International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Study on Anti-Inflammatory Effect of Baclofen in Albino Rats

Dr. Mangala Devi .R[1], Dr. Sarojini .R[2], Dr. Ahil .M .S[3], Dr. Vasanth .S[4]

[1]Post Graduate, Institute of Pharmacology, Madurai Medical College

[2]Professor, Institute of Pharmacology, Madurai Medical College

[3]Assistant Professor, Institute of Pharmacology Madurai Medical College

[4]Assistant Professor, Department of Pharmacology, Govt Thiruvarurmedical College

Abstract: ***Introduction: Inflammation is a response to any noxious stimuli such as physical, chemical, immunological or infection, which produces cellular damage. Inflammation is characterized by the classic signs of rubor, calor, tumor, dolor, and functiolaesa. Baclofen is a selective GABA- B agonist. Diclofenac is an NSAID acts by inhibiting cyclooxygenase enzyme. Baclofen is known to interfere with the functions of proinflammatory chemokine receptors In this present study, baclofen was evaluated for its anti-inflammatory activity in acute inflammation.AIM: To evaluate the anti-inflammatory activity of baclofen in adult albino male rats. MethodS: Eighteen adult male albino rats weighing about 150-200gms were used for this study. They were divided into 3 groups of 6 rats in each group I control normal feed and water group IIstandard normal feed and water and received diclofenac 10 mg/kg orally and group III received normal feed and water and baclofen 8 mg/kg orally.Carrageenan was used to induce edema in mice and anti-inflammatory effect was evaluated using mercury plethysmography Results: There was a statistically significant anti-inflammatory activity with Baclofen comparable to Diclofenac, after three hours. The percentage inhibition of edema was 64% with diclofenec (group II) and 56.5% with baclofen (Group III). Conclusion: Study showed that baclofen has significant anti-inflammatory activity in acute inflammatory animal model.***

Keywords: Ant inflammation,Baclofen,Diclofenac,Paw edema,Swiss albino rat

1. Introduction

Inflammation is a complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants, and is a protective response involving immune cells, blood vessels, and molecular mediators. The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and to initiate tissue repair. The classical signs of inflammation are heat, pain, redness, swelling, and loss of function. Inflammation is a generic response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen. Too little inflammation could lead to progressive tissue destruction by the harmful stimulus and compromise the survival of the organism. In contrast, chronic inflammation may lead to a host of diseases, such as hay fever, periodontitis, atherosclerosis, rheumatoid arthritis, and even cancerThe inflammatory process is mediated by release of various cytokines like interleukins, tumor necrosis factor alpha, leukotrienes, prostaglandins, nitric oxide and oxygen derived free radical. They increase local blood flow, vascular permeability, and leukocyte infiltration followed by release of lysosomal contents of neutrophils which eventually cause cellular damage.Inflammation is a protective mechanism but if it runs amok, it may turn potentially harmful to the host.[1] Inflammation is therefore normally closely regulated by the body. Inflammation can be classified as either acute or chronic. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes from the blood into the injured tissues. A series of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged inflammation, known as chronic inflammation, leads to a progressive shift in the type of cells present at the site of inflammation, such as mononuclear cells, and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.[2]Anti-inflammatory drugs help to reduce inflammation and are useful in chronic inflammatory diseases. Diclofenac, a NSAID, act by blocking the enzyme cycloxygenase which catalyse the biosynthesis of prostaglandins and thromboxanes from arachidonic acid and it also inhibits neutrophil chemotaxis and superoxide production at the inflammatory sites.[3]Baclofen is a selective GABA- B agonist. It is a β - chlorphenyl derivative of the neurotransmitter Gama Amino Butyric Acid (GABA) and it is a centrally acting muscle relaxant.[4] Baclofen is known to interfere with the functions of proinflammatory chemokine receptors which are upregulated in cutaneous inflammation. In this present study, baclofen was evaluated for its anti-inflammatory activity in acute inflammation.

2. Aim and Objective

To evaluate the anti-inflammatory activity of baclofen in adult albino male rats.

3. Materials

Study Centre: The study was carried out in the Institute of Pharmacology, Madurai Medical College, Madurai after getting clearance from the Institutional Animal Ethical Committee.(Ref no:5953/E1/5/2015)

Study Design: Eighteen adult male albino rats weighing about 150-200gms were used for this study. They were divided into 3 groups of 6 rats in each. Animals were kept in cages for seven days prior to the study and allowed to acclimatize with the lab environment. They were housed at room temperature with free access to food and water. The animals were on overnight fast prior to study

Table 1: Treatment groups

Group	Study	Treatment
I	Control	Normal feed and water
II	Standard	Normal feed, water and T. Diclofenac –10 mg/kg (oral)
III	Test	Normal feed, water and T.Baclofen-8mg/kg (oral)

4. Methodology

Carrageenan Induced Paw Edema[5]

Baseline paw volume of left hind paw was measured using mercury plethysmograph. One hour after administration of the drugs, a subplantar injection of 0.1 ml of 1% carrageenan was given to the left hind paw of each rat. A marking was done at the level of lateral malleolus to ensure that, the rat paw was dipped to the same level, every time. The left hind paw volume was measured using the mercury plethysmograph after 1hour, 2 hours and 3 hours.

Extent of edema was obtained by subtracting base line left hind paw volume from volume of the same paw at 1 hour, 2 hours and 3 hours after injecting carrageenan. The mean paw volume in animals treated with standard drug and test drug were compared with untreated control group and the anti-inflammatory activity of the drugs were calculated using the formula

$$\text{Percentage inhibition in edema} = \frac{[V_c - V_t]}{V_c} \times 100$$

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 paw edema of the rats, measured at one hour, two hour & three hours were tabulated and analyzed by one way ANOVA. P value < 0.05 (95% confidence limit) was considered statistically significant. Data analysis was done with SPSS software.

5. Results

There was a statistically significant anti-inflammatory activity with Baclofen comparable to Diclofenac, after three hours. The percentage inhibition of edema was 64% with diclofenec (group II) and 56.5% with baclofen (Group III).

Table 2: Mean paw volume and percentage reduction

Group	1 hour	2 hours	3 hours	% inhibition
I	0.997±0.44	1.24±0.04	1.48±0.03	-
II	1.06±0.03	1.037±0.02	0.96±0.04*	64%
III	0.972±0.2	1.027±0.01	0.99±0.03*	56.5%

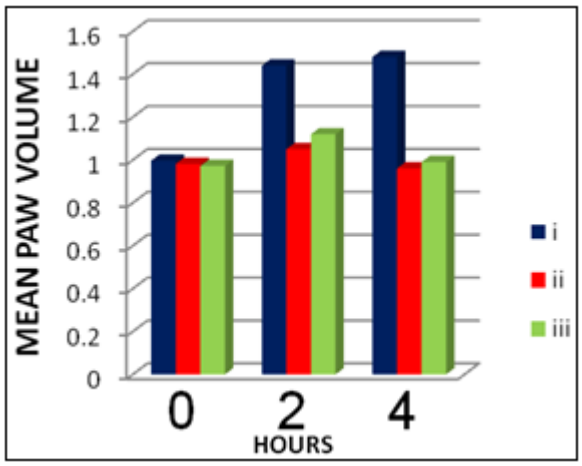

Figure 1: Mean paw volume in 1 hour, 2 hour and 3 hour

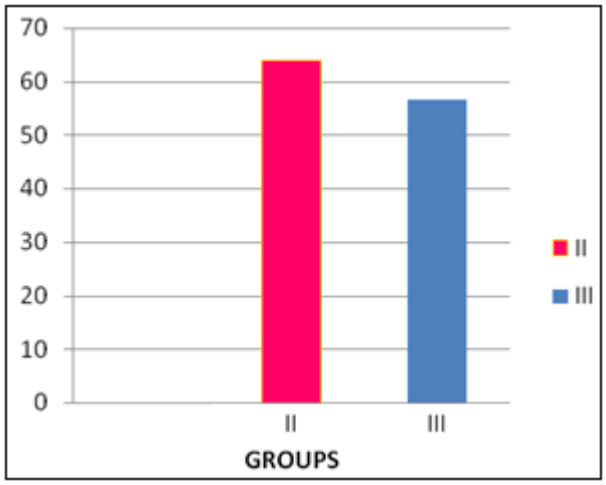

Figure 2: Percentage inhibition of paw edema

6. Discussion

In the present study, anti-inflammatory effect of baclofen was studied using acute inflammatory animal model namely carrageenan induced rat paw edema. Carrageenan is regarded as an established edemogen and edema induced by subplantar injection of carrageenan in rat hind paw is reported to be inhibited by a number of steroidal and non-steroidalanti-inflammatory drugs. It has a biphasic effect. The first phase is due to release of histamine and serotonin (0-2 hrs), plateau phase is maintained by kinin receptors (3hours). The second accelerating phase of swelling is due to PG release (>4 hours).

In this study, the test drug baclofen significantly reduced edema induced by caraggenan. PI (percentage inhibition) of paw edema by baclofen was 56.5% and while diclofenac group showed 64%. Hence baclofen group showed anti-inflammatory activity in acute inflammatory animal model which is comparable to that of diclofenac group.

GABA receptors are G- protein coupled receptors. They are found along with the chemokine receptors on the immune cells. They can undergo heterologous desensitization.[6] Baclofen is known to interfere with the functions of proinflammatory chemokine receptors which are upregulated in cutaneous inflammation. The probable mechanism could be inhibition of synthesis of

prostaglandins, histamine and other inflammatory mediators in the early hours of inflammation.[7]

7. Conclusion

Baclofen is a GABA-B selective receptor agonist. It is a centrally acting muscle relaxant. It is used in the treatment of neurological disorders like multiple sclerosis, spinal injuries and flexor spasms. From the present study it is shown that baclofen has significant anti-inflammatory activity in acute inflammatory animal model. The probable mechanism for the anti-inflammatory action could be due to inhibition of synthesis of prostaglandins and other inflammatory mediators.

Further studies need to be done in various acute and chronic inflammatory animal models along with human studies to strengthen the results. Safety and efficacy of long term administration of baclofen, as a potential anti-inflammatory agent in clinical practice, should be proved.

8. Acknowledgement

We would like to thank Dr.R.Parameshwari Director, Institute of pharmacology, Madurai medical college for permitting us to do the study we would like to thank Dr.S.Vijayalakshmi and Dr.M.Shanthi for helping us to complete the study.

References

[1] Hall, John. Guyton and Hall textbook of medical physiology 12th ed.. Philadelphia, Pa.: Saunders Elsevier. 2011 p. 428.
[2] Porth, Carol .Essentials of pahtophysiology: concepts of altered health states. Hagerstown, MD: Lippincott Williams & Wilkins.2007 p. 270.
[3] Small R E.Diclofenacsodium.Clin Pharm. 1989 Aug;8(8):545-58.
[4] Jin S, Merchant ML, Ritzenthaler JD, McLeish KR, Lederer ED, Torres-Gonzalez E, et al. (2015) Baclofen, a $GABA_BR$ Agonist, Ameliorates Immune-Complex Mediated Acute Lung Injury by Modulating Pro-Inflammatory Mediators. PLoS ONE 10(4): e0121637
[5] FereidoniaM,AhmadianiaA,Semnanianb S,JavanM.An accurate and simple method for measurement of paw edema .Journal of pharmacological and toxicological methods 2000 ;43:11-14
[6] Ward PA. Recruitment of inflammatory cells into lung: roles of cytokines, adhesion molecules, and complement. J Lab Clin Med. 1997;129(4):400–4.
[7] Nielsen, J. F.; Hansen, H. J.; Sunde, N.; Christensen, J. J. "Evidence of tolerance to baclofen in treatment of severe spasticity with intrathecal baclofen". Clinical neurology and neurosurgery. 104 (2): 142–145.