International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

Evaluation of Anti Inflammatory Activity of Benazepril in Albino Rats

Meenambal .S[1], *Israel Raja Johnley .I

[1]Assistant Professor of Pharmacology, Government Thoothukudi Medical College, Thoothukudi, India
*Assistant Professor of Pharmacology, Government Thoothukudi Medical College, Thoothukudi, India

Abstract: ***Inflammation is a component of the biological response of the body to harmful stimuli like pathogens, damaged cells, irritants, etc[1]. It plays a protective role by the process of innate defense of the body and indicate itself clinically by four cardinal signs such as redness, heat, pain, and edema.***

Keywords: Benazepril, Indomethacin, Carrageenan, Paw edema, Rats

1. Introduction

Inflammation is a component of the biological response of the body to harmful stimuli like pathogens, damaged cells, irritants, etc[1]. It plays a protective role by the process of innate defense of the body and indicate itself clinically by four cardinal signs such as redness, heat, pain, and edema.

Treating inflammation with the analgesic, non steroidal anti-inflammatory drugs (NSAIDs), and corticosteroids leads to many adverse effects like gastric discomfort, gastric erosion, cardiovascular and renal effects precipitation of diabetes mellitus, and increased susceptibility to infection[2].Indomethacin was also particularly active in the carrageenan-induced rat paw model of inflammation[3].

Indomethacin is a non steroidal anti-inflammatory drug (NSAID) and its mechanism of action is by inhibiting cyclooxygenase nonselectively. It also inhibits phospholipase A and C. It acts by reducing neutrophil migration and by decreasing T cell and B cell proliferation. NSAIDS are obviously known for their gastrointestinal and cardiovascular side effects[4].

Benazepril is anACE inhibitor and it inhibits angiotensin II molecule formation[5]. Evidence shows, there is an alteration in angiotensin II molecule is implied in the anti inflammatory effect of benazepril and it is found to be lack of the side effects of NSAIDs[6]. Benazepril exerts its anti inflammatory property by acting on intracellular ROS (reactive oxygen species) production in rats with LV hypertrophy by the downregulation of both NF-κB and TGF – β signaling pathways[7]. Hence, it suggests that benazepril has an anti inflammatory effect.

2. Aim

To evaluate the anti-inflammatory activity of benazepril in adult albino rats, in comparison with the standard drug Indomethacin using carrageenan induced paw edema model.

3. Materials and Methods

Study Centre:

The study was carried out in the Central animal house, Institute of Pharmacology, Madurai Medical College after getting clearance from the Institutional Animal Ethical Committee.

Experimental design:

The study involves 30 inbred adult albino rats of either sex divided into 5 groups – each group containing 6 rats. Animals were kept in cages and allowed to acclimatize for a period of one week prior to the study. They were housed at an ambient temperature and kept on overnight fasting with access to water ad libitum.

Groups	Study	Treatment
1.	Control	Normal feed and water
2	Standard	Normal feed, water and Indomethacin 10mg/kg po
3	Test – 1	Normal feed, water and TabBenazepril 5mg/kg p.o.
4	Test – 2	Normal feed, water and Tab Benazepril 10 mg/kg p.o.
5	Test – 3	Normal feed, water and Tab Benazepril 15 mg/kg p.o.

4. Methodology

1% Carrageenan induced paw edema in rats[8].

Paw edema was induced by subplantar injection of 0.1ml of 1% sterile Carrageenan in saline into left hind paw. The standard drug and test drug were administered one hour prior to the carrageenan injection. The paw edema was measured (by marking it at the level of ankle joint) by using plethysmograph, immediately after 30 minutes, 1 hour, 2 hours and 3 hours of injecting carrageenan. The difference between the left and right paw edema volume was determined and the percentage reduction in edema was calculated in comparison to the control animals.

Percentage inhibition in edema $\frac{V_c - Vt \times 100}{V_c}$

V_c - Mean volume of paw edema in control group
V_t - Mean volume of paw edema in the drug treated groups

Statistical Analysis:

The statistical analysis was done by one way ANOVA. P values < 0.05 (95% confidence limit) was considered statistically significant and a Fisher's least significant difference post hoc test was done. Data analysis was done using SPSS software.

5. Results

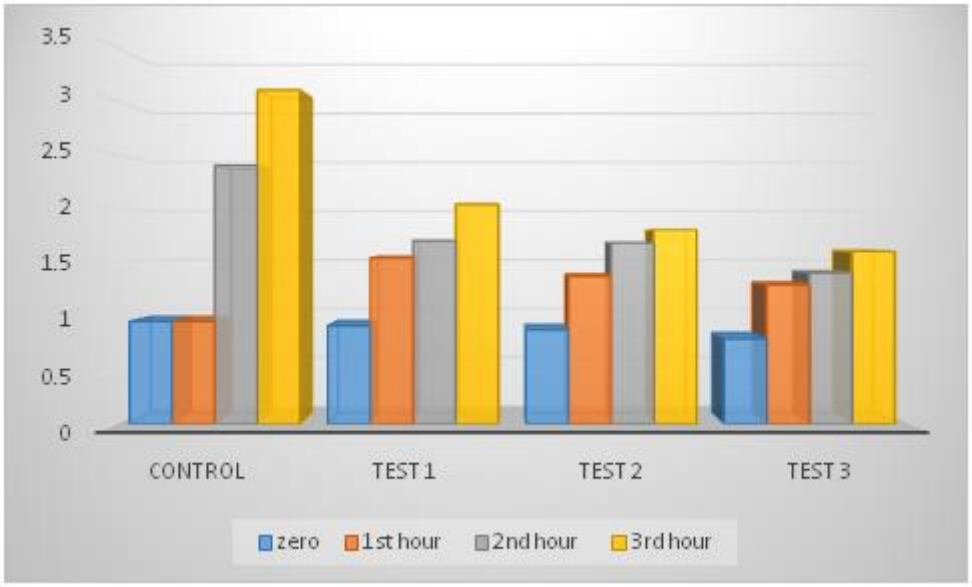
The control group were provided with only food and water ad libitum. Standard group(Group II) received T.Indomethacin 10 mg/kg orally and Groups III, IV and V received 5, 10, 15 mg/kg doses of Tab Benazepril on the day of the experiment, 1 hour before carrageenan injection.

Paw volume was measured in all the groups at baseline, 1 hour, 2 hour and 3 hours of carageenan injection. All groups showed no significant difference at their corresponding baseline values. As given in table 1, the paw volume of control group increased from baseline (0.95+ 0.29) to the third hour (3.2+ 0.43). The standard group had a volume of 0.83+0.25 at baseline, and 1.4+ 0.20 at third hour. Similarly, test groups III, IV, V had a paw volume of 0.91+0.26, 0.87+0.26, 0.79+0.33 at baseline and 2.04+ 0.36, 1.8 +0.26, 1.6+ 0.33 at third hour respectively.

Table 1: Paw volume (ml) as Mean + S.D. among the groups

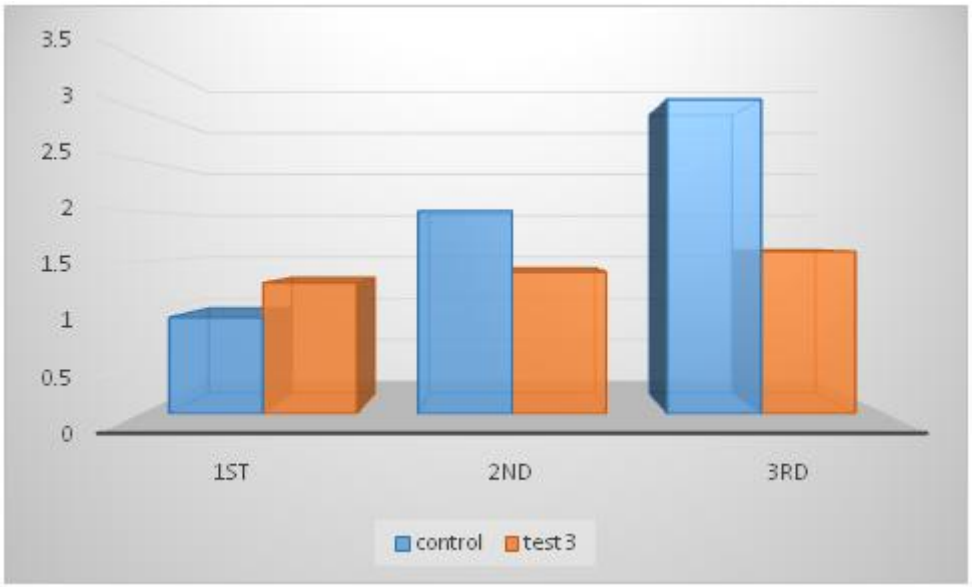
Time / Groups	Zero hour	First hour	Second hour	Third hour
Control	0.95+0.29	0.95±0.29	2.4±0.46	3.2±0.43
Standard	0.83±0.25	1.15±0.12	1.33±0.12	1.4±0.20
Tab Benazepril 5mg/kg	0.91±0.26	1.54±0.18	1.7±0.27	2.04±0.36
Tab Benazepril 10mg/kg	0.87±0.26	1.37±0.13	1.68±0.21	1.8±0.26
Tab Benazepril 15mg/kg	0.79±0.33	1.29±0.24	1.4±0.33	1.6±0.33

Graph 1: Paw volume in ml among the groups



Graph 2: Comparison between control and test groups

Graph 3: Comparison between test groups



Graph 4: Comparison between control and test group 3

Table 2: Percentage inhibition of paw edema between the groups Vs control.

GROUPS	% INHIBITION IN 1ST HOUR	% INHIBITION IN 2ND HOUR	% INHIBITION IN 3RD HOUR
Indomethacin 10mg / kg p. o.	31.95	44.81	54.63
Tab Benazepril 5mg/kg p.o	8.87	26.97	34.36
Tab Benazepril 10mg/kg p.o.	18.63	30.15	39.67
Tab Benazepril 15mg/kg p.o.	23.66	38.45	46.91

*P value less than 0.05 is significant

The standard and test drug treated groups showed a statistically significant difference in their anti-inflammatory activity when compared with the control group. A following post hoc test showed that the anti inflammatory activity for the test drug when compared to the control was in the order of Group V > Group IV > Group III > Control.

6. Discussion

In this present study anti inflammatory effect of Benazepril, an ACE inhibitor was evaluated in albino rats by using carrageenan induced paw edema model and it was found to be statistically significant.

Angiotensin II (Ang II) is a vasoconstrictor molecule. It acts by stimulating sympathetic nervous system and it increases aldosterone secretion. The other actions are induction of growth, cell migration, and mitosis of vascular smooth muscle cells, increased synthesis of collagen type I and III in fibroblasts, leading to thickening of the vascular wall and myocardium, and fibrosis[9].

Ang II is a potent vasoconstrictor that magnifies endothelial dysfunction, decreases NO, and induces inflammatory states by enhancing release of interleukin (IL)-6 and other inflammatory markers. Nuclear factor-κB (NF-κB) is central to the inflammatory response, stimulating expression of tumor necrosis factor-α (TNF-α), IL-1, IL-6, and, via a feedback pathway, further NF-κB production.

The central role of the renin-angiotensin system in the pathogenesis of cardiovascular disease is well established. Elevated levels of Ang II, a potent vasoconstrictor, combined with a reduction in NO levels, enhances vasoconstriction, inflammation, and the atherogenic process[10]. Blocking the formation of Ang II with an ACE inhibitor increases NO availability, improving flow-mediated vasodilation, blood flow, and cGMP production as well as reducing oxidant stress and inflammation in the endothelium.

Importance of ACE inhibition as a mechanism for restoring the balance in the NO-cGMP pathway to prevent inflammation, ischemia, and cardiac hypertrophy. The AT2 receptor is stimulated in left ventricular hypertrophy and is coupled to NO-cGMP signaling. The NO-cGMP pathway may, therefore, be an important protective mechanism to prevent left ventricular hypertrophy, ventricular dilatation, and heart failure. Benazepril alone significantly improved CIF levels of NOX, cGMP, and inflammatory markers, and attenuated infarct expansion[11].

Clinical observations of ACEI/ARB and statin treatment combination among patients with heart failure can further improve ventricular remodeling and decline inflammatory factors, such as CRP[12].

Further elaborative studies are needed to potentiate this claim.

References

[1] Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018 Jan 23;9(6):7204.
[2] Crofford LJ. Use of NSAIDs in treating patients with arthritis. Arthritis research & therapy. 2013 Jul 1;15(S3):S2.
[3] Brune K, Hinz B. The discovery and development of antiinflammatory drugs. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2004 Aug;50(8):2391-9.
[4] Moore N, Pollack C, Butkerait P. Adverse drug reactions and drug–drug interactions with over-the-counter NSAIDs. Therapeutics and clinical risk management. 2015;11:1061.
[5] Liu XP, Pang YJ, Zhu WW, Zhao TT, Zheng M, Wang YB, Sun ZJ, Sun SJ. Benazepril, an angiotensin-converting enzyme inhibitor, alleviates renal injury in spontaneously hypertensive rats by inhibiting advanced glycation end-product-mediated pathways. Clinical and Experimental Pharmacology and Physiology. 2009 Mar;36(3):287-96.
[6] Bregonzio C, Armando I, Ando H, Jezova M, Baiardi G, Saavedra JM. Anti-inflammatory effects of angiotensin II AT1 receptor antagonism prevent stress-induced gastric injury. American Journal of Physiology-Gastrointestinal and Liver Physiology. 2003 Aug;285(2):G414-23.
[7] Ranjbar R, Shafiee M, Hesari A, Ferns GA, Ghasemi F, Avan A. The potential therapeutic use of renin–angiotensin system inhibitors in the treatment of inflammatory diseases. Journal of cellular physiology. 2019 Mar;234(3):2277-95.
[8] Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs. Proceedings of the society for experimental biology and medicine. 1962 Dec;111(3):544-7.

[9] Fyhrquist F, Metsärinne K, Tikkanen I. Role of angiotensin II in blood pressure regulation and in the pathophysiology of cardiovascular disorders. Journal of human hypertension. 1995 Nov;9:S19-24.
[10] Vallance P, Chan N. Endothelial function and nitric oxide: clinical relevance. Heart. 2001 Mar 1;85(3):342-50.
[11] Siragy HM, Xue C, Webb RL. Beneficial effects of combined benazepril-amlodipine on cardiac nitric oxide, cGMP, and TNF-α production after cardiac ischemia. Journal of cardiovascular pharmacology. 2006 May 1;47(5):636-42
[12] Tang SY, Peng DF, Hu YJ, Chen J. Protective effects of valsartan and benazepril combined with atorvastatin on cardiorenal syndrome in rats. Eur Rev Med Pharmacol Sci. 2015 Mar 1;19(5):759-66