TREATMENT OF ALLERGIC DISORDER FROM THE TRADITIONAL ERA TO THE MODERN ERA

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ABSTRACT

The human being appears to be affected with more disease than any other animal species most common disorders such as allergy, cold, fever, etc. Allergy is a state of hypersensitivity of the immunosystem against the allergen, which is entered into the body. Various clinical disorders associated with allergy-like asthma, hay fever, food allergy, Urticaria, delayed hypersensitivity. The allergic disorder can be treated by three ways of control of the environment, drug therapy, and Novel strategies. Treatment of allergic disorders from the traditional era to the modern era, people used herbal drug therapy and in the modern era, allopathic treatment most commonly used. Allopathic drug therapy having various side effects and researchers work on overcoming the side effect of the allopathic drug. Novel strategies are used in the treatment of allergy-like peptide vaccines and specific allergen immunotherapy after reviewed we concluded that from the traditional era to modern era, treatment of allergy is better than better for previous treatment and further study continue for the develop a stable and effective technique for the treatment of allergy.

KEYWORDS: Histamines, Herbal drug, Allopathic drug, Novel strategies, etc.

INTRODUCTION

Phytomedicines has gained increasing popularity due to the lesser side effect and improve conventional treatment. Allergic rhinitis has two phases Early and late phase. It also is known as the initial phase, this type of response is seen within minutes after allergen exposure. It is also known as quick response phase. The late-phase response starts 4 to 8 hrs after allergenic exposure.
The herbal drug has a wide range of therapeutic benefits for treating allergic conditions. Generally, corticosteroids and antihistamine are used in the treatment of allergy. Herbal drug shows anti-allergic properties which are present in plants; they contain the flavonoids, Triterpenes, alkaloids, and xanthenes. Herbal medicine shows the therapeutical response by Specific and non-specific mechanisms. It contains the various bioactive compounds having specific action. Researcher study on the in-vivo and in-vitro model.to investigates the anti-allergic properties of herbal medicines. Phytomedicines can act in acute and chronic conditions.

Pathophysiology
When the allergens enter into the body. The defense mechanism of the body is activated and captures the allergen by producing IgE-antibodies. Block the release of histamine. Immediate hypersensitivity response is mainly mediated by mast cells and basophils. In the early phase of allergic rhinitis occurs after a few minutes of degranulation and production of other mediators activated by allergens and late-phase response starts at the 4-8 hour after exposure of allergens.

Mechanisms of Anti-allergic(Anti-histaminic) Drug
When the drug administered it blocks the release of histamines and stabilizes the mast cell and other mediators responsible for allergy and inflammations. Few drugs block the COX₁ and COX₂ receptors along with prostaglandin synthesis and Archidinic acid pathways (inhibit Leukotrienes).

Figure No.1: Early phase and late phase.
Clinical disorders associated with the allergy

There are four general principles for clinical management of allergy (Willsie et al., 2002)
1) Avoid allergens and triggering factors.
2) Evaluation of allergy vaccine therapy.
3) Use of appropriate therapy.
4) Patient education and follow up guidelines.

Global condition of Allergic Disorder

1) Globally more than 6000 millions peoples suffering from an allergic disorder like rhinitis. Allergic rhinitis and its impact on asthma guidelines, second-generation antihistaminic is the first choice to recommend in both children and adults. (Kuna et al., 2016) Due to it
observed that Anti-histaminic have a 40.4% share in the total market of allergic rhinitis, then the second-largest used drug is a corticosteroid and followed by Decongestant and other options of treatment. In England, 65% of patients who suffer from allergy. They used as herbal therapy as Complimentary alternative medicine. In general, literature observed that 25-50% population and up to 70% of children herbal therapy is preferred. (Sayin et al., 2013) The global market of allergic rhinitis, based on the number of patients is found in that region. It divided into America (1st largest), Europe (2nd larger), Asia-Pacific, and Middle East & Africa.

2) American dominates the global market of allergic rhinitis, In America increase the cases of allergic rhinitis cases of allergic disorders, the American Academy of allergy asthma and immunology estimated that more than 50 million Americans suffer from the allergic disease annually this represents the 20% of USA population. (Mullol et al., 2008)

3) European region holds the second-larger market, allergic rhinitis patient compare to the globally approximately 25% patient in Europe suffer from allergic rhinitis. (Kuna et al., 2016)

4) Asia-Pacific regions, Most of the developing countries like China and India, Maximum cases due to tobacco, smoke, and other pollutants.

Drug affecting the respiratory system
(Davis et al., 1980)

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Therapeutic action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cromoglycate</td>
<td>Anti-allergic activity</td>
</tr>
<tr>
<td>Doxantrazole</td>
<td>Anti-allergic activity</td>
</tr>
<tr>
<td>Pyrimido[4,5-b]quinoline</td>
<td>Anti-allergic activity</td>
</tr>
<tr>
<td>Phenylendioxamic acid</td>
<td>Anti-allergic activity</td>
</tr>
<tr>
<td>Diphenhydramine Hydrochloride</td>
<td>Antihistaminic</td>
</tr>
<tr>
<td>Meclizine Hydrochloride</td>
<td>Antihistaminic</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Antihistamine(Nonsedative)</td>
</tr>
<tr>
<td>Dextromethorphan HBr</td>
<td>Antitussive agent</td>
</tr>
<tr>
<td>Codeine Phosphate</td>
<td>Antitussive agents</td>
</tr>
</tbody>
</table>

Role of vitamins in allergic disorder
A) Vitamin D
Vitamin D is regulating the immunosystem and various diseases are linked with vitamin D level in blood. Vitamin D and endocrine systems also associate with Allergic disorders like rhinitis, Asthma, Atopic-dermatic. Vitamin D acts by binding its receptor site which is
present in various tissues. It is induced the cellular response by triggering cytokines activity. (Tian et al., 2017).

**Mechanism of Action**

![Mechanism of Action Diagram]

(By increasing WBC and triggered the function of cytokines)

**B) Vitamin C**

Vitamin C is also known as ascorbate. Vitamin C has reduced allergic conditions such as respiratory and cutaneous allergy. It is a powerful antioxidant, vitamin C boost the immune system and reduced free radicals in the body. (Claudia et al., 2018).

Vitamin C Increases the level of epinephrine (secreted from the adrenal medulla) level in blood and vitamin c act as a potent antidote of allergic disorders. Vitamin C most commonly used in skin allergy and some clinical trials already perform by the iv route to check the inflammatory response of vitamin c.

**Mechanism of action**

![Vitamin C Mechanism Diagram]

(It responsible for the destruction of histamine structure)
Treatment of allergic rhinitis is done in three ways: (Bousquet et al., 2008)

1) Control of the environment
2) Drug therapy (Herbal and allopathic)
3) Novel strategies (Peptide vaccine and Allergen-specific immunotherapy).

Control of the environment

An allergic disorder like hay fever and other allergies, which is caused by pollens, dust, and other pollutants. We can use to remove allergen by HEPA- filter and purification efficacy is 99.95%.

Proper sunlight is required to kill the virus-like rhinovirus which is responsible for cold and other symptoms of allergy because our body produced vitamin d in the presence of sunlight and vitamin d is important to regulate the immune system. Few peoples are sensitive to change in the environment in that case dehumidifier and the air conditioner is used because it controls the change in temperature.

Plants provide the fresh oxygenated air to the living species and due to deforestation level of oxygen are reduced and pollutant level is increased. Therefore we need to purify the air. Air purifier mask is used to remove the pollutant from the air, Air purifier mask contain Two layers of activated carbon and it is enhanced the purification process. The best air purifier mask is N99. Which is 99.5% efficacy and purification power. N95 is most commonly used for purifying the oil pollutants present in the environment.

Herbal Drug Used in allergic disorders

1) Curcuma longa: Curcuma longa is traditional remedies and Curcumin is the active ingredient of Curcuma longa. Curcuma longa has various pharmacological activities such as anti-inflammatory activity, anti-allergic activity. In 2018, the Researcher is studied that Curcumin suppressed compound 48/80. Induced rat peritoneal mast cell degranulation and release of histamine. Curcumin can inhibit non-specific and mast cell-dependent allergic reactions. (Yun et al., 2010) The primary obstacle to utilizing Curcumin therapeutically has been its limited systemic bioavailability but the researcher is involved in try to increase bioavailability (Louay et al., 2014). Marketed available Curcumin gives along with black pepper to enhance the bioavailability.

2) Stinging Nettle: Stinging Nettle(Urtica Dioica) is a member of the Urticaceae family. Nettle is effective for treating seasonal allergy. researcher observed that in the research
extract of Urtica Dioica inhibits the histamine secretion and the release of other mediators is responsible for inflammation. It also blocks the COX₁ and COX₂ receptor by inhibiting prostaglandin formation and stabilizes the mast cells. (Roscchek et al., 2009) Dose: ½ to 1 teaspoon of Urtica tincture three times a day. (Yarnell et al., 1998).

3) **Liquorice**: liquorice contains glycyrrhizinic acid and its derivatives responsible for Antiallergic, antitumorigenic and anti-inflammatory activity. Glycyrrhizin inhibits the phospholipase A₂ enzyme, which is taking part in inflammatory reaction. liquorice contains steroidal moiety which is the equivalent action of hydrocortisone. (Kaur et al., 2013).

4) **Ginseng**: Ginseng is an herbal drug. And genocide is an active phytoconstituents which is responsible for Antiallergic activity. In 1996, the researcher observed that the extract of ginseng inhibits the release of beta hexamidase-enzyme from rat basophils cell in the rat. (Choie et al., 1996) And further Investigation observed that genocide and their metabolites an antagonistic effect on the release of histamine receptors by using ileum strip of guinea pig. (Choo et al., 2003).

5) **Rosemary**: Rosemary contains Rosemarinic acid, Ursolic acid. Rosemarinic acid is used in the treatment of allergic conditions and respiratory problems. In 2014, The Researcher observed that 150mg of Rosemarinic acid dose is reduced the Neutrophils and eosinophils count. (Stansbury et al., 2014).

6) **Hardy kiwi**: In vivo study conduct by researcher in 2009, In the study observed that reduce the interleukins-5, eotaxin, MCP-1, TARC, and IgE antibodies. (Kim et al., 2009).

7) **Apple**: In 2005, the researcher observed that apple reduced the cytokines secretion and reduced the intestinal mast cell protease, T helper cells, and Pro-inflammatory mediators which is responsible for allergic symptoms. (Tokura et al., 2005).

8) **Tomato**: Tomato contains Vitamin C and other phytoconstituents which is reduced the allergic rhinitis symptoms like sneezing, rhinorrhea, and nasal obstructions. It also overcomes the IgE antibodies and eosinophils counts. (Yoshimura et al., 2007).

9) **Amomum compactum**: In 2008, In vivo study on mice, aqueous and alcoholic extract of amomum compactum seed reduced the mucus production, count of eosinophils, and interleukakines and IgE level. Dose: 100-200mg. (Lee et al., 2008).

10) **Khairi**: It is also known as the Kalahari Christmas tree. In 2011 Researcher gives an Ethanolic extract of Dichrostachys cinerea (Khairi) bark to the mice and he observed that reduced tracheal contraction dependent on epithelium and k-Channels, Dose: 1mg/ml (Irie et al., 2011).
11) **Daphnegnidium**: It blocks the Cox₂ receptor and TNF-α factor due to reducing the inflammation, Dose:25-100µg/ml.(Harizi ret al.,2011).

12) **Echinodorus grandiflorus**: Aqueous leaf extract of echinoderms help to the reduction in the inflammation by Inhibition the synthesis of the Interluekines, eosinophils and IgE antibodies Dose:23mg/kg.(Harizi ret al.,2011).

13) **Withania somnifera**: Withania somnifera contain withanolide –A. Researchers observed that splenocyte, IFN-α, and Interleukins reduced when a dose of Withania introduced in mice. Dose: 0.1-10ng (Malik et al., 2007).

14) **Solanum nigrum**: Solanum nigrum contains alkaloids, Cinnamic acid esters, and steroids. It blocks the LTC₄ release and other mediators responsible for Inflammation. Dose/Concentration: 10.3µl.

15) **Bacopa Monieri**: Bacopa monieri contains Bacoside, alkaloid, Flavanoids, and anthraquinone. these are the phytoconstituents that are responsible for therapeutic activity. It observed that the Ethanolic extract of Bacopa monieri leaves shows mast cell stabilizing activity. (Samiulla et al., 2001).

16) **Neem**: Neem (Azadirachta indica) contains Nimbin, nimbinine, nimbandiol, and quercetin. Ethanolic leaves of Neem show mast cell stabilizing activity (Acharya et al., 2003) as well as antifungal and antibacterial activity.

**Allopathic medicine used in allergic disorders**

A) **Antihistamines**: Antihistamine has prevented the release of histamine from the mast cell. The first-generation antihistamine is reduced the itching, sneezing, rhinorrhea, and also causes sedation. Examples: Diphenhydramine, Hydroxyzine, and brompheniramine and second-generation histamine used to reduce the side effect like sedation examples: Loratadine, Cetirizine.

**Mechanism of action**

- **Antihistaminic drug**
- **Bind with receptors**
- **Block the release of histamine from the mast cells.**
  
  (Generally H1 receptors)
B) **Decongestants:** These are the three type’s oral, topical, and nasal decongestants. Oral decongestant like Pseudoephedrine is a few side effects like headache, hypertension but it is contraindicated in cardiovascular disorders. Topical decongestants are used for 4 to 5 days. Because of topical decongestants having a limitation is rebound the worsening and hyperemia of symptoms with chronic use. (Kushnir et al., 2011).

**Mechanism of action**

![Diagram of Decongestant mechanism](image)

C) **Corticosteroids:** Corticosteroids are used for the predominant nasal obstruction. Beclomethasone, fluticasone propionate is the most commonly used corticosteroids in nasal obstruction.

D) **Mast cell stabilizers:** Cromyline sodium (Cromoglycate) is effective in allergic rhinitis by preventing the release of histamine from mast cells. (Davis et al., 1980).

**Mechanism of action**

![Diagram of Mast cell stabilizer mechanism](image)

(Indirectly increase the level of Cyclic AMP levels)
E) **Leukotrienes receptor antagonists**: Montelukast is used in the treatment of asthma but also used in the treatment of allergic rhinitis. Leukotrienes receptor antagonist (Leukotrine modifier) are the inhibit the 5-Lipoxygenase enzyme. The clinical trial demonstrated with Montelukast is given in the combination with Loratadine and It observed that better result in a cause of seasonal allergic rhinitis. (Meltzer *et al.*, 2000).

**Mechanism of action**

![Mechanism of action diagram](image)

**Marketed products**

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Name of a marketed product</th>
<th>Chemical Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alerid 10 mg (Tablet)</td>
<td>Cetirizine Hydrochloride</td>
</tr>
<tr>
<td>2</td>
<td>Avabast 10 (Tablet)</td>
<td>Ebastine</td>
</tr>
<tr>
<td>3</td>
<td>Avil (Injection)</td>
<td>Pheniramine Maleate</td>
</tr>
<tr>
<td>4</td>
<td>ELC-M (Tablet)</td>
<td>Montelukast sodium and levocetirizine Hydrochloride</td>
</tr>
<tr>
<td>5</td>
<td>Sonocet-AL(Tablet)</td>
<td>Levocetirizine, Paracetamol, Phenylephrine, and Ambroxol</td>
</tr>
<tr>
<td>6</td>
<td>Allegra(Tablet)</td>
<td>Fexofenadine</td>
</tr>
<tr>
<td>7</td>
<td>Salcet (Syrup)</td>
<td>Cetirizine Dihydrochloride and Salbutamol</td>
</tr>
<tr>
<td>8</td>
<td>Alexo-180 (Tablet)</td>
<td>Fexofenadine</td>
</tr>
<tr>
<td>9</td>
<td>Punlix (Capsule)</td>
<td>Diphenyl hydramine</td>
</tr>
<tr>
<td>10</td>
<td>Polyhist (syrup)</td>
<td>Pheniramine Maleate</td>
</tr>
</tbody>
</table>

**Diagnostic test for Allergy**

Diagnostics test used to identify the allergy. Skin allergy identifies by using skin test (scratch test), skin injection test, and patch test. For the identification of allergen done by the blood test (by measures the IgE antibodies). Challenge test performed under the supervision of allergist, Challenge test done for the food and medicine. (Ansotgui *et al.*, 2020).
<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Diagnostic test for allergy</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diagnostic test for Skin allergy</td>
<td>Clean the test site by alcohol then, Needle penetrates the skin surface. Draw the mark on the skin. After 15 minutes observe the skin for the sign of allergic reaction like red spot(like mosquito bites) measure the size of spot. after record the result your skin clean by alcohol to remove marks</td>
</tr>
<tr>
<td></td>
<td>Scratch test</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skin Injection test (Intradermal test)</td>
<td>Inject the small amount of allergen into the skin on your arm. Injection site examined after 15 min for signs of an allergic reaction. Note: Physicians generally inject penicillin/insect venom as an allergen.</td>
</tr>
<tr>
<td></td>
<td>Patch test</td>
<td>Allergen apply to the patch, this patch placed on the skin (Arm/Back) due to causes contact dermatitis after 48 hours to wear the patch, Irritation on the skin at the patch indicated an allergy</td>
</tr>
<tr>
<td>2</td>
<td>Blood test</td>
<td>The blood test measures the IgE antibodies to certain allergen into the blood.</td>
</tr>
<tr>
<td>3</td>
<td>Challenge test</td>
<td>This test performs under the supervision of an allergist. You can eat/breathe a small amount of allergen. Challenged test perform for check food and medicine allergy.</td>
</tr>
</tbody>
</table>

Novel strategies for allergic disorder

1) Peptide vaccine (containing T cell epitopes)

The peptide vaccines are novel strategies by the usage of short peptide fragments in the treatment of allergy. It is a highly targeted immunosystem. The genuine concept of peptide-induced T-Cell from in vitro studies various clinical trials already done and it observed that T-cell Reactive short allergen peptide and other peptides are overlapped. When it intra-dermal administered into the skin immunological mechanism concept already resolved but specific anergy. Peptide vaccines are used in the food allergy and also used in allergy caused by pollens. Vaccines are developed for the treatment of chronic disease and most of the condition protein peptide vaccine is preferred in infections, cancer treatment, and serious allergic disorders. (Hehir et al., 2016).
2) Allergen-specific immunotherapy

Allergen-specific immunotherapy is used as a preventive allergy vaccination (for a specific allergen, food as well as venom allergen). It is based on DNA Technology and peptides. DNA technology is one of the tools to make allergen-specific immunotherapy. A specific gene is responsible for a specific activity. We can change the code of gene, which is responsible for allergy. Specific Recombinant and synthetic allergy vaccination are more safe, effective, and convenient. (Valenta et al., 2016).

Figure No.5: Specific Immunotherapy.
Future Study
Allopathic medicine shows quick relief and various side effects and not completely cure the disease. In that condition, we can use the herbal drug and allopathic drugs in combination. Herbal drugs contain more than one constituents . they overcome the side effect of the allopathic drug, such combination we can use in Acute and chronic disorders. Peptide vaccine has the potential to treat the food allergy in the future, strict avoidance of the allergen and the new approach for treat food allergy and management of food allergy. Specific immunotherapy is one of the best approaches for the treatment of allergic disorders as well as DNA Technology is used to correct the genetic code of gene which is responsible for allergic conditions. Various vitamins are used in the treatment of allergy, further research carried out for the development of new treatment strategies.

CONCLUSION
After reviewed, we concluded that from the traditional era to the modern era allergic treatment is better that better for previous treatment, and further study is required to develop a new, stable and effective technique for the treatment of allergy.

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REFERENCE


