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EVALUATION OF ANALGESIC ACTIVITY OF BENAZEPRIL IN ALBINO RATS

Pharmacology

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ABSTRACT

AIM AND OBJECTIVE: To evaluate the analgesic activity of Benazepril in adult male albino rats in comparison with Aspirin.

MATERIALS AND METHODS: Twenty four inbred adult male albino rats weighing about 150-200 gms were selected from central animal house, Madurai Medical college, Madurai. They were divided into four groups, with six rats in each. Group Iserved as control received normal feed and water. Group II served as standard received T.Aspirin– 100 mg/kg (oral). Group III was test 1 group and it receivedT. Benazepril - 5mg/kg (oral).Group IV was test 2 group and it receivedT. Benazepril - 10mg/kg (oral). The analgesic effect of benazepril was evaluated using Eddy's hot plate method and tail-flick method and compared with the standard analgesic Aspirin.The values obtained are expressed as mean±SEM. Statistical analysis of differences between groups was carried out using one-way analysis of variance (ANOVA). Probability (P) value of <0.05 was taken as the level of statistical significance.

RESULTS: Benazepril showed statistically significant analgesic activity in comparison with control group and standard group ($P < 0.05$).

KEYWORDS

Analgesic effect,Rat, Eddys hot plate, Tail flick, Benazepril

1.INTRODUCTION:

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Analgesic medications are the first line of treatment in pain management.Over the course of human history pain has been treated by psychological technique, physical method (surgical intervention, electrical stimulant, pressure, cold, heat, counter irritant, acupuncture) and by drugs[1].PGE2 sensitizes pain receptors at efferent nerve endings to mediators of pain and amplify algesia[2]. NSAIDs being most commonly employed drug for pain management has side effects like peptic ulcer, increase in bleeding time, worsening of renal function etc[3]. Severe pain due to cancer metastasis and postoperative pain needs the use of strong analgesics like opioid drugs but addiction liability of opioid is a major drawback[4]. In spite of vast number of drugs,search for new analgesics having better efficacy and minimal adverse effect are continuing throughout the world. Benazepril, anACE inhibitor inhibits the formation of angiotensin II molecule. There is an evidence indicating that alteration in angiotensin II molecule is involved in the antinociceptive effect of benazepril and it is found to be devoid of the side effects of NSAIDs.Aspirin, a NSAID, acts by blocking the enzyme cycloxygenase which catalyses the biosynthesis of prostaglandins and thromboxanes from arachidonic acid.

2.MATERIALS AND METHODS:

The study was carried out in the Institute of Pharmacology, Madurai medical college, Madurai after getting clearance from the Institutional AnimalEthical Committee 24 adult male albino rats weighing 150-250gm were obtained from central animal house, Madurai Medical College, Madurai. The animals had free access to food and water ad libitum.The animals were divided into four groups of 6 animals each. Group1 served as control, Group 2 as standard T. Aspirin - 100 mg/kg (oral). Group 3 and Group 4 as test 1 and test 2 respectively T. Benazepril - 5mg/kg (oral) &T. Benazepril – 10mg/kg (oral) .

METHODS FOR EVALUATION OF ANALGESIC EFFECT

Tail flick method

Eddy's hot plate method

ANALGESIOMETER BY TAIL FLICK METHOD:

Tail flick latencies (reaction time) of the animal were assessed by the analgesiometer. The strength of the current passing through the naked nichrome wire was kept constant at 5 amps. The distance between the heat source & tail skin was 1.5 cm. The site of application of the radiant heat in the tail was maintained at 2.5 cm, measured from the root of the tail. The time taken by the animal to withdraw (flick) its tail from the hot wire was noted and taken as the 'reaction time. This tail flicking was considered as the end point of this test and time taken for tail flicking was measured for each rat. The cut-off time of 10 sec was planned to avoid any tissue damage. After drug administration , the reaction time of each rat was recorded at 30mins, 60mins, 90mins, 120mins. The mean of the observed values was considered for statistical analysis.

EDDY'S HOT PLATE METHOD:

The rats were placed on a hot plate, one by one, which was maintained at a temperature of 55 ± 0.5^{0}C throughout the test. A cut-off period of 15 sec was considered as maximal latency to avoid injury to the paws. The time taken by the animals to lick the hind paw or jump away was taken as the reaction time and measured. After drug administration, the reaction time of the rats was recorded at 30mins, 60mins, 90mins,120mins. The mean of the observed values was considered for statistical analysis.

STATISTICAL METHODS:

The values obtained were expressed as mean±SD. Statistical analysis of differences between groups was carried out using one-way analysis of variance (ANOVA). Probability (P) value of <0.05 was taken as the level of statistical significance.

3.RESULTS:

In Tail flick test, the reaction time of the rats were recorded at 30mins, 60mins, 90mins, 120mins, after drug administration. The results obtained were expressed as mean±SD. Benazepril showed statistically significant ($P < 0.05$) elevation in pain threshold in comparison to control, as represented in **Table 1**. The results also demonstrated that analgesic activity produced by benazepril was comparable to that of standard group that received Aspirin**.**

Table 1: Analgesic Activity Of Benazepril By Tail Flick Response In Rats.

Groups	30min	60min	90min	120min
Group I	5.01±0.46	5.34±0.56	5.40±0.38	5.31±0.38
Group II	5.72±0.20	7.15±0.55*	9.30±0.76*	8.60±0.73*
Group III	5.22±0.30	5.73±0.37	7.83±0.26*	7.31±0.41*
Group IV	5.56±0.37	6.83±0.29*	7.63±0.26*	7.67±0.43*

* $P < 0.05$

In hot plate method, the reaction time of the rats were recorded at 30mins, 60mins, 90min, 120mins, after drug administration.The results obtained were expressed as mean±SD.

Benazepril showed statistically significant ($P < 0.05$) elevation in pain threshold in comparison to control, as represented in **Table 2**. The results also demonstrated that analgesic activity produced by benazepril was comparable to that of standard group, which received aspirin.

Table 2. Analgesic Effect Of Benazepril By Eddy's Hot Plate:

Groups	30min	60min	90mins	120mins
Group I	4.08±0.38	3.85±1.00	3.98±0.85	4.46±0.58
Group II	4.32±0.61	5.54±0.50*	7.70±0.51*	8.49±0.51*
Group III	4.24± 0.51	5.19± 0.48	6.41± 0.34	7.66± 0.51*
Group IV	4.24± 0.62	5.49± 0.29*	6.78 ±0.20*	7.99± 0.49*

* $P < 0.05$

4.DISCUSSION:

In tail flick method, 10mg of benazepril showed an earlier response at 60 minutes onwards than 5mg of benazepril.In hot plate method, 10mg of benazepril showed an earlier response at 60 minutes onwards than 5mg of benazepril.In this present study analgesic effect of Benazepril, an ACE inhibitor was evaluated in albino rats by tail flick and Eddy's hot plate method and it was found to be statistically significant.Angiotensin II increases the formation of PGE2by increasing the cyclo-oxygenase 2 activity and also it increases the sympathetic tone thus causing pain. Benazepril inhibits the synthesis of angiotensin II and by decreasing the central sympathetic activity causes analgesic effect[5]. Also, Benazepril inhibit enkephalinase responsible for hydrolysis of enkephalins, hence increasing the endogenous opioids[6].

Benazepril increases the levels of angiotensin(1-7) by bypassing the production of angiotensin II and by inhibiting angiotensin(1-7) hydrolysis. Angiotensin(1-7) increases NOS-derived NO levels. Midbrain periaqueductal gray (PAG) is a neural site for several physiological functions related to pain modulation[7]. Increased NO decreases the discharge rate of spontaneous action potential in dorsolateral-PAG neurons. Angiotensin(1-7) is involved in pain modulation by acting on PAG through NO dependent signaling.The main nociceptive mechanism of benazepril may be due to the inhibition of synthesis of algesic molecule angiotensin II and by decreasing central sympathetic tone.

6.CONCLUSION:

In the present study, Benazepril showed promising results as an analgesic when compared to the control group. It may be a lead compound for identifying newer adjuvant analgesic agents. Further studies are however needed to explore the mechanism(s) of action in depth.

7.REFERENCES:

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