

Original research article

A Study of Role of Diethylcarbamazine in Allergic Rhinitis with Eosinophilia

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Abstract

Background and Objectives: Although not as glamorous as its surgical counterparts, the management of allergic rhinitis constitutes a large proportion of the day-to-day practice of the general otolaryngologists. In addition to its primary effect, inhalant allergy of the upper respiratory tract might affect the development and clinical course of other disease states such as sinusitis, otitis media, and asthma accounting upto half the patients encountered in an otolaryngological practice. Diethylcarbamazine an antifilarial drug used in the treatment of tropical pulmonary eosinophilia was used in this study to know its role in allergic rhinitis.

Method: A Descriptive study was conducted for one year at Department of DMCH Darbhanga. Selected Patients were administered Tab Diethylcarbamazine 5mg/kg body wt BD for 21 days and their effect on symptom control, blood eosinophilia and nasal eosinophilia was studied. **Results:** About 100 patients were recruited. 78 patients had eosinophilia either in blood, nasal smear or both which accounted to significant amount. After treatment with Diethylcarbamazine blood Eosinophilia decreased significantly in both blood and nasal tissue and blood eosinophilia only group. Nasal Eosinophilia decreased significantly in both blood and nasal tissue and nasal tissue only group. Symptoms of sneezing, rhinorrhea, nasal obstruction, nasal pruritis, eye watering and eye itching improved significantly in all 3 groups after treatment. Pharyngeal itching improved only in blood & nasal eosinophilia and blood eosinophilia group. No improvement in Anosmia in all 3 groups.

Conclusion: Eosinophilia was associated in significant number of population and Diethylcarbamazine is useful in reducing the symptom scores in patients of allergic rhinitis with eosinophilia. It also reduces the eosinophil scores in both blood and nasal tissue. Diethylcarbamazine can be used in the treatment of allergic rhinitis with eosinophilia as an adjunctive drug.

Keywords: Allergic rhinitis, Eosinophilia, Diethylcarbamazine.

Introduction

It is very seldom that diseases are found pure and unmixed, as they are commonly described by authors, and there is almost an endless variety of constitutions. The treatment must be adapted to this mixture and variety in order to be as successful as circumstances will permit.

Allergic rhinitis is a heterogenous disorder that despite its high prevalence is often

undiagnosed.¹ It affects population irrespective of age, sex, race, or socioeconomic status.² It is one of the most common chronic condition in the industrialised world with significant lifestyle impacts³. Some would describe allergic disease as "the epidemic of the 21st century". The head and neck are the most common portals of entry of inhalant and food sensitizers and it is in this region where the most common allergy induced diseases, such as rhinitis, sinusitis, otitis media, laryngitis, conjunctivitis and asthma occur.^{4,5} Otolaryngologist is frequently called on to evaluate as nose is usually the first site of a hypersensitivity response.² Most co-morbidities can be explained on the basis of anatomic relationships between nasal cavities and the respectively affected organs. However, it is important to consider the possibility that, allergic rhinitis has a systemic aspect and that this aspect may bear responsibility in the manifestation of co-morbidities. Furthermore, the systemic aspect of allergic rhinitis may be involved in the perpetuation and intensification of its local manifestation which include acute and chronic inflammation of the nasal mucosa and their functional consequences.³ Environmental condition may be responsible for doubling of the number of children who have allergic rhinitis. There is evidence that doubling of atmospheric CO₂ concentration, increased ragweed pollen production by 61%, leading to increased exposure to allergic pollen which possibly is related to the effects of global warming.⁶ In addition it is difficult to make a clear distinction between a normal state and a disease. Everyone occasionally has nasal symptoms, but this does not necessarily imply that he/she suffers from rhinitis. At present there are no epidemiological investigations using stringent criteria that allow us to define borderline between normal and abnormal.⁵ Allergic rhinitis occurs in atopic individuals who are exposed to common aeroallergens. Allergic rhinitis is either seasonal or perennial. Although frequently trivialised by patients and doctors, allergic rhinitis remains a common cause of morbidity, social embarrassment and impaired performance either at school or in workplace.⁷ Most allergic rhinitis patient can be diagnosed by a combination of history, clinical examination, skin prick test, radioallergosorbent test for specific IgE with other nonspecific allergy tests like peripheral blood eosinophilia, total serum IgE level, nasal secretions for eosinophils.^{5,8} Management of allergic rhinitis includes allergen avoidance, pharmacotherapy, education and possibly immunotherapy. Surgery is rarely needed.⁹ Various groups of drugs are available for use in management of allergic rhinitis. Antihistamines are effective in reducing symptoms of itching, sneezing and rhinorrhea and are first line therapy for treatment of allergic rhinitis. Sedation and performance impairment are undesirable and potentially dangerous side effects of 1st generation antihistamines. Consequently 2nd generation antihistamines with less sedating side effects were introduced. But these drugs caused cardiac effects with overdose, administration with certain concomitant medications and in the presence of liver disease.⁹ Oral nasal decongestants like pseudoephedrine and phenylephrine were useful in reducing nasal congestion. Allergen immunotherapy is unique and effective. But costs associated with this excellent drug therapy place this form of therapy in a position of relative cost effectiveness with monitoring from an allergist.⁹ Various trials are being undertaken to treat the disease but complete cure still remains an enigma. Patients with allergic rhinitis exhibit peripheral eosinophilia and basophilia, the magnitude of which correlates with severity of symptoms. Many other diseases which exhibit eosinophilia are; infections with helminths, eosinophilic pneumonitis, asthma, inflammatory bowel disease, eosinophilic gastroenteritis, allergic colitis, idiopathic hypereosinophilic syndrome, vasculitis to name a few.¹⁰ Eosinophilia in blood and sputum is seen in Tropical pulmonary eosinophilia, which was successfully treated with an antifilarial drug Diethylcarbamazine.¹¹ Allergic rhinitis is also associated with blood and nasal eosinophilia and hence a new indication was found for Diethylcarbamazine, a familiar antifilarial drug. It is likely that it is the blocking agent of

mediator release in particular SRS-A, from basophil or mast cell.¹²

Objectives

To study the association of blood and nasal eosinophilia in patients with allergic rhinitis.
To know the efficacy of Diethylcarbamazine in reducing symptoms in patients with allergic rhinitis and nasal eosinophilia or blood eosinophilia or both.
To study the effect of Diethylcarbamazine on nasal and blood eosinophil counts.

Materials and methods

The Descriptive study, Data for this study was collected from patients attending Out Patient Department of E.N.T at Darbhanga Medical College and Hospital, Darbhanga Laheriasarai, Bihar. Study duration of Two Years. Patients presenting to out patient department of ENT with symptoms of allergic rhinitis were carefully evaluated by means of proper history taking with help of proforma, clinical examination and laboratory investigations like absolute eosinophil count and nasal smear for eosinophils. Nasal symptoms of sneezing, rhinorrhea, nasal pruritis, nasal obstruction and Non nasal symptoms of eye itching, eye watering, pharyngeal itching anosmia were recorded on symptom evaluation scale of 4. A total of 100 patients were recruited over one year and then subjected to evaluation for inclusion into the study after fulfilment of both inclusion and exclusion criteria.

Inclusion criteria

Age: 10 – 40 years

Symptoms of allergic rhinitis – sneezing, nasal pruritis, rhinorrhoea, nasal congestion, eye watering and itching, nasal and pharyngeal itching. At least 2 of the above symptoms

Table 1:

Symptom evaluation scale	Description	Definition
0	Absent	No symptom
1	Mild	Symptom occasionally present, but not troublesome to the patient
2	Moderate	Symptom frequently present and annoying
3	Severe	ously present and interfering withwork or sleep

Symptom evaluation score scale

- Allergic rhinitis patients with nasal smear eosinophilia > 1+ according to the grading for nasal cytology or Absolute blood eosinophil count \geq 350 or both.
- Patients should not be on any antiallergic medications for 2 weeks.

Exclusion criteria

- Vasomotor rinitis,
- Atrophic rinitis,
- Tumors of nose and paranasal sinuses, nasopharynx,
- Drug induced rhinitis,
- HIV, Pregnancy,
- H/o worm infestation,

This study was conducted to know the efficacy of Tab Diethylcarbamazine on allergic rhinitis with eosinophilia. Consent was obtained from all the patients recruited to the study. Prior to the study, clearance was taken from the ethical committee of the institution. Patients were

selected for the study after proper history taking, clinical examination and laboratory examination like absolute eosinophil count and nasal smear for eosinophil using the predefined inclusion criteria and exclusion criterias. Absolute eosinophil count was done by Direct method. The principle of the method is; blood drawn from patient is diluted 10 times in a WBC pipette with special diluting fluid called Dunger solution, which removes red cells and stains the eosinophils. The diluted blood specimen is then charged in a Neubauer's counting chamber and the cells are counted under a high power objective. After fulfilment of both inclusion and exclusion criteria patients were then categorised into three groups. Group 1 had both nasal and blood eosinophilia, Group 2 had only nasal eosinophilia and Group 3 had only blood eosinophilia. Patients were started on Tab Diethylcarbamazine for 21 days. Patients were followed up after 21 days and they were evaluated for symptoms of allergic rhinitis and then graded on symptom evaluation scale. Absolute eosinophil count and nasal smear for eosinophil count were also done and the values recorded after 21 days. None of the patients had any adverse effects to the drug during the study period. If the symptoms persisted after 21 days patients were then treated by antihistamines and steroid sprays according to the severity of the symptoms.

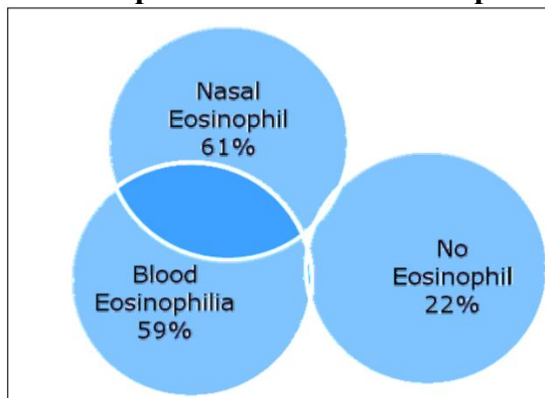
Results

About **100** patients of allergic rhinitis were recruited to the study.

Nasal eosinophilia was found in **61%** pts

Blood eosinophilia was found in **59%** pts

No eosinophilia was found in 22% pts



Shows distribution of eosinophils in study population

Out of which only 78 patients fulfilled the criteria for Diethylcarbamazine drug trial.

These 78 patients were subsequently grouped into 3 groups and the results were studied in these 3 groups.

Group 1 had eosinophils in both nasal and blood smears.

n=42 Group 2 had eosinophils in nasal smear only. n=19

Group 3 had eosinophils in blood smear only. n=17

Table 2: Difference between groups

1-2	< 0.01, S	< 0.01, S	< 0.01, S
1-3	< 0.01, S	< 0.01, S	0.37, NS
2-3	< 0.01, S	< 0.01, S	< 0.01, S

Post treatment difference between the groups in allergic rhinitis

Kruskal Wallis Test

Mann-Whitney Test

Absolute Eosinophil Count decreased significantly in group 1 and group 3 after treatment with Diethylcarbamazine. But the reduction in the Absolute eosinophil Count in group 2 was not significant. Among the groups difference was significant between 1 and 2 and between 2 and 3.

Table 3: Effect on nasal eosinophilia

GROUPS		Pre	Post	Diff	% reduction	Significance**
1.B+N+	Median+/-SD	1.8+/-0.9	1.1+/-1.0	0.7+/-1.4	39%	<0.01, S
	Median					
2.B0N+	Median +/-SD	1.9+/-0.8	1.3+/-0.8	0.6+/-0.7	32%	< 0.01, S
	Median					
3.B+N0	Median +/-SD	0.3+/-0.3	0.5+/-0.7	(-)0.2+/-0.8	67%	0.29, NS
	Median					
K-W ANOVA* , H		42.5	17.6	11.41		
P		< 0.01, S	< 0.01, S	< 0.01, S		

Post treatment changes in nasal eosinophilia in allergic rhinitis**Table 4: Difference between groups**

1-2	0.72, NS	0.15, NS	0.40, NS
1-3	< 0.01, S	< 0.01, S	< 0.01, S
2-3	< 0.01, S	< 0.01, S	< 0.01, S

Post treatment difference in nasal eosinophilia between groups in allergic rhinitis

Kruskal Wallis Test

Mann-Whitney Test

Nasal Eosinophil Count decreased significantly in group 1 and group 2 after treatment with Diethylcarbamazine. But the reduction in the Absolute eosinophil Count in group 3 was not significant.

Among the groups difference was significant between 1 and 3.

Association of blood and nasal eosinophilia in allergic rhinitis according to severity of symptoms (all together) in three groups

Table 4:

Groups	Symptom severity (total score)	No. of cases	AEC	Nasal eosinophilia				
				0	1	2	3	4
1.B+N +	TS<10 Absent/mild	14	1432+/-1153	-	6	1	7	-
	TS>10 Mod/severe	28	1015+/-615	-	17	4	3	1
	Significance*		P=0.49(ns)		P=0.22 (ns)			
2.B0N+	TS<10 Absent/mild	10	250+/-54	-	4	4	2	-
	TS>10 Mod/severe	9	223+/-68	-	3	5	-	1
	Significance*		P=0.32(ns)		P=0.95 (ns)			
3.B+N0	TS<10 Absent/mild	7	496+/-239	2	5	-	-	-
	TS>10 Mod/severe	10	595+/-230	7	3	-	-	-
	Significance*		P=0.43(ns)		P=0.11 (ns)			

Association of blood and nasal eosinophilia in allergic rhinitis according to severity of symptoms (all together) in three groups

*Mann – Whitney U test P > 0.05 not significant

Above table indicates that association of blood and nasal eosinophilia in allergic rhinitis according to severity of symptoms (all together) in three groups is NOT SIGNIFICANT

Inter group significance of reduction of symptoms in allergic rhinitis patients. Symptoms of allergic rhinitis were assessed between the groups also. Sneezing, rhinorrhea, nasal pruritis, nasal obstruction, eye itching, eye watering, pharyngeal itching and anosmia was found to be insignificant according to Kruskal Wallis Anova test between the groups.

Discussion

Allergic rhinitis is the commonest immunologic disease and is the one of the commonest chronic disease experienced by humans. Even today despite the advances in the understanding of the numerous chemical mediators of allergy, only two major categories of drugs are in common use for the management, namely antihistamines and corticosteroids and the quest for the effective drug continues. Allergic rhinitis with its attendant complications is a common condition today, affecting all the age groups with more predilection in the younger ones upto 3rd decade. The mean age of subjects, who entered our study was 27.46 years which is in accordance with the studies of Vervloet (1998) 29 years, Darnell¹³ (1998) 28 years, Bunnag¹³(1998) 30 years. One reason for this may be the lifestyle and activity in this age group, who are more active compared to older age group and children which will increase the chances of bringing them into contact with a wide variety of allergens. In this study, males constituted 57% and females constituted 43%. Sex incidence according to the studies of C. Bachert¹⁴ (2001) showed, males 43% and females 49% and Abhey Sood¹⁵ (2005) males 45% and females 55%. However, allergic rhinitis perse does not differ in its presentation and clinical course between males and females. Hence this difference in sex does not affect the comparison of groups, who were selected after randomization. During the past 2 decades, considerable information has been obtained about the function of eosinophils and its role in human disease. Presently, the eosinophil is recognised as a pro-inflammatory granulocyte

implicated in protection, and parasitic infestations are believed to play a major role in allergic diseases such as allergic asthma, allergic rhinitis, atopic dermatitis. Eosinophils normally account for only 1 to 3% of peripheral-blood leukocytes, and the upper limit of the normal range is 350 cells per cubic millimetre of blood. Eosinophilia occurs in a variety of disorders and is arbitrarily classified as mild (351 to 1500 cells per cubic millimetre), moderate (>1500 to 5000 cells per cubic millimetre), or severe (>5000 cells per cubic millimetre). In allergic rhinitis eosinophils are found both in peripheral blood and nasal tissue.¹⁰ Eosinophil is a major source of cytotoxic cationic protein, such as major basic protein, eosinophil peroxidase, eosinophilic cationic protein. These proteins potentially act as two edged sword; on the one hand, they protect the host against overwhelming helminth infections, but on the other hand, they damage the host's tissues. Eosinophils also induce inflammation by releasing lipid mediators, oxygen metabolites, and cytokines. Numerous studies have shown the association of eosinophils and various human parasitic and allergic diseases.¹⁶ Atopy and parasitism are two important causes of eosinophilia. But etiology remains idiopathic in most patients. Allergy and atopy is described as the leading cause in developed countries and parasitism in travellers returning from the developing countries. Lower down in the list of etiology of eosinophilia are the drugs, malignancies, and collagen vascular diseases. In about 70% of the patients, no diagnosis could be made. Considerable debate exists in the literature regarding optimal work up of patients with eosinophilia. Abhey Sood in 2005 conducted a study on 30 cases of allergic rhinitis and found nasal eosinophilia in 80% of the patients on specimen collected from middle and inferior turbinates. Bryan and Bryan concluded that, increased number of eosinophils are found in active allergic nasal disease. In contrast, the normal nasal mucosal cytology usually demonstrates no eosinophilia or basophilic cells. High degree of correlation between nasal allergy and eosinophilia was also demonstrated by Sasaki et al.¹⁵ Miri S in 2006 conducted a study on 4584

children with allergic rhinitis aged 11-15 yr of both sexes from May 1995 to April 1996. Symptoms of allergic rhinitis and nasal smears were recorded and results were compared with healthy children. Nasal eosinophilia was present in 62% of children with nasal symptoms and signs of allergic rhinitis.

Conclusion

Allergic rhinitis is one of the most common chronic condition in the industrialised world with significant lifestyle impacts.

Eosinophilia was found in significant number of population in allergic rhinitis.

Blood and nasal eosinophilia can occur independent of each other in allergic rhinitis.

Association of blood and nasal eosinophilia in allergic rhinitis according to severity of symptoms was not significant in all the three groups.

Treatment with Diethylcarbamazine was found to reduce the symptom score significantly except anosmia.

Diethylcarbamazine was found to reduce the blood eosinophil counts significantly in Group 1 and 3.

Diethylcarbamazine was found to reduce the nasal eosinophil counts significantly in Group 1 and 2.

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