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A comparative study of nicardipine with diclofenac sodium in chemically induced inflammatory models in rats and mice

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ABSTRACT

The present study is to compare the anti-inflammatory effect of Nicardipine with diclofenac sodium in rats and mice. The study was conducted using carrageenan-induced rat and mice paw inflammation models. Albino mice and wistar rats of either sex were divided in to four groups of six each. One of the groups was chosen as control, while the remaining three groups were drug treated groups. The control group received only normal saline intraperitoneally. While the other three groups received Diclofenac sodium (25mg/kg), Nicardipine (10mg/kg) and low dose Nicardipine (5mg/kg) intraperitoneally. After 30 minutes all the animals were injected with 0.1ml and 0.05 ml 1 % carrageenan respectively in to the animal hind paws. Paw volume measured by dipping in to the mercury plethysmograph. After carrageenan injection the time for number of licks were noted. Nicardipine in the dose of 10mg/kg was found to be equally effective with diclofenac sodium (25 mg/kg) in reducing edema in rats. In mice Nicardipine in the dose of (25 mg/kg) was found to be more effective than diclofenac sodium (25 mg/kg) in reducing pain and edema.

Key words: Acute Inflammation, Diclofenac sodium, Nicardipine, Carrageenan

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INTRODUCTION

Inflammation is the reaction of vascularized connective tissue to local injury. Inflammation is fundamentally a protective response the ultimate goal of which is to rid the organism of both initial cause of cell injury and the consequences of such injury. Without inflammation infections would go unchecked; wounds would never heal and injured organs would become permanent festering sores.

Inflammation and repair may be potentially harmful. However, inflammatory reactions for example underlie life threatening hypersensitivity reactions to insect bites, drugs and toxins as well as some chronic diseases such as rheumatoid arthritis, atherosclerosis and lung fibrosis. Repair by fibrosis may lead to disfiguring scars or fibrous bands that cause intestinal obstruction or limit the mobility of joints.

Any drug, which can prevent or suppress any or more of the components of inflammation are termed anti-inflammatory agents. Plenty of drugs have flooded the market and there is continuing flow of preparations, because of the fact that none is ideal in controlling or modifying the signs and symptoms of inflammation, particularly in the common inflammatory joint diseases. None of these NSAIDs are without a side effect. Hence there is a need for intense research for an anti inflammatory agent free from side effects. Most of the currently available anti inflammatory drugs Like NSAIDs will inhibit the cyclooxygenase pathway and therefore inhibits the synthesis of

prostaglandins. Another group consisting mainly of steroidal anti-inflammatory drugs exerts their actions by inhibiting the enzyme phospholipase-A2.

Calcium ions play an important role in the synthesis and release of chemical mediators of inflammation. While increased calcium may potentiate inflammatory events, decreased calcium may reduce such events. In inflammation, arachidonic acid metabolites are the most important mediators. Calcium ions increase the lipoxygenase products by activating 5-lipoxygenase enzyme and eicosanoid synthesis by activating cytosolic Phospholipase-A2. Elastase and superoxide anion radicals are also activated by calcium ions. So inhibiting these calcium ions proves to be a potential target for anti-inflammatory drugs. These calcium ions mainly act on L-type of calcium channels.

My present work is based on the induction of inflammation by a chemical carrageenan and evaluation of effect of Nicardipine, which is a L-type of calcium channel blocker on the signs of inflammation mainly on pain and edema in rats and mice.

MATERIALS AND METHODS

Albino mice and Wistar rats of either sex were divided in to four groups of six each. One of the groups was chosen as control, while the remaining three groups were designated as the drug treated groups.

On each day of the experiment one animal was taken from the each group, and an anatomical marking made at the level of the malleolus of the right hind paw of the animal, in order to fix a constant level up to which the animal paw must be dipped in the plethysmograph every time.

The control group received only normal saline intraperitoneally. While the other three groups received Diclofenac sodium (25mg/kg), Nicardipine (10mg/kg) and low dose Nicardipine (5mg/kg) intraperitoneally. After 30 minutes all the animals were injected with 0.1ml and 0.05 ml 1 % carrageenan respectively in to the animal hind paws. Immediately after the sub plantar injection of carrageenan, paw volume measured by dipping in to the mercury plethysmograph (zero hour value). Similar recordings were taken at 30, 60 and 120 minutes.

After carrageenan injection the time for number of licks in early phase (10-15 minutes) and number of licks in late phase (30-40 minutes) were noted.

RESULTS AND DISCUSSION

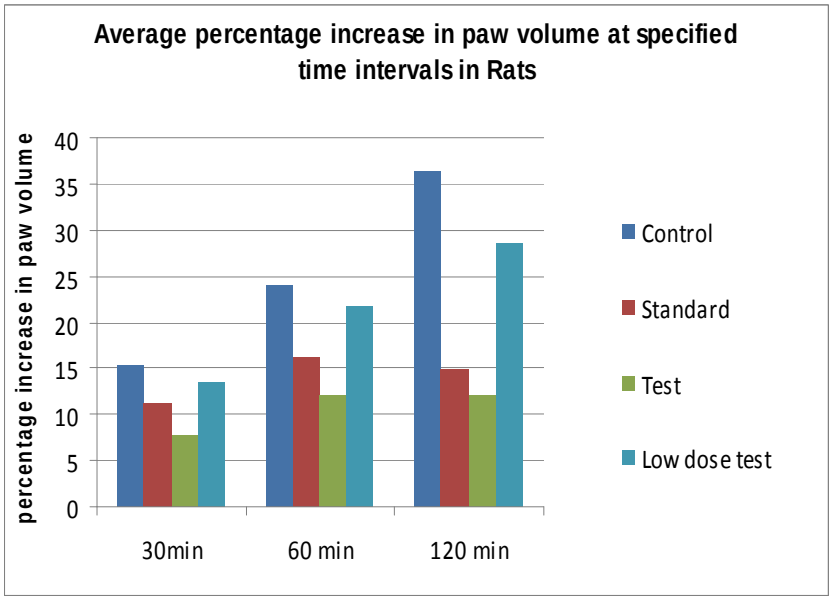
In this study inflammation was assessed by two parameters mainly edema and pain, induced by carrageenan.

Results obtained with the test drug, standard drug were compared. For testing statistical significance ANOVA was used to assess paw edema and unpaired ‘t’ test for assessment of pain.

In rats Nicardipine (10mg/kg) showed a potent anti-inflammatory effect similar to that of diclofenac sodium (25mg/kg) in reducing the edema.

In mouse Nicardipine (10mg/kg) was more effective compared to diclofenac sodium (25 mg/kg) in reducing the edema.

Nicardipine (10mg/kg) was more effective compared to diclofenac sodium (25 mg/kg) in reducing pain, both in rats and mice.


Average percentage increase in paw volume at specified time intervals in Rats
percentage increase in paw volume
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15
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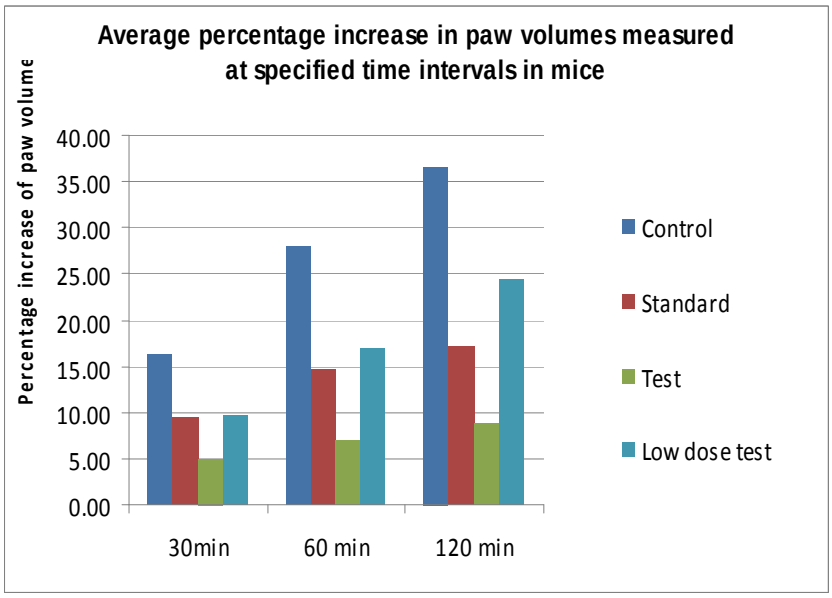
120 min
Control
Standard
Test
Low dose test


Average percentage increase in paw volumes measured at specified time intervals in mice
Percentage increase of paw volume
40.00
35.00
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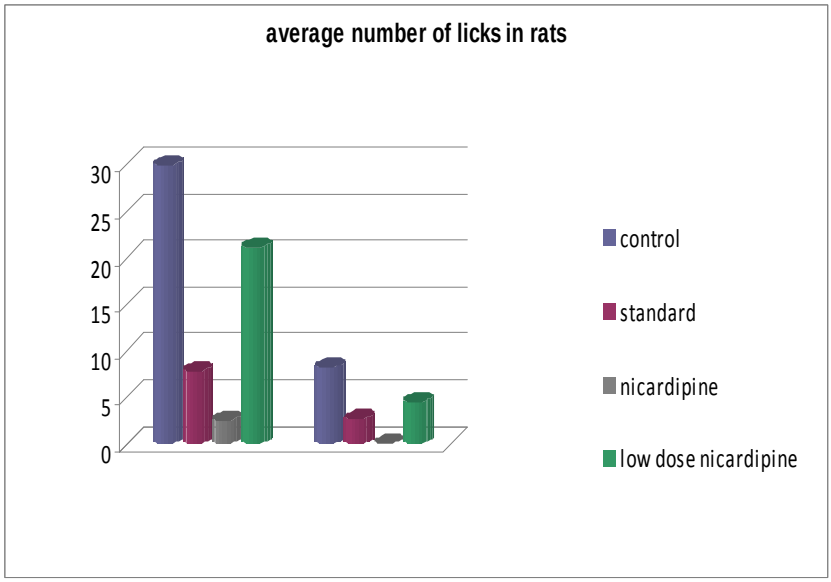
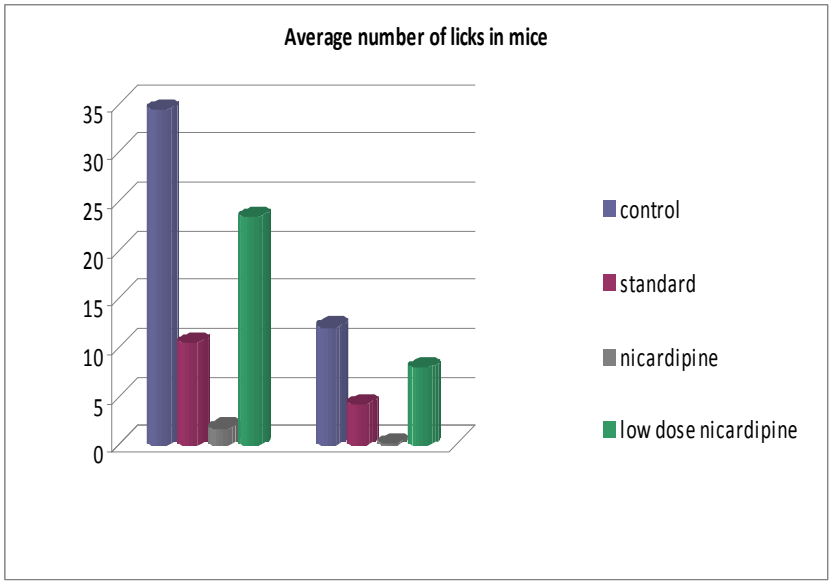
Control
Standard
Test
Low dose test





CONCLUSION

Finally based on the above study conclusion has been drawn. To conclude it may be said that

Nicardipine in the dose of 10mg/kg was found to be equally effective with diclofenac sodium (25 mg/kg) in reducing edema in rats.

In mice Nicardipine in the dose of (25 mg/kg) was found to be more effective than diclofenac sodium (25 mg/kg) in reducing pain and edema.

Nicardipine in the dose of 5mg/kg was found to be less effective than Diclofenac sodium (25 mg/kg) in rats and mice.

However studies with other models of inflammation and with other calcium channel blockers on experimental animals and human beings would be needed to substantiate the present work.

REFERENCES

[1] ***Robbins and Cotran, Pathologic Basis of Disease***, Page no 48-85. -7th edition, Kumar, Abbas and Fausto. Anti-inflammatory effect of L- type of calcium channel blockers, Tukiye, Klinikleri journal of medical sciences **2007**, 27; 328-334.
[2] Hypertension: ***management of hypertension*** in adults in primary care. Clinical guideline G34. National Institute for Health and Clinical Excellence (NICE), June **2006.**
[3] ***Grossman E, Messerli FH, Grodzicki T, Kowey*** P (1996). "Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudo emergencies". JAMA 276 (16): 1328–31.
[4] **King JF, Flenady VJ, Papatsonis DN, Dekker GA, Carbonne** *B* (**2003**). "Calcium channel blockers for inhibiting preterm labour".
[5] ***De Vries GW, Mc Laughlin A, Wenzel MB, Perez J, Harcourt D, Lee G, et al***. The anti-inflammatory activity of topically applied novel calcium channel antagonists. Inflammation **1995**; 19:261-75.
[6] ***Lake BG, Lyubsky S.*** Dose dependent effect of continuous subcutaneous verapamil infusion on experimental acute pancreatitis in mice. Dig Dis Sci **1995;** 40:2349-55.
[7] ***Yeole, P.G., Khan, S., and Patel, V.F.,*** Ind. J. Pharm. Sci**., 2005**, 67(3), 265-272
[8] ***Klausner, E.A., Lavy, E., Friedman, M., Hoffman*** A. J. Control. Rel. **2003**, 90, 143-162.
[9] ***Gollasch M, Haase H, Ried C, Lindschau C, Morano I, Luft FC, Haller H***. L-type calcium channel expression depends on the differentiated state of vascular smooth muscle cells. FASEB J. **1998**; 12:593-601.
[10] ***Stokes L, Gordon J, Grafton G***. Non-voltage-gated L-type Calcium channels in human T cells: pharmacology and molecular characterization of the major alpha pore-forming and auxiliary beta-subunits. J Biol Chem. **2004**; 279:19566 –19573.
[11] ***G.N,Aditya,R.N Chattopadhyay, S. Mandal, R.K.Roy. H.L.Lahiri***, Department of Indian Journal of pharmacology, **1997**,preliminary study on anti-inflammatory effect of calcium channel blockers in Albino rats: 132-134.
[12] Drugs, volume 66, special issue 1, **2006**, pp 28 – 30 Publisher ***Adis international. Anti- inflammatory effect of nifedipine.***