Indian J Physiol Pharmacol 1992; 36(2) : 133-134

SHORT COMMUNICATION

FAILURE TO REDUCE EXPERIMENTAL MYOCARDIAL INFARCT SIZE WITH IBUPROFEN PRE-TREATMENT IN RATS

A. LAL* AND M. L. SHARMA

Department of Pharmacology,
M.G.I.M.S., Sevagram - 442 102
Distt. Wardha (Maharashtra State)

(**Received on January 7, 1992**)

Abstract : The prophylactic role of ibuprofen in experimental myocardial infarction has not been reported. Twentyfour rats pre-treated with ibuprofen (30 mg/kg), po, for 21 days were subjected to myocardial infarction by administration of isoprenaline hydrochloride (85 mg/kg), sc, on two consecutive days. An equal number of rats were given saline to serve as control. Heart specimens were taken for macroscopic and microscopic examination after 1 day, 5 days, 12 days and 21 days, following myocardial infarction. Ibuprofen pre-treatment caused a significant increase in infarct size at all the intervals studied ($P< 0.01$), indicating that ibuprofen exerted a harmful effect in increasing the size of experimental myocardial infarction.

Key words : ibuprofen myocardial infarction isoprenaline

INTRODUCTION

There exists certain similarities between the pathophysiological processes involved in acute myocardial infarction and acute inflammatory reaction. This has led to the notion that non-steroidal anti-inflammatory drugs (NSAID) may protect against ischemic myocardial damage (1, 2). However, NSAID have been shown both to protect against (1, 3, 4) as well as to increase (5, 6) experimental myocardial infarction.

Ibuprofen has been reported to reduce myocardial infarct size in rats and dogs, when used after the production of experimental myocardial infarction (3, 4). But its prophylactic role in myocardial infarction has not been reported yet. The present study was aimed at assessing such a prophylactic role of ibuprofen. The myocardial infarction was produced by high doses of isoprenaline as this model has certain advantages that it does not require any expertise or expensive equipment, and is less time consuming, coupled with low mortality (7).

METHODS

Fortyeight albino rats of either sex, weighing 200 ± 50 gm, were divided into two groups of 24 rats each. In one group ibuprofen 30 mg/kg was administered in 1 ml of saline, po, for 21 days. The control group was fed with an equal volume of saline. During this period both the groups were given standard rat feed and water *ad libitum*. At the end of 21 days myocardial infarction was induced in both groups by the method of Rona et al (7), by giving them isoprenaline hydrochloride 85 mg/kg, sc, daily for 2 consecutive days. The animals were then divided into 4 sub groups of 6 animals each. They were sacrificed and hearts removed after 1 day, 5 days, 12 days, and 21 days, following myocardial infarction. The macroscopic and microscopic findings were graded according to the method of Rona et al (7).

The results were compared using Mann-Whitney U test and the $P< 0.05$ was considered statistically significant (8).

*Corresponding Author

RESULTS

Table I, summarising the results, shows a significant increase in macroscopically and microscopically studied myocardial infarct size in ibuprofen pre-treated group, as compared to the control group, on all the post-infarction intervals studied ($P < 0.01$).

TABLE I : Macroscopic and microscopic findings in the control (C) and ibuprofen pre-treated (I) groups after 1 day, 5 days, 12 days, and 21 days following myocardial infarction in rats.

	After 1 day		*After 5 days*		*After 12 days*		*After 21 days*	
	C	*I*	*C*	*I*	*C*	*I*	*C*	*I*
Macroscopic finding	1.67± 0.21	3.17± 0.17*	2.67± 0.21	3.67± 0.21*	3.00± 0.00	4.00± 0.00*	2.83± 0.17	4.00± 0.00*
Microscopic findings	1.67° 0.21	3.17± 0.17*	2.67± 0.21*	3.67± 0.21*	3.00± 0.00	4.00± 0.00*	2.83± 0.17	4.00± 0.00*

*P<0.01 vs control at respective interval.

(Data are mean±SEM of 6 animals in each group)

DISCUSSION

In the present study, prolonged oral pre-treatment of rats with ibuprofen 30 mg/kg, resulted in a significant increase in experimentally produced myocardial infarct size as compared to the normal saline pre-treated controls. This is in agreement with the studies of some other workers who have reported an increase in myocardial infarct size after pre-treatment of animals with NSAID (5, 6). But these are not in consonance with the observations of some other workers who showed a protective effect of ibuprofen on experimental myocardial infarction (3, 4). However, they had used ibuprofen, 12.5 mg/kg, im, after the production of experimental myocardial infarction.

It has been reported that small doses of ibuprofen suppress lysozyme release by stabilizing the lysosomal membrane (9), prevent platelets aggregation by inhibiting thromboxane synthesis (10), and inhibit the leukocyte migration (11). However, in large doses ibuprofen produce lysis of lysosomal membrane, leading to the leakage of lysozyme (12), and inhibit the prostaglandins synthesis which have vasodilatory properties (13, 14). These could be the mechanism by which ibuprofen 30 mg/kg, po, increased the myocardial infarct size in the present study.

REFERENCES

1. Ogletree ML, Lefer AM. Influence of non-steroidal anti-inflammatory agents on myocardial ischemia in cats. *J Pharmacol Exp Ther* 1976; 197 : 582-593.
2. Libby P, Maroko PR, Bloor CM, Sobel BE, Braunwald E. Reduction of experimental myocardial infarct size by corticosteroids administration. *J Clin Invest* 1973; 52 : 599-607.
3. Maclean D, Fishbein MC, Blum RI, Braunwald E, Maroko PR. Long term preservation of ischemic myocardium by ibuprofen after experimental coronary artery occlusion (abstr). *Am J Cardiol* 1978; 41 : 394.
4. Ribeiro LGT, Yusuda T, Lowenstein E, Braunwald E, Maroko PR. Comparative effects on anatomic infarct size of verapamil, ibuprofen, and morphine-promethazine-chlorpromazine combination (abstr). *Am J Cardiol* 1979 ; 43: 396.
5. Jugdutt BI, Hutchins GM, Bulkley BH, Bechker LC. Effect of indomethacin on collateral blood flow and infarct size in the conscious dog. *Circulation* 1979 ; 59: 734-743.
6. Sharma S, Arora S, Sanan S. Failure of acetyl salicylic acid (aspirin) to reduce experimental myocardial ischemic damage. *Ind J Physiol Pharmacol* 1981 ; 25: 325-330.
7. Rona G, Chappel CI, Balazs T, Gaudry R. An infarct like myocardial lesion and other toxic manifestations produced by isoproterenol in the rats. *Arch Pathol* 1959; 67 : 443-455.
8. Shortcut and non-parametric methods. In : Snedecor GW, Cochran WG, eds. Statistical Methods. India : Oxford & IBH Publishing Co Pvt. Ltd. 1967; 120-134.
9. Smith RJ, Sabin C, Gilchrest H, Williams S. Effect of anti-inflammatory drugs on lysosomes and lysosomal enzymes from rat liver. *Biochem Pharmacol* 1976; 27: 2171-2177.
10. Packham MA, Mustard JF. Clinical Pharmacology of platelets. *Blood* 1977 ; 50 : 555-573.
11. Brown KA, Collins AJ. Action of non-steroidal anti-inflammatory drugs on human and rat peripheral leukocyte migration *in vitro*. *Ann Rheum Dis* 1977 ; 36 : 239-243.
12. Lewis DA. The action of some non-steroidal drugs of lysosomes. *J Pharm Pharmacol* 1970 ; 22: 909-912.
13. Bloor CM, White FC, Sobel BE. Coronary and systemic hemodynamic effects of prostaglandins in the unanesthetized dog. *Cardiovasc Res* 1973; 7: 156.
14. Rowe GG, Afonoso S. Systemic and coronary hemodynamic effects of intracoronary administration of prostaglandins E_1 and E_2. *Am Heart J* 1974; 88: 51.