



Efficacy of Diethylcarbamazine in Allergic Rhinitis as an Adjuvant to Antihistamines : A Comparative Study

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ABSTRACT

Background: Allergic rhinitis is a type of inflammation in the nose that occurs when the immune system overreacts to allergens in the air. Underlying mechanism involves IgE antibodies that attach to allergen resulting in release of histamine from mast cells. Signs and symptoms include a runny or stuffy nose, sneezing, redness and watering of eyes. Symptom onset is often within minutes following allergen exposure and can affect sleep and ability to work or study. People with allergic rhinitis may have associated asthma, allergic conjunctivitis, atopic dermatitis. The study aims to know the efficacy of diethyl carbamazine in reducing the severity of symptoms in patients with allergic rhinitis when added to the antihistaminic treatment.

Methods: This is a single blind randomized control trial study involving 50 allergic rhinitis patients between 13-60 years as cases and 50 as controls. The patients were classified as mild, moderate and severe based on the severity of symptoms. The cases were prescribed Tablet Diethyl carbamazine 300mg along with Tablet cetirizine 10mg for a period of 21 days. The controls were prescribed Tablet cetirizine 10mg with placebo. Patients were followed up for 3 months and watched for any reduction in the severity of symptoms. Results were compared between the study and control groups.

Results: Out of 50 patients in the study group, 20 cases showed improvement, 30 cases did not show any improvement; Out of 50 controls, 6 showed improvement and 44 didn't show any improvement. P value is significant (0.003)

Conclusion: Diethyl carbamazine is an ant filarial drug which is found to have an effect in reducing the mediators of inflammation thereby useful in reducing the severity of symptoms in allergic rhinitis, as an adjuvant.

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Introduction

Allergic rhinitis is a very common problem that we come across in daily practice in otolaryngology. A close association between allergic rhinitis and asthma has been explained by several studies. Childhood allergic rhinitis is strongly associated with adult-onset asthma (1). Symptoms of allergic rhinitis include pruritus, sneeze, discharge, and stuffiness

(2). Allergic rhinitis affects one's quality of life and can lead to conditions like asthma, Eustachian tube dysfunction, sinusitis, and conjunctivitis. Important Allergens include seasonal pollens, moulds, perennial indoor allergens like dust, mites, pests and pet dander (3). Allergic rhinitis has a strong association with positive family history (4). After sensitization of the nasal mucosa to an allergen, subsequent

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exposure to that same allergen leads to cross-linking of specific IgE receptors on mast cells and their degranulation, with the release of inflammatory mediators most importantly eosinophil products and cytokines. As a consequence of mucosal inflammation, mucosa becomes more reactive to the allergen resulting in nasal symptoms.

Though there are many standard medications in use for allergic rhinitis, symptoms are found to recur once the drug is withdrawn leading to a challenge in cure. Diethyl carbamazine is an antifilarial drug commonly used in clinical practice, which has significant role in reducing inflammation. It inhibits the formation of LTB₄ and sulfidopeptide leukotrienes, which are potent vaso/bronchoconstrictors, in mastocytomas, while stimulating the formation of 5-hydroxyeicosatetraenoic acid, suggesting that the site of action of DEC for inhibiting leukotrienes formation may be the leukotriene A₄ synthetase reaction. Considering this, DEC is being selected as the tool of study and its efficacy is studied (5). This is a comparative study to evaluate whether there is an advantage of adding Diethyl carbamazine 300mg for 21 days to the standard treatment regime of allergic rhinitis. This study aims to know the efficacy of Diethyl carbamazine as an adjuvant to antihistamines in controlling the severity of symptoms of Allergic rhinitis.

Methods

A Randomized control trial is done in a tertiary care teaching hospital. The study population comprises 100 patients with allergic rhinitis. 50 were included in the study group and 50 were included in the control group. Patients diagnosed with allergic rhinitis (history of at least one year) in the age group 13-60 years and followed up for one year. Patients with vasomotor rhinitis, atrophic rhinitis, pregnancy and hypersensitivity to Diethyl carbamazine were excluded. The information such as name, a medical record number of patients will not be included in the database or reports of the results.

Once diagnosed with allergic rhinitis through proper history and clinical examination, patients were classified based on mARIA (Modified three level severity of symptoms in Allergic rhinitis and its impact on Asthma) classification of Allergic Rhinitis (6) as mild/moderate/severe. Depending on the frequency of symptoms, classified them as intermittent/persistent. All the patients were explained about the study in detail and informed consent was obtained. They underwent through detailed history taking, clinical examination and all basic blood and radiological investigations. They were randomly placed in

study and control groups. 50 study group patients were prescribed Diethyl carbamazine 300 mg for 21 days (as this is the recommended dose and duration of treatment) (7).

Patients were being asked to make their first review visit, a week after the completion of the course of treatment (both control and study group) to confirm the adherence to drug and completion of course. Then, they were followed up during the course of treatment and at the end of 4th, 8th and 12th weeks. During the time, the frequency of attacks, the severity of symptoms was documented using VAS score (8). Downgrading of severity was taken as improvement in treatment. A comparison was made between the study group who received Diethyl carbamazine with antihistamines and the control group who received antihistamines with placebo.

Data are presented as percentages and the number of cases. Categorical data were analysed with Pearson chi-square tests. Significance was defined by P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

Results

The study group consists of total 50 patients, out of which 22 were in mild category, 19 in moderate and 9 were in severe category according to the severity of symptoms (Figure 1). They received Tablet. Diethyl carbamazine 300 mg for 21 days along with antihistamine Tab. cetirizine 10 mg. After the follow up period, it was found that, Diethyl carbamazine had a significant reduction in severity. Out of 50 study group patients, 20 had downgrading of severity. 30 patients had no change in severity of symptoms (Table 2).

Table 1. Age and Gender distribution.

	AGE GROUP	MALE	FEMALE
1	13-20	11	12
2	21-30	10	8
3	31-40	9	10
4	41-50	12	7
5	51-60	10	11
		52	48

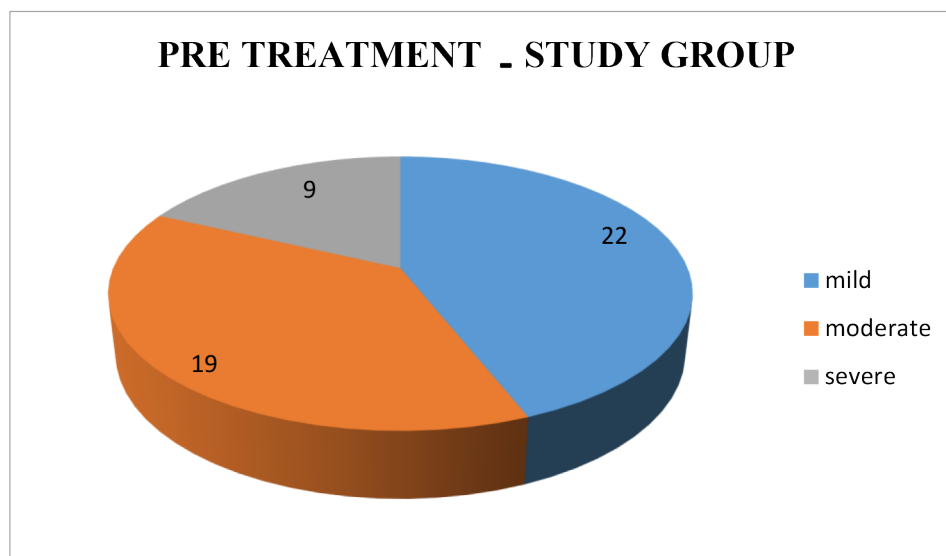


Figure1. Pre Treatment Distribution of patients among study group according to severity of symptoms

Table 2. Post treatment evaluation of severity of symptoms among study group patients.

Study Group (N = 50)			
Pre Treatment	Post Treatment (after 12 weeks)		
Symptom free N = 0	Same Severity	Increased Severity	Reduced Severity
Mild N = 22	14 (mild)	0	8 (No Symptoms)
Moderate N = 19	10 (Moderate)	0	4 (No Symptoms) 5 (Mild)
Severe N = 9	6 (Severe)	0	0 (No Symptoms) 1 (Mild) 2 (Moderate)
Total Improved			20

Out of 50 control group patients, 22 were in mild category, 19 in moderate and 9 were in severe category according to the severity of symptoms (Figure 2). They received a placebo tablet for 21 days along with antihistamine Tab.

cetirizine 10 mg. After the follow up period, it was found that only 6 patients had reduction in severity. 2 patients had increased severity of symptoms and 42 patients remained with same severity (Table 3).

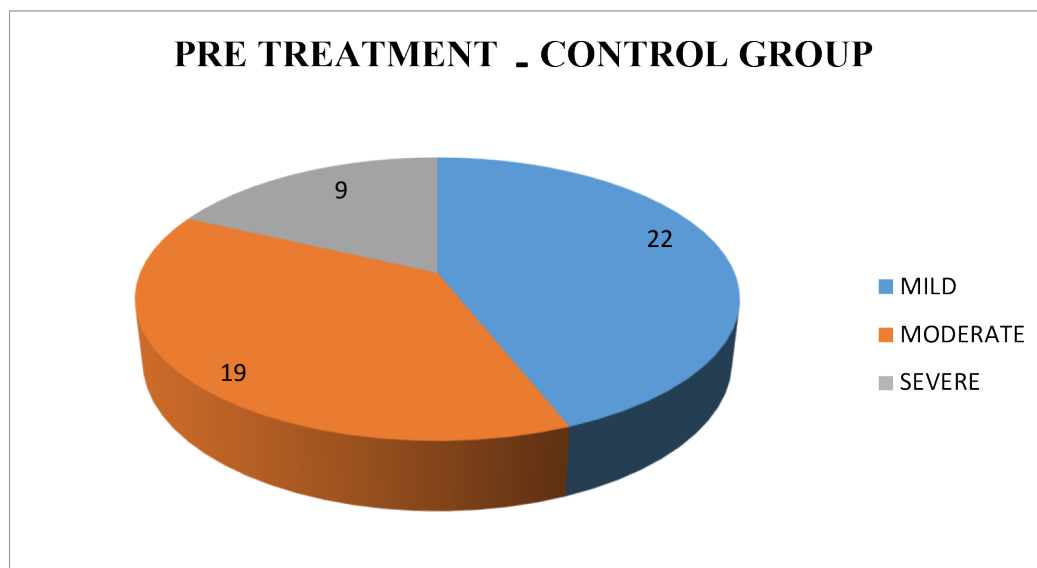


Figure 2. Pre Treatment Distribution of patients among control group according to severity of symptoms.

Table 3. Post treatment evaluation of severity of symptoms among control group patients

Control Group (N = 50)			
Pre Treatment	Post Treatment (after 12 weeks)		
Symptom free	Same Severity	Increased Severity	Reduced Severity
Mild N = 22	18 (mild)	2 (Moderate)	2 (No Symptoms)
Moderate N = 19	15 (Moderate)	0	3 (No Symptoms) 1 (Mild)
Severe N = 9	9 (Severe)	0	0 (No Symptoms) 0 (Mild) 0 (Moderate)
Total Improved			6

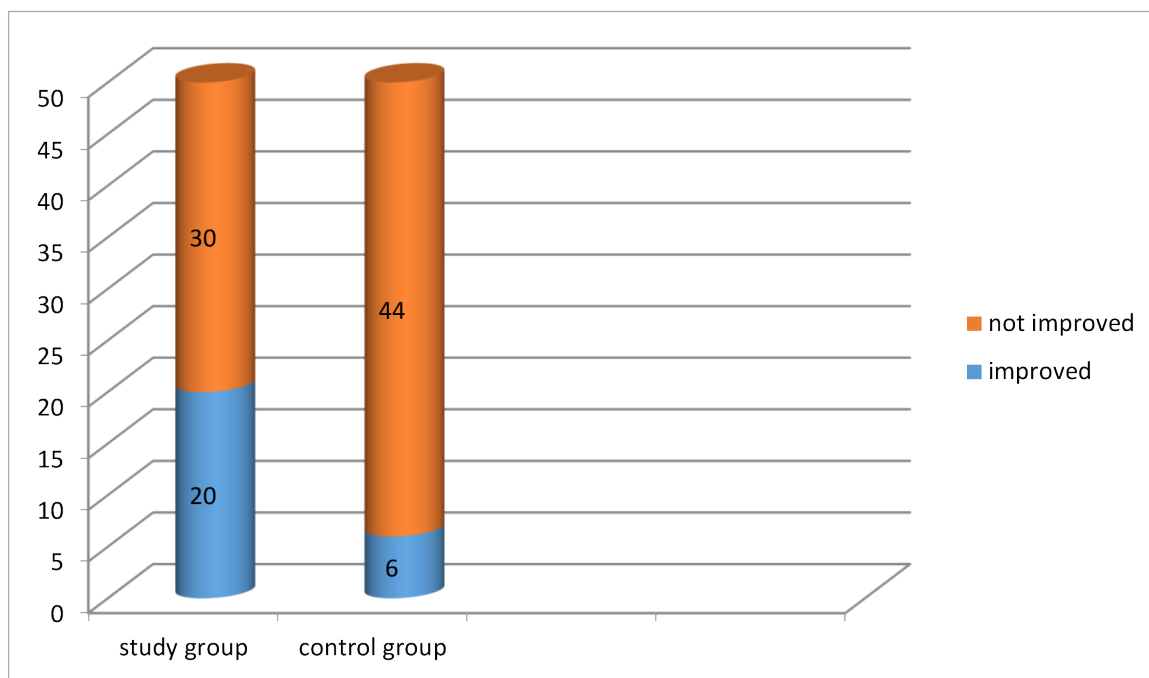


Figure 3. Post treatment Improvement in the symptoms.

Discussion

On getting exposed to an allergen, Antigen presenting cells (APCs), such as dendritic cells present in the mucosal surface, process allergens and present some peptides from allergens on the major histocompatibility complex (MHC) class II molecule. This MHC class II molecule and antigen complex take a role as the ligand of T-cell receptors on Naive CD4+ T cells, resulting in differentiation of Naive CD4+ T cells to allergen-specific Th2 cell. Activated Th2 cells secrete cytokines, which induce B cells in IgE production and eosinophils proliferation, mast cells and neutrophils proliferation. Antigen-specific IgE binds to IgE receptors on mast cells and basophils (9).

When allergic rhinitis patients are getting exposed to allergens, allergic reactions develop in 2 different patterns according to time sequence. One is the early reaction, in which sneezing and rhinorrhoea develops in 30 minutes and disappears. The other is the late reaction, approximately 6 hours after exposure to allergens and subsides slowly. The early reaction is the response of mast cells to offending allergens (type I hypersensitivity) (10). Stimulated mast cells induce nasal symptoms by secreting chemical mediators such as histamine, prostaglandins and leukotrienes. In contrast to the early reaction, eosinophil chemotaxis is the chief mechanism in the late reaction, which is caused by chemical mediators produced in the early reaction. Several inflammatory cells, eosinophils, mast cells and T cells

migrate to nasal mucosa, break up and remodel normal nasal tissue, which result in nasal obstruction which stands out to be the main symptom in allergic rhinitis patients.

Antihistamines/topical /oral steroids remain the standard treatment for allergic rhinitis. However, recurrence is common in many patients, after treatment withdrawal. Diethyl carbamazazine has anti-inflammatory action as a result of its interference with the arachidonic acid metabolism, which includes lipoxygenase and cycloxygenases enzymes with an antileukotriene action. When it is administered for period of 21 days, it has shown to significantly reduce the severity of symptoms (11).

Limitations of the study encountered was the sample size and the duration study. In our present study sample size was 100 and duration of study was 3 months. In future, a multicentre study on a huge sample size will benefit for more accurate interpretation of the outcome.

The outcome is that the study group who received Diethyl carbamazazine in addition to antihistamines had downgrading of severity and frequency when compared to the control group who received only antihistamines. Diethyl carbamazazine is an antifilarial drug which is found to have an effect in reducing the mediators of inflammation thereby useful in reducing the severity of symptoms in allergic rhinitis, as an adjuvant. Diethyl carbamazazine in time shortens the duration of late allergic response although it

has less effect on the immediate response. This may explain the better response in the study group.

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