EFFECT OF BETAMETHASONE VALERATE WITH BIOPOLYMER ON SKIN INFLAMMATORY MODELS IN ALBINO MICE AND WISTAR RATS

Satish Kumar MC[3], Sachidananda Adiga[4], Avin D'Souza[5], Purnima Sirigiri[5], Deepa Ayappa[5], Veena Nayak[3], Bharti Chogtu*[1], K.L. Bairy[2]

1. Associate Professor, Kasturba Medical College, Manipal University, Manipal, Karnataka- 576104, India.
2. Professor and Head, Kasturba Medical College, Manipal University, Manipal, Karnataka- 576104, India.
3. Assistant professor, Kasturba Medical College, Manipal University, Manipal, Karnataka- 576104, India.
4. Associate Professor, Perunthalaivar Kamaraj medical college, Puducherry, India.
5. MSc student, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.

***Email:** bhartimagazine@gmail.com

ABSTRACT

There is always a need for better antiflammatory drugs for conditions like atopic dermatitis. A newer formulation is biopolymer based betamethasone valerate. This study was done to compare the efficacy of betamethasone valerate with neomycin (Betnovate N) with betamethasone valerate with biopolymer in animal models of superficial skin inflammation in rats and mice. The inflammatory models croton oil ear edema in rats and topical application of arachadonic acid in mice were used. In both the models, the animals treated with betamethasone valerate with biopolymer showed a significant decrease in inflammation as compared to Betnovate N group.

Keywords: Inflammation, betamethasone valerate with biopolymer.

INTRODUCTION

Inflammation though a protective mechanism, in some situations if untreated can lead to serious complications. To know the efficacy of drugs used in inflammation various animal models are used. Inflammatory changes can be induced in these animals by administration of various agents and anti-inflammatory efficacy of different drugs can be compared.

Inflammation is a complex biological response of vascular tissues to harmful stimuli, pathogens or irritants[1]. Exposure to chemicals, irritants and allergens leads to various inflammatory disorders. The treatment for such disorder includes avoidance of allergens, irritants, adequate cutaneous hydration and judicious use of low to moderate potency corticosteroids. There is always a search for more efficacious preparations.

Betamethasone is a moderately potent glucocorticoid with anti-inflammatory and immunosuppressive properties. This drug is available in various forms and one of them is betamethasone valerate with neomycin marketed as Betnovate N. In this study we are comparing the anti-inflammatory activity of Betnovate N with a new formulation betamethasone valerate with biopolymer on superficial skin inflammation in rats and mice.

MATERIALS AND METHODS

Animals

Adult male Wistar rats weighing between 150-200g and albino mice weighing 25 g were used. Animals were acclimatized to the laboratory environment for 5-7 days before entering in the study. They were allowed free access to water and were maintained on standard rat diet under laboratory conditions. 12- hour light/dark cycle was maintained. All procedures were carried with approval of Institutional Animal Ethics Committee (IAEC).

Drugs

Betnovate N (Betamethasone valerate + Neomycin)

Betamethasone valerate with biopolymer (Apex Labs Chennai)

Antiinflammatory studies

Croton oil ear edema in rats:

The study was conducted in male Wistar rats. The irritant croton oil was prepared by dissolving 4 parts of croton oil, 10 parts of ethanol, 20 parts of pyridine and 66 parts of ethyl ether. The test compounds were dissolved (5mg/ml strength) in the croton oil. The animals were divided into three groups of 10 animals each. The control and the test animals were anaesthetized with ether and then received the drugs in following doses

Group I - 0.02ml of croton oil solution.

Group II - 0.02ml of croton oil solution containing dissolved Betnovate N (5mg/ml)

Group III - 0.02ml of croton oil solution containing Betamethasone valerate with biopolymer (5mg/ml)

The drug was applied externally to the outer surface of right ear of each rat. The animals were sacrificed by cervical dislocation after four hours and discs of 8mm punches were made with a cork borer. Each ear disc was weighed and compared with control.

Topical application of arachidonic acid

This method was carried out in mice. Mice were divided into three groups of 10 animals each**.** The control and the test animals received the drug in following doses

Group I- 1mg arachadonic acid

Group II- Betnovate N (5mg/ml) in acetone 30 min prior to 1mg arachidonic acid

Group III- Betamethasone valerate with biopolymer (5mg/ml) in acetone 30 min prior to 1mg arachidonic acid

All the drugs were applied topically on the external surface of right ear of each rat. The left ear served as control. Ear swelling was estimated by weighing it after arachidonic acid treatment.

Statistical analysis

Results are expressed as mean ± SEM and were analyzed statistically by analysis of variance (ANOVA). P values of less than 0.05 were considered significant.

RESULTS

Croton oil edema in rats**:**

Topical application of croton oil induced cutaneous inflammation which caused a significant increase in ear plug weight. The two treatment groups were compared with control. The difference in weight between two plugs was taken as a measure of edematous response. Drug effects were calculated as percent inhibition of edema using the equation[2]

$$\frac{\text{Weight of left minus control ear- Weight of left minus test ear}}{\text{Weight of left control ear}} \times 100$$

The percentage of edema in three groups is shown in table 1

Table 1: Croton oil ear edema- percentage of edema

Groups (n=10)	Mean ± SEM
Control	101.34 ± 22.63
Betnovate N	56.88 ± 10.52
Betamethasone valerate with biopolymer	45.29 ± 7.00*

* Significant p< 0.05

Topical application of arachidonic acid**:**

The difference in weight between right and left ear gives a measure of inflammation. The percentage decrease in edema in test groups is calculated**.** Table 2 shows the percentage of edema in three groups.

Table 2: Topical application of arachadonic acid- percentage of edema

Groups (n=10)	Mean ± SEM
Control	46.20 ± 8.58
Betnovate N	26.74 ± 4.55
Betamethasone valerate with biopolymer	12.54 ± 5.36*

*Significant p< 0.05

DISCUSSION

Corticosteroids play an important role in treatment of inflammation. It has been established that inflammation induced by croton oil is related to the activation of phopholipase A_2, which releases arachidonic acid from the cell membrane. Arachidonic acid, in turn, is metabolized to prostaglandins (PG's) and leukotrienes. Substances able to inhibit edema could be inhibitors of cyclooxygenase (COX) and/or 5-lipoxygenase[3]. The anti-inflammatory action of glucocorticoids is mediated mainly by lipocortin 1, which inhibits phospholipase A_2 on the arachidonic acid cascade[4] resulting in decreased synthesis of PG's. In this study there was a significant decrease in edema in rats treated with Betamethasone valerate with biopolymer as compared to Betnovate N.

Topical application of arachidonic acid is based on the principle of its metabolism by COX which leads to generation of PGs and thromboxanes that mediate pain and edema associated with inflammation. The inhibition of these mediators by test drug is evaluated. Application of arachidonic acid to the ears of mice produces immediate vasodilatation and erythema (5 min) followed by the abrupt development of edema which is maximal at 40-60 min[5]. In this inflammatory model as well, the mice treated with betamethasone valerate with biopolymer showed a significant decrease in inflammation as compared to betnovate N.

Many drugs have limited efficacy because of sub-optimal pharmacokinetics and advances in drug delivery are needed to improve the pharmacokinetics of such drug[6]. Biopolymer based drugs play an important role in development of drug formulations as they have specific advantages[7]. Biopolymers are generally nontoxic and biocompatible. It is most probably the better pharmacokinetics of the biopolymers that gives them an advantage over the conventional preparations.

In conclusion, advances in drug delivery improve the pharmacokinetics of promising drugs for many diseases and biopolymers have great potential for delivery of pharmaceuticals. Biopolymer based formulations can be promising candidates for various types of inflammation in which conventional preparations have shown less efficacy.

REFERENCES

1. Meena MK, Jain AK, Jain CP, Gaur K, Kori ML, Kakde A etal. Screening of anti-inflammatory and analgesic activity of Cassia grandis Linn. Academic Journal of Plant Sciences 2009; 2: 51-55.
2. Paula ACB, Hayashi LSS, Freitas JC. Anti-inflammatory and antispasmodic activity of Ipomoea imperati (Vah) Griseb (Convolvulaceae) Braz J Med Biol Res 2003;36:105-12
3. Benito PB, Abad Martinez MJ, Silván Sem AM, San Gómez A, Fernández Matellano L, Sánchez Contreras S & Diaz Lanza AM. In vivo and in vitro

anti-inflammatory activity of saikosaponins. Life Sciences 1998; 63: 1147-56.

4. Goulding NJ, Guyre PM. Glucocorticoids, lipocortins and the immune response. Curr Opin Immunol 1993; 5: 108-113.

5. Young JM, Spires DA, Bedord CJ, Wagner B, Ballaron SJ, De Young LM. The mouse ear inflammatory response to topical arachidonic acid. J Invest Dermatol 1984; 82: 367-71.

6. Chow D, Nunalee ML, Lim DW, Simnick AJ, Chilkoti A. Peptide based biopolymers in biomedicine and biotechnology. Mater Sci Eng R Rep 2008 ; 62: 125–55.

7. Sinha V.R., Kumria R. Polysaccharides in colonspecific drug delivery. Int. J. Pharm 2001; 224**:** 19-38.

****