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Effects of oral administration of nonsteroidal anti-inflammatory drugs: aspirin and paracetamol in mice

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Abstract

An experiment work was carried out to investigate the effects of oral administration of nonsteroidal anti-inflammatory drugs (NSAIDs) on blood glucose level and haematological parameters (TEC, TLC, Hb%, DLC) in mice. Out of three groups of mice (each containing 10 mice), one group was kept as control without giving any drug. Another two groups of mice received separately aspirin (Ecospirin®, 620 mg/kg b.wt.) and paracetamol (Napa®, 333 mg/kg b.wt.) orally along with normal feed. In treated groups, the blood glucose level and total leucocyte count were increased significantly ($p<0.01$) but the total erythrocyte count (TEC) and haemoglobin content (Hb%) were decreased significantly ($p<0.01$). In case of differential leukocyte count (DLC), neutrophil count was decreased significantly ($p<0.01$) but lymphocyte count was increased significantly ($p<0.01$) in treated groups. In post-mortem examination, congested and hyalinized liver, enlarged kidney and spleen, hemorrhagic stomach and ulcerated intestine were found in NSAIDs treated mice. Long-term oral administration of NSAID is not recommended due to side effects.

Key words: Aspirin, Paracetamol, Blood glucose, Haematology

Introduction

The first drugs which were recognized as providing a reliable and powerful anti-inflammatory effect were glucocorticoids. However, exogenous glucocorticoids administered at therapeutic level quickly bring an unpleasant and other dangerous side effects. Thus alternative means of controlling the various manifestations of the inflammatory process have been pursued. Current interest has been focused more on a group of drugs, which contains many diverse chemicals such as "nonsteroidal anti-inflammatory drugs." The ability of the NSAIDs is to diminish the production of prostaglandin which acts as mediators of inflammatory response (e.g., pyrexia) and as modulators in pain perception (Brander *et al.*, 1991).

NSAIDs are not free from toxic effects both in humans and livestock. The common clinical signs of toxicosis are vomition, diarrhoea, CNS depression and circulatory dysfunctions (Jonnes *et al.*, 1992). The NSAIDs frequently cause irritation, bleeding and gastric ulcer. The major toxic effects included gastric ulcer, hepato-toxicity, impair platelet activity and analgesic nephropathy (Lewis, 1984). The other side-effects associated with the use of NSAIDs include aseptic meningitis (Clemmons and Meyers, 1984, Syvlia *et al.*, 1988) and oral ulcerations (Tobin and Chay, 1986). The information on the effects of NSAIDs (aspirin and paracetamol) in most animals is limited. But the use of NSAIDs (aspirin and paracetamol) has been increasing with their greater effectiveness against fever, pain and inflammation. The present study was undertaken to investigate the effects of two different preparations of oral NSAIDs drugs e.g., aspirin and paracetamol on blood glucose and haematological parameters e.g., TEC, TLC, Hb%, DLC in mice.

Materials and Methods

The experiment was conducted for a period of 70 days (1st August, 2001 to 9th October, 2001). Eight weeks old 30 male swiss albino mice (*Mus muscularis*) were collected from International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR, B), Mohakhali, Dhaka. The mice in house were kept under close observation in order to acclimatize to the new environment for a period of one week prior to commencement of the experiment. The mice were divided randomly into 3 (A, B, C) equal groups of 10 in each group. Group A was kept as control without giving any treatment. Two oral NSAIDs drugs were used i.e. aspirin 620 mg/kg b.wt. (Ecospirin®, The ACME Laboratories Limited, Bangladesh) in group B and paracetamol 333 mg/kg b.wt (Napa®, Beximco Pharma. Ltd., Bangladesh) in group C. The animals were given a basal ration.

The blood was collected from tail and heart of mice in the vials containing EDTA. Blood glucose level was recorded on day 0 (pretreatment) and on 7th, 21st, 42nd and 70th day of experimental period using glucose meter (Glucotrend). Hematological parameters (TEC, TLC, Hb%, DLC) were determined using standard methods as described by Coffin (1955) and Schalm (1965).

The mice of all groups were sacrificed on the 70th day for post-mortem examination to detect gross pathological changes. The data were analyzed statistically by using student's 't' test for the significance of differences in control and treated groups.

Results and Discussion

The effects of oral administration of two nonsteroidal anti-inflammatory drugs i.e. aspirin (620 mg/kg b.wt.) and paracetamol (333 mg/kg b.wt.) on blood glucose level and certain haematological parameters were shown in Table 1. A significant ($p<0.01$) increase of blood glucose level was found on days 7, 21, 42 and 70 following oral administration of aspirin and paracetamol. This result is agreeable with the findings of Bhaumik and Sharma (1993). The increase of blood glucose level might be due to NSAIDs increasing the output of glucocorticoids, displacing glucocorticoids from plasma-protein binding and increasing concentration of glucocorticoids. These glucocorticoids increase gluconeogenesis, decrease protein synthesis and reduce peripheral glucose utilization (Brander *et al.*, 1991, Adams, 1995). Total erythrocyte count (TEC) decreased significantly ($p<0.01$) at 7th, 21st, 42nd and 70th day in aspirin and paracetamol treated groups. Haemoglobin content (Hb%) was also decreased significantly ($p<0.01$) in treated groups. The total leukocyte count (TLC) increased significantly ($p<0.01$) from day 7 to day 70 in all treated groups. In case of differential leukocyte count, neutrophil count decreased significantly ($p<0.01$) while lymphocyte count was increased significantly ($p<0.01$) from day 7 and contained upto last day of experimental period (70th day) in treated groups. The haematologic findings were in conformity with the earlier workers (Sharma *et al.*, 1993, Bhaumik and Sharma, 1993, Ramesh *et al.*, 2001). The decrease of TEC and Hb% might be due to shortened the life span of RBC and oxidization of haemoglobin to methomoglobin and sulphaemoglobin caused by NSAIDs respectively (Brander *et al.* 1991). The other white blood cells were unaffected.

Congested and hyalinized liver, enlarged kidney and spleen, haemorrhagic stomach and ulcerated intestine were the frequent necropsy findings in all treated groups. These findings were supported by previous reports (Davis, 1985, Saxena *et al.*, 1987, Mohapatra *et al.*, 1993, Reimer *et al.*, 1999, Saekwang *et al.*, 2000).

Table 1. Effects of NSAIDs (aspirin and paracetamol) on blood glucose and certain haematological parameters in mice

Parameters	Groups	Drugs	Pretreatment (Mean± SE)	Post-treatment (days) (Mean± SE)			
			Day 0	7	21	42	70
Blood glucose (mg/dl)	A	-	8.30±0.1	8.30±0.0	8.30±0.2	8.30±0.1	8.26±0.1
	B	Aspirin	8.24±0.1	8.52±0.1**	9.00±0.1**	9.54±0.1**	9.80±0.1**
	C	Paracetamol	8.32±0.1	8.70±0.1**	9.12±0.1**	9.78±0.1**	10.16±0.1**
Total erythrocyte (million/cu.mm.)	A	-	6.80±0.1	6.85±0.2	6.89±0.0	6.86±0.2	6.87±0.2
	B	Aspirin	6.84±0.1	6.50±0.2**	5.86±0.1**	5.70±0.2**	5.33±0.2**
	C	Paracetamol	6.89±0.1	6.52±0.2**	6.20±0.2**	5.63±0.2**	5.40±0.2**
Total leucocyte (thousand/cu.mm.)	A	-	8.23±0.1	8.26±0.1	8.14±0.2	8.22±0.1	8.18±0.1
	B	Aspirin	8.26±0.1	8.92±0.1**	9.11±0.1**	9.62±0.1**	10.97±0.1**
	C	Paracetamol	8.22±0.2	9.10±0.2**	9.84±0.2**	10.22±0.2**	10.97±0.3**
Haemoglobin (gm%)	A	-	12.67±0.2	12.58±0.1	12.71±0.1	12.76±0.1	12.73±0.1
	B	Aspirin	12.76±0.5	11.09±0.1**	10.80±0.3**	10.73±0.2**	10.29±0.2**
	C	Paracetamol	12.44±0.5	11.49±0.2**	11.06±0.3**	11.21±0.2**	10.04±0.2**
Lymphocyte (%)	A	-	63.00±2.1	65.00±1.4	62.00±1.0	60.00±1.4	64.00±1.7
	B	Aspirin	66.00±1.0	71.80±1.2**	72.66±3.5**	73.00±1.4**	74.00±1.6**
	C	Paracetamol	65.20±1.8	71.00±1.4**	73.00±3.5**	73.00±3.5**	74.00±2.3**
Neutrophil (%)	A	-	19.20±1.1	19.20±1.6	19.25±1.6	19.00±1.2	19.00±1.6
	B	Aspirin	19.00±1.6	17.00±1.1**	16.85±1.3**	15.00±0.7**	12.00±1.1**
	C	Paracetamol	20.00±1.9	17.75±1.3**	17.00±1.1**	12.00±1.7**	11.00±1.1**

** = Significant at 1% level

It may be concluded that oral administration of NSAIDs not only increased the blood glucose level but also had variable effects on haematological parameters in mice.

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