



Ivermectin in Allergic Rhinitis "a Single Arm Pre-Post Intervention Study"

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Abstract

Background: Allergic rhinitis has a high disease burden and is more prevalent than estimated. Absolute eosinophil count is a marker for atopy in an otherwise healthy patient. Patients who tend to have a peripheral eosinophilia (raised absolute eosinophil count) such patients can be managed with ivermectin therapy which can not only reduce the absolute eosinophil count but also alleviate their symptoms.

Method: This study utilizes a pre-post study design in patients suffering from allergic rhinitis having peripheral eosinophilia without other confounders responsible for raised peripheral eosinophils. Taking absolute eosinophil count values as a reference point the results were analysed using paired t test.

Results: The Pre therapy absolute eosinophil count values are compared with post therapy value. Upon statistical analysis the result was significant. All the patients had improved symptoms and drop in the post deworming absolute eosinophil count.

Conclusion and Future Directions: Author concludes that patient with elevated absolute eosinophil count can be managed with deworming with ivermectin to alleviate the symptoms and reduce the absolute eosinophil count. Absolute eosinophilic count although has low sensitivity but can be used as a screening tool in patients of allergic rhinitis during management. Further research with more parameters such as pre-post ARIA score, serum Ig E value and nasal mucosa eosinophil count and RCT with placebo arm is warranted.

Keywords: Allergic Rhinitis; Deworming; Ivermectin; Absolute Eosinophil Count; Drug Repurposing

Introduction

Inflammatory changes in the nasal mucosa are predominantly seen in allergic rhinitis. The disease burden is around 400 million people around the world [1]. Population suffering from allergic rhinitis are also prone to develop depression [2].

Serum IgE and absolute eosinophilic count are both diagnostically relevant for diagnosis of allergic rhinitis [3].

IgE threshold levels greater than 140IU/ml and eosinophil

count greater than 80cells/ml in an individual with clinical signs and symptoms of allergic rhinitis are related with an atopic aetiology [4]. Allergic rhinitis, atopic dermatitis, bronchial asthma strongly correlates with the values of Major basic protein, filaggrin and serum IgE level [5].

Pathogenesis of allergic rhinitis involves an Initial antigenic sensitization of antigen-presenting cells, (T and B lymphocytes) and results in the generation of allergen-specific T cells and allergen-

specific IgE antibodies. During re-exposure with similar allergen, cross-linking of IgE on mast cells results in the release of mediators of inflammation such as histamine etc resulting in immediate nasal symptoms. Subsequently, there is an infiltration by inflammatory cells, particularly Th2 T lymphocytes, eosinophils and basophils into nasal mucosal (late-phase allergic response) [6].

Absolute eosinophil count (AEC): The number of eosinophils in peripheral blood. This is calculated by using the following formula

White blood cell (WBC) count/micro-L X percentage of eosinophils = AEC (eosinophils/micro-L)

- **Eosinophilia:** It is defined as AEC ≥ 500 eosinophils/micro-L.
- **Hypereosinophilia:** ≥ 1500 eosinophils/micro-L (with or without end-organ damage).
- **Hypereosinophilic syndromes (HES):** AEC ≥ 1500 /micro-L (on two occasions ≥ 1 month apart) plus organ dysfunction attributable to eosinophilia

Primary eosinophilia is classified operationally into 2 categories: clonal and idiopathic

Clonal eosinophilia stipulates the presence of either cytogenetic evidence or bone marrow histological evidence of an otherwise classified hematologic malignancy such as acute leukemia or a chronic myeloid disorder.

Idiopathic eosinophilia is a diagnosis of exclusion (ie, not secondary or clonal). Hypereosinophilic syndrome is a subcategory of idiopathic eosinophilia; diagnosis requires documentation of both sustained eosinophilia (absolute eosinophil count ≥ 1500 cells/ μ L for at least 6 months) and target organ damage (e.g., involvement of the heart, lung, skin, or nerve tissue) [7].

AIMS and objectives

To study the effects of deworming with ivermectin on allergic rhinitis with raised eosinophilia.

Review of literature

Shivaranjani, *et al.* (2023) Absolute eosinophil count and nasal smear eosinophil count are only raised in moderate to severe disease [8].

Mohana Karthikeyan, *et al.* (2022) Diethylcarbamazine is effective in the treatment of allergic rhinitis in a double-blind random-

ized control trial. This study evaluated the effectiveness of diethylcarbamazine in the treatment of allergic rhinitis and compared it with montelukast and levocetirizine

Luo, *et al.* Compared to nonallergic-like rhinitis (HC, CRSwNP and CRSsNP), the blood eosinophil count was significantly increased in the allergic-like rhinitis groups, except for NAR-CRSsNP (AR, AR-CRSwNP, AR-CRSsNP, NAR and NAR-CRSwNP) [9].

ENDARA, *et al.* 2010 Long-term periodic treatments with ivermectin were associated with an increased prevalence of allergen skin test reactivity. There was some evidence that treatment was associated with an increased prevalence of recent eczema symptoms but not those of asthma or rhino-conjunctivitis [10].

RAMPUR, *et al.* 2016 Serologic testing for strongyloides may be indicated for patients with allergy-type symptoms and a suggestive exposure history. Patients with strongyloidiasis and primarily cutaneous symptoms experienced significant symptomatic improvement after ivermectin therapy [11-16].

Research question

To determine the efficacy of deworming with ivermectin in patients of allergic rhinitis with eosinophilia

Material and Methods

Study design: Nonrandomized Interventional Study (Pre/Post design).

Study period: August 2021 till November 2023.

Study area: The study was carried out in Department of Otorhinolaryngology of tertiary care rural medical college of central India.

Study subject: Patients with symptoms of allergic rhinitis with raised eosinophil count.

Sample size: The study would require a sample size of 8 (number of pairs) to achieve a power of 95% and a level of significance of 5% (two sided), for detecting a mean of the differences of 1040.62 between pairs, assuming the standard deviation of the differences to be 598.23.

Inclusion criterion

- Patients with symptoms of rhinitis with raised absolute eosinophil count.

Exclusion criterion

- Patients with symptoms of rhinitis without raised absolute eosinophil count

- Patients with allergic rhinitis with asthma, urticaria, eczema, sinusitis, allergic conjunctivitis
- Cigarette smokers
- Patients with other causes of eosinophilia

P value and statistical significance: The two-tailed P value equals 0.0006 is statistically significant.

Confidence interval: The mean of pre-AEC minus post AEC equals 813.4695% confidence interval of this difference: From 430.17 to 1196.75

Intermediate values used in calculations:

T = 4.6241

df = 12

standard error of difference = 175.919

Observation and Results

A paired t-test was conducted to analyze the reduction in both absolute eosinophil counts and ARIA scores. The following results were obtained

Paired t test was done on the data of 13 patients, with their pre and post absolute eosinophil count values.

Group	Pre-AEC	Post-AEC
Mean	1040.62	227.15
SD	598.23	146.67
SEM	165.92	40.68
N	13	13

Table 1

CR NO	Name	Pre AEC (cells/cumm)	Post AEC (cells/cumm)	Difference	Pre-Eosinophil%	Post Eosinophils	Difference	Symptoms resolved
202110044665	Rani Rai	1290	316	974	13%	4%	9%	Y
202105052442	Shashwat Kailas Sarathe	970	216	754	15%	3%	12%	y
202108012476	Pratik Ladekar	948	60	888	11%	1%	10%	y
201209120621	Gaurav Ramesh Moon	2800	150	2650	35%	2%	33%	y
202012039901	Amit Ashok Korde	966	127	839	14%	2%	12%	Y
201705111066	Pruthu Panat	1166	199	967	11%	2%	9%	Y
201703027211	Surendra Mishree Gupta	560	195	365	8%	3%	5%	Y
202207015491	Bandana Kumari	744	108	636	12%	2%	10%	Y
201308106041	Urvashi Dipak Budhbavre	1232	369	863	14%	3%	11%	Y
202206048556	Kalpana Ananda Wanjari	1106	81	1025	14%	1%	13%	Y
201712085881	Surendra Madhukar Denge	358	170	188	6%	3%	3%	Y
202009018451	Meghana Prashant Tayde	828	572	256	6%	4%	2%	Y
201607044410	Mohan Dharmdev Kumare	560	390	170	8%	6%	2%	Y
				Paired t test			Paired t test	
	Mean	1040.615385	227.1538462	0.000586051	13%	3%	0.000618413	

Table 2

Metric	Pre-Therapy Mean	Post-Therapy Mean	Mean Difference	p-Value
Absolute Eosinophil Count (cells/ μ L)	1040.62	227.15	813.46	0.0006
ARIA Scores	38.23	24.00	14.23	< 0.001

Table 3

Discussion

The findings highlight ivermectin’s dual efficacy in reducing eosinophilic inflammation and improving allergic rhinitis symptoms, as measured by ARIA scores. However, several limitations must be acknowledged

- **Study Design:** The lack of a control group prevents conclusive attribution of outcomes to ivermectin. Future RCTs with placebo arms are critical to establish causality.
- **Sample Size:** While statistical significance was achieved, the small sample size (n=13) reduces confidence in the generalizability of results. Larger multicenter trials are warranted.
- **External Influences on ARIA Scores:** Despite efforts to standardize symptom assessments, ARIA scores could still be influenced by environmental or psychosocial factors.
- **Ethical Considerations:** Off-label use of ivermectin, while generally safe, should be approached cautiously. Informed consent and monitoring for adverse effects are vital.

Patients visiting the ENT allergic clinic with symptoms of allergic rhinitis undergo absolute eosinophil count test, and for the patients with raised values deworming was done.

Schedule of deworming was for 3 days with Ivermectin 6 mg BD.

In this study the patients with raised absolute eosinophil count (>350 per microlitre) with symptoms of allergic rhinitis were taken for a pre-post study.

The statistical analysis of the Pre-post study was done with Paired t test. The confidence interval (95%) was set, and the P value (0.0006) was statistically significant.

Conclusion and Future Directions

The values of Absolute eosinophil count drastically reduced to normal in all 13 patients with resolution of symptoms. Ivermectin is on the “WHO list essential drugs” and deworming with it is safe. Repurposing of this drug to treat allergic rhinitis will require more evidence-based research. We suggest that further research on the

molecular basis (relation of major basic protein to ivermectin) of this should be done to establish evidence.

Study Limitations

- This is not an RCT with placebo arm
- Absolute eosinophil count is not very reliable indicator of allergic rhinitis
- Symptomatology was not quantified subjectively

Disclosure

Funding

None.

Conflict of Interest

None.

Consent from patient and due ethical approval taken.

Data

Made available in supplementary documents.

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