.01$ in relation to control (CRD)

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