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ASSESSMENT OF ROLE OF DIETHYLCARBAMAZINE IN MANAGING ALLERGIC RHINITIS WITH EOSINOPHILIA

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ABSTRACT

Introduction: Managing allergic rhinitis constitutes a substantial part of the daily practice for general otolaryngologists. This study aimed to investigate the role of diethylcarbamazine, an antifilarial drug used in treating tropical pulmonary eosinophilia, in managing allergic rhinitis.

Methods: A descriptive study was conducted in an Indian tertiary level Hospital. Patients selected for the study were administered Tab Diethylcarbamazine at a dose of 5mg/kg body weight twice daily for 21 days. The study evaluated the drug's effects on symptom control, blood eosinophilia, and nasal eosinophilia.

Results: A total of 145 patients were enrolled, with 113 showing eosinophilia either in blood, nasal smear, or both, constituting a significant proportion. Following treatment with Diethylcarbamazine, there was a significant decrease in blood eosinophilia in both the blood and nasal tissue eosinophilia groups. Nasal eosinophilia also decreased significantly in both the blood and nasal tissue eosinophilia groups, as well as the nasal tissue-only eosinophilia group. Symptom improvement was observed across all three groups. Pharyngeal itching improved only in the blood and nasal eosinophilia group and the blood eosinophilia group. However, there was no improvement in anosmia across all three groups.

Conclusion: A significant proportion of the study population exhibited eosinophilia, and Diethylcarbamazine demonstrated utility in reducing symptom scores in allergic rhinitis patients with eosinophilia. The drug also reduced eosinophil scores in both blood and nasal tissue, suggesting its potential as an adjunctive treatment for allergic rhinitis with eosinophilia.

Keywords: Eosinophil, Allergic Rhinitis, Nose, Diethylcarbamazine.

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INTRODUCTION

Allergic rhinitis, despite its high prevalence, is frequently undiagnosed. It affects individuals across all age groups, genders, races, and socioeconomic backgrounds. This condition ranks among the most prevalent chronic ailments in industrialized nations, significantly impacting lifestyle [1-3]. Some experts label allergic diseases as "the epidemic of the 21st century." The head and neck regions serve as primary entry points for airborne and dietary allergens, contributing to common allergy-induced disorders such as rhinitis, sinusitis, otitis media, laryngitis, conjunctivitis, and asthma [4,5]. Otolaryngologists often assess these conditions as the nasal region typically initiates a hypersensitivity response. The majority of associated conditions can be explained by anatomical connections between the nasal cavities and affected organs. However, it's crucial to consider the systemic nature of allergic rhinitis, which may play a role in the development of comorbidities. Furthermore, the systemic aspect could contribute to the perpetuation and aggravation of local symptoms, including acute and chronic inflammation of the nasal mucosa and their functional repercussions [3].

Environmental factors may exacerbate pediatric allergic rhinitis, with CO2 doubling potentially increasing ragweed pollen by 61%, linked to global warming. Differentiating normal from pathological states is challenging, lacking stringent criteria in epidemiological studies. Atopic individuals exposed to common allergens are primarily affected seasonally or year-round, impacting morbidity and performance. Diagnosis involves medical history, clinical examination, skin prick tests, radioallergosorbent tests, and peripheral blood eosinophilia, serum IgE levels, and nasal eosinophil counts [6-8].

Management of allergic rhinitis includes allergen avoidance, pharmacotherapy, patient education, and potentially immunotherapy, with surgery being a rare necessity [9]. Several drug classes are available for managing allergic rhinitis, with antihistamines serving as first-line therapy to alleviate itching, sneezing, and runny nose symptoms. However, first-generation antihistamines pose sedation and performance impairment risks, leading to the development of second-generation antihistamines with reduced sedative effects. Nonetheless, these drugs may induce cardiac effects under certain conditions such as overdosing, concomitant medication use, or in the presence of liver disease [9]. Oral nasal decongestants like pseudoephedrine and phenylephrine are effective in relieving nasal congestion. Immunotherapy targeting allergens has shown unique efficacy, although its costs often place it in a less cost-effective position unless monitored by an allergist [9]. Despite ongoing clinical trials, a definitive cure for allergic rhinitis remains elusive. Peripheral eosinophilia and basophilia in allergic rhinitis patients correlate with symptom severity, mirroring similar patterns observed in various eosinophil-related diseases such as helminthic infections, eosinophilic pneumonitis, asthma, inflammatory bowel disease, eosinophilic gastroenteritis, allergic colitis, idiopathic hypereosinophilic syndrome, and vasculitis [10].

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Tropical pulmonary eosinophilia, characterized by eosinophilia in blood and sputum, has been successfully treated with the antifilarial drug Diethylcarbamazine [11]. Notably, Diethylcarbamazine has also found a new indication in allergic rhinitis due to its ability to block mediator release, particularly SRS-A, from basophils or mast cells [12]. Objectives of this study were: Investigate the correlation between blood and nasal eosinophilia in allergic rhinitis patients; assess the effectiveness of Diethylcarbamazine in alleviating symptoms in individuals with allergic rhinitis and either nasal eosinophilia, blood eosinophilia, or both; evaluate the impact of Diethylcarbamazine on nasal and blood eosinophil levels.

MATERIALS AND METHODS

A descriptive study was conducted, collecting data from patients visiting Outpatient Department at an Indian Medical College and Hospital. Patients with allergic rhinitis symptoms were assessed through thorough history-taking using a proforma, clinical examinations, and laboratory investigations including absolute eosinophil count and nasal smear for eosinophils. Symptoms such as sneezing, rhinorrhea, nasal pruritus, nasal obstruction, eye itching, eye watering, pharyngeal itching, and anosmia were evaluated using a 4-point symptom evaluation scale. 145 patients were enrolled and evaluated for inclusion.

The inclusion criteria for this study encompassed individuals aged between 10 and 40 years who exhibited symptoms indicative of allergic rhinitis, including sneezing, nasal pruritus, rhinorrhea, nasal congestion, eye watering and itching, as well as nasal and pharyngeal itching. To qualify for inclusion, participants needed to experience at least two of these symptoms. Additionally, a symptom evaluation score scale was utilized, categorizing patients as having allergic rhinitis if they presented with nasal smear eosinophilia greater than 1+ or an absolute blood eosinophil count of at least 350, or both, and were not taking any antiallergic medications for a minimum of two weeks. Conversely, exclusion criteria were established to exclude individuals with vasomotor rhinitis, atrophic rhinitis, nasal, paranasal sinus, or nasopharyngeal tumors, drug-induced rhinitis, HIV infection, pregnancy, or a history of worm infestation from the study cohort.

Patients meeting the inclusion and exclusion criteria underwent history-taking, clinical examination, and laboratory tests for absolute eosinophil count and nasal eosinophil smear. Absolute eosinophil count was determined using the Direct method, where blood samples were diluted and stained to count eosinophils under a high-power microscope. Patients were categorized into three groups based on eosinophil counts (both nasal and blood, only nasal, or only blood) and were prescribed Diethylcarbamazine tablets for 21 days.

After 21 days, patients were reassessed for allergic rhinitis symptoms, graded on the symptom evaluation scale, and underwent repeat absolute eosinophil count and nasal smear for eosinophil

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count. No adverse effects were reported during the study. Patients with persistent symptoms after 21 days received treatment with antihistamines and steroid sprays based on symptom severity.

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RESULTS

Among the 145 participants, 113 individuals (77.93%) exhibited eosinophilia either in nasal tissue, blood, or both, as detailed in Table 1.

Following treatment with Diethylcarbamazine, a significant decrease in nasal eosinophil count was observed in both group 1 and group 2. However, the reduction in group 3 was not statistically significant, as indicated in Table 2.

Table 3 provides an overview of the correlation between blood and nasal eosinophilia in allergic rhinitis patients, categorized by the severity of symptoms across three groups. The results show that this association lacked statistical significance.

Moreover, the analysis included an assessment of intergroup significance regarding symptom reduction among allergic rhinitis patients. Various symptoms such as sneezing, rhinorrhea, nasal pruritis, nasal obstruction, eye itching, eye watering, pharyngeal itching, and anosmia were evaluated. The ANOVA test revealed no significant differences in these symptoms between the groups.

Table 1: Distribution of study participants into groups

Group	n	%
Nasal Eosinophilia; N+B0	28	19.31
Blood Eosinophilia; N0B+	25	17.24
Both Nasal and Blood Eosinophilia; N+B+	60	41.38
No Eosinophilia	32	22.07

Table 2: Effect of Diethylcarbamazine on Nasal Eosinophilia

Group	Pre	Post	Diff	% reduction	p
N+B+	1.7 ± 0.8	1.2 ± 1.2	0.5 ± 1.5	42	<0.05
N+B0	2.0 ± 0.7	1.4 ± 0.9	0.6 ± 0.6	30	<0.05
N0B+	0.4 ± 0.2	0.4 ± 0.6	(-)0.1 ± 0.7	75	0.31

Table 3: Association of blood and nasal eosinophilia in AR as per symptom severity

Group	Symptom Severity (Total Score)	n	AEC	Nasal Eosinophilia				
				0	1	2	3	4
N+B+	TS<10; Absent/Mild	20	1397 ± 1167	-	9	1	10	-
	TS>10; Moderate/Severe	40	1050 ± 610	-	27	6	5	2
	P Value		0.47	0.25				

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N+B0	TS<10; Absent/Mild	15	245 ± 56	-	6	6	3	-
	TS>10; Moderate/Severe	13	230 ± 65	-	4	8	-	1
	P Value		0.35	0.91				
N0B+	TS<10; Absent/Mild	10	509 ± 235	3	7	-	-	-
	TS>10; Moderate/Severe	15	602 ± 225	11	4	-	-	-
	P Value		0.45	0.15				

DISCUSSION

Allergic rhinitis, along with its associated complications, is a prevalent condition affecting individuals across all age groups, with a higher incidence observed in younger individuals up to the third decade of life. In our study, the average age of participants was 28.50 years, consistent with findings from studies [13,14]. This demographic trend may be attributed to the lifestyle and increased activity levels among younger age groups, potentially exposing them to a wider array of allergens. Our study included 58% males and 42% females, which aligns with sex distribution patterns reported by C. Bachert [15] (males 43%, females 49%) and Abhey Sood [16] (males 45%, females 55%). However, the presentation and clinical course of allergic rhinitis do not significantly differ between males and females, thereby not impacting group comparisons post-randomization.

Over the past two decades, considerable insights have been gained regarding the role of eosinophils and their involvement in human diseases. Eosinophils are now recognized as pro-inflammatory granulocytes implicated in protective responses and associated with parasitic infestations, as well as allergic conditions such as allergic asthma, allergic rhinitis, and atopic dermatitis [7]. Normally constituting only 1 to 3% of peripheral-blood leukocytes, eosinophil levels up to 350 cells per cubic millimeter are considered within the normal range. Eosinophilia, defined as an elevated eosinophil count, can range from mild (351 to 1500 cells per cubic millimeter) to moderate (>1500 to 5000 cells per cubic millimeter) or severe (>5000 cells per cubic millimeter) and is observed in various disorders [8]. In allergic rhinitis, eosinophils are found both in peripheral blood and nasal tissue [9]. Eosinophils play a significant role as a major source of cytotoxic cationic proteins, including major basic protein, eosinophil peroxidase, and eosinophilic cationic protein. These proteins have dual effects, providing host protection against helminth infections while also causing tissue damage. Additionally, eosinophils contribute to inflammation through the release of lipid mediators, oxygen metabolites, and cytokines [10].

Numerous studies have demonstrated the association between eosinophils and various parasitic and allergic diseases [11]. Atopy and parasitism are key contributors to eosinophilia, although the etiology remains idiopathic in most cases. In developed countries, allergy and atopy are prominent causes, whereas parasitism is more common among travelers returning from developing regions. Other less common causes of eosinophilia include drug reactions, malignancies, and collagen vascular diseases. Approximately 70% of patients with eosinophilia

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present without a definitive diagnosis. The optimal approach to investigating patients with eosinophilia remains a topic of debate in medical literature.

A study conducted by Abhey Sood in 2005 [16] involving 30 cases of allergic rhinitis found nasal eosinophilia in 80% of patients based on specimens collected from middle and inferior turbinates. Similarly, Bryan and Bryan reported increased eosinophil numbers in active allergic nasal disease, while normal nasal mucosal cytology typically does not show eosinophilia or basophilic cells. The strong correlation between nasal allergy and eosinophilia was also highlighted in studies by Sasaki et al. [17] and Miri S [18], emphasizing the significance of eosinophils in allergic rhinitis among different age groups.

CONCLUSION

Treatment with Diethylcarbamazine demonstrated notable effectiveness in reducing symptom scores, although anosmia was not significantly improved. Additionally, Diethylcarbamazine was found to significantly decrease blood eosinophil counts in Group 1 and 3, as well as nasal eosinophil counts in Group 1 and 2. These findings highlight the potential therapeutic value of Diethylcarbamazine in managing allergic rhinitis with eosinophilia, emphasizing the need for further research to explore its efficacy in different patient populations and symptom presentations.

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