

A DOUBLE BLIND CLINICAL TRIAL OF DIOSMIN (VENEX) A BIOFLAVONOID IN ACUTE ALLERGIC RHINITIS.

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A double blind randomised clinical trial of Diosmin against placebo was conducted in 150 patients with acute allergic rhinitis. Patients who satisfied the inclusion criteria were included into the study. Diosmin and placebo were given 300 mg three times daily in respective groups. The treatment lasted for a week and follow up for another week. The Parameters studied included rhinorrhoea, sneezings and nasal obstruction. The nasal smear was also studied for eosinophil count. At the end of the clinical trial patients who received Diosmin were significantly improved in all the parameters and the eosino phil count has also reduced in the nasal smear in comparison to the patients who received placebo. Diosmin hastens the recovery from acute phase and offers therapeutic promise in acute allergic rhinitis compared to placebo. No Significant side effects were observed with the drug.

Flavonoids in general have been known to interfere nonspecifically with number of cellular and membrane functions such as PI turnover, protein kinase C activity, calcium fluxes and pathways of arachadonic acid metabolism. The pure synthetic bioflavonoid, DIOSMIN (venex) chemically 5, 7, 3-trihydroxy-4 methoxy flavone-7-rhamnoglycoside. DIOSMIN is well absorbed from the small intestine following oral administration. The glycoside portion of the molecule is split off enzymatically in the organism producing rhamnose, Glucose and diosmetin. In the second phase diosmetin is split at the B-ring with the formation of various metabolities in particular methoxy-hydroxyphenyl- propionic acid which could be responsible for the pharmacological effect. Diosmin affects the venous wall, decreases capillary permiability by increasing its resistance. The primary objective of the present study is to investigate the efficacy of diosmin in acute allergic rhinitis with its established pharmacological actions^{2,5} such as antiphlogistic (inhibition of synthesis of prostaglandins PGE 2, PGF2 alpha and throm boxane Tx), anti odemeatous and physiological antagonism to

histamine. We report here a controlled, double-blind randomized trial with Diosmin in patients with acute allergic rhinitis.

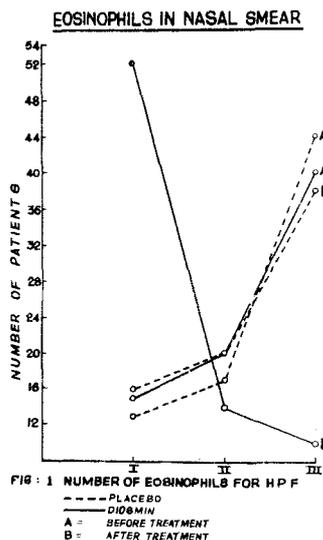


Fig. 1:

MATERIAL AND METHODS :

This double blind study was carried out in 161 patients (93 men and 68 women) aged 16-60 Years with symptoms of acute allergic rhinitis

of less than 5-7 days, duration. Patients on corticosteroids, undergoing desensitization therapy, those with liver and kidney diseases and pregnant and lactating women were excluded from the study. Patients less than 15 years of age were also eliminated from the study. Acute allergic rhinitis was diagnosed on the basis of clinical features including rhinorrhoea, sneezings and nasal obstruction. All the patients included in the study had routine haematological examination, urine analysis, liver function tests, X-ray paranasal sinuses and vestibular function tests done before and after the treatment. Nasal smear for eosinophil count was done in all the cases before and after the treatment.

Venex tablet contained 300mg of pure synthetic diosmin. This tablet was powdered and filled into yellow capsules. Lactose powder 300 mg was used as placebo capsules. This clinical trial was approved by the hospital ethics committee. Informed written consent was obtained from all patients

The trial was conducted on outpatients at Government general Hospital, Guntur. Patients were randomly allocated to receive either placebo (79 patients) or Diosmin. Diosmin was administered as 300 mg thrice daily for 7 days. Placebo capsules were administered in the same dose. Patients were followed for 7 days after stopping the drug. Patients were not prescribed any other drugs during the trial period. They were evaluated after the drug treatment.

The severity of the symptoms (rhinorrhoea, sneezing and nasal obstruction) Were evaluated on a three point scoring scale, 0 to 2 (0 absent ;

grade I 0-50% response and grade II 51-100% response) Eosinophils in nasal smear was graded as I to III depending on the number of eosinophils per high power field (grade=I 0-1 ; II=3-4 ; III=more than 4). Thereapeutic response was judged by improvement in clinical symptoms and reduction in eosinophils in nasal smear. Chi square test was used to determine the statistical significance between the two groups.

RESULTS:

One hundred and fifty patients (87 men, 63 women), 76 in the Diosmin group and 74 in the placebo group, Completed the trial. There were no significant differences in clinical and biochemical parameters between the two groups before treatment. This randomised double blind study with Diosmin and placebo lasted for one week and the follow up period for one week. Diosmin was given 300 mg three times a day and placebo was also administered in the same dose as identical capsules as Diosmin. Significant difference in the response between the two groups for the individual parameters was observed. With Diosmin rhinorrhoea subsided in 58 patients (51-100%) while it was in 19 patients (51-100%) in placebo group (table I). Sneezing were decreased in 76 patients (51-100%) (P < 0.001) in Diosmin group and 19 patients in placebo group (table I). There was considerable reduction in eosinophilic count of Diosmin group compared to placebo group (Fig 1). There were eleven drop outs (6males, 5 females). No side effects were observed in placebo group but one female and three males complained mild fever in Diosmin group.

TABLE-I

Shows the effects of placebo and diosmin in rhinorrhoea, sneezings and nasal obstruction. Significant relief is seen in all the parameters at the end of treatment with Diosmin.

	PLACEBO				DIOSMIN			
	No change	Grade I 0-50%	Grade II 51-100%	Total	No change	Grade I 0-50%	Grade II 51-100%	Total
RHINORRHOEA	50 (67.6%)	5 (6.8%)	19 (25.6%)	74	6 (7.9%)	12 (15.8%)	58 (76.3%)	76
SNEEZING	45 (60.8%)	7 (9.5%)	22 (29.7%)	74	8 (10.8%)	12 (15.8%)	56 (73.7%)	76
NASAL OBSTRUCTION	48 (64.9%)	7 (9.5%)	19 (25.7%)	74	12 (15.8%)	14 (18.4%)	50 (65.8%)	76

P < 0.001

DISCUSSION:

Allergic rhinitis is very common problem affecting about 10-15% of the population. Antihistamines are the most frequently used drugs for the treatment of allergic rhinitis. Decongestants and sympathomimetics are useful in both oral and topical forms for symptom control, often as adjuvant to anti histamines. Corticosteroids, especially the topical intranasal preparations and systemic forms have become increasingly important in thrapy of allergic rhinitis. Antihistamines, decongestants and corticosteroids can not be used injudiciously for long periods due to their variety of side effects.

Diosmin a bioflavonoid found to be antiphlogistic, antiödematous and physiological antagonist to histamine. It increases capillary resistance and decreases capillary permia bility

1. The preparations used in treating allergic diseases may have three pharmacological effects; modifying mediator effects in sensitive target organs and mediator release⁴. Diosmin affects the microcirculation and on certain

inflammatory reaction mediators. The physiological antagonism to histamine, inhibition of synthesis of prostaglandins, the lymphogogue property and antiödematous effects might have responsible in relieving rhinorrhoea, sneezing and nasal obstruction. In addition Diosmin has shown a decrease in eosinophils in the nasal smear at the end of seven days of treatment. It was reported earlier by Das Gupta and Gambhir³ that Bioflavonoids have mast cell stabilisation action. The administration of Diosmin may be beneficial in the treatment of acute allergic rhinitis as indicated by rapid clinical recovery. The drug deserves further studies.

ACKNOWLEDGEMENTS:

We wish to thank Dr. YDS Ravi Professor and Head ENT department, Dr. K. Indira Assistant Professor of Pathology and Dr. Ch. Suryakantham Tutor in Clinical Pharmacology. We also thank Elder Pharmaceuticals, Bombay for their kind support in carrying out this study.

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