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Do Oral Prescriptions Overrule Topical Medications in The Management of Allergic Rhinitis: Observations and Opinions?

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Original Research Article

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Abstract: Allergy is one of the major causes of illness in present day that ranges from dust mite contact to anaphylaxis. It occurs when body defences get weak; immunity becomes sensitized and overreacts to an allergen. Hence, early identification has become apt to avoid allergens that trigger overt symptoms. With progression of both economy and education, people have begun adapting effective drug measures to get rid of the source of its occurrence and thus implementing lifestyle changes to improve quality of life. To study how effective is clearing the root cause of allergy from the system in comparison to topical regimen in its management. 480 patients were clinically evaluated, categorised based on their chronicity of symptoms. All were subjected to absolute eosinophil count test. Patients with and without eosinophilia were then treated accordingly. As per the observations, patients were divided into 2 groups with and without eosinophilia and were compared following treating both systemic and local cause separately. Patients dealt for systemic cause of eosinophilia showed far better outcomes compared to other group. Eradicating systemic cause of eosinophilia is mandatory to attain favourable results in treatment protocols.
Keywords: Allergy, allergen, immunity, anaphylaxis, eosinophilia

INTRODUCTION

In this present day materialistic lifestyle, quantum of health has been completely outlined. In this rat race to mint money and lead life in luxury, health often tops the list from bottom. This has led to low self- immunity making body liable to any health perils ranging from a simple common cold to shocking cancer [4, 19, 31].

In a population of > 50 million, 1 in 5 have allergy as a major cause of illness in the present scenario, with its presentation from contact to dust mite to severe anaphylaxis reaction [12, 35, 47]. According to American Academy of Allergy, Asthma & Immunology, 10- 30% of the worldwide population have AR. People get probed with symptoms when the body defences get weak, immune system becomes sensitized and overreacts to an allergen [6, 33, 42]. An allergen is a harmless substance that causes an allergic reaction. AR is an allergic response to these specific allergens. Hence, early identification of these triggering factors is appropriate to evade allergens. With the evolution of both economy and education, people have begun adapting effective drug therapy measures and implementing certain lifestyle modifications to eliminate the cause and improve quality of life[10,24,49].

AIMS AND OBJECTIVES

To study the role of conservative management in eradicating systemic cause of allergy compared to usage of topical medications in AR.

To understand the effectiveness in eliminating eosinophilia in blood to exterminate allergic response in AR.

To know how well are the response rates of systemic medications over topical drug usage in AR.

METHODOLOGY

A prospective study among 480 patients was conducted in a random mixed spectrum of patients with AR over a period of 3 months. Among them, study was conducted only in 452 patients with AR were considered, while the rest were excluded from the study due to other causes of rhinitis. All 452 of them were clinically diagnosed based on their symptomatology and were categorised into 3 groups based on their chronicity of symptoms (< 6 months , 6 months-2 years, > 2 years) as Group A, B and C. Treatment protocols were posed to these 3 groups over a period of around 2 months based on which results were drawn. The observed results are pictorially represented below.

Inclusion criteria

Only patients with Allergic rhinitis were considered i the study.

No gender bias.

Only adults were included in the study.

Exclusion criteria

All other causes of rhinitis are excluded from the study.

Children were excluded from the study.

RESULTS

Out of 480 patients who consulted OPD with rhinitis, 452 patients were considered for the study as they were diagnosed with Allergic rhinitis and rest 28 were excluded from the study due to other causes of rhinitis.

Out of 295 patients with positive AEC test, 68 of them were lost to follow up.

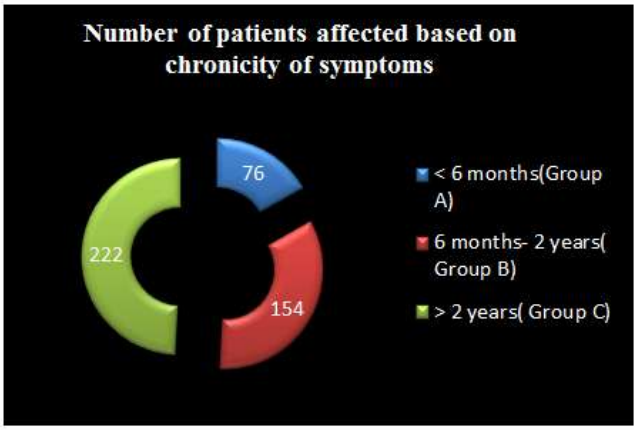

Fig-1: Doughnut diagram showing the number of patients affected with Allergic rhinitis based on their chronicity of symptoms. 76 patients presented symptoms within a period of 6 months (Group A), 154 patients between 6 months to 2 years (Group B) and 222 patients had symptoms for over > 2 years (Group C)

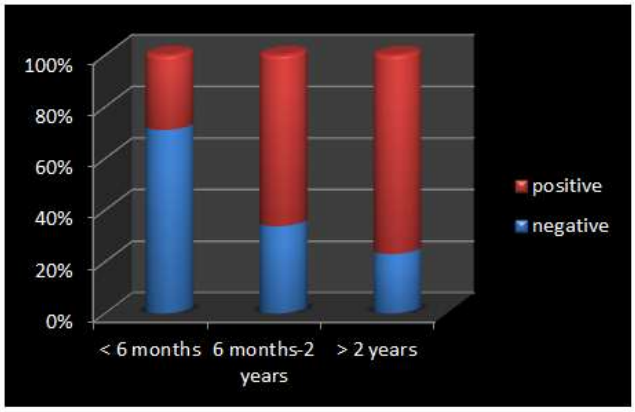

Fig-2: Column diagram showing the results of positive AEC test in 295 patients categorised into 3 groups based on their chronicity of symptoms. 54(71%) had negative eosinophil test while 22 (29%) had positive test in Group A. In Group B, 52(34%) had negative eosinophil test while 102(66%) had positive test. 51(23%) had negative eosinophil test while 171(77%) had positive test in Group C.

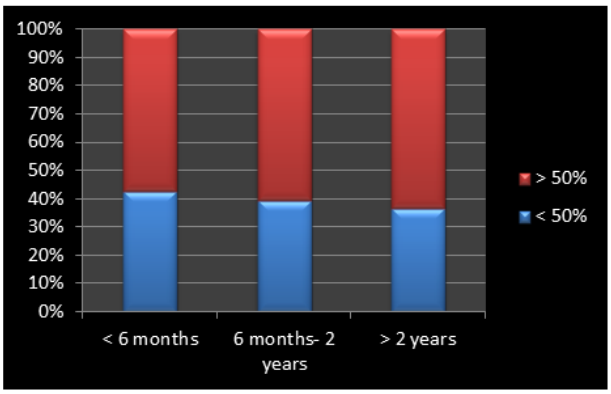

Fig-3: Stacked column diagram showing results of improvement as per their verbal statements on follow up in 227 patients after 21 days of treatment for eosinophilia. In Group A, 6 patients showed < 50% improvement while 8 showed > 50% improvement. 31 patients showed < 50% improvement while 48 showed > 50% improvement in Group B. Group C, 49 patients showed < 50% improvement while 85 showed > 50% improvement. Thus, total 62% of patients showed > 50 % results of improvement

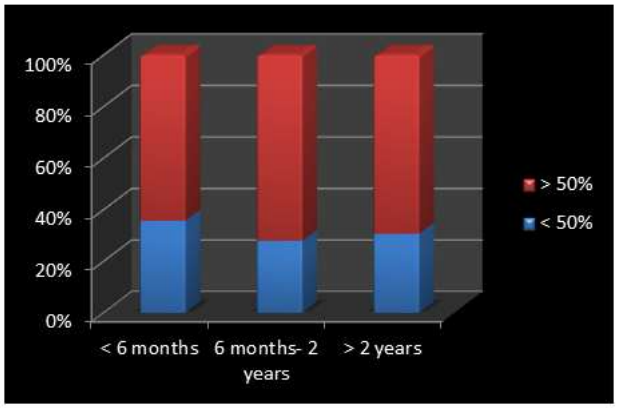

Fig-4: Column diagram depicting results of signs of improvement based on AEC test results in 227 patients following treatment for 21 days for eosinophilia. 5 patients showed < 50% of improvement while 9 showed > 50% improvement in Group A. In Group B, 22 patients showed < 50% improvement while 57 showed > 50% improvement. 41 patients showed < 50% improvement while 93 showed > 50% improvement. Hence, total 70% of patients showed > 50 % results of improvement

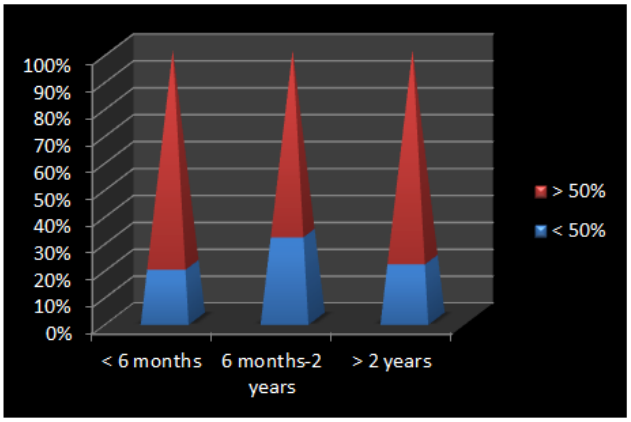

Fig-5: Column diagram representing rest 68 patients who showed < 50 % improvement that were treated for another 15 more days for eosinophilia and were followed up with their AEC test. 1 patient showed < 50% results of improvement while 4 showed > 50% improvement in Group A. In Group B, 7 patients showed < 50% improvement while 15 showed > 50% improvement. 9 patients showed < 50% improvement while 32 showed > 50% improvement in Group C. So, total 75% of patients showed > 50 % results of improvement

Out of 227 patients who were tested positive for AEC test, 17 patients showed < 50% improvement even after the period of 36 days treatment for eosinophilia. This number was considered negligible as it was accounting to only 17 patients (7%) from the entire group of 227 patients.

Now the remaining 210 patients were treated with AR treatment for 15 days with topical steroid nasal sprays and combination of antihistamines with nasal decongestants after systemic course of treatment for eosinophilia. The results are represented in diagram below in Figure 6-

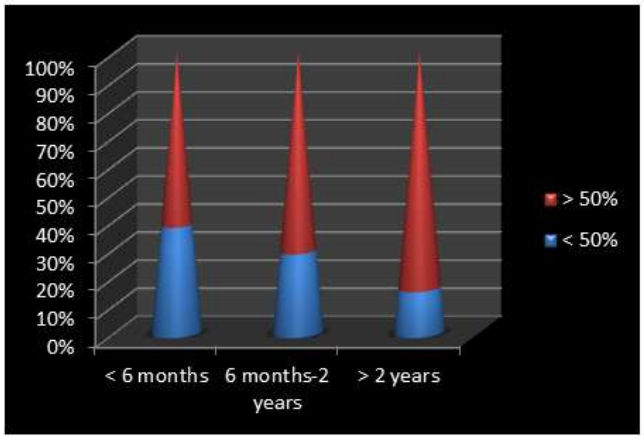

Fig-6: In this Column diagram representation, 5 patients showed < 50% improvement while 8 showed > 50% improvement in Group A. In Group B, 21 patients showed < 50% improvement while 51 showed > 50% improvement. 20 patients showed < 50% improvement while 105 of them showed > 50% improvement. Hence, total 78% of patients showed > 50 % results of improvement

From 452 patients, 157 of them were selected for treatment of AR based on negative AEC test results or AEC within normal range. Among them, 27 patients did not follow up. So, the results was then calculated among the remaining 130 patients depicted in Figure 7 below-

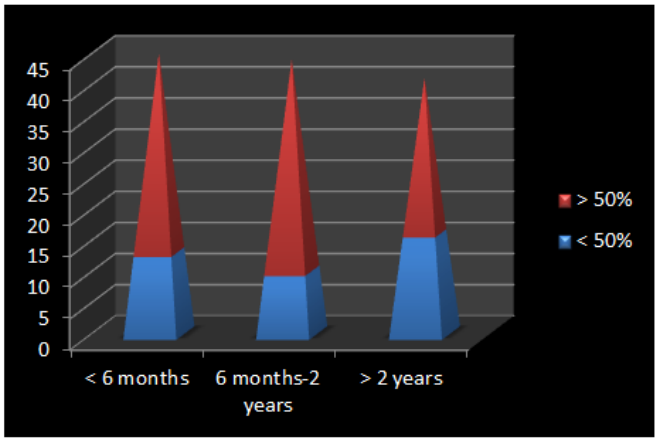

Fig-7: As per depiction in the Column diagram, in Group A, 13 patients showed < 50% improvement while 32 showed > 50% improvement. 10 patients showed < 50% improvement while 34 showed > 50% improvement in Group B. In Group C, 16 patients showed < 50% improvement while 25 showed > 50% improvement. Thus in total 91(70%) out of 130 patients showed > 50 % results of improvement.

DISCUSSION

A prospective study was conducted among 480 patients in a random mixed spectrum of population over a period of 3 months looking for Allergic rhinitis. Patients were divided into 3 groups based on their chronicity of symptomatology. Among the 452 patients diagnosed with Allergic rhinitis, AEC test was done and they were categorised into 2 groups based on blood eosinophil levels. Treatment was then given based on the test results. Medications were then posed over a period of around 2 months based on which results were drawn.

Among 480 patients who consulted ENT outpatient department with rhinitis, 452 patients were included in the study as they were diagnosed with

Allergic rhinitis while the rest 28 were omitted due to various other causes of rhinitis.

An allergen is a harmless substance that causes an allergic reaction. Allergic rhinitis or Hay fever is an allergic response to certain specific allergens. When the body comes in contact with an allergen, it releases histamine, which is a natural chemical that defends the body from it. This chemical haywire can cause Allergic rhinitis and its symptoms. It is a self-treatable and usually self-diagnosable condition which lasts for years as it is chronic in nature [5, 23, 38]. The most common contact allergens are grass pollen (during seasons), dust mites (contact on daily basis), animal dander (specifically its old skin), cat saliva and moulds. There are a set of symptoms seen encountered with people suffering either one of them or all of them immediately when they come in contact of these triggering factors not just during change of seasons but even otherwise which are sneezing (typically continuous 10-12 at a time), watery rhinorrhoea, nasal obstruction, itching and watering in the nose, eyes, dry cough (due to postnasal drip), sore throat, frequent headaches [2, 17, 36, 42]. Though can be easily diagnosable due to its chronicity of symptoms and is treatable by getting the routine blood counts done more specifically absolute eosinophil counts test alone is done which turns out to be an important investigation of choice to know the eosinophil levels in the blood [6,19,26,45]. The more is the eosinophilia in the blood; the more chronic is the occurrence of this condition. Apart from topical and systemic role of drug therapy which has been adapted since decades, the latest treatment mode are radiofrequency diathermy and immunotherapy which are not proven beneficial with no upto the mark expected results as per literature when compared to the age old drug regimens which were efficient both then and now [16,23,39,41].

Out of 452 patients with symptoms of Allergic rhinitis, patients were then categorised into 3 groups based on the chronicity of their symptoms. Of which, patients with allergic symptoms over 2 years and close to 2 years outnumbered inferring existence of the condition on a higher spectrum in the general population in the present scenario. 76 patients in Group A presented with symptoms within 6 months, 154 patients presented symptoms between 6 months to 2 years in Group B and Group C showed 222 patients with symptoms for over > 2 years.

Of the 452 patients with Allergic rhinitis, which were later divided in to 2 groups based on AEC test results (Normal AEC count ranges from 40-440) results.

White blood cells (WBC's) forms an important part of the body's immune system that protects it from invading microorganisms. Bone marrow produces 5 different kinds of WBC's in the body which continually replenishes the body's WBC supply [2,17,43]. Each WBC lives for hours to days in the blood stream. An eosinophil is a type of WBC stored in the body tissues that survives for several weeks [9,22,45].

Elevated levels of WBC's in the blood can be an indicator of an infection. An eosinophil count is a blood test that measures the quantity of eosinophils in the body. 2 important functions of eosinophils [1, 20, 42] within the immune system are to destroy the invading viruses, bacteria or parasites and also have a role in the inflammatory response such as allergy [8, 44].

In adults, a normal AEC reading will show < 500 eosinophil cells / microliter of blood. In children, eosinophil levels vary with age while if counts are > 500 eosinophil cells/microliter of blood, it indicates to a disorder known as eosinophilia. Eosinophilia is classified as either mild (500–1,500 eosinophil cells per microliter), moderate (1,500 to 5,000 eosinophil cells per microliter) or severe (> 5,000 eosinophil cells / microliter) [5, 23, 37, 41].

Eosinophilia can occur due to Allergy, Parasitic infestations, Autoimmune disease, Eczema, Asthma, Leukemia, Inflammatory bowel diseases, Scarlet fever, Lupus, drug reactions, Organ transplant rejection, severe allergic reactions. Medications that cause an increased eosinophil count are diet pills, Interferons, certain antibiotics, Laxatives that contain psyllium, Tranquilizers and Warfarin [3, 15, 32, 40].

An abnormally low eosinophil count can be the result of intoxication from alcohol or excessive production of cortisol as in Cushing's disease. Under normal conditions, eosinophil counts are lowest in the morning and highest in the evening [7, 21]. Unless alcohol abuse or Cushing's disease is suspected, low levels of eosinophils are not usually of concern unless other WBC's are also abnormally low. If all WBC's are low, this can signal a problem with the bone marrow [11, 29]. If there is an allergy or parasitic infection, short-term treatment is prescribed to alleviate symptoms and revert WBC count to normal.

The 2 groups were; 295 patients (65%) showed positive AEC counts with 3-4 times more than the range values (> 440) while the rest 157 patients (35%) who showed negative or within normal range AEC counts.

Out of 295 patients with raised eosinophil levels, were then treated with only Diethylcarbamazine twice daily for a period of 21 days.

Diethylcarbamazine (DEC), an inhibitor of arachidonic acid and also prostaglandin G/H synthase-1 inhibitor. Though it belongs to the class of

Anthelmintics but does not resemble other antiparasitic compounds [13,27]. It has mainly both micro and macro filaricidal in action. It is a synthetic organic compound which is highly specific to several parasites and does not contain toxic metallic elements. It gets rapidly and readily absorbed with no volume of distribution and protein binding with half of life of 8 hours [16, 39]. It is used as treatment of Lymphatic filariasis, Tropical pulmonary eosinophilia, Loaisis, Onchocerciasis. It involves in sensitising the microfilariae to phagocytosis. Though active against microfilariae, it is dependent on inducible nitric oxide synthase and cyclooxygenase pathway [30, 46]. It also has an important role of arachidonic acid metabolic pathway in its invivo mechanism of action. In addition to its effect on 5- lipooxygenase pathway, it also targets the cyclooxygenase and COX-1 pathways [34, 48].

It is given in the dose of 6mg/kg/day in divided TID doses of 15 or 21 days. In allergic rhinitis, as it has a blocking agent of mediator release in particular of SRS-A from the sensitised basophil or mast cell. There is no much literature regarding its usefulness in Allergic rhinitis till date with respect to this drug. There was some light put on the effectiveness of this drug shown in the study [51,52,53] with more effective results were shown in this study similarly.

Among 295 patients, 68 patients did not follow up. Reason behind patient non-follow up may be one of the following- they must have been either cured or there is no improvement with the treatment prescribed to them or no proper intake of medications meticulously prescribed to the patients.

As per verbal statement of the remaining 227 patients on follow up after 21 days course of treatment with Diethylcarbamazine twice daily; 141(62%) patients showed > 50% improvement.

These 227 patients were evaluated once again with a repeat AEC test following treatment therapy of 21 days of Diethylcarbamazine twice daily. The results were gauged based on their blood test reports. 159 (70%) patients that showed > 50% improvement.

The remaining 68 patients out of 227 patients who showed < 50% improvement were again treated with Diethylcarbamazine twice daily for another 15 more days. They were once again followed up with their AEC test reports after the 15 days treatment therapy. Of which 51(75%) patients showed >50% improvement and rest 17(7%) showed < 50% improvement which were ignored as the number was considered negligible among a total of 227 patients who were treated for positive AEC test.

Out of 295 patients, 210 of them who were treated for 36 days with Diethylcarbamazine and 157 patients of initial 452 patients with negative or normal eosinophil counts were now put to Allergic rhinitis treatment for 15 days (that is topical steroid nasal sprays and combination of oral antihistaminic and nasal decongestants).

Corticosteroids are either used singly or in combination for better effects and results. Corticosteroids are very effective at reducing inflammation especially caused by allergies by relieving nasal passages [14,25]. They relieve symptoms such as nasal and sinus congestion, mucus production caused by conditions such as hay fever or allergic rhinitis.

Regular use of nasal corticosteroids can make the nasal passages less sensitive to triggers such as pollen, animal dander or dust mites. They work best when used daily with a specific schedule of number of puffs to each nostril as regular usage gives good results [18, 36]. It takes at the most 2 weeks to get the effective results which can sometimes vary as relieving symptoms helps to feel and sleep better and lessen the symptoms during day [3,14].

They are Azelastine hydrochloride, Beclomethasone dipropionate, Budesonide, Ciclesonide, Fluticasone propionate and furoate, Flunisolide, Mometasone furoate, Triamcinolone acetonide in a preparation designed for nasal use [26,35].

Nasal corticosteroid sprays are safe for all adults and are even safe for children of age 2 and above. The sprays are even safe to use in pregnant women. Side effects may include any of these symptoms: dryness / burning in the nasal passages, sneezing, throat irritation, headaches, epistaxis and in rare cases, septal perforation as the spray is used into centre of the septum instead of towards the outer wall [28,38,50].

Flutiflo FT (Fluticasone furoate) was a random choice of steroid nasal spray in this study as it provided excellent outcomes in terms of patient's response to usage with very limited side effects and is cost effective [8,22,34,47].

Antihistamines are the class of drugs that opposes the activity of histamine receptors in the body. These drugs are used to treat allergic rhinitis and other allergies. They give relief from nasal congestion, sneezing from hives of pollen, dust mites or animal dander. They are preferred as they are inexpensive, generic, over-the-counter drugs with few side effects [12, 33, 49]. They are usually taken as short-term treatment course as long term use is harmful. Chronic allergies increase the risk of health problems wherein

antihistamines might not treat conditions such as asthma, sinusitis and lower respiratory tract infections [6, 17, 23].

Antihistamines are subclassified according to histamine receptor that they act upon. 2 largest classes of antihistamines are H1-antihistamines and H2-antihistamines. Antihistamines that target H1-receptor are used to treat allergic reactions in the nose as well as for insomnia. They also treat motion sickness. H1-antihistamines [11, 22, 31, 47] work by binding to histamine H1 receptors in mast cells, smooth muscle and endothelium in the body as well as in the tubero-mammillary nucleus in the brain Antihistamines that target the H2-receptor are used to treat peptic ulcers and acid reflux. H3 and H4 antihistamines which are latest additions to this group.

Histamine produces increased vascular permeability causing fluid to escape from capillaries into tissues leading to classic symptoms of an allergic reaction. Histamine also promotes angiogenesis [2,19]. Antihistamines suppress the histamine-induced wheal and flare response by blocking binding of histamine to its receptors or reducing histamine receptor activity on nerves, vascular smooth muscles, glandular cells, endothelium, and mast cells. Itching, sneezing and inflammatory responses are suppressed by antihistamines that act on H1-receptors [27,46].

H1-antihistamines are used to treat allergic reactions and mast cell-related disorders. They can reduce inflammation as the expression of NF-κB (transcription factor) regulating inflammatory processes and is promoted by both receptor's constitutive activity and agonist binding at the H1 receptor [24,37,48]. First- generation antihistamines having analgesic-sparing (potentiating) effects on opioid analgesics and to some extent with non-opioid ones as well. The most commonly used for the purpose include Hydroxyzine, Promethazine etc.

H1 antagonists include: Azelastine, Cetirizine, Chlorpheniramine, Clemastine, Cyclizine, Cyproheptadine, Dimenhydrinate, Diphenhydramine, Ebastine [4,16,28,43], Fexofenadine, Hydroxyzine, Loratadine, Meclizine, Mirtazapine Olopatadine, Promethazine, Quetiapine, Rupatadine, Triprolidine etc while H1 inverse agonists: Cetirizine, Levocetirizine.

Nasal Decongestants are used to relieve nasal congestion in the upper respiratory tract. The active ingredient in most decongestants is either pseudoephedrine or phenylephrine. Intranasal corticosteroids can also be used as decongestants and antihistamines can be used to alleviate allergic symptoms [13, 36, 45]. Topical decongestants produce local vasoconstriction. Regular use of decongestants for long periods should be avoided because mucosal ciliary function is impaired as in atrophic rhinitis and anosmia which can occur due to persistent vasoconstriction. Decongestants can be absorbed from the nose via an inhaler and produce systemic effects mainly CNS stimulation and rise in blood pressure. These drugs should be used cautiously in hypertensives and in those receiving MAO inhibitors as they can cause hypertensive crisis. These are used to treat nasal congestion in allergies, URI, influenza, sinus infection and nasal polyps [5,17,33].

The vast majority of decongestants act via enhancing noradrenaline and adrenaline or adrenergic activity by stimulating the α-adrenergic receptors. This induces vasoconstriction of the blood vessels in the nose [7,37,42], throat and PNS which results in reduced inflammation and mucus formation in these areas.

Decongestant nasal sprays and eye drops often contain Oxymetazoline are used for topical decongestion. Pseudoephedrine acts indirectly on the adrenergic receptor system, whereas Phenylephrine and Oxymetazoline are direct agonists. The effects are not limited to the nose, and these medicines mainly causes hypertension through vasoconstriction hence to be avoided them[1,14,28].

Topical nasal or ophthalmic are Ephedrine, Pseudoephedrine, Loratadine, Cyclopentamine, Mephentermine. The α-Adrenergic receptor agonists are Naphazoline, Oxymetazoline, Phenylephrine [8,19,42], Xylometazoline, Epinephrine, Norepinephrine.

The combination of Antihistamine with Nasal decongestant chosen in this study is Tablet Ebast-DC (Ebastine hydrochloride + Phenylephrine) [6,14,26,39,44] as it was found to have good efficacy, cost effective with very good result outcomes in patients when prescribed.

Out of 210 patients, 164 (78%) patients showed > 50% improvement to Allergic rhinitis treatment. So, among the 130 patients, 91 (70%) patients showed > 50% improvement with Allergic rhinitis treatment therapy and the rest 27 patients failed to follow up.

CONCLUSION

The various treatment protocols were established for Allergic rhinitis from ages as per literature. Moreover the studies showed that the medical line of management was preferred over surgical mode of treatment therapy. This study is one of its kinds with efficacy shown with conservative line of treatment moreover beneficial with clearance of blood eosinophilia as a primary goal for treating Allergic rhinitis.

As per the observations made in the study, AEC test has served as an important diagnostic tool for

diagnosis of Allergic rhinitis. Usually by treating only local allergic symptoms conservatively has not provided needed results as systemic clearance of eosinophils is often neglected, which is the root cause. By just treating the local cause per se is not at all found beneficial among patients when followed up on a long term basis.

The role of conservative management in eradicating systemic cause of allergy compared to usage of topical medications in Allergic rhinitis is very well proven in this study with an 8% difference in the test results when both the groups with and without eosinophilia were compared after treatment therapy.

The effectiveness in eliminating eosinophilia in blood to exterminate allergic response in Allergic rhinitis has achieved 78% success rates, which was the basis of this study.

The response rates of systemic medications over topical drug usage in Allergic rhinitis has not only proven effective in this study with the results achieved but also the feedback received from the patients were satisfactory.

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