A Dissertation on

"EFFECT OF IMMUNOTHERAPY ON ALLERGIC RHINITIS"

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BRANCH-IV

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MADRAS MEDICAL COLLEGE
CHENNAI

APRIL 2014

BONAFIDE CERTIFICATE

This is to certify that this dissertation is a bonafide record of work done by **Dr.S.SHENBAGAVALLI** on **"EFFECT OF IMMUNOTHERAPY ON ALLERGIC RHINITIS",** during her M.S. ENT course from April 2011 to April 2014 at the Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai. She is appearing for her M.S. Branch-IV Degree examination in April 2014 and her work has been done with partial fulfillment of the regulations of The Tamil Nadu Dr.M.G.R. Medical University, Chennai. I forward this to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I, **Dr.S.SHENBAGAVALLI**, solemnly declare that this dissertation entitled **"EFFECT OF IMMUNOTHERAPY ON ALLERGIC RHINITIS"** is a bonafide work done by me in upgraded Institute of Otorhinolaryngology, Madras Medical College and Rajiv Gandhi Government General hospital, Chennai, during the period 2011 to 2014 under the guidance of **Prof. Dr. G. GANANATHAN, M.S., D.L.O.,** Director, Institute of Otorhinolaryngology, Madras Medical College and Government General Hospital, Chennai – 3 and submitted to **The Tamilnadu Dr. MGR Medical University,** Guindy, Chennai – 32, in the partial fulfillment of the requirements for the award of the degree of M.S., E.N.T., (Branch IV).

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EFFECT OF IMMUNOTHERAPY ON ALLERGIC RHINITIS

Dr. S. SHENBAGAVALLI

Guide : Prof. Dr. G. GANANATHAN, M.S. D.L.O.,

ABSTRACT

Objective : Effect of SCIT in allergic rhinitis patients sensitive to multiple allergens.

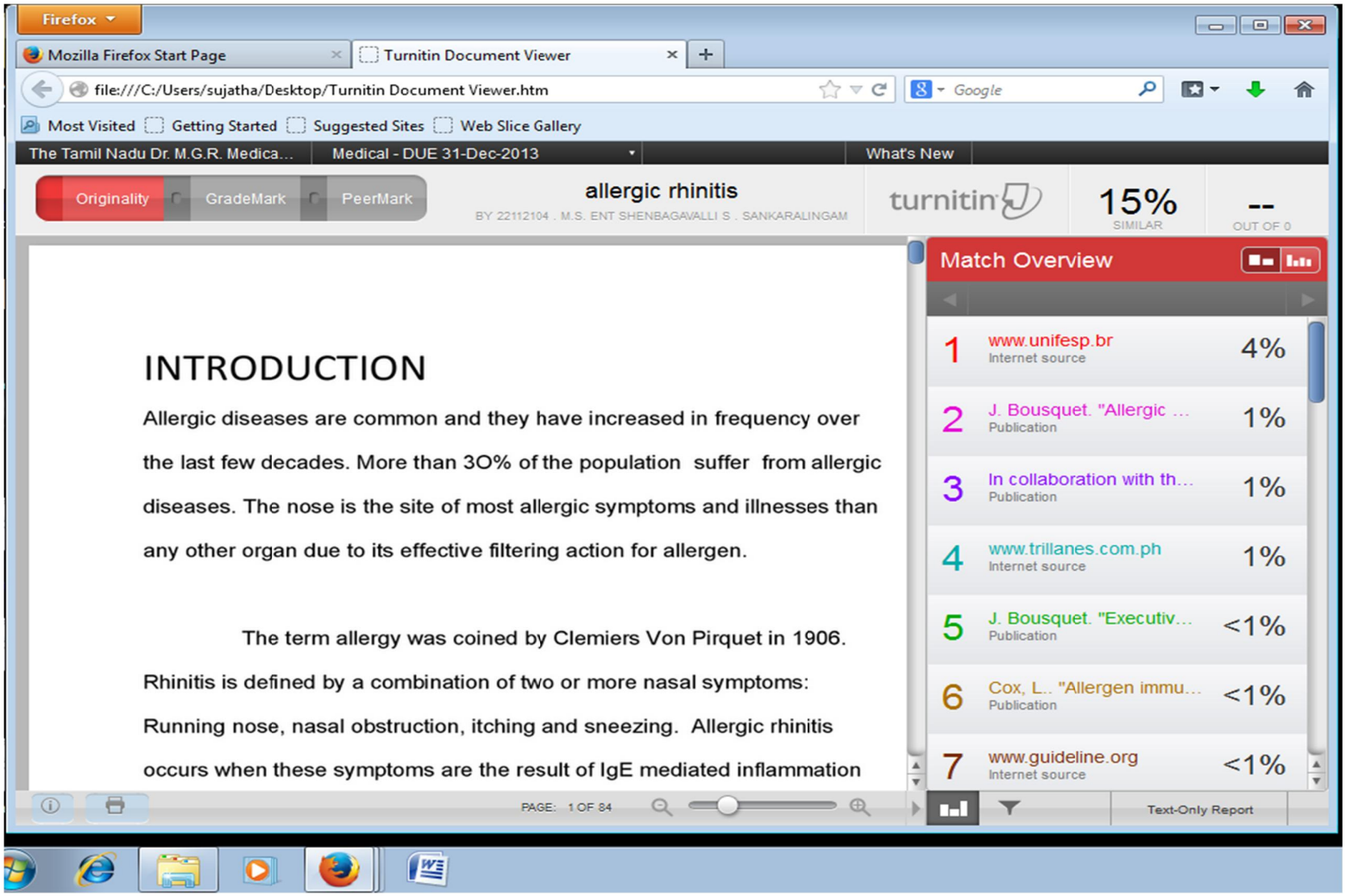
Methods : In this study symptom score medication score of 30 allergic rhinitis patient's were collected. Intradermal skin test, Absolute Eosinophil Count and FEV1% were performed at baseline and 12 months after treatment with subcutaneous Immunotherapy.

Result: There is significant improvement in Nasal symptoms and Non-Nasal symptoms. There is better improvement in nasal symptoms compared to non nasal symptoms. Subcutaneous immunotherapy reduces medication requirement. Skin sensitivity reactions have reduced. Patients showed significant symptomatic improvement even when skin sensitivity reactions were present. Immunotherapy lowers total IgE and absolute eosinophil count.

Conclusion : SCIT demonstrated clinical improvement in Allergic rhinitis/ Asthma, sensitive to multiple allergen.

Key Words:

Allergy, subcutaneous Immunotherapy, FEV1%, IgE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INTRODUCTION
Allergic diseases are common and they have increased in frequency over the last few decades. More than 3O% of the population suffer from allergic diseases. The nose is the site of most allergic symptoms and illnesses than any other organ due to its effective filtering action for allergen.
The term allergy was coined by Clemiers Von Pirquet in 1906. Rhinitis is defined by a combination of two or more nasal symptoms: Running nose, nasal obstruction, itching and sneezing. Allergic rhinitis occurs when these symptoms are the result of IgE mediated inflammation
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INTRODUCTION

Allergic diseases are common and they have increased in frequency over the last few decades. More than 3O% of the population suffer from allergic diseases. The nose is the site of most allergic symptoms and illnesses than any other organ due to its effective filtering action for allergen.

The term allergy was coined by Clemiers Von Pirquet in1906. Rhinitis is defined by a combination of two or more nasal symptoms: Running nose, nasal obstruction, itching and sneezing. Allergic rhinitis occurs when these symptoms are the result of IgE mediated inflammation following exposure to allergens.

Management involves allergen avoidance, use of antihistamines, topical steroids and allergen immunotherapy Immunotherapy involves the step-wise incremental injection of increasing subcutaneous doses of allergen, in order to suppress symptoms on subsequent re-exposure to that allergen. In contrast to topical corticosteroids, immunotherapy, when given monthly for three to four years, has been shown to induce long-term remission for at least three years following discontinuation of treatment. Studies strongly suggest that immunotherapy is the only treatment that has the potential to modify the course of allergic disease.

AIMS AND OBJECTIVE

To evaluate the effect of immunotherapy for

1. Reduction of symptoms during allergic rhinitis
2. Reduction of medication requirements
3. Alteration of immunological markers- IgEs, absolute eosinophil count.
4. Alteration in pulmonary function test

REVIEW OF LITERATURE

ANATOMY OF NOSE

The Vestibule, a skin lined area bearing coarse hairs and vibrissae is a dilated passageway leading from external nares to nasal cavity and limited superiorly by limen nasi.

Pyriform aperture is a pyramidal shaped opening bound by nasal bones superiorly and inferolaterally by maxilla. Anterior nasal spine lies inferiorly. All nasal cartilages are hyaline cartilage. Cartilaginous framework of external nose is formed by upper lateral and lower lateral or alar cartilages. The lower lateral cartilage gives rise to medial and lateral crus which forms the dome of nasal tip. Dorsal branch of ophthalmic artery and infra orbital branch of maxillary artery supplies dorsum and lateral wall of external nose.

Venous network- Frontomedian area drains into facial vein while the orbitopalpebral area drains to ophthalmic vein. Supratrochlear and

supraorbital veins join to form angular vein at the inner canthus and continues as facial vein.

The skin of external nose is supplied by ophthalmic and maxillary branch of trigeminal nerve. Lymphatic drainage terminates into submandibular and submental nodes

NASAL CAVITY

Nasal cavity extends from external nares to posterior choana and continues as nasopharynx. It extends vertically from palate to cribriform plate. Superiorly cavity narrows down to form the olfactory cleft. Floor is formed by horizontal process of palatine bone and palatine process of maxilla. Terminal branches of nasopalatine nerve, greater palatine artery and stensons organ enters the nasal cavity through incisive canal which lies about 12 mm behind the end of floor.

Roof is divided into frontonasal, ethmoidal and sphenoidal parts. Frontonasal and sphenoidal parts of roof slopes downwards while ethmoidal part is almost in the horizontal plane. Olfactory epithelium lines the roof and upper third of medial and lateral walls of nasal cavity. Respiratory epithelium lines the remaining part of nasal cavity and continuous with paranasal sinuses, nasolacrimal duct and nasopharynx.

NASAL SEPTUM

Septum is composed of membranous, cartilaginous and bony parts. Quadrilateral cartilage forms the major bulk of septum while upper and lower lateral alar cartilages provides a minimal contribution to the formation of septum.

The bony part of septum is formed by vomer and perpendicular plate of ethmoid . Perpendicular plate forms the anterosuperior part of bony septum. It continues with the cribriform plate and crista galli. Vomer forms the posteroinferior bony nasal septum and articulates with the rostrum of sphenoid, palatine and maxillary crests, perpendicular plate above and quadrilateral cartilage below. Posteriorly it forms the posterior free border of septum.

HISTOLOGY

The nasal cavity is predominantly lined by respiratory epithelium composed of either ciliated or non ciliated pseudostratified columnar epithelium. A small area in the roof is lined by olfactory epithelium. The columnar cells bears 300-400 microvilli which aids in increasing the surface area and prevent drying.

The Olfactory epithelium spreads from cribriform plate to upper septum. It is composed of receptor cells, supporting cells and brain stem cells. The brain stem cells is responsible for regenerative capacity of olfactory epihelium.

BLOOD SUPPLY

The rich blood supply of septum is contributed by both the internal and external carotid arteries. Septum is supplied by sphenopalatine artery posteroinferiorly, greater palatine artery anteroinferiorly, superior labial branches of facial artery anteriorly and anterior and posterior ethmoidal arteries superiorly.

NERVE SUPPLY

Major part of sensory supply of nasal septum is by maxillary division of trigeminal nerve. Anterosuperior part of nasal septum is supplied by anterior ethmoidal nerve while anteroinferior part is supplied by anterior superior alveolar nerve. Posteroinferior septum receives a small supply from nerve to pterygoid canal and anterior palatine nerve branches.

Sensory nerves are accompanied by postganglionic sympathetic fibers and parasympathetic secretomotor fibers.

LATERAL NASAL WALL

INFERIOR MEATUS- it's the largest meatus and forms part of lateral wall of nose. It lies lateral to inferior turbinate and extends almost along the whole length of nasal cavity. The opening of nasolacrimal duct is

seen anterior to the junction of anterior and middle third of inferior meatus. Hasner's valve, a mucosal fold covers the opening of the duct.

INFERIOR TURBINATE- it is formed by an independent bone. The bone has an irregular surface grooved by vascular channels and mucoperiosteum is firmly attached to the same. The maxillary process of inferior concha articulates with inferior margin of maxillary hiatus. The other bony articulations are formed by palatine bone, ethmoid and lacrimal bones. It forms the medial wall of nasolacrimal duct. It has an extensive submucosal cavernous plexus under autonomic control. This provides the major contribution to nasal resistance. The respiratory epithelium lining the inferior turbinate is rich in goblet cells which decrease in density from anterior to posterior.

MIDDLE MEATUS- it is the part of lateral nasal wall lying lateral to middle turbinate. The frontal, maxillary and anterior ethmoidal sinuses drain into middle meatus. The maxillary ostium is bounded posteriorly by perpendicular plate of palatine bone, inferiorly by maxillary process of inferior turbinate bone, superiorly by uncinate and bulla and lastly anterosuperiorly by lacrimal bone. The anterior and posterior fontanelle is the membranous portion seen anterior and posterior to uncinate.

Accessory ostium, may be formed as a result of infection, usually is seen in the posterior fontanelle.

The uncinate is a thin crescent shaped bone with concavity posteriorly running parallel to the anterior face of ethmoidal bulla. Anteriorly it's attached to maxillary hiatus. Superiorly it may attach to skull base or may fuse with the insertion of middle turbinate. In these two situations, both frontal and maxillary sinuses drain into ethmoidal infundibulum with obvious pathological consequences. Sometimes uncinate may insert laterally to lamina papyracea such that the ethmoidal infundibulum ends as a blind pouch known as terminal recess.

The aggernasi is a small mound lying anterior to middle turbinate on the lateral wall of nose. It may be pneumatised in 5 to 80 % population. Hiatus semilunaris is a 2 dimensional space between the anterior surface of ethmoidal bulla and posterior free border of uncinate. It is also known as inferior hiatus semilunaris coined by Grunwald. Superior hiatus semilunaris lies between the basal lamella of middle turbinate and ethmoidal bulla. This sickle shaped cleft leads into retrobullar recess.

Ethmoidal infundibulum is a 3 dimensional funnel shaped space connecting maxillaryostium to middle meatus via hiatus semilunaris. Uncinate and hiatus semilunaris forms the medial boundary of this space. The anterior face of bulla lies posteriorly and lamina papyracea lies laterally. Superior boundary depends on the attachment of uncinate process.

Ethmoidal bulla is the most constant aircell .It is the largest ethmoidal air cell. A poorly pneumatised or completely unpneumatised bulla known as torus lateralis is seen in 8 % of population. Anterior face of bulla forms the posterior margin of ethmoidal infundibulum and hiatus semilunaris. The posterior face may fuse with the basal lamella of middle turbinate. If it does not fuse with middle turbinate, it forms a retrobullar recess known as lateral sinus or recessus supraethmoidalis. Superiorly it forms the posterior wall of frontal recess when it reaches the roof of ethmoid.

Anatomical variations such as concha bullosa, paradoxical middle turbinate, enlarged ethmoidal bulla, haller cells, septal deflection, medialised uncinate process etc., contributes to the pathogenesis of sinusitis.

SUPERIOR TURBINATE- is seen above the superior meatus. Posterior ethmoidal cell opens into superior meatus. Spenoid sinus opens into spenoethmoidal recess which lies medial to superior turbinate.

HISTOLOGY OF LATERAL WALL

Respiratory epithelium composed of ciliated columnar epithelium lines majority of the lateral wall of nose. A small portion over the superior turbinate is lined by olfactory epithelium. Areas of squamous metaplasia is seen in anterior inferior turbinate as it is subject to greatest air flow.

BLOOD SUPPLY OF LATERAL WALL

The external and internal carotid artery branches supply the lateral wall of nose. Sphenopalatine artery enters the nose through sphenopalatine foramen and supplies all turbinates and meatus Sphenopalatine foramen lies inferior to the horizontal attachment of middle turbinate.

Excessive enlargement of middle meatal antrostomy may damage the sphenopalatine artery. The anterior part of lateral wall of nose is supplied by facial artery branches. Greater palatine artery supplies the

lateral wall of nose adjacent to palate. Anterior and posterior ethmoidal arteries supplies superior lateral wall.

Venous drainage is carried through facial and ophthalmic vessels to sphenopalatine vein. Intracranially via ethmoidal veins to veins of dura and also to superior sagittal sinus via foramen caecum.

NERVE SUPPLY OF LATERAL WALL

The anterosuperior part is supplied by anterior ethmoidal nerves. Posteriorly by branches of pterygopalatine ganglion and anterior palatine nerves. Infraorbital nerve, a branch of maxillary nerve supplies a small area anteriorly. The anterior inferior meatal region is supplied by anterior superior alveolar nerves .

LYMPHATIC DRAINAGE

Anteriorly drains into submandibular node and posteriorly to lateral pharyngeal, retropharyngeal and upper deep cervical nodes.

NASAL AIRWAY AND FACTORS INFLUENCING NASAL RESISTANCE TO AIRFLOW

Nose contributes to two thirds of total airway resistance in adults. Nasal resistance is divided into three compartments. They are turbinated nasal passage, nasal valve and nasal vestibule.

Nasal vestibule acts as a flow limiting area as its walls are compliant and easily collapsible under the influence of negative pressure generated during inspiration.

Nasal valve is the narrowest part of nose and it is an important determining factor of nasal resistance to airflow. It is formed by the inferior edge of upper lateral cartilage, anterior end of inferior turbinate along with adjacent part of nasal septum.

The degree of engorgement of venous erectile tissue is one of the major determining factor for nasal resistance. Accessory respiratory muscles also influence nasal resistance by maintaining the patency of nostril during inspiration. Sympathetic autonomic nervous system plays a major role in regulating nasal resistance.

Airflow through nasal passage is inversely related to nasal resistance. The oscillations in nasal resistance are referred to as the nasal cycle. Hence airflow through nasal passage is essentially asymmetrical.

IMMUNOLOGY

Immunology was initially a study of response of animal to infection. Now it involves the study of allergy, immunochemistry, immunopathology, clinical immunology, tumor immunology and transplantation.

Allergy is a type of hypersensitivity reactions with harmful immune response resulting in tissue injury and serious diseases. Type I is an Ig E mediated hypersensitivity reaction due to allergen mediated crosslinking of preformed Ig E antibody bound to FC receptors on mast cells.

IMMUNE SYSTEM

The main role of immune system comprising of lymphocytes and antibodies is to distinguish between macromolecules that are indigenous or foreign. The specificity is the ability of immune system to produce specific antibody directed against non-self macro molecules which acts as an antigen and stimulates immunity.

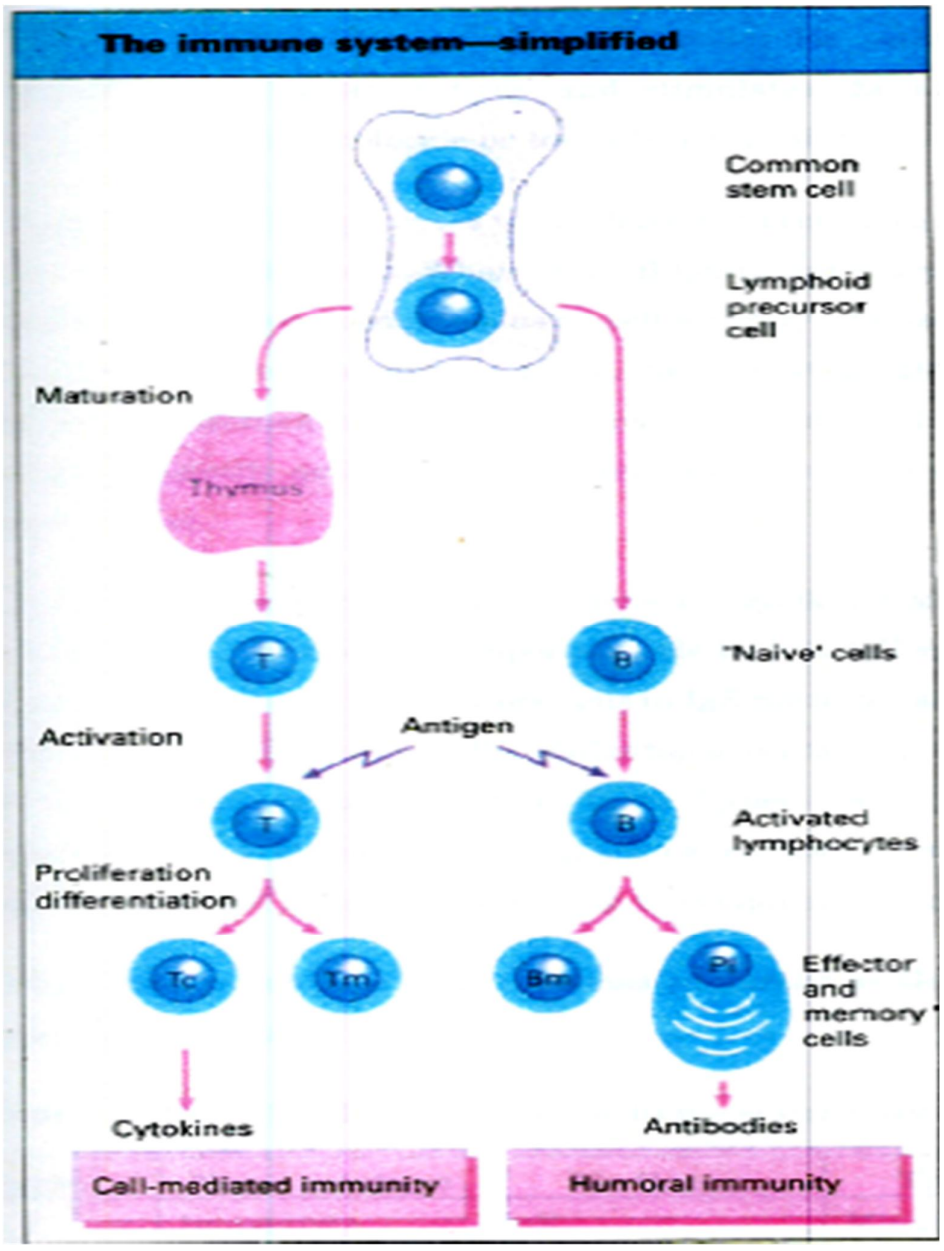
B and T Cells- naïve cells are lymphocytes which have not yet been exposed to any antigen. On stimulation of these naïve B cells by antigen, they are converted into plasma cells which synthesize antibody.

This is known as humoral immune response. Naïve T lymphocytes on stimulation by antigens transform to activated T cells which secrete proteins, cytokines. This type of immune response is termed cell mediated immune response. T helper cells, cytokines and their signal proteins control entire immune responses. IgE synthesis, recruitment and activation of inflammatory cells in IgE mediated reactions is under the influence of T helper cells. Effector cells or cytotoxic T cells destroy antigen containing cells by release of cytokines or by direct contact.

The term hypersensitivity refers to an exaggerated response due to an reaction between antigen and antibody or sensitized lymphocytes leading to morbidity.

CLASSIFICATION OF HYPERSENSITIVY REACTIONS

TYPE	NOMENCLATURE	TIME FRAME	MEDIATOR
I	Immediate	Minutes	IgE
II	Cytotoxic	Minutes to days	Ag- Ab complex
III	Immune complex	Hours	IgG, complement, IgM
IV	Cell mediated	Days	T cells


The immune system—simplified
Common stem cell
Lymphoid precursor cell
Maturation
Thymus
T
B
'Naive' cells
Activation
Antigen
T
B
Activated lymphocytes
Proliferation differentiation
Tc
Tm
Bm
Pl
Effector and memory cells
Cytokines
Antibodies
Cell-mediated immunity
Humoral immunity

TYPE I HYPERSENSITIVITY

Mast cells coated with IgE antibody, when comes in contact with allergen degranulates with the release of histamine and chemical mediators. This is known as type I hypersensitivity reaction. Immediate symptoms occur within minutes due to release of vasoactive amines. Late phase response occurs 4 to 6 hours later. Late phase response occurs by action of inflammatory cells that migrates into the involved area under the influence of cytokines released from mast cells and T cells.

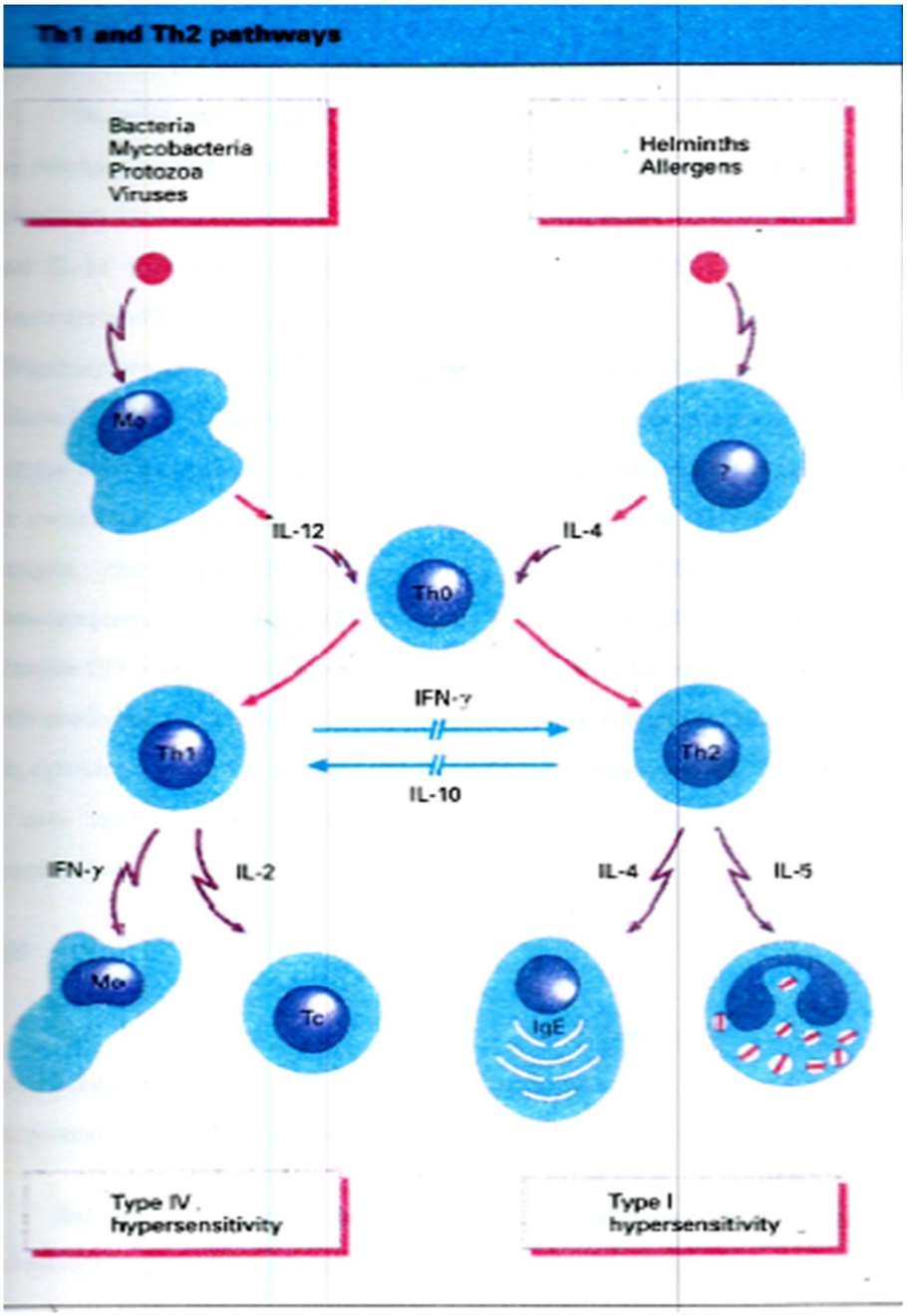
ANTIGEN PRESENTING CELLS

An antigen presented by an antigen presenting cell alone can be recognized by T lymphocytes. Some common antigen presenting cells are macrophages and langherhan's cells. Langerhan's cells pick up antigen proteins and break them into small peptide fragments which are recognized by T lymphocytes . They travel to regional lymph nodes and activate T cells. The first step In immune response is handling of antigens by antigen presenting cells. The next steps is stimulation of T lymphocytes and requires specific antigen recognition. This is effected by specific protein molecules in cell membranes known as cell receptors

through which cell communicates with the environment. Cell receptor has specificity for its ligand which is also a protein molecule.

CYTOKINES

These are soluble protein molecules synthesized by one cell and alter the properties of another cell. Cytokines are signal proteins that co-ordinates the activities of different cells and thus help in proper functioning of immune system. They collaborate together to form a cytokine network which forms the basis of immune response and inflammation. It act as a chemotactic factor and hemopoietic growth factor. They have proinflammatory and cytotoxic effect. Interleukin 3 stimulates the growth of precursors of basophils, eosinophils and mast cells. IL 4 acts on B lymphocytes and stimulate the production of IgE. IL 5 acts as an eosinophilic growth factor. IL 5 is responsible for eosinophilia in allergic diseases. Cytokines in allergic diseases are produced by Th 2 subset of T lymphocytes, mast cells and by other cell types. Th 1 and Th2 are the two type of T helper cells. Th1 cells are stimulated mainly by microbial antigens while Th 2 cells are preferably stimulated by allergens. IL2 ,TNF and gammainterferon secreted byTh1 cells. Th 2 cells synthesize IL 4, IL 5, IL 6and IL 10, IL 13. GM- CSF and IL 13 are produced by both Th 1 and Th 2 cells. Th 0


Th1 and Th2 pathways
Bacteria
Mycobacteria
Protozoa
Viruses
Helminths
Allergens
Mφ
IL-12
IL-4
Th0
IFN-γ
Th1
Th2
IL-10
IFN-γ
IL-2
IL-4
IL-5
Mφ
Tc
IgE
Type IV
hypersensitivity
Type I
hypersensitivity

cells are obligatory precursors of both Th 1 and Th 2 cells, hence they produce cytokines similar to both type of cells. Th 1 activate macrophages and support delayed type hypersensitivity. Immunoglobulin isotype switching to IgG2a is also mediated by Th1 cells. On the other hand switching of Ig to IgG1 and IgE isotype is by Th 2 cells. Thus Th2 cells provide efficient help for B cell activations. Differentiation of naïve CD 4 T cells into specific Th subsets depends on dose of antigen, major histocompatibility complex class 1 haplotype and type of antigen presenting cells. Th1 cytokines predominantly causes delayed hypersensitivity and Ig G synthesis while Th2 cytokines induce Ig E synthesis and eosiniophilia. Interstingly these two cytokine systems mutually suppress each other.

IgE

Ig E is secreted by B lymphocytes and plasma cells in respiratory tract, gastrointestinal tract and regional lymph nodes. It contributes to less than 0.001 % of circulating immunoglobulins.

The initial formation of Ig E antibodies requires signals from Th 2 lymphocytes and IL 4. However the gamma interferons secreted by Th 1 cells antagonize the production of Ig E antibodies. Hence the ratio between activated Th 2 and Th 1 cells is important in the regulation of

Ig E synthesis. Mast cells have greater affinity receptors for Ig E(FcR1), thus contributing to the skin sensitizing ability of Ig E. As T cells, eosinophils and antigen presenting cells have low affinity receptors (FcR2), their role in allergic reaction is uncertain.

IgE is a heat labile molecule and has a molecular weight of 188000. It is composed of two heavy chains and two light chains

MAST CELLLS AND BASOPHILS

Both cells have greater affinity receptors for Ig E. As they synthesize and release histamine and chemical mediators, they are the primary cells of IgE mediated allergy.

Mast cells are seen predominantly in skin, respiratory tract and gastrointestinal tract. They contain granules bearing histamine, prostaglandins and leukotrienes. There are two types of mast cells. Connective tissue mast cells are mast cells containing tryptase and chynase (MCTC). Another subgroup of mast cells known as mucosal mast cells contain only tryptase and are referred to as MCT. When connective tissue mast cells predominate in skin, it’s the mucosal mast cells which migrate into nasal and bronchial epithelium and participate in allergic reaction.

IL 5 is an important growth and differentiation factor for basophils. Basophils are circulating mast cells and mediate systemic allergic reactions.

Degranulation and activation of mast cells is mediated by interaction of allergen with Ig E antibody bound to FcR1 receptors. Non immunological factors like mechanical trauma, thermal trauma, drugs, some cytokines, radio contrast agents etc., also cause degranulation and mediator release.

EOSINOPHIL

They are most important factor mediating allergic inflammation. It contains bright red granules made up of eosinophil specific proteins name major basic protein and eosinophilic cationic proteins which are cytotoxic. Cytokine growth factors, GM CSF, IL 3, IL 5 which are produced by Th 2 cells influence the formation of eosinophils in bone marrow. After circulating in blood for few days, it leaves the circulation in response to adhesion molecules expressed over inflamed tissues.

Adhesion molecules are grouped into selectins and integrins. The selectin immunoglobulin super family contains ICAM-1 & VCAM-1. These molecules are present on leukocytes and endothelial cell surface. They are responsible for cell to cell contact by making the cells stick to

each other through the interaction between adhesion molecule and its ligand. These molecules are upregulated by the release of cytokines in the inflamed area. The freely circulating eosinophils attach to endothelial cells through these molecules, migrates between the cells towards chemotactic factors. Eosinophils become activated in the inflamed tissue and release cytotoxic proteins, leukotriene C4, prostaglandin E2 and platelet activating factor. During allergic inflammation, the survival of eosinophils is prolonged. Allergic provocation test is used for studying allergic inflammation. It results in an early and late response.

The early response starts within minutes and resolve within an hour. This occurs due to mast cell degranulation. This early response is characterized by itching, wheel and flare reactions due to histamine release. Histamine release in nose is characterized by sneezing, watery rhinorrhea and nasal blockage. Late response usually develops after 4 to 6 hours. This is due to accumulation and activation of eosinophils, Th 2 cells and other cell and its inflammatory proteins namely cytokines, mediator and cytotoxic protein.

ALLERGIC RHINITIS

Atopy refers to a predisposition to develop exaggerated immunoglobulin E (IgE)-antibody responses against common inhaled aeroallergens. Atopy is defined clinically as a positive skin prick test and/or elevated serum allergen-specific IgE. The term 'allergy' refers to the clinical expression of atopic allergic disease such as allergic rhinitis, allergic bronchial asthma, atopic eczema and IgE-mediated food allergy.

Allergic rhinitis is a global health problem and is increasing in prevalence. It is an Ig E mediated inflammation of nasal mucosa caused by allergen. It presents with 3 cardinal symptoms of sneezing, nasal discharge and nasal obstruction. Now a global health problem with impact on school, work and social life.

Allergic rhinitis has been classified as intermittent allergic rhinitis (IAR) and persistent allergic rhinitis[PER] as per the ARIA document. However seasonal and perennial rhinitis as per the conventional classification cannot be used interchangeable with the IAR and PER . To categorize a patient as PER, he should be symptomatic for atleast more than 4 consecutive days in a week.

Based on symptoms and quality of life allergic rhinitis is graded as mild, moderate or severe. In mild allergic rhinitis, symptoms are

present but not troublesome. There is no sleep disturbance or any impairment of school work or daily activities. In moderate or severe cases, symptoms are troublesome. Sleep is disturbed, daily activities are impaired and school /work is impaired.

Rhinitis is the inflammation of nasal mucosal lining characterized by nasal symptoms of rhinorrhea, sneezing, nasal blockage with or without itching. Post nasal drip occurs with profuse anterior rhinorrhea in allergic rhinitis cases. Sleep, school and work are adversely affected by allergic rhinitis. Symptoms may revert spontaneously or on treatment. Sinusitis does not exist without rhinitis as paranasal sinus mucosa is in continuous with nasal mucosa and any nasal mucosal congestion causes ostial congestion which eventually results in sinusitis. Asthma and rhinitis are so interrelated that while 80% of astmatics have rhinitis, about 40 % of rhinitis patients will eventually develop asthma.

The two important objective tests for the diagnosis of IgE mediated allergy are Skin prick tests and allergen specific IgE. SAPALDIA conducted a randomized study to compare the diagnostic efficiency of skin prick tests and IGE. Positive predictive value of skin prick test and total serum IgE were about 48.7 % and 31.6% respectively.

OTHER CAUSES OF RHINITIS

Drug Induced Rhinitis -Non steroidal anti inflammatory drugs like aspirin, diclofenac, ibuprofen, mefenamic acid etc commonly induce rhinitis and asthma. They inhibit cyclooxygenase enzyme and precipitate asthma.

Work Related Rhinitis.

Rhinitis Medicamentosa -Chronic use of intranasal vasoconstrictors results in rebound nasal obstruction.

Hormonal Rhinitis

Rhinitis related to Physical and Chemical factors

Rhinitis in smokers -Tobacco smoke alter the mucociliary clearance.

NARES[Nonallergic rhinitis with eosinophilia syndrome] - It is characterized by the presence of nasal eosinophilia, absence of demonstrable allergy, sneezing, rhinorrhea, itchinig and hyposmia. It occurs in children and adults. It responds usually to intranasal glucocorticosteroids.

Senile Rhinitis

Emotion -Due to autonomic stimulation as in stress and sexual arousal rhinitis has been seen.

Rhinosinusitis -In acute viral rhinosinusitis or common cold symptoms last for less than 10 days.

RISK FACTORS FOR ALLERGIC RHINITIS

GENETIC FACTORS

The best established risk factor for allergic rhinitis is a family history of allergy, especially of allergic rhinitis. there are several genes which appear to be involved in atopy. These include 5q chromosome, where genes exist for interleukin - 4 and IL-13, with markers associated with the presence of a high level of serum IgE. Other possible susceptibility loci exist on chromosome 11q, 13, 12q.

ENVIRONMENTAL FACTORS

Factors such as lifestyle changes, increased exposure to allergen, pollution and irritants, dietary modifications are responsible for diminution of protective nutrients, decrease in infections, leading to reduction in Th1- type immune response (hygiene hypothesis) .Pollution and diesel exhaust particles may induce a Th2-like inflammation.

ALLERGENS

Allergens are antigens that induce specific IgE antibodies and react with the same. They are proteins or glycoproteins and rarely glycans.

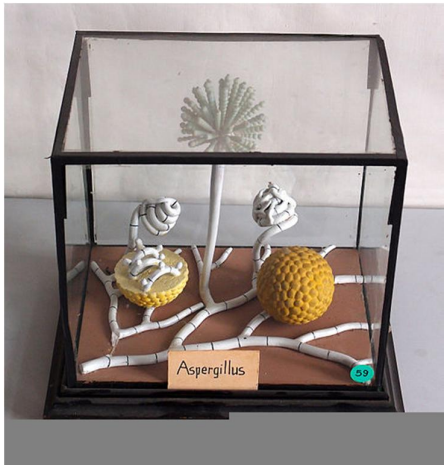
INHALANT ALLERGENS

Inhalant allergens are of two types- outdoor and indoor allergens. The common indoor allergens are house dust mites, pet animals, insects and plant origin. Outdoor allergens are pollens and molds or occupational agents. Association of greater risk with outdoor allergens is seasonal rhinitis, Indoor allergens is asthma and perennial rhinitis.

HOUSE DUST MITES.

The most important species are D.Pteronyssinus, Dermatophagoides farinae, Euroglyphusmaynei, Lepidoglyphus destructor and Blomia tropicalis. It may potentiate a Th2 cell response. They are abundant in mattresses, pillows, bed bases, carpets, fluffy toys, fecal pellets. For sensitizing an infant 100 mites per gram of house dust is sufficient . It is equivalent to 2 micrograms of Der p in 1 gram of dust. The sensitized patients are more prone for developing asthma .

ALLERGENS



POLLENS

Two types namely anemophilous and entomophilous pollens. The anemophilous pollen are in aerodynamic form .The entomophilous pollens are carried by insects. The pollens causing the common allergies are grasses, weed and trees.

FUNGAL ALLERGENS

Molds and yeast are plants which liberate allergenic spores in large quantities into indoor and outdoor environments. Fungi and molds are present in hot and humid conditions. As mold spores are small in size, they can penetrate deeply into the respiratory tract and can provoke rhinitis and asthma. Three important types of mold and yeast are outdoor molds, indoor molds and molds present over food. The atmospheric outdoor molds are Cladosporium, Alternaria, Aspergillus and Penicillium.

Domestic indoor molds are present in the home . They grow in aeration, climatization ducts, and in water pipes. They are abundant in bathrooms and kitchens. .Molds that are present in foods are Penicillium, Aspergillus and Fusarium

INSECTS

Cockroach allergen- it is found in gastrointestinal secretions and on its chitin shell. As the allergen is distributed in large particles, they do not become airborne. They are mostly seen in high-rise apartments, urban settings, and households with low income. Allergies to cockroaches are more frequent in tropical areas such as South East Asia

FOOD ALLERGENS

Food allergy is rare in allergic rhinitis. Most common food allergens are cow's milk , soya, peanuts, fish, eggs, milk, soyabeans, and fruits like apples and peaches.

Automobile Pollutants that are associated with allergic rhinitis are-

1) OXIDANT POLLUTANTS are carbon monoxide, nitric oxide, volatile organic compounds.
2) SULPHUR POLLUTANTS- sulphur dioxide.
3) ORGANIC CHEMICAL AGENTS- polyaromatic hydrocarbons like benzopyrene, benzofluoranthene, benzoanthracene, benzofluoranthene and benzopirylene.
4) CARBON DIOXIDE
5) METALS

DIAGNOSIS OF ALLERGIC RHINITIS

The diagnosis of allergic rhinitis is made by history of allergic symptoms and diagnostic tests.

SYMPTOMS

Two or more of the following symptoms lasting for more than one hour on most days :

Sneezing, Watery rhinorrhea, Nasal pruritis, Nasal obstruction- usually bilateral, Conjunctivitis- ocular symptoms are more common in pollen induced rhinitis

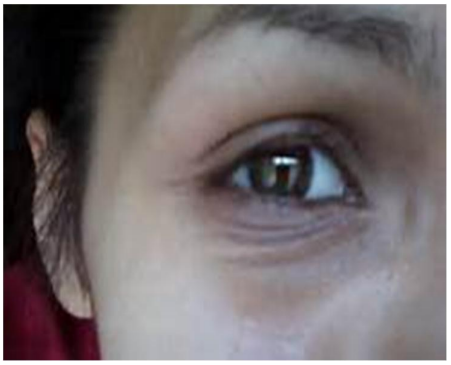
Other symptoms & signs:

Hyposmia or anosmia, Snoring, sleep problems, Postnasal drip or chronic cough.

Diagnostic tests

skin tests - by demonstration of allergen-specific IgE in the skin

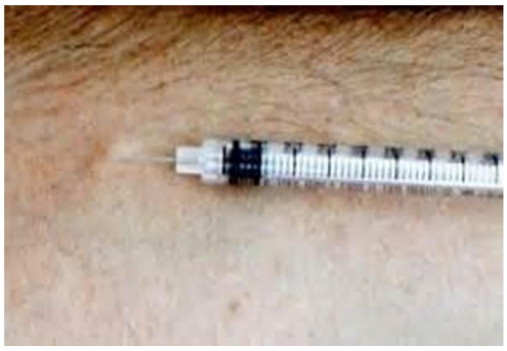
blood - allergen specific IgE



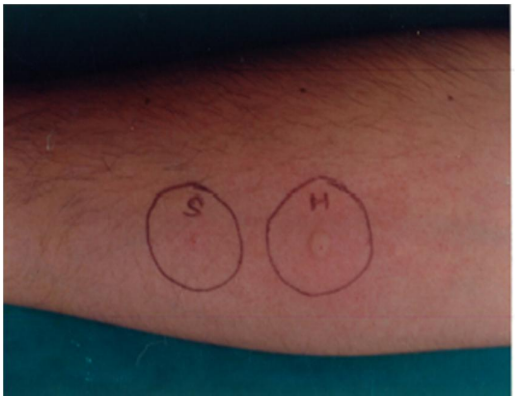
Denniemorgan fold

allergic salute

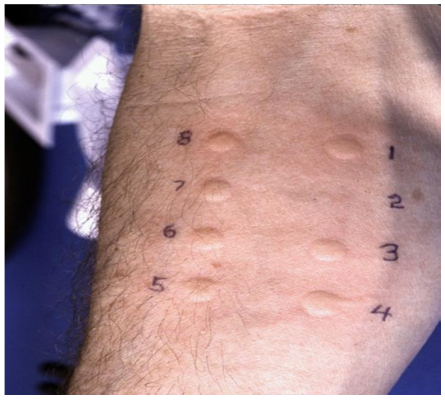
allergen vaccine vial



Intradermal skin tests



positive and negative control



Intradermal skin test

SKIN TESTS

Immediate-hypersensitivity skin tests are used to demonstrate IgE mediated allergic reaction. They are major diagnostic tools in the field of allergy. They give confirmatory evidence for a diagnosis of specific allergy.

Scratch Tests- done by making multiple cuts and apply a drop of antigen. It is simple and quick procedure but of historical interest only.

Skin Prick Tests-

Modified skin prick test was introduced by Pepys. A drop of glycerinated allergen extract is placed on the volar surface of forearm. Skin is pricked through the drop using a lancet needle. Positive reaction is measured by wheal and flare reaction.

Intradermal Skin Tests – are done by Injection of diluted liquid allergen into the dermal layer of skin on the volar surface of forearm using a mantoux syringe. 4 mm intra cutaneous wheal is created. The wheal is remeasured within 10 to 20 minutes. Induration of 3 mm more than control is considered as positive.

The positive control intradermal test is done by administration of 0.004 mg/ml of histamine to create a 4mm wheal which after 10 minutes

increase to 7 mm or more. If this test fails to produce a positive response, then false negative responses should be expected.

Negative control tests is done using Phenolated saline or human serum albumin. This is injected to create a 4 mm wheal and it should not enlarge more than 5 mm after 10 minutes.

PATCH TESTS

It is difficult to differentiate between allergic reactions and irritative reactions.

IN VITRO TESTS

Serum-total IgE is measured by radioimmunoassay or enzyme immunoassay. In adults, levels of 100–150 KU/l are normal.

Serum-specific IgE is considered to be positive when more than 0.35 KU/l. measurement of serum specific IgE is less sensitive than skin tests.

Nasal challenge test

They are used for research purpose. It is not useful to confirm the diagnosis of inhalant allergy. However it can be of use in diagnosis of

occupational allergy. Methacholine or histamine is widely used for nasal challenge test. Both induce dose dependant increase in secretions

ROLE OF IMAGING

Computerized tomography is of limited use in the diagnosis of allergic rhinitis. Computerized tomography is done:

- to rule out other conditions
- to exclude CRS
- to eliminate complications in rhinitis;
- in patients not responding to treatment and
- in patients with unilateral rhinitis

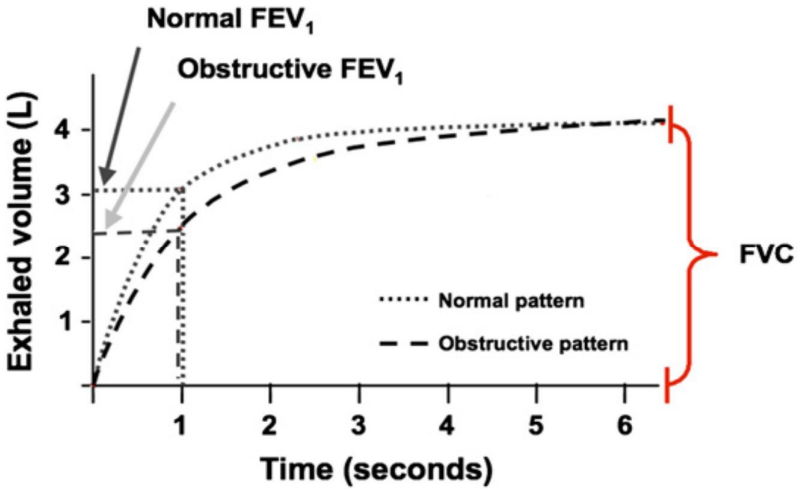
ASSESSMENT OF SEVERITY

PULMONARY FUNCTION TESTS

There is a strong relationship between asthma and allergic rhinitis as they share a common pathophysiology and anatomy, this entity has been called the ‘‘unified airway disease’’. Pulmonary function tests (PFT) help in diagnosis and predict severity. They can be used to monitor both disease progression and therapeutic response. Pulmonary function tests are used to obtain objective data. PFT include

(1) spirometry, (2) assessment of lung volumes, (3) body plethysmography, (4) diffusion capacity and (5) flow-volume loops.

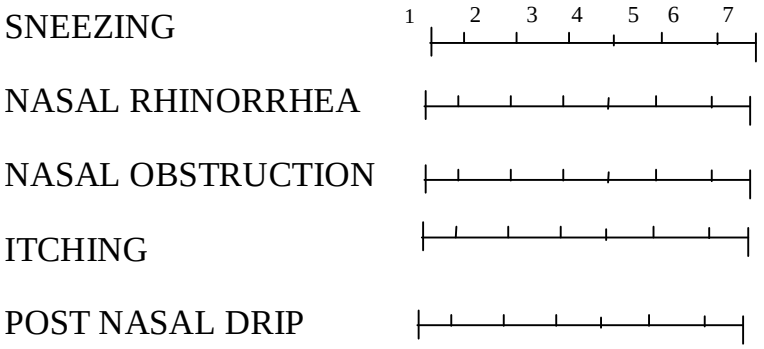
Spirometry is used to evaluate FVC and FEV1. The graphs can indicate normal patterns or abnormal patterns of obstructive, restrictive, or mixed lung disease. Spirometry alone cannot establish a diagnosis, but it is used to assess and monitor disease and also to gauge response to treatment. Normal FEV1 is 80% of the FVC. FEV1/FVC ratio is also used. Asthma is characterized by normal to decreased FVC, decreased FEV1 and FEV1/FVC ratio. Restrctive lung disease is characterized by a normal or increased FEV1/FVC ratio and a decrease in all lung volumes. Lower airway obstruction is assessed by FEV1. A predicted value of FEV1 between 70% and 85% is mild, while a value between 60% and 69% is considered as moderate. Values between 50% to 59% is moderately severe, between 35% and 49% is considered as severe, and less than 35% is very severe obstruction.



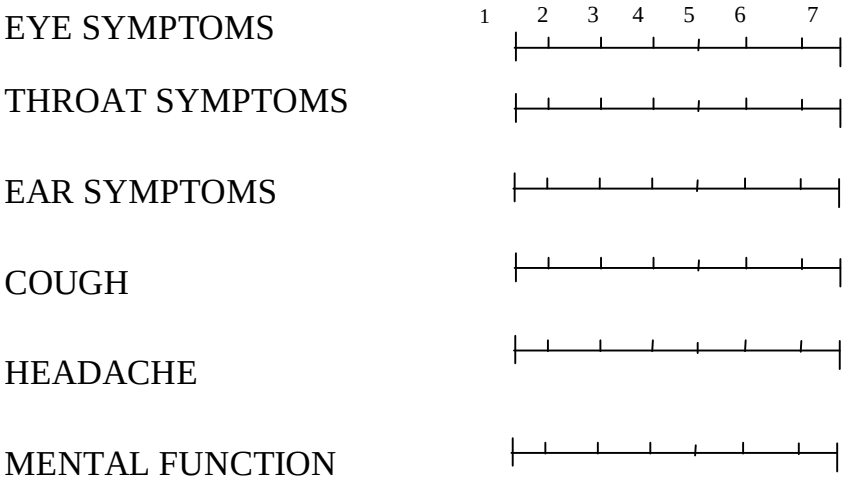
VISUAL ANALOGUE SCALE

The joint task force on practice parameters proposed visual analogue scale for the symptom severity assessment for allergic rhinitis. 7 point visual analog scale is used.

ASSESSING NASAL SYMPTOM SEVERITY



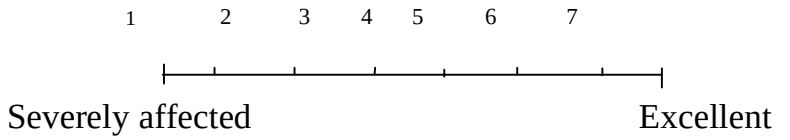
ASSESSING NON NASAL SYMPTOM SEVERITY



KEY

1. Occasional episodes
2. Mild but easily tolerable
3. moderate but symptoms are hard to tolerate and may interfere with daily activities
4. severe symptoms such that patient cannot function all the time

QUALITY OF LIFE ASSESSMENT OF RHINITIS SEVERITY



1. **QOL** is terribly affected in terms of sleep disturbance at night and /impairment of work performance and/impairment of social activities.
2. **QOL** is affected almost all the time.
3. **QOL** is affected often.
4. **QOL** is affected occasionally but it is tolerable.
5. **QOL** is hardly affected.
6. **QOL** is mildly affected.
7. Excellent quality of life.

MANAGEMENT

PREVENTION: Allergen avoidance is mandatory

PHARMACOTHERAPY

Oral or intranasal of Second-generation antihistamines are used for allergic rhinitis. Intranasal steroids are also used in allergic rhinitis. Montelukast is used for seasonal allergic rhinitis in children more than 6 years. Topical cromones are modestly effective in allergic rhinitis. Intranasal decongestants is also recommended. Intranasal ipratropium is used for rhinorrhoea associated with allergic rhinitis. Despite optimal pharmacotherapy some patients with moderate/severe allergic rhinitis do not become symptom free.

ALLERGEN SPECIFIC IMMUNOTHERAPY

Noon and Freeman introduced Allergen immunotherapy in 1911. Immunotherapy involves the step-wise incremental injection of increasing subcutaneous doses of allergen, in order to suppress symptoms on subsequent re-exposure to that allergen. Immunotherapy, given monthly for three to four years, has been shown to induce long-term remission for at least three years following discontinuation of treatment. In children, immunotherapy reduces the risk of physician-

diagnosed asthma at three to five years after commencing treatment and prevents the onset of new allergen sensitivities in children. Studies strongly suggest that immunotherapy is the only treatment that has the potential to modify the course of allergic disease. Thus immunotherapy favourably improves quality of life. Allergen-specific immunotherapy can be administered by sublingual and subcutaneous routes. It is effective in pollen and mite allergy. It alters the natural course of allergic diseases. Subcutaneous immunotherapy provides symptomatic improvement for many years even after completion of treatment. It prevents sensitization to other allergens in future.

SUBCUTANEOUS IMMUNOTHERAPY

The optimal dose is the dose of allergen vaccine that gives a clinically relevant effect in most of the patients without any adverse effects. 5–20 micro grams is the optimal dose used clinically.

INDICATIONS

- Symptomatic on allergen exposure.
- Rhinitis and lower airway symptoms during peak allergen exposure symptoms during pollen seasons.
- Patients with inadequate symptom control despite antihistamines and topical steroids.

- Patients with side effects to pharmacotherapy.
- To avoid long-term pharmacotherapy

CONTRAINDICATIONS

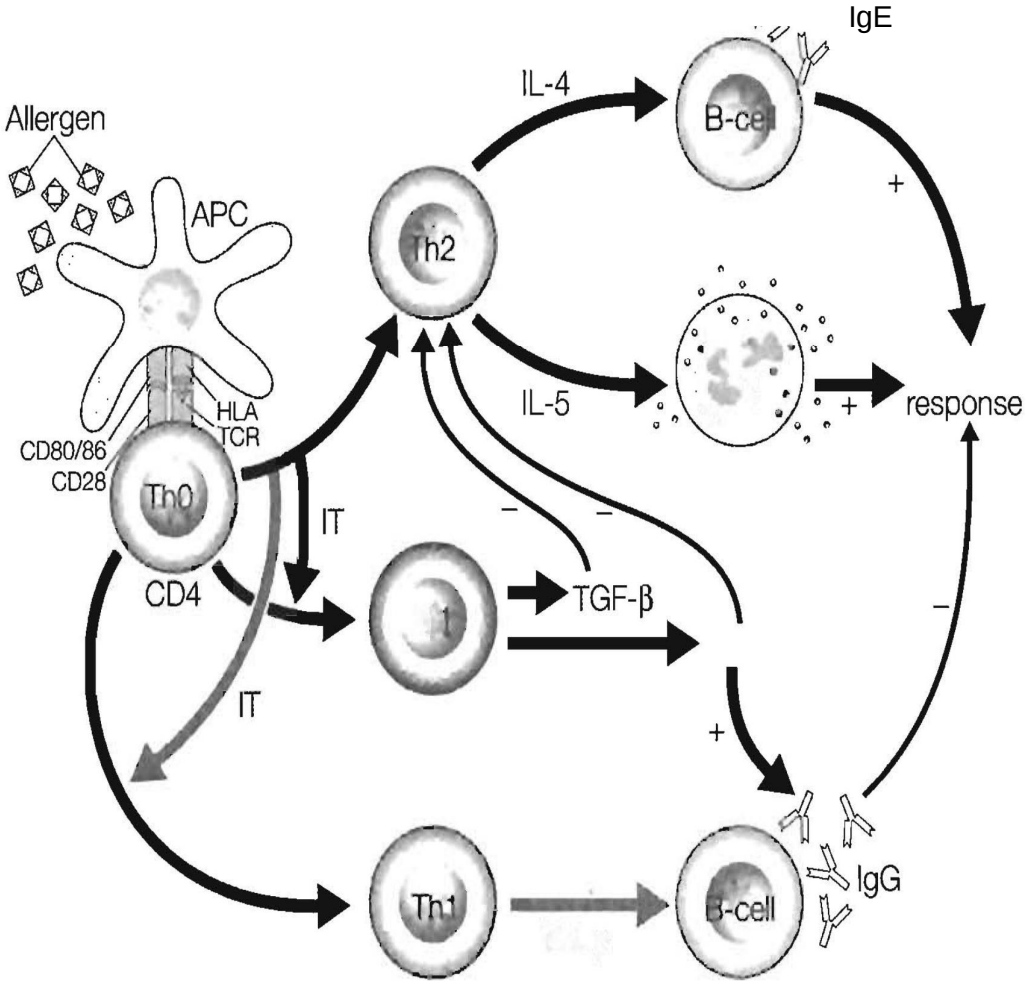
- Patients on ß-blockers
- Patients with any other immunologic disease
- Patients with poor compliance
- Starting immunotherapy during known pregnancy

Immunologic changes observed with immunotherapy treatment

Initially IgG1 increases; after treatment for 2 years with immunotherapy, Reduction in IgG1 noted, Gradual increase in IgG4

Reduced neutrophils, esinophils, Decrease in antigen-specific IgE and reduced post seasonal increase in IgE, Decrease in IL 13, Decrease in serum prolactin, Reduction in T cell proliferation, Increased IL-10 production, Decrease in serum ECP, Decrease in urinary leukotriene levels, Decrease in nasal tryptase and specific IgE.

IMMUNOTHERAPY



ALGORITHM FOR IMMUNOTHERAPY

suspected allergic rhinitis, allergic asthma

↓

detailed history, physical examination, laboratory tests.

↓

Consider immunotherapy when specific IgE antibodies are positive and correlate with suspected triggers and patient exposure

↓

Assess benefit/ risk/ costs of appropriate management options
-patient preference
-allergen avoidance
-pharmacotherapy
-severity of disease
-response to prior treatment
-immunotherapy

↓

Consider immunotherapy for symptoms not controlled by medications and allergen avoidance/ require high medication dose or long term use/ multiple medications

↓

Informed consent/ counsel about duration of immunotherapy and onset of efficacy

↓

Identification of specific allergenic extracts
Starting dose- 1000 to 10,000 fold less than maintenance dose
Build up schedule- gradually increasing doses from 8 to 28 weeks every 1- 3 times a week

↓

maintenance dose- 500 to 2000 allergy units/ 5 to 20 micro gram every 2-4 weeks

↓

Patient should wait 30 mins in clinic after injection; well equipped to manage any complications of immunotherapy

↓

Follow up every 6- 12 weeks
Clinical response to immunotherapy based on symptoms and medication use

↓

Usual duration-3 to 5 years
Based on severity of disease, convenience of treatment, benefits sustained from treatment- decide to continue or stop immunotherapy

SIDE EFFECTS OF IMMUNOTHERAPY

Severe systemic reactions occur only in less than 1 % of patients receiving immunotherapy.

Grade I- Cutaneous- pruritis, urticarial. URI- sneezing, rhinorrhea, pruritis or itchy throat, cough, Conjuctival- pruritis, Nausea, headache

Grade II- Lower respiratory – cough, wheeze. GIT- cramps, diarrhea, vomiting. Uterine cramps.

Grade III- Asthma not responding to bronchodilators. Laryngeal edema with or without stridor. Cardiovascular.

Grade IV- Respiratory failure, loss of consciousness. Hypotension

Grade V- death

MATERIALS AND METHODS

Cases of ALLERGIC RHINITIS coming to Upgraded Institute of Otorhinolaryngology, Rajiv Gandhi Government General Hospital, who satisfy the inclusion criteria that are studied during the year Oct 2011 – OCt 2013. Study material consists of 30 cases.

INCLUSION CRITERIA :

- Age above 12 years
- Sex- both male and female
- Allergic rhinitis not responding to pharmacotherapy with positive allergic skin tests with or without polyposis

EXCLUSION CRITERIA :

- Children less than 12 years
- Pregnancy.
- Extreme response to skin tests.
- Uncontrolled severe asthma
- Patients on beta blockers
- Other medical/ immunological disease

A total of 30 patients with symptoms suggestive of allergic rhinitis were evaluated by visual analogue scale.

Following nasal symptoms are assessed for severity

Sneezing, Nasal Rhinorrhea, Nasal Obstruction, Itching, Post nasal Drip.

Following non nasal symptoms are assessed for severity

Eye symptoms, Throat symptoms, Ear symptoms, Cough, Headache, Mental function, Wheeze,

History of medications taken for allergic rhinitis was noted.

Hematological Investigations:

Complete hemogram- hemoglobin percentage, total count, differential count(polymorphs, lymphocytes, eosinophils).

Absolute eosinophil count

Total IgE

Pulmonary Function Tests- FEV1 %

SKIN TESTS

Intradermal skin tests was used. 0.02 ml of test allergen introduced intradermally with mantoux syringe on the volar aspect of forearm. Result is read at varying period and induration and erythema measured against the control. An induration of 3 mm more than control is considered as positive. Result is graded as +,++,+++ measured in mm.

Allergic skin tests is done for following allergens:

INHALANT ALLERGEN:

House Dust, Cotton Dust, Aspergillus, Pollen, Parthenium, Cockroach.

MEAT PROTEINS:

Beef/ chicken/ crab/ egg/ mutton/ prawns/ fish

FRUITS AND VEGETABLES:

Tomato/ apple/ potato

PULSES:

Bengal gram/ black gram/ channaetc

MILK PROTEINS:

Milk/ butter/ cheese/ curd

BUILD UP PHASE

Allergen extract is slowly increased from 0.05 ml to 0.5 ml of 1 in 1,00,000 dilution on weekly twice interval

DILUTIONS

DOSE	100000	10000	1000	100	50
0.05 ml	1	7	13	19	25
0.1 ml	2	8	14	20	26
0.2 ml	3	9	15	21	27
0.3 ml	4	10	16	22	28
0.4 ml	5	11	17	23	29
0.5 ml	6	12	18	24	30

Maintenance phase- 0.5 ml of 1 in 50 dilution of allergen is given at monthly twice interval.

BOOSTER DOSE

months	I	II	III	IV	V	VI	VII
FIRST	1	1	1	1	1	1	1
	2	2	2	2	2	2	2
SECOND	3	3	3	3	3	3	3
	4	4	4	4	4	4	4
THIRD	5	5	5	5	5	5	5
	6	6	6	6	6	6	6
FOURTH	7	7	7	7	7	7	7
	8	8	8	8	8	8	8
FIFTH	9	9	9	9	9	9	9
	10	10	10	10	10	10	10
SIXTH	11	11	11	11	11	11	11
	12	12	12	12	12	12	12

After one year of treatment, symptom severity is assessed. Absolute eosinophil count, IgE and pulmonary function tests are measured. Skin tests are done for six inhalant allergens. Reduction of other medicines taken following initiation of immunotherapy was also studied.

RESULTS AND ANALYSIS

SEX	FREQUENCY	PERCENT
Male	15	50.0
Female	15	50.0
Total	30	100.0

INDIVIDUAL SYMPTOM ANALYSIS

SNEEZE BEFORE AND AFTER TREATMENT

VAS-BT	FREQUENCY	PERCENT
Absent	1	3.3
5	2	6.7
7	27	90.0
Total	30	100.0

VAS – AT	FREQUENCY	PERCENT
Absent	20	66.7
3	9	30.0
7	1	3.3
Total	30	100.0

Sneezing was present in 96.7% of the subjects and reduced to 33.3% after immunotherapy. Immunotherapy was effective in completely relieving sneezing in 63.4%.

RUNNING NOSE BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
Absent	0	0
3	1	3.3
5	4	13.3
7	25	83.3
Total	30	100.0

VAS - AT	FRE	%
Absent	21	70.0
3	8	26.7
-	-	-
7	1	3.3
Total	30	100.0

Running nose was present in all patients. On using immunotherapy, 70% symptomatic relief is noted in rhinorrhea while 26.7% had reduction in symptoms.

NASAL OBSTRUCTION BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
Absent	18	60.0
3	4	13.3
5	6	20.0
7	2	6.7
Total	30	100.0

VAS - AT	FRE	%
Absent	27	90
3	2	6.7
-	-	-
7	1	3.3
Total	30	100

Nasal obstruction which was present in 40% of patients and reduced to 10% after immunotherapy.

ITCHING BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
Absent	6	20.0
3	4	13.3
5	7	23.3
7	13	43.3
Total	30	100.0

VAS - AT	FRE	%
Absent	20	66.7
3	7	23.3
5	2	6.7
7	1	3.3
TOTAL	30	100

Itching was present in 80% of patients and reduced to 33.3% after immunotherapy.

POST NASAL DRIP BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
Absent	20	66.7
3	2	6.7
5	2	6.7
7	6	20.0
Total	30	100.0

VAS - AT	FRE	%
Absent	27	90
3	3	10.0
-	-	-
-	-	-
Total	30	100

Post nasal drip was seen in 33.3% of patients and was reduced to 10% after immunotherapy

WHEEZE BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
ABSENT	24	80.0
3	1	3.3
5	5	16.7
Total	30	100.0

VAS - AT	FRE	%
ABSENT	29	96.7
3	1	3.3
-	-	-
Total	30	100.0

Wheeze was seen in 20% of patients and was reduced to 3.3% after immunotherapy. 83.3% of patients with wheeze were relieved from symptom.

EYE SYMPTOMS BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
ABSENT	16	53.3
3	2	6.7
5	6	20.0
7	6	20.0
Total	30	100.0

VAS - AT	FRE	%
1	21	70
3	6	20
5	2	6.7
7	1	3.3
Total	30	100.0

Irritation of eye was seen in 46.7% which was reduced to 30% after immunotherapy.

EAR SYMPTOMS BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
1	18	60.0
3	1	3.3
5	7	23.3
7	4	13.3
Total	30	100.0

VAS - AT	FRE	%
1	22	73.3
3	5	16.7
5	2	6.7
7	1	3.3
TOTAL	30	100

Ear symptoms were seen in 40% of patients and reduced to 26.7% after immunotherapy.

THROAT SYMPTOMS BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
1	20	66.7
-	-	-
5	6	20.0
7	4	13.3
Total	30	100.0

VAS - AT	FRE	%
1	24	80.0
3	3	10.0
5	2	6.7
7	1	3.3
TOTAL	30	100

Throat symptoms were seen in 33.7% of patients which was reduced to 20% after immunotherapy.

COUGH BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
1	25	83.3
3	1	3.3
5	3	10.0
7	1	3.3
Total	30	100.0

VAS - AT	FRE	%
1	29	96.7
3	1	3.3
-	-	-
-	-	-
TOTAL	30	100

Cough was seen in 16.6% of patients and it was reduced to 3.3% after immunotherapy

HEADACHE BEFORE AND AFTER TREATMENT

VAS-BT	FRE	%
1	21	70.0
3	3	10.0
5	5	16.7
7	1	3.3
Total	30	100.0

VAS - AT	FRE	%
1	25	83.3
3	5	16.7
-	-	-
-	-	-
Total	30	100

Headache was seen in 30% of study group and was reduced to 16.7% after immunotherapy

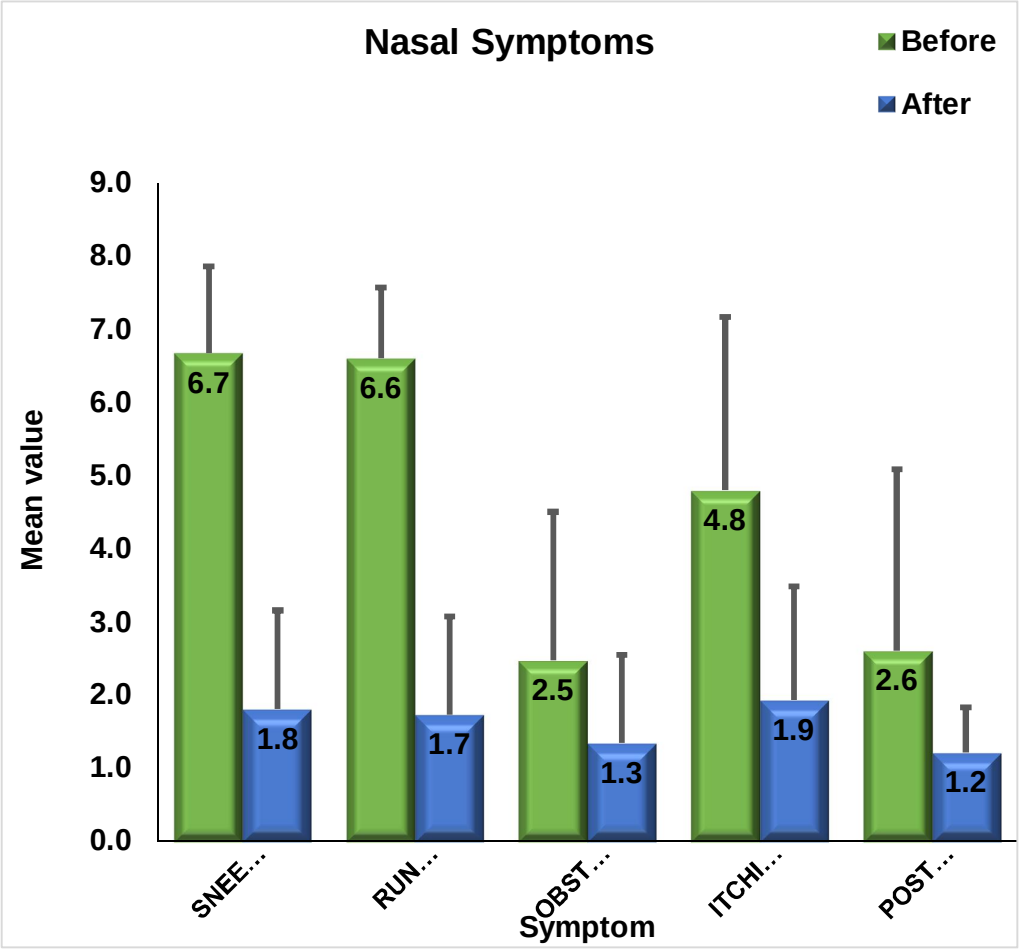
DESCRIPTIVE STATISTICS FOR NASAL SYMPTOMS BEFORE AND AFTER IMMUNOTHERAPY

STATISTIC	N	MEAN	STD. DEVIATION	1ST QUARTILE	MEDIAN	3RD QUARTILE
SNEEZE	30	6.67	1.184	7	7	7
RUNNING NOSE	30	6.6	0.968	7	7	7
OBSTRUCTION	30	2.47	2.03	1	1	5
ITCHING	30	4.8	2.369	3	5	7
POST NASAL DRIP	30	2.6	2.486	1	1	5
SNEEZE – AT	30	1.8	1.349	1	1	3
RUNNING NOSE – AT	30	1.73	1.337	1	1	3
OBSTRUCTION – AT	29	1.34	1.203	1	1	1
ITCHING – AT	30	1.93	1.552	1	1	3
POST NASAL DRIP – AT	29	1.21	0.62	1	1	1

WILCOXON SIGNED RANKS TEST TO COMPARE THE MEAN NASAL SYMPTOMS BEFORE AND AFTER INTERVENTION

VARIABLE	RANKS	N	MEAN RANK	P-VALUE
SNEEZE - AT – SNEEZE	Negative Ranks	28	14.50	<0.001
	Positive Ranks	0	.00	
RUNNING NOSE - AT - RUNNING NOSE	Negative Ranks	29	15.00	<0.001
	Positive Ranks	0	.00	
OBSTRUCTION - AT – OBSTRUCTION	Negative Ranks	10	5.50	0.004
	Positive Ranks	0	.00	
ITCHING - AT – ITCHING	Negative Ranks	23	12.00	<0.001
	Positive Ranks	0	.00	
POST NASAL DRIP - AT - POST NASAL DRIP	Negative Ranks	10	5.50	0.004
	Positive Ranks	0	.00	

Reduction of all nasal symptoms –sneeze, running nose, nasal obstruction, itching, post nasal drip were statistically significant as seen in the above table.


Nasal Symptoms
Before
After
Mean value
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
6.7
1.8
6.6
1.7
2.5
1.3
4.8
1.9
2.6
1.2
SNEE...
RUN...
OBST...
ITCHI...
POST...
Symptom

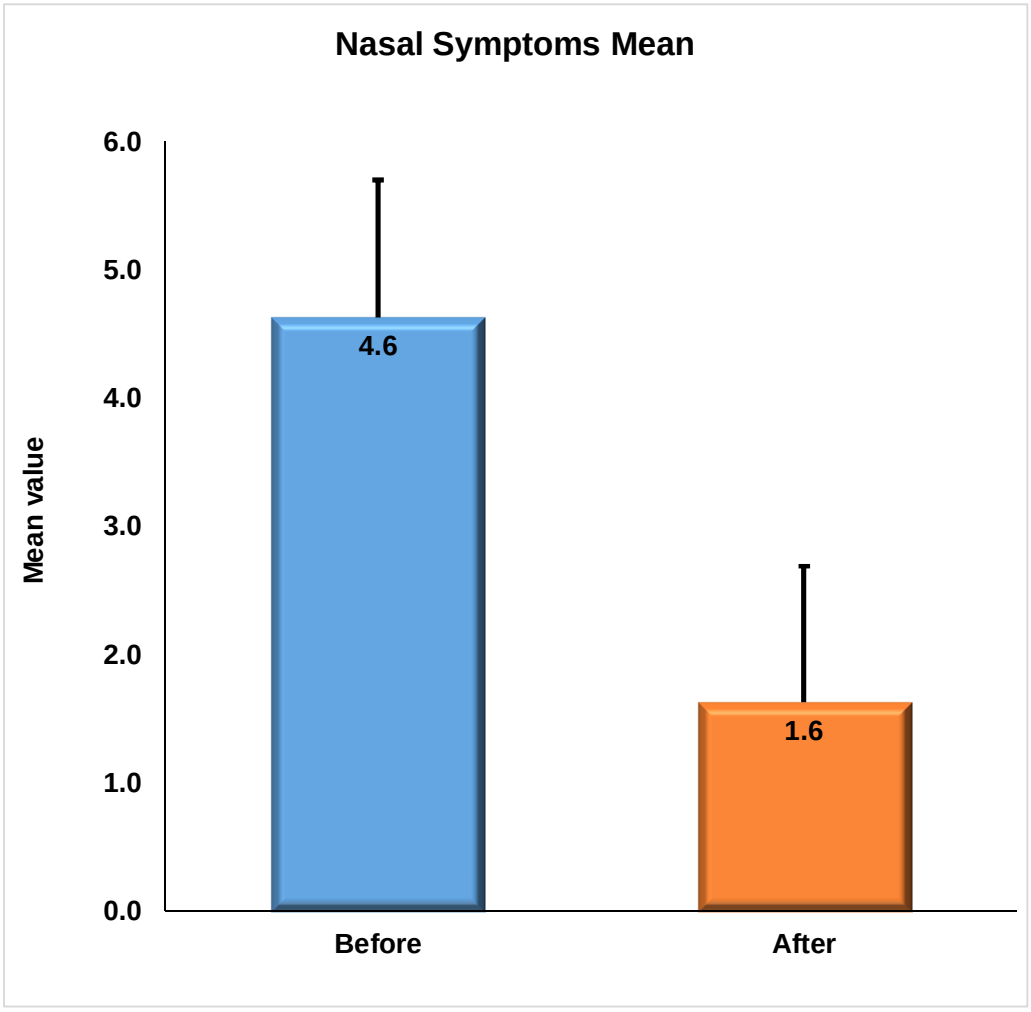
DESCRIPTIVE STATISTICS

STATISTICS	N	MEAN	STD DEVIATION
NASAL SYMPTOMS MEAN	30	4.627	1.0657
NASAL SYMPTOMS MEAN AT	30	1.627	1.0593

WILCOXON SIGNED RANKS TEST TO COMPARE THE MEAN NASAL SYMPTOMS BEFORE AND AFTER INTERVENTION

VARIABLE	RANKS	N	MEAN RANK	P-VALUE
NASAL SYMPTOMS (MEAN) – AT – NASAL SYMPTOMS (MEAN)	Negative Ranks	29	15.00	<0.001
	Positive Ranks	0	.00	

Reduction of nasal symptom mean score was statistically significant after immunotherapy as seen in the above tables


Nasal Symptoms Mean
Mean value
6.0
5.0
4.0
3.0
2.0
1.0
0.0
4.6
1.6
Before
After

DESCRIPTIVE STATISTICS FOR NON NASAL SYMPTOMS BEFORE AND AFTER IMMUNOTHERAPY

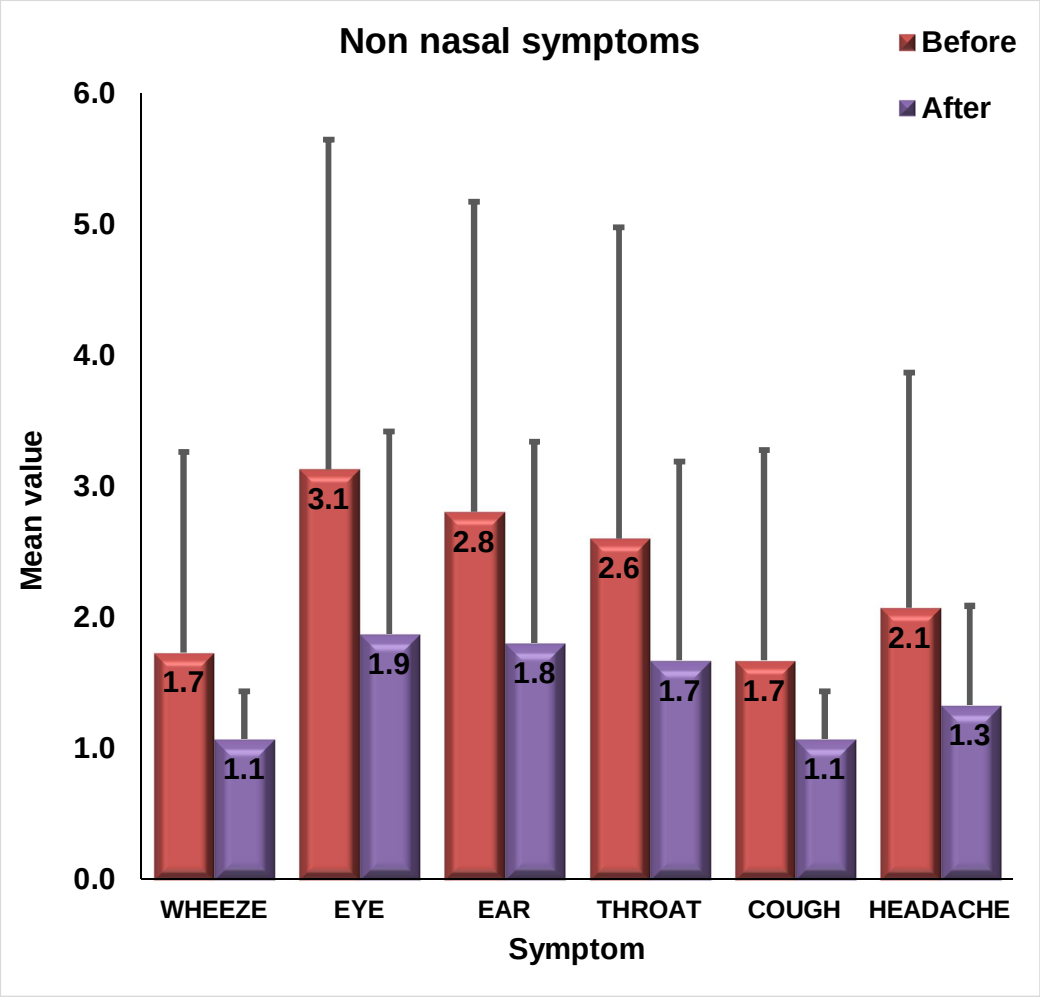
STATISTIC	N	MEAN	STD. DEVIATION	1ST QUARTILE	MEDIAN	3RD QUARTILE
WHEEZE	30	1.73	1.53	1	1	1
EYE	30	3.13	2.515	1	1	5
EAR	30	2.8	2.369	1	1	5
THROAT	30	2.6	2.372	1	1	5
COUGH	30	1.67	1.605	1	1	1
HEADACHE	30	2.07	1.799	1	1	3
WHEEZE – AT	30	1.07	0.365	1	1	1
EYE – AT	30	1.87	1.548	1	1	3
EAR – AT	30	1.8	1.54	1	1	3
THROAT – AT	30	1.67	1.516	1	1	1
COUGH – AT	30	1.07	0.365	1	1	1
HEADACHE – AT	30	1.33	0.758	1	1	1

WILCOXON SIGNED RANKS TEST TO COMPARE THE BEFORE AND AFTER INTERVENTION

VARIABLES	RANKS	N	MEAN RANK	P-VALUE
WHEEZE - AT – WHEEZE	Negative Ranks	6	3.50	0.023
	Positive Ranks	0	.00	
EYE - AT – EYE	Negative Ranks	13	7.00	0.001
	Positive Ranks	0	.00	
EAR - AT – EAR	Negative Ranks	11	6.00	0.002
	Positive Ranks	0	.00	
THROAT - AT – THROAT	Negative Ranks	9	5.00	0.006
	Positive Ranks	0	.00	
COUGH - AT – COUGH	Negative Ranks	5	3.00	0.041
	Positive Ranks	0	.00	
HEADACHE - AT – HEADACHE	Negative Ranks	9	5.00	0.004
	Positive Ranks	0	.00	

Reduction of wheeze was statistically significant as seen in the above table.

Reduction of all non nasal symptoms –eye symptoms , ear symptoms, throat symptom, cough, headache were statistically significant as seen in the above table.


Non nasal symptoms
Before
After
Mean value
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.7
1.1
3.1
1.9
2.8
1.8
2.6
1.7
1.7
1.1
2.1
1.3
WHEEZE
EYE
EAR
THROAT
COUGH
HEADACHE
Symptom

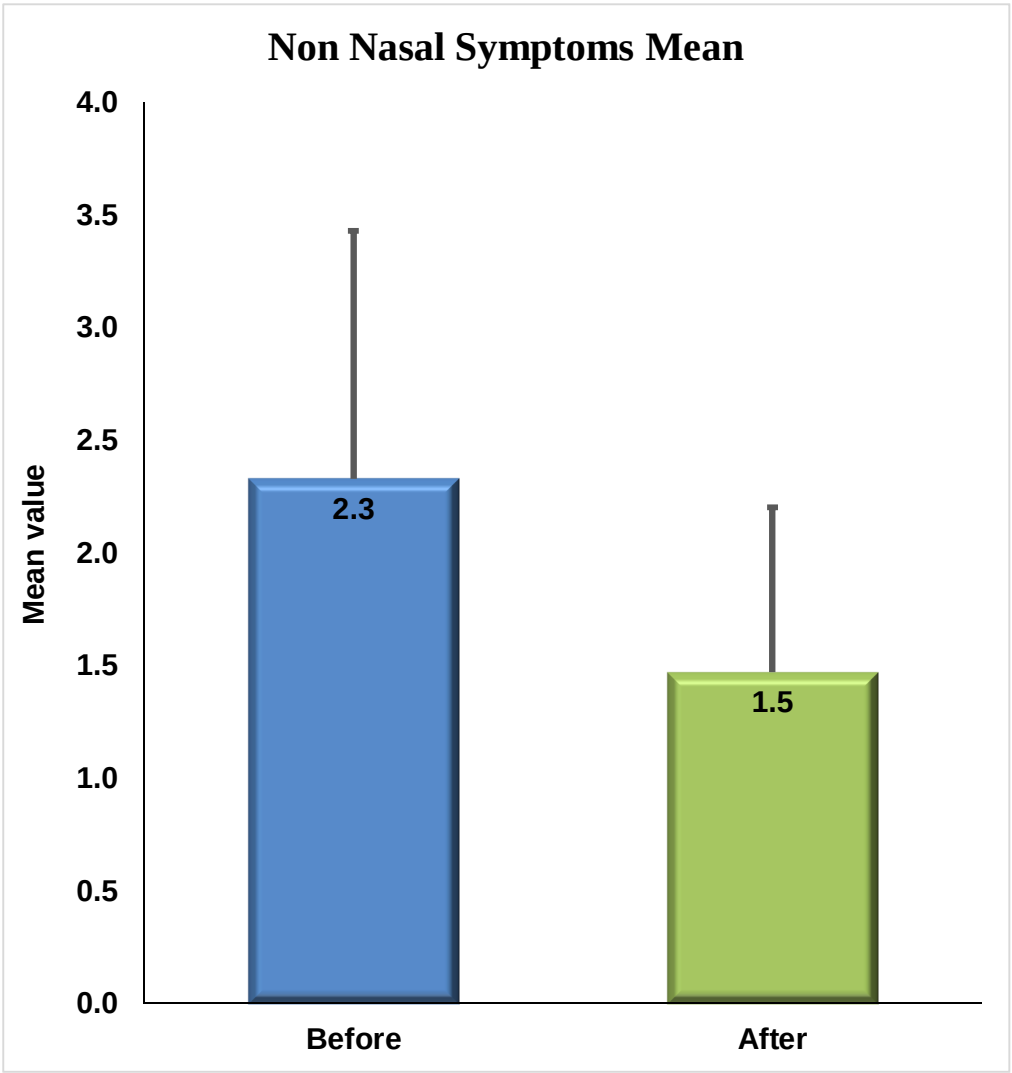
DESCRIPTIVE STATISTICS FOR MEAN NON NASAL SYMPTOMS BEFORE AND AFTER IMMUNOTHERAPY

STATISTICS	N	MEAN	STD DEVIATION
NON NASAL SYMPTOMS MEAN	30	2.33	1.10
NON NASAL SYMPTOMS MEAN AT	30	1.47	0.73

WILCOXON SIGNED RANKS TEST TO COMPARE THE MEAN NON NASAL SYMPTOMS BEFORE AND AFTER INTERVENTION

VARIABLE	RANKS	N	MEAN RANK	P-VALUE
Non Nasal Symptoms Mean - AT - Non Nasal Symptoms Mean	Negative Ranks	23	12.00	<0.001
	Positive Ranks	0	.00	

Reduction of non nasal symptoms mean was statistically significant after immunotherapy as seen in the above table


Non Nasal Symptoms Mean
Mean value
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.3
1.5
Before
After

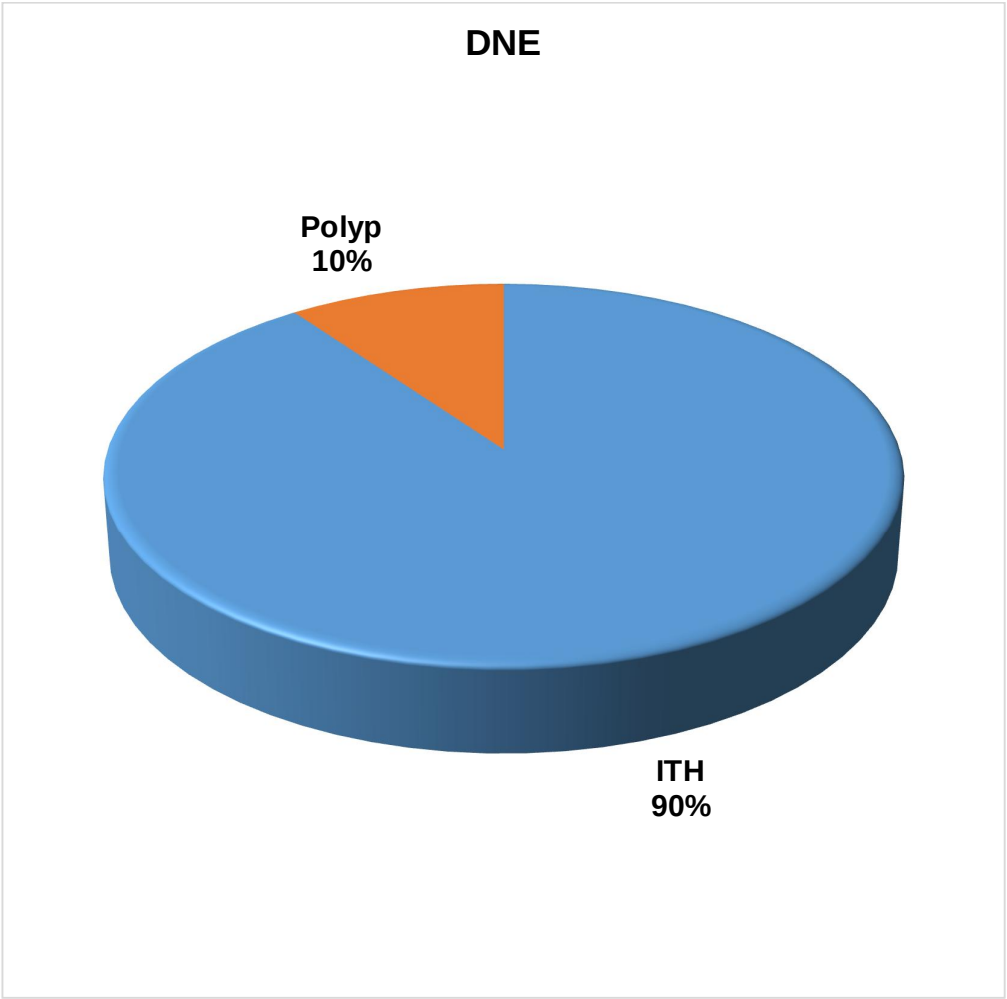
DIAGNOSTIC NASAL ENDOSCOPY

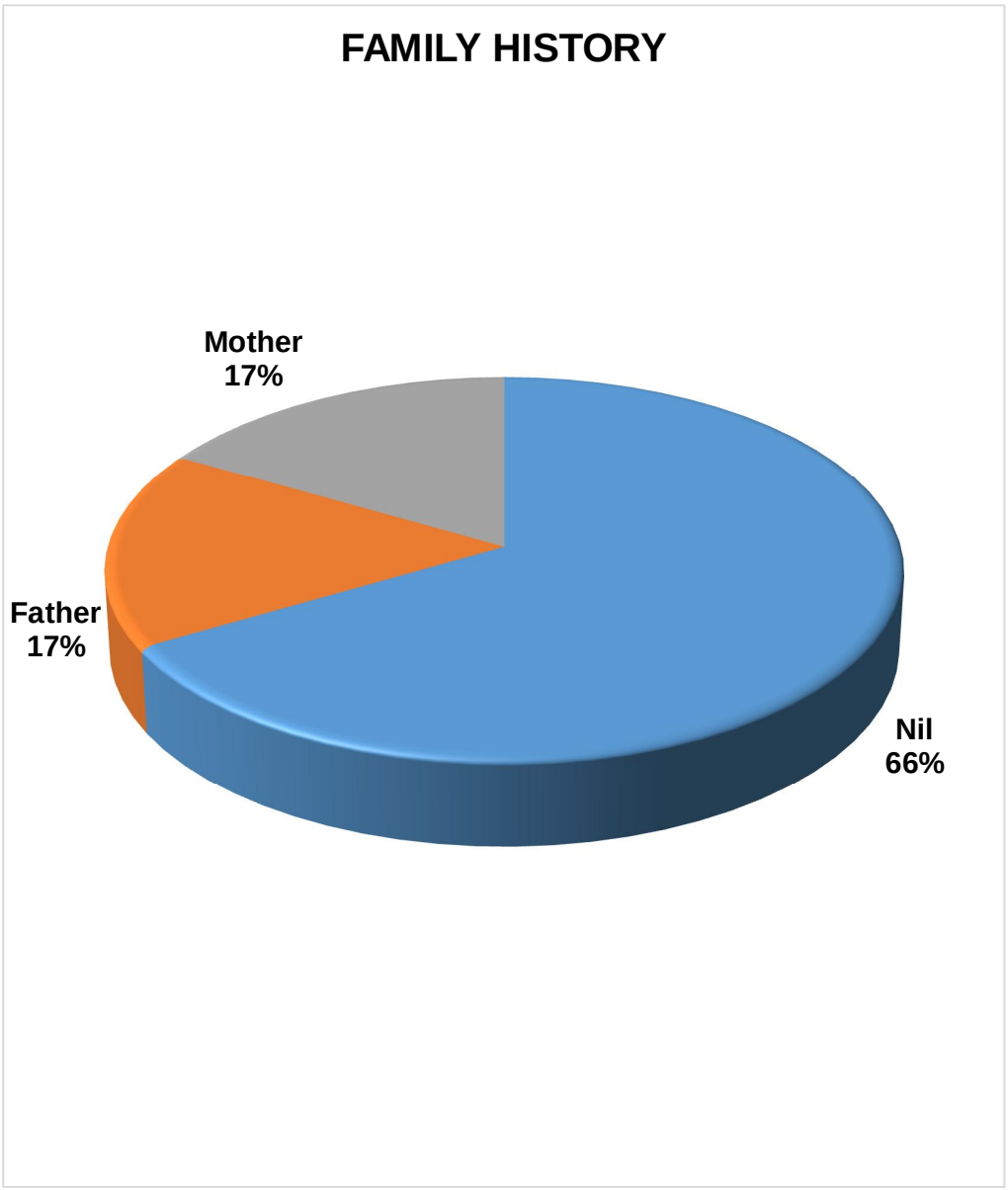
DNE	FREQUENCY	PERCENT
ITH	27	90.0
Polyp	3	10.0
Total	30	100.0

POLYP was seen in 10% of patients. All these patients had no recurrence after post FESS immunotherapy.

FAMILY HISTORY	FREQUENCY	PERCENT
Nil	20	66.7
Father	5	16.7
Mother	5	16.7
Total	30	100.0

33.4% people had family history.


DNE
Polyp
10%
ITH
90%


FAMILY HISTORY
Mother
17%
Father
17%
Nil
66%

MEDICATIONS REQUIREMENTS BEFORE AND AFTER TREATMENT

FREQUENCY OF MEDICATIONS	N	PER
1	16	53.3
2	12	40
3	2	6.7
Total	30	100

FREQUENCY OF MEDICATIONS	N	PER
2	3	10.0
3	11	36.7
4	10	33.3
5	6	20.0
Total	30	100.0

Key

1. Not taken treatment
2. Occasionally taken antihistamines
3. Use of antihistamines regularly/ intermittently
4. Use of antihistamines daily.
5. Use of topical steroids and antihistamines.

DESCRIPTIVE STATISTICS

STATISTICS	**N**	**MEAN**	**STD DEVIATION**
Total score	30	3.376	0.831
Total score-AT	30	1.539	0.654

WILCOXON SIGNED RANKS TEST

VARIABLE	**NO**	**RANK**	**MEAN**	**P**
Total score – AT total score	30	Negative rank	15.50	<o.oo1
		Positive rank	.0	

Reduction of medication requirement was statistically significant.

DESCRIPTIVE STATISTICS FOR ALLERGENS

HOUSE DUST SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	4	13.3
1	6	20.0
2	13	43.3
3	6	20.0
4	1	3.3
Total	30	100.0

AT	FRE	%
Negative	13	43.3
1	11	36.7
2	6	20.9
-	-	-
-	-	-
Total	30	100.0

86.6 % of patients sensitized with house dust allergen.34.6% of them becomes negative 65.3% of them showed reduction in sensitivity.

COTTON SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	3	10.0
1	7	23.3
2	16	53.3
3	4	13.3
Total	30	100.0

AT	FRE	%
Negative	14	46.7
1	16	53.3
-	-	-
-	-	-
TOTAL	30	100

90% of study groups were sensitive to cotton dust.40% of them becomes negative. 60% of them showed reduction in sensitivity

ASPERGILLUS SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	9	30.0
1	12	40.0
2	6	20.0
3	3	10.0
Total	30	100.0

AT	FRE	%
Negative	20	66.7
1	8	26.7
3	2	6.7
-	-	-
Total	30	100.0

70% of study groups were sensitive to Aspergillus.52% becomes negative. 48% showed reduction in sensitivity.

POLLEN SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	1	3.3
1	13	43.3
2	10	33.3
3	6	20.0
Total	30	100.0

AT	FRE	%
Negative	7	23.3
1	15	50.0
2	8	26.7
-	-	-
Total	30	100.0

96.6% of patients showed pollen sensitivity.20% of them becomes negative. 80% of them showed reduced sensitivity

COCKROACH SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	4	13.3
1	3	10.0
2	14	46.7
3	9	30.0
Total	30	100.0

AT	FRE	%
Negative	5	16.7
1	15	50.0
2	10	33.3
-	-	-
Total	30	100.0

86.7% of the study group had sensitivity to cockroach.3.8% becomes negative. 96.2% of them showed reduction in sensitivity

PARTHENIUM SENSITIVITY BEFORE AND AFTER TREATMENT

BT	FRE	%
Negative	1	3.3
1	1	3.3
2	19	63.3
3	8	26.7
4	1	3.3

AT	FRE	%
Negative	5	16.7
1	18	60.0
2	5	16.7
3	2	6.7
Total	30	100.0

96.7% of the study groups had sensitivity to Parthenium.13.7% of them becomes negative . 86.3% of them showed reduction in sensitivity.

DESCRIPTIVE STATISTICS FOR ALLERGEN

STATISTICS	N	MEAN	STD. DEVIATION
HOUSE DUST	30	1.8	1.031
COTTON	30	1.7	0.837
ASPER	30	1.1	0.96
POLLEN	30	1.7	0.837
COCKROACH	30	1.93	0.98
PARTHENIUM	30	2.23	0.728

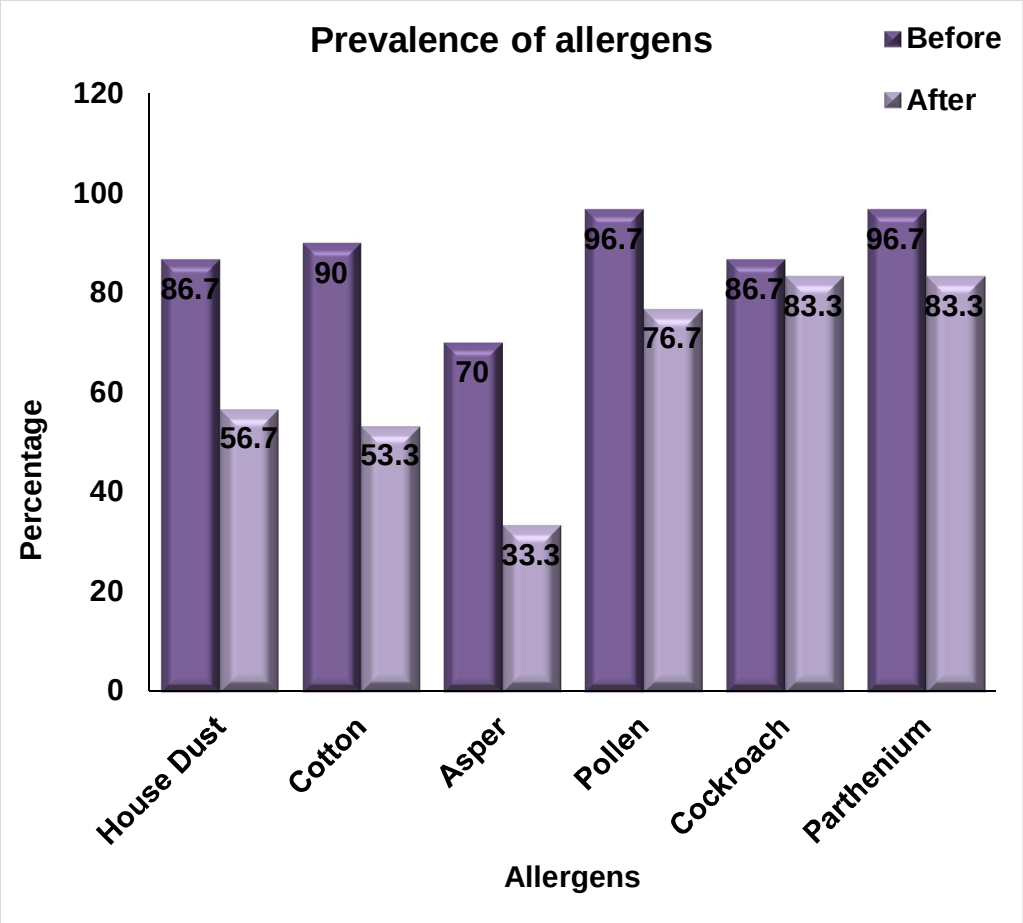
DESCRIPTIVE STATISTICS FOR ALLERGEN AFTER IMMUNOTHERAPY

STATISTICS	N	MEAN	STD. DEVIATION
HOUSE DUST	30	0.77	0.774
COTTON	30	0.53	0.507
ASPER	30	0.47	0.819
POLLEN	30	1.03	0.718
COCKROACH	30	1.17	0.699
PARTHENIUM	30	1.13	0.776

WILCOXON SIGNED RANKS TEST

VARIABLE	RANKS	N	MEAN RANK	P-VALUE
HOUSE DUST - AT - HOUSE DUST	Negative Ranks	23	13.35	0.001
	Positive Ranks	3	14.67	
COTTON - AT – COTTON	Negative Ranks	25	13.00	<0.001
	Positive Ranks	0	.00	
ASPER - AT - ASPER	Negative Ranks	14	8.21	0.001
	Positive Ranks	1	5.00	
POLLEN - AT - POLLEN	Negative Ranks	16	8.50	<0.001
	Positive Ranks	0	.00	
COCKROACH - AT – COCKROACH	Negative Ranks	16	10.06	0.001
	Positive Ranks	2	5.00	
PARTHENIUM - AT – PARTHENIUM	Negative Ranks	25	14.40	<0.001
	Positive Ranks	2	9.00	

Reduction in skin sensitivity for all allergen was statistically significant. Response to house dust and aspergillus were better than pollen.


Prevalence of allergens
Before
After
120
100
80
60
40
20
0
Percentage
86.7
56.7
90
53.3
70
33.3
96.7
76.7
86.7
83.3
96.7
83.3
House Dust
Cotton
Asper
Pollen
Cockroach
Parthenium
Allergens

DESCRIPTIVE STATISTICS FOR AEC AND IGE

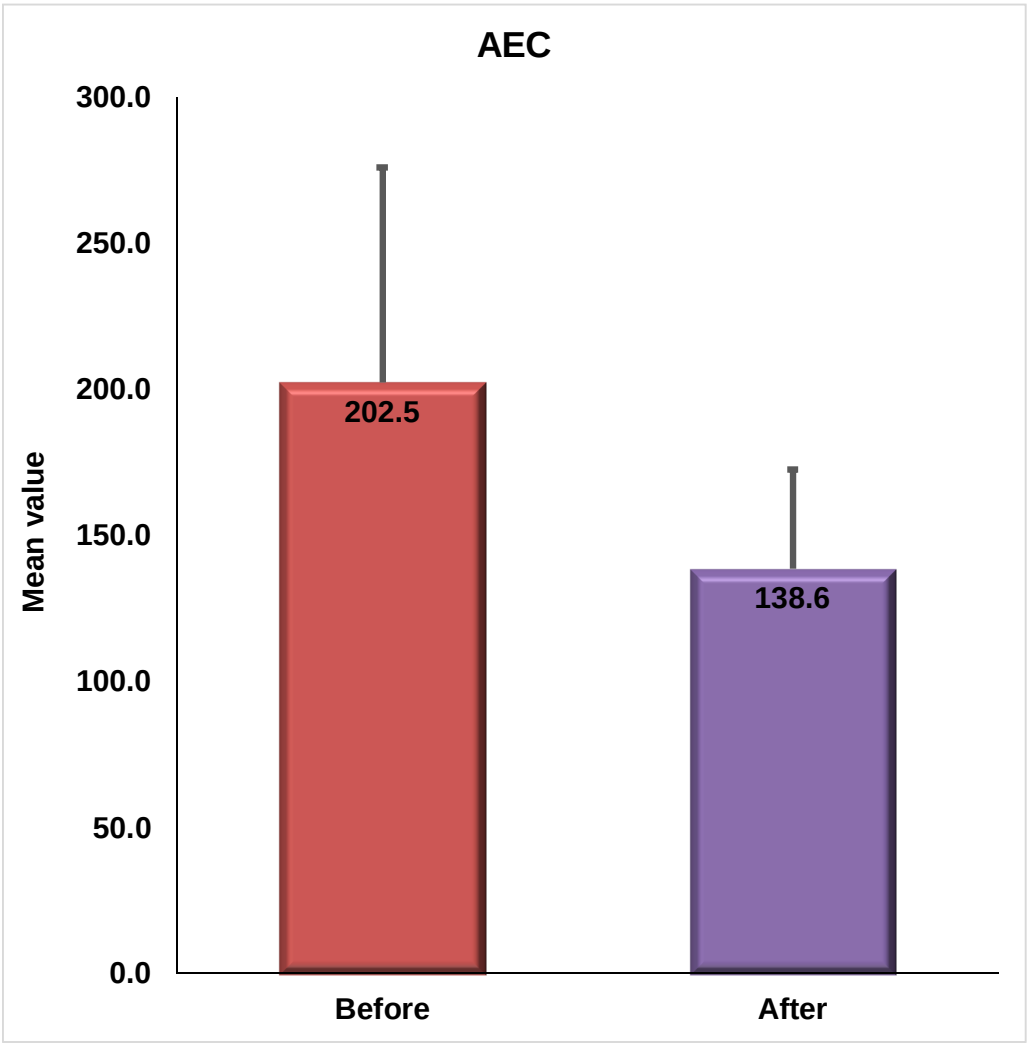
STATISTIC	**N**	**MEAN**	**STD DEVIATION**
AEC	30	202.5	73.5
AEC-AT	30	138.6	33.988
IGE	30	547.8	74.1
IGE –AT	30	136.7	33.988

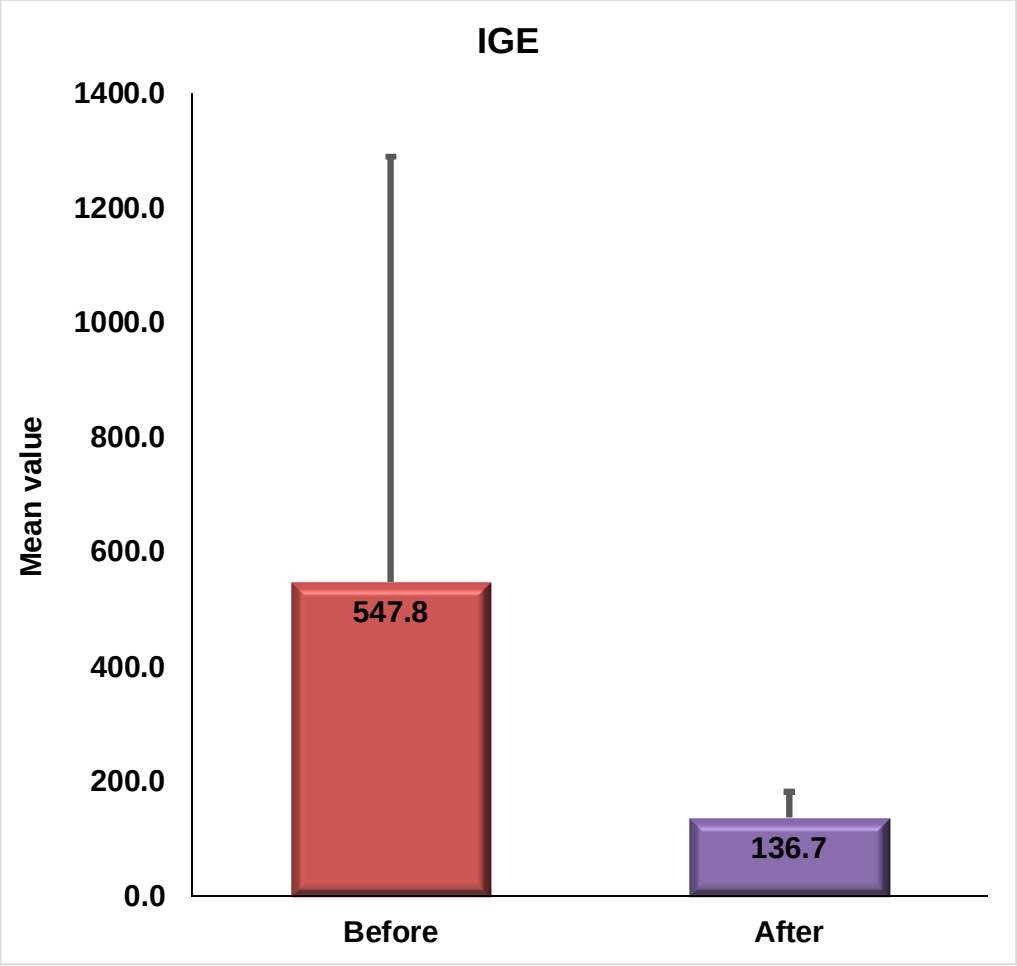
The mean value of AEC and IGE reduced after immunotherapy

WILCOXON SIGNED RANKS TEST TO COMPARE THE BEFORE AND AFTER INTERVENTION

Variable	Ranks	N	Mean Rank	P-Value
AEC - AT - AEC	Negative Ranks	30	15.50	<0.001
	Positive Ranks	0	.00	
IGE - AT - IGE	Negative Ranks	29	15.45	<0.001
	Positive Ranks	1	17.00	
	Positive Ranks	7	4.00	

Reduction of absolute eosinophil count and IG E were statistically significant as seen in the above table. IgE count was more than 200 in 15 cases after treatment only 2 patients had more than 200 IU.


AEC
300.0
250.0
200.0
150.0
100.0
50.0
0.0
Mean value
202.5
138.6
Before
After


IGE
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0.0
Mean value
547.8
136.7
Before
After

DESCRIPTIVE STATISTICS

STATISTICS	N	MEAN	STD DEVIATION
FEV1%	30	80.563	7.086
FEV1% - AT	30	86.933	5.164

Mean value for FEV1% was increased from 80.56 to 86.933% after immunotherapy.

WILCOXON SIGNED RANKS TEST

Variable	Ranks	N	MEAN	P VALUE
FEV1%-AT-FEV1%	Negative ranks	0	00	<0.001
	Positive ranks	30	15.50	

Improvement in pulmonary function was statistically significant.

SIDE EFFECTS

AT	**FRE**	**%**
None	28	93.3
LOCAL REACTION	2	6.7
Total	30	100.0

Only -6.7 percent of study group had side effects –Local reaction at the site of injection. No patients had severe systemic reaction

QUALITY OF LIFE BEFORE AND AFTER TREATMENT

BT	FRE	%
1	1	3.3
2	14	46.7
3	10	33.3
4	5	16.7
Total	30	100.0

AT	FRE	%
5	8	26.7
6	13	43.3
7	9	30.0
-	-	-
Total	30	100.0

DESCRIPTIVE STATISTICS

STATISTICS	N	MEAN	STD DEVIATION
Quality of life	30	2.630	0.809
Quality of life- AT	30	6.030	0.765

WILCOXON SIGNED RANKS TEST

Variable	Ranks	N	mean	P value
Quality of life-AT-quality of life	Negative ranks	0	.00	<0.001
	Positive ranks	30	15.50	

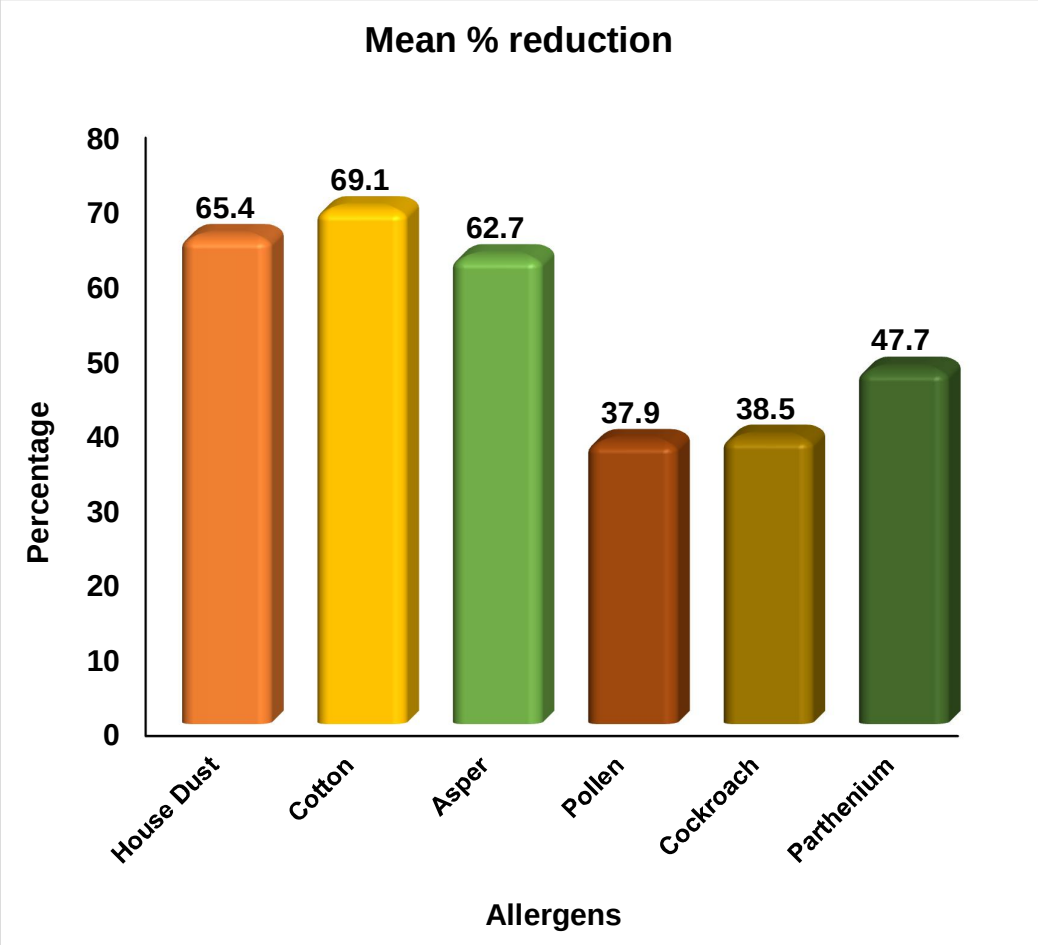
Improvement in Quality of life was statistically significant.


QUALITY OF LIFE
Before
After
Mean value
8
7
6
5
4
3
2
1
0
2.63
6.03
Before
After

PERCENTAGE IMPROVEMENT

VARIABLES	N	MEAN	STD. DEVIATION	1ST QUARTILE	MEDIAN	3RD QUARTILE
% improvement in Nasal Symptoms	30	64.9	18.6	52.2	72.1	76.2
% improvement in Non-nasal Symptoms	30	31.7	21.7	15.0	38.2	45.8
% improvement in total score	30	54.1	15.8	47.3	58.2	64.6
% reduction in House dust	26	65.4	45.0	50.0	66.7	100.0
% reduction in Cotton	27	69.1	30.2	50.0	66.7	100.0
% reduction in Asper	21	62.7	47.1	0.0	100.0	100.0
% reduction in Pollen	29	37.9	40.1	0.0	33.3	66.7
% reduction in Cockroach	26	38.5	35.5	0.0	41.7	66.7
% reduction in Parthenium	29	47.7	36.4	41.7	50.0	66.7
% improvement in Quality of life	30	148.9	78.6	93.8	141.7	200.0

Nasal symptoms have improved by 64.9%. Improvement in Nasal symptoms is better than Non-Nasal symptoms.


Mean % reduction
Percentage
80
70
60
50
40
30
20
10
0
65.4
69.1
62.7
37.9
38.5
47.7
House Dust
Cotton
Asper
Pollen
Cockroach
Parthenium
Allergens

DISCUSSION

JOHNSTONE AND DUTTON[7] (1968)-14 yr study in 173 children with bronchial asthma. After 4yrs of SCIT symptomatic improvement was assessed.78% of rate of remission of asthma was observed.

In my study 83.3% rate of remission of asthma was observed.

LOWELL AND FRANKLIN[8] (1965)- Study in 24 adults with rhinoconjunctivitis with a mixture of ragweed & multiple allergens conducted over a period of 8 months. Study result showed significant improvement in median symptom score.

In my study,median significant score showed improvement.

FRANKLIN &LOWELL[14] (1967)- Study in 24 individuals with allergic rhinitis with low dose & high dose mixture of ragweed extract in multiple pollen allergens. Symptom scores were significantly reduced with high dose ragweed extract than with the lower dose.

In my study, I have used high dose of multiple pollen allergens. Symptom score was significantly reduced.

GB PAJNO[9] et al- Over a 6 yr follow up study, in 134 children with asthma with or without rhinitis, HDM Specific immunotherapy was given. New sensitization had occurred in 24.6% of children administered with immunotherapy.

In the study I have conducted, 13.3% new sensitization recorded.4patients developed new sensitization after immunotherapy.

A.O.EIFAN[10] et al- This study compared SCIT vs sublingual immunotherapy in 43 individuals. The median percentage improvement in SCIT was

Total rhinitis symptom score -67%

Total asthma symptom score- 93%

Total symptom score- 81%.

In my study,

Total rhinitis symptom score -72.1%

Total asthma symptom score- 83.3%

Total symptom score- 58.2%.[both nasal non nasal symptoms]

VISNJAMILAVEC-PURETIC[11] etal- In 87 allergic rhinitis patients, retrospective study was conducted with SCIT.

There was a significant decrease in total IgE and specific IgE

Total IgE value of 441-1034 kU/l is decreased to 220-800 after 36 months of immunotherapy

In my study

The mean value of total Ig E547.8 is decreased to 136.7 after immunotherapy.

SUSMITHA J, VIJAYALAKSHMI[20] et al conducted a study on "combination of allergens in specific immunotherapy for IgE mediated allergies". It was noted that 58% showed no improvement in symptoms due to incorrect combination of allergens.

THOMAS REINHOLD etal- study conducted on "Influence of subcutaneous specific immunotherapy on drug costs in children suffering from allergic asthma" .Decline in medication cost became statistically significant after 3yrs SCIT.

PFAAR O[19] etal-2yr study 285 pts with mixed pollen sensitization SCIT given.SMS assessed by VAS .Significant reduction in median SMS 5.7 compared with placebo .Quality of life were significantly better for active group compared with placebo.

EWASWIEBOCKA etal study compared the efficacy of SCIT-pre seasonal versus maintenance. In maintenance group, the intensity of symptoms reduced in successive years.

ABRAMSON MJ[17] etal in his Cochrane review reduced asthma symptoms and medication requirements and bronchial hyperreactivity.

BLUMBERGA[18] et al- 3 years of subcutaneous immunotherapy showed improvement in skin reactivitiy and late asthmatic reactions

JACOBSEN[16] etal- In study group of allergic rhinitis patients, only 25 % of SCIT group had asthma while 45 % of controls had asthma.

PURELLO-D[15] ambrosia conducted a study on 8000 allergic adults, out of which 27 % developed new sensitization after immunotherapy.

SRIVASTAVA D[13] etal-conducted study on patients with coakroach allergy, significant improvement was noted after one year of subcutaneous therapy.

CONCLUSION

Allergic rhinitis patients may progress to rhinosinusitis, sinonasal polyposis and asthma.. Immunotherapy is the only treatment that has potential to modify the course of allergic disease.

- My study has revealed subcutaneous immunotherapy for patients with allergic rhinitis with or without polyposis reduces nasal and non nasal symptoms significantly
- There is better improvement in nasal symptoms compared to non nasal symptoms.
- Subcutaneous immunotherapy reduces medication requirement.
- Skin sensitivity reactions have reduced.
- Patients showed significant symptomatic improvement even when skin sensitivity reactions were present.
- Immunotherapy lowers total IgE and absolute eosinophil count.
- Immunotherapy improves quality of life.
- Immunotherapy increases predicted value of FEV 1, thus reduces the incidence of development of asthma in allergic rhinitis.
- In my study I would like to conclude that simultaneous administration of different unrelated allergens in adequate dosage and duration of treatment is the most effective.

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ABBREVIATIONS

AEC - Absolute Eosinophil Count

ARIA- Allergic Rhinitis and its Impact on Asthma

AT - After Treatment

BT- Before Treatment

DNE- Diagnostic Nasal Endoscopy

FEV1% - predicted value of Forced Expiratory Volume in 1 second

FRE- Frequency

IgE - Immunoglobulin E

ITH- Inferior Turbinate Hypertrophy

QOL- Quality of life.

SAPALDIA- Swiss study on Air Pollution And Lung Disease In adult

VAS- Visual Analogue Scale

Absolute eosinophil count.

Total IgE.

Pulmonary Function Tests- FEV1 %.

SKIN TESTS:

House Dust.

Cotton Dust.

Aspergillus.

Pollen.

Parthenium.

Cockroach.

DIAGNOSTIC NASAL ENDOSCOPY.

PROFORMA

Name Age Sex:

OP No. Occupation:

PERSONAL DATA:

1. Smoking :
2. Drug Allergy :
3. Asthma :
4. DM/HT :

FAMILY HISTORY:

Allergy/Asthma/ Eczema

SYMPTOMS:

Sneezing, Nasal Rhinorrhea, Nasal Obstruction, Itching, Post nasal Drip,Eye symptoms, Wheeze Throat symptoms, Ear symptoms, Cough, Headache, Mental function.

HISTORY OF MEDICATIONS:

HEMATOLOGICAL INVESTIGATIONS:

Complete hemogram- hemoglobin percentage, total count, differential count(polymorphs, lymphocytes, eosinophils).

CONSENT FORM

STUDY TITLE : A STUDY ON "EFFECT OF IMMUNOTHERAPY ON ALLERGIC RHINITIS"

I …… hereby give consent to participate in the study conducted by Dr.S. SHENBAGAVALLI, Post Graduate in Upgraded Institute of Otorhinolaryngology, Madras Medical College & Rajiv Gandhi Govt. General Hospital, Chennai and to use my personal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations.

Signature / Thumb impression of the patient / relative Place Date

Patient Name and Address

Signature of the Investigator

Signature of the Guide

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970
EC RegNo.ECR/270/Inst./TN/2013

CERTIFICATE OF APPROVAL

To
Dr.S.Shenbagavalli Dch,
MS ENT (PG),
Madras Medical College, Chennai-3.

Dear S.Shenbagavalli,

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Effect of Immune therapy on Allergic Rhinitis" No.14062013.

The following members of Ethics Committee were present in the meeting held on 11.05.2013 conducted at Madras Medical College, Chennai -3.

1. Dr.SivaKumar, MS FICS FAIS --- Chairperson
2. Prof. R. Nandhini MD -- Member Secretary
   Director, Instt. of Pharmacology ,MMC, Ch-3
3. Prof. Shyamraj MD -- Member
   Director i/c , Instt. of Biochemistry , MMC, Ch-3
4. Prof. P. Karkuzhali. MD -- Member
   Prof., Instt. of Pathology, MMC, Ch-3
5. Prof. A. Radhakrishnan MD -- Member
   Prof of Internal Medicine, MMC, Ch-3
6. Prof. S. Deivanayagam MS -- Member
   Prof of Surgery, MMC, Ch-3
7. Thiru. S. Govindsamy. BABL -- Lawyer
8. Tmt. Arnold Saulina MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nadhini 12/2/13
Member Secretary, Ethics Committee

MASTER CHART

no	DURATION (YRS)	AGE	SEX	SNEEZE	RUNNING NOSE	OBSTRUCTION	ITCHING	POST NASAL DRIP	NASAL SYMPTOMS (MEAN)	WHEEZE	EYE	EAR	THROAT	COUGH	HEADACHE	DNE/AR	POLY	LYM	EOS	AEC	IGE	FEV1%	HOUSE DUST	COTTON	ASPER	POLLEN	COCKROACH	PARTHENIUM	frequency of medications	s/e	FAMILY HISTORY	QUALITY OF LIFE
1	2	25	Male	5	5	1	3	5	3.8	3	3	3	1	3	1	ITH	54	44	2	156	1199	80.2	1	1	1	2	3	2	4		Father	2
2	2	14	Male	7	7	3	3	1	4.2	1	1	1	1	5	1	ITH	56	41	2	216	283	96	Negative	Negative	Negative	1	2	3	2		Nil	2
3	2	53	Male	7	7	5	7	1	5.4	1	1	5	1	1	1	ITH	63	36	1	221	178	82	3	2	1	1	2	3	3		Father	3
4	1	37	Male	7	7	1	5	1	4.2	5	5	5	1	1	5	ITH	54	44	2	166	1265	68.6	2	2	2	2	3	2	5		Nil	2
5	2	39	Female	7	7	1	7	7	5.8	5	7	7	7	1	1	ITH	67	31	2	498	182	62	2	2	3	2	2	2	5		Mother	2
6	1	15	Female	7	7	1	1	1	3.4	5	1	1	1	1	1	ITH	65	33	2	158	765	72.4	3	2	1	3	3	2	4		Nil	1
7	2	23	Male	7	7	1	7	7	5.8	1	7	7	7	1	1	ITH	63	36	1	168	258	80.4	Negative	Negative	Negative	2	2	2	2		Nil	4
8	2	33	Male	1	7	1	1	1	2.2	5	1	1	1	7	1	ITH	63	35	1	159	176	72.3	Negative	2	1	Negative	Negative	2	3		Father	4
9	1	25	Female	7	7	1	7	7	5.8	1	7	7	7	1	1	ITH	62	34	2	162	180	83	2	2	1	3	2	2	4		Nil	3
10	1	17	Female	7	3	1	3	3	3.4	1	1	1	1	1	1	ITH	52	36	2	165	132	85	2	1	1	1	1	Negative	4		Nil	3
11	1	24	Female	7	7	3	1	1	3.8	1	3	1	1	1	3	ITH	56	42	2	169	611	80.5	1	1	2	1	Negative	2	3		Nil	3
12	3	30	Male	7	7	3	7	3	5.4	5	1	1	1	1	1	ITH	70	28	2	134	3641	79	1	2	3	3	1	3	4	PALA	Father	2
13	2	44	Female	7	7	1	5	1	4.2	1	5	5	1	1	5	Polyp	59	39	2	176	172	81	3	3	1	1	Negative	2	2		Nil	4
14	2	24	Female	7	7	5	7	5	6.2	1	5	1	5	1	5	ITH	59	39	2	182	80	79	3	3	Negative	3	3	3	3		Nil	3
15	3	26	Male	7	7	1	7	1	4.6	1	7	5	5	1	3	Polyp	62	36	1	316	1420	80.7	2	2	2	2	3	2	4		Mother	3
16	2	19	Male	7	5	1	5	1	3.8	1	1	1	1	1	1	ITH	58	40	2	178	174	88	3	3	Negative	3	3	3	3		Nil	2
17	2	26	Male	7	7	5	5	1	5	1	5	1	1	1	1	ITH	60	38	2	166	210	87.9	1	1	Negative	1	2	2	3		Nil	2
18	1	35	Male	7	7	7	7	1	5.8	1	1	1	1	1	1	Polyp	60	38	2	166	210	81.6	1	1	Negative	1	2	2	3		Nil	3
19	1	56	Male	7	5	1	1	1	3	1	1	5	1	5	1	ITH	56	42	2	196	153	83.7	1	1	Negative	1	2	2	4		Mother	2
20	1	29	Female	5	5	5	5	1	4.2	1	1	1	5	1	7	ITH	55	43	2	165	132	80.4	2	2	2	2	2	2	5		Nil	2
21	2	52	Female	7	7	1	7	7	5.8	1	1	1	1	1	1	ITH	58	40	2	192	97	84.7	2	2	Negative	1	2	3	3		Nil	4
22	1	18	Female	7	7	7	7	7	7	1	1	1	1	1	1	ITH	54	44	2	157	1106	83	2	2	2	3	3	3	5		Father	2
23	1	45	Female	7	7	5	1	1	4.2	1	5	1	1	1	5	ITH	60	38	2	185	218	85.3	4	2	1	2	3	4	4		Nil	3
24	1	19	Male	7	7	5	1	1	4.2	1	1	1	5	1	1	ITH	64	37	2	167	172	80.5	2	2	1	2	2	2	3		Nil	3
25	1	29	Female	7	7	1	7	1	4.6	1	1	1	5	1	1	ITH	60	44	2	178	152	84.5	2	1	1	1	1	1	4		Mother	2
26	2	15	Female	7	7	1	5	1	4.2	1	1	1	1	1	1	ITH	58	40	1	185	154	85	2	2	1	1	2	2	3		Nil	4
27	2	26	Male	7	7	3	3	1	4.2	1	1	1	1	5	1	ITH	56	41	2	216	203	83.2	Negative	Negative	Negative	1	2	3	5		Nil	2
28	3	24	Male	7	7	1	7	1	4.6	1	7	5	5	1	3	ITH	62	36	1	316	1420	81.4	2	2	2	2	3	2	3		Nil	3
29	2	18	Female	7	7	1	5	1	4.2	1	5	5	1	1	5	ITH	59	39	2	246	172	83.6	3	3	1	1	Negative	2	4		Mother	2
30	2	26	Female	7	7	1	7	7	5.8	1	7	7	7	1	1	ITH	67	31	2	316	1320	62	2	2	3	2	2	2	5		Nil	2

no	SNEEZE - AT	RUNNING NOSE - AT	OBSTRUC ION - AT	ITCHING - AT	POST ASAL DRIP - AT	NASAL SYMPTOMS (MEAN) - AT	WHEEZE - AT	EYE - AT	EAR - AT	THROAT - AT	COUGH - AT	HEADACHE - AT	DNE/AR -AT	POLY - AT	LYM - AT	EOS - AT	AEC - AT	IGE - AT	PUL FN TEST - AT	FEV1% - AT	HOUSE UST - AT	COTTON - AT	ASPER - AT	POLLEN - AT	COCKROACH - AT	PARTHENIUM - AT	frequency of medications - AT	s/e - AT	FAMILY HISTORY - AT	QUALITY OF LIFE - AT
1	1	1	1	1	1	1	1	1	1	1	1	1					146	138		83.2	Negative	Negative	1	1	1	Negative	2			6
2	1	1	1	1	1	1	1	1	1	1	1	1		58	48	1	78	240		97	2	Negative	Negative	1	2	1	1			7
3	1	1	1	1	1	1	1	1	3	1	1	1					156	148		86	1	1	Negative	1	2	1	1			6
4	1	1	1	3	1	1.4	3	3	3	1	1	3					145	130		78.6	1	1	Negative	1	1	2	2			5
5	3	3	1	5	3	3	1	5	5	5	1	1		67	31	2	186	120		75	Negative	Negative	3	2	2	1	3			6
6	1	1	1	1	1	1	1	1	1	1	1	1					130	153		78.8	1	1	Negative	2	1	1	2			5
7	1	1	1	1	1	1	1	1	1	1	1	1					146	172		90.3	Negative	Negative	Negative	Negative	Negative	1	1			7
8	1	1	1	1	1	1	1	1	1	1	1	1					148	166		80.2	Negative	1	Negative	Negative	Negative	1	1			6
9	1	1	1	1	1	1	1	7	7	7	1	1					154	148		87.5	1	1	1	2	2	1	1			6
10	1	1	1	1	1	1	1	1	1	1	1	1					140	82		90.5	1	Negative	Negative	Negative	1	Negative	2			7
11	1	1	1	1	1	1	1	1	1	1	1	1					145	153		89.9	Negative	Negative	1	1	Negative	1	1			6
12	3	3	3	3	1	2.6	1	1	1	1	1	1		53	46	1	78	83		85.2	2	1	1	2	1	2	2			6
13	1	1	1	1	1	1	1	3	1	1	1	3	0				158	153		86.7	1	1	Negative	Negative	1	Negative	1	PAIN		7
14	1	1	1	1	1	1	1	1	1	1	1	3					138	72		88.8	1	1	Negative	1	2	2	1			6
15	3	3	1	3	1	2.2	1	3	3	1	1	1					58	108		87.9	2	1	Negative	1	1	3	2			6
16	3	1	1	1	1	1.4	1	1	1	1	1	1					165	86		94.5	1	1	Negative	1	2	1	1			5
17	1	1	1	1	1	1	1	1	1	1	1	1					156	180		94.6	Negative	Negative	Negative	1	1	1	1			7
18	7	7	7	7	1	5.8	1	1	1	1	1	1					156	180		86.8	Negative	Negative	Negative	1	1	1	1			6
19	1	1	1	1	1	1	1	1	3	1	3	1					185	97		88.4	Negative	1	1	Negative	Negative	Negative	1			6
20	1	1	1	1	1	1	1	1	1	3	1	1					156	130		86.8	Negative	Negative	Negative	2	1	1	2			7
21	1	1	1	1	1	1	1	1	1	1	1	1					142	72		89.8	Negative	Negative	Negative	1	Negative	2	2			7
22	1	1	1	3	3	1.8	1	1	1	1	1	1					146	153		88	Negative	Negative	Negative	1	2	1	2			5
23	1	1	1	1	1	1	1	3	1	1	1	3					172	145		89.6	2	1	1	2	1	2	1			6
24	3	3	3	1	1	2.2	1	1	1	3	1	1					156	146		88.2	1	1	1	2	2	1	1			5
25	3	3	1	3	1	2.2	1	1	1	3	1	1					156	106		88.9	1	1	1	1	1	1	2			5
26	3	3		3	1	3	1	1	1	1	1	1					132	134		89	Negative	Negative	Negative	Negative	1	1	1			7
27	1	1	1	1	1	1	1	1	1	1	1	1					78	263		87.9	2	Negative	Negative	1	2	1	2			7
28	3	3	1	3	1	2.2	1	3	3	1	1	1					58	108		85.9	2	1	Negative	1	1	3	1			5
29	1	1	1	1	1	1	1	3	1	1	1	3					158	153		89	1	1	Negative	Negative	1	Negative	2	PAIN		6
30	3	3	1	5	3	3	1	5	5	5	1	1					136	82	35.00%	75	Negative	Negative	3	2	2	1	3			5