THE TREATMENT OF ALLERGIC RHINITIS: CURRENT VIEW

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ABSTRACT

Allergic rhinitis has become a global health problem affecting about 500million of the world population of which 20% of these are estimated to be in developing countries. This figure underestimates the true prevalence of allergic rhinitis primarily due to under-diagnosis, misdiagnosis, and patients' not seeking medical attention. Allergic rhinitis though not a fatal disease, significantly affects quality of life and is associated with comorbid conditions with a strong link with asthma. The primary goal of allergic rhinitis treatment is to treat current symptoms and to prevent comorbidities without interfering with the patient's ability to function on a daily basis. Treatment of allergic rhinitis should begin with proper avoidance measures when allergic triggers have been identified through skin prick testing or radioallergosorbent test. Pharmacologic management includes first and second generation antihistamines, intranasal corticosteroids, leukotriene receptor antagonists, mast cell stabilizers, and decongestants. Allergen specific immunotherapy remains the only disease modifying treatment available for AR treatment at present.

KEYWORDS: Allergic rhinitis, Treatment of Allergic rhinitis. Sub Saharan Africa.

INTRODUCTION

Allergic rhinitis is an IgE mediated inflammatory disease of the nose which manifests with the symptoms of sneezing, runny nose, nasal obstruction, itchy nose and ocular symptoms. The disease condition is now posing an increasing global problem. This is due to the increasing prevalence, the impact on quality life and economic burden.[1] Studies from developed countries especially Europe and America have estimated very high costs of treatment of the disease.[2,3] In developing countries there is paucity of data on the estimated economic costs of treating this disease but it is also likely to be high. Its link with asthma and other comorbid conditions also has made it imperative that measures to treat this disease condition adequately needs to be reviewed periodically as treatment of allergic rhinitis can be challenging. There is paucity of data on controlled clinical trials of treatment outcomes of allergic rhinitis in sub Saharan Africa and Nigeria in particular. This narrative review article aims at highlighting the current concepts in the treatment of allergic rhinitis and the challenges especially in Nigeria.

TREATMENT METHODS

The treatment methods for allergic rhinitis include: Allergen avoidance, Pharmacotherapy, Immunotherapy and Surgery.

Allergen Avoidance

Exposure to specific allergens is the main underlying mechanism in the pathophysiology of allergic rhintis.[4] Thus avoiding exposure to these allergens should be an effective method of treatment. An important step in allergen avoidance is the identification of the specific allergens that the patient is sensitive to. This requires appropriate allergen specific testing to determine the variety of allergens the individual is sensitized to.[5,6] There are methods by which some allergens can be avoided or the exposure levels minimized. These include removal of pets, avoidance of exposure to dust, trees, weeds, fungal spores, molds and fumes.[7,8] Other allergen avoidance measures have been proposed for indoor allergens. These include removal of carpets, use of allergen-impermeable bedding covers for the mattress and pillow and indoor air filtration with a high-efficiency particulate air (HEPA) filter.[9–13] Also washing of bed sheets in hot water (60℃) and use of acaricides which are chemical agents formulated to kill dust mites are measures that have been shown to reduce exposure to house dust mites.[14] A Cochrane review in 2010 on avoidance measures for house dust mites (HDMs) evaluated the effectiveness of measures to decrease exposures to HDMs. The use of Acaricides alone was found to have a similar efficacy as a combination of the other environmental control measures in reducing dust mite exposure and improving symptoms of allergic

rhinitis. The combined environmental measures assessed were removal of carpets, use of allergen-impermeable bedding covers and indoor air filtration.[15] However, the long term toxicity profile of the acaricides has not been well elucidated.

Reductions in exposure to allergens have been shown to correlate with improvement in symptoms. With the reduction in allergen levels in the environment, the risk of allergen triggers, progression of the disease and increased frequency of medication can be reduced. However, adequate avoidance is not always possible and is often difficult for patients to comply with.[9,12,14] In developing countries like Nigeria, a major challenge is the difficulty in identification of specific allergens of patients with AR. The allergy testing kits used for skin prick test is imported from developed countries and the allergen extracts used for testing do not adequately represent the variety of allergens in our environment. Thus, the results are not usually useful in accurate evaluation of allergens that patients are sensitized to. The commonest allergens that have been reported from such tests in Nigeria are the House dust mites (Dermatophagoides pteronyssimus and farina) and fungal spores of aspergillus species.[16,17] The others that have been reported such as ragweed and grass mix are not specific in our environment.[17] Palynological studies in Nigeria have shown and characterized an abundance of Pollen grains in the coastal belt and in the hinterland vegetation.[18–21] However, their extracts for specific allergen testing have not been widely produced. The issue of poly-sensitization as against mono-sensitization poses a peculiar challenge to allergen avoidance. In poly-sensitization, the individual is sensitized to two or more allergens. Thus exposure to any of these allergens can trigger a reaction even when an identifiable allergen is being avoided. Ciprandi et al in 2011 performed a cross-sectional study aimed at evaluating a large cohort of AR patients to define the percentage and the features of mono- and poly-sensitized subjects. They noted that Poly-sensitization was common in patients with allergic rhinitis with only 25.7% being mono-sensitized. They concluded that mono-sensitized and Poly-sensitized patients could constitute two different categories as the disease severity was significantly higher among the poly-sensitized patients (p < 0.05).[22] It is most likely that many patients with allergic rhinitis in Nigeria are poly-sensitized.

The role of air pollution is now a known factor in aggravation of the symptoms of allergic rhinitis. The epidemiological study by von Mutius et al in two different cities in Germany showed that air pollution with smoke from diesel and automobiles was a significant factor in inducing allergic disease.[23] Molecular studies have also shown that the Carbon molecule has a high affinity to trap several allergenic proteins into a single particle that can be inhaled.[24] In the urban cities in Nigeria, fumes from automobiles and wide use of generators are thus likely to pose a

significant challenge with allergen avoidance as the main treatment or control of allergic rhinitis.

Allergen avoidance still has a role to play in the management of allergic rhinitis in sub Saharan Africa as in other parts of the world. Adequate care of pets by keeping them outdoors and indoor environmental control measures are practicable. Indoor environmental control measures include removal of carpets from the house, wet mopping of the indoor floors, regular cleaning of shoes and books to prevent fungal mold formation, washing of bed sheets with hot water at 60^0C and exposure of mattresses to ultra violet rays from sunlight in tropical environments. These will reduce the load of house dust mites indoors. However, controlled randomized studies using these measures need to be performed to provide evidence of their effectiveness in sub Saharan Africa.

Pharmacotherapy
Pharmacotherapy involves the use of drugs in the treatment of allergic rhinitis. There are different groups of drugs that have been found useful in the treatment of allergic rhinitis. These groups of drugs are discussed below.

Oral H1 Antihistamines
Histamine is naturally synthesized from L –histidine by the enzyme histidine carboxylase and stored in cytoplasmic granules in tissue mast cells and basophils. It is an important chemical mediator which is released from the mast cells in the early phase of an allergic reaction.[25] Histamine is known to play a major role in human health, in immune modulation and in acute and chronic allergic inflammation through 4 known histamine receptors. Most of the effects of histamine in allergic diseases are mediated by H1 receptor stimulation. Some of its effects are mediated through H2 receptors and others through H3 and H4 receptors.[26] Studies have shown that histamine exerts effects in the central nervous system through the H1 receptors. These effects include; the sleep – wake cycle, appetite, memory, learning, locomotion and emotion.[26] The H1 antihistamines were previously thought to be H1 receptor blockers or antagonists. However, recent evidence has established them as inverse agonists.[27,28] The H1 receptor exists in two forms namely, the inactive form and the active form. Normally, the active form and the inactive form of the H1 receptors coexist functionally in equilibrium. Histamine binds preferentially with the active form of the receptor to stabilize it. This shifts the equilibrium by activating the active form to stimulate the cells. On the other hand, antihistamines bind with the inactive form to stabilize it. This shifts the equilibrium in the opposite direction by stimulating the inactive form to inactivate the cells. Therefore, the degree of histamine induced stimulation of the cells in a tissue depends on the balance between histamine and antihistamines. Studies have also shown that the H1 antihistamines down – regulate allergic inflammation directly through H1 receptors and indirectly through a transcription factor

(Nuclear factor-Kb) which also down – regulates allergen presentation, expression of cytokines and chemotaxis.[29–32] The oral H1 antihistamines are classified into the first generation antihistamines and the second generation antihistamines. The former are highly lipophilic which makes them easily cross the blood – brain barrier resulting in sedation and other CNS side effects. The latter are much less lipophilic and have strong plasma protein – binding/hydrogen binding capacity which makes them much less likely to cross the blood – brain barrier and relatively non - sedating.[33]

First Generation Oral Antihistamines
These include Chlorpheniramine, Diphenhydramine, Prometazine and Hydroxyzine. They have been in use since the 1940s. They readily cross the blood – brain barrier even at low doses and cause side effects of sedation. These drugs have actions which suggest poor receptor selectivity which include anticholinergic effects, muscarinic effects and tachyphylaxis. Thus, they have adverse effects of drowsiness, impaired psychomotor function, poor concentration, fatigue, dry mouth, urinary retention and gastrointestinal upset. The literature suggests that the pharmacokinetics have not been investigated optimally. Clinical information on half-life and time of maximal plasma concentrations are available for only a few of them. There are also few prospective controlled studies on infants, children, elderly and patients with impaired renal and hepatic function.[34] These drugs are available as over the counter (OTC) drugs, are cheap and widely used for self – medication in Nigeria. Their use is not encouraged for allergic rhinitis.

Second Generation Antihistamines
The second generation antihistamines were developed in the 1980s with goal of producing drugs with less sedating effects with improved efficacy. They have been found to show high level of H1 receptor selectivity and poor anticholinergic / muscarinic effects.[33] Positron emission tomographic scan studies have demonstrated that the second generation antihistamines occupy between 0% and 30% of H1 receptors in the CNS.[35] This is due to their poor ability to cross the blood brain barrier. These drugs include astemizole, terfenadine, cetirizine, loratadine, levocetirizine, desloratadine, fexofenadine and descarboethoxyloratadine. The pharmacokinetic and pharmacodynamics of these drugs have been studied extensively in infants, children, healthy adults, the elderly and in individuals with impaired renal and hepatic function.[36]

The drugs are well absorbed after oral administration and peak plasma levels have been found to peak between 1 to 2 hours. While some of them are oxidatively metabolized in the liver by the hepatic cytochrome P450 enzyme, cetirizine, levocetirizine and fexofenadine are not and are eliminated unchanged in the urine and faeces respectively.[37,38] The clinical implication is that the half-life of the drugs that are metabolized in the liver is prolonged in patients with hepatic disease and those

receiving treatment with cytochrome P450 inhibitors like Erythromycin and Ketoconazole. This makes them more prone to side effects.[39] The duration of action of the second generation antihistamines is about 24hours which allows for a daily dose regimen. This has the advantage of easy drug compliance.[33] Also studies have shown that the plasma concentrations of these antihistamines correlate well with tissue concentrations. This has implication for improved efficacy as it is the tissue concentration that is clinically relevant. Tolerance to their effects during regular daily use has not been shown to occur. After discontinuation of daily use, the effects have been reported to last from 1 to 4 days.[39–41]

Astemizole and terfenadine have been reported to be cardiac toxic by prolongation of the QT interval with potentially fatal ventricular arrhythmias. This effect has been shown to be due to blockade of cardiac ion currents and this is not a H1 antihistamine effect.[42] Thus, these drugs have been withdrawn from use. Cetirizine, levocetirizine, loratadine and fexofenadine have been reported to have long term safety profiles.[36–38] Systematic review articles of controlled randomized trials have shown that they are not cardio-toxic even with high doses.[39] Studies have documented their efficacy in the relief of the early symptoms of allergic rhinitis such as sneezing, rhinorrhea and itching.[43,44] Astemizole was available in Nigeria in the 1980s and early 1990s but has been withdrawn. Loratadine, Cetirizine and Ketotifen are available in Nigeria. A controlled comparative study on the efficacy of Loratadine and Chlorpheniramine in Nigerian patients with allergic rhinitis showed that loratadine was significantly better than Chlorpheniramine in the overall relief of the symptoms of sneezing and rhinorrhea but no significant relief of nasal obstruction.[45] The efficacy of the second generation antihistamines in the relief of nasal obstruction is mild to moderate.[46] These drugs are recommended for the treatment of mild intermittent and mild persistent allergic rhinitis.

INTRANASAL ANTIHISTAMINES
Topical antihistamines that belong to second generation H1 receptor antagonists have been developed over past three decades. Currently two intranasal antihistamines are approved by the US FDA for treatment of AR. They are Azelastine and Olopatadine. The benefits of intranasal antihistamines include direct delivery of the drug to the nasal mucosa, increased concentration in the nasal tissues, rapid onset of action and reduced potential for systemic effects. Their mode of action is same as the second generation antihistamines. A lot of well-designed randomized, controlled, and blinded studies have shown equal efficacy to oral antihistamines for the treatment of nasal symptoms of allergic rhinitis especially with nasal congestion.[46,47]

The side effects of intranasal antihistamines are bitter taste, burning sensation in the nose, epistaxis and headaches. These tend reduce the compliance level of

patients. The common formulations in use are Azelastine 0.1% and Azelastine 0.15% solution plus sorbitol and sucralose (added to improve taste). Taste aversion has been demonstrated to all intranasal antihistamines.[48] Intranasal antihistamines are an effective treatment for AR but they are expensive and not widely available. ARIA recommendation is for use as first- or second-line therapy especially in episodic allergic rhinitis. This group of drugs has not been studied in Nigeria.

SYMPATHOMIMETICS
The sympathomimetic used in allergic rhinitis are pseudoephedrine and phenylephrine. They are available in oral and topical forms.

Pseudoephedrine acts on α- adrenergic receptors in the muscles lining the walls of the blood vessels to cause vasoconstriction. The constricted blood vessels in the nasal mucosa results in decreased inflammation of nasal membranes, as well as decreased mucus production which leads to reduction in the symptoms of nasal congestion.[49] Pseudoephedrine easily crosses the blood brain barrier to activate the adrenergic receptors thus stimulating the central nervous system to cause insomnia, nervousness, excitability, dizziness and anxiety. Also due to its vasoconstrictive action, it can lead hypertension, tachycardia and palpitations. Its use has been restricted because it is used in the illicit production of methamphetamine. The oral form is marketed as Actifed and Sudafed. The topical form is available as Oxymetazoline and Xylometazoline.[50] These are recommended for short term use mainly 3 to 5 days. Prolonged use is associated with progressive tolerance and rebound effects.[51] Rhinitis medicamentosa is also a risk with long term use.

Phenylephrine is used as an alternative for pseudoephedrine in over the counter decongestant medicines due to pseudoephedrine's use in the illicit manufacture of methamphetamine. However, it's efficacy as an oral decongestant is now controversial, as recent independent studies have shown that it not significantly more efficacious than placebo.[52]

Due to adverse effects, current ARIA guidelines recommend a very short course (not longer than 5 days) of topically administered decongestants. Patients with allergic rhinitis are not advised to use sympathomimetics regularly. However, this group of drugs are widely available as OTC in Nigeria and commonly used as self - medication because they are cheap and easily available.

ORAL LEUKOTRIENERECEPTOR ANTAGONISTS (LTRAs)
The Leukotriene inhibitors were introduced because of the role of Leukotrienes in the allergic rhinitis.[53] They block the inflammatory effects of leukotrienes and are useful in the relief of nasal congestion and other symptoms associated with allergic rhinitis.[54] The main Leukotriene receptor antagonist (LTRA) that is

recommended for use is Montelukast and it can be used alone or in conjunction with antihistamines.[55] Systematic literature reviews show that LTRAs are more effective in controlling symptoms and improving quality of life than placebo in patients with allergic rhinitis.[56] Montelukast has been shown to be well tolerated and is not associated with drowsiness. However, recent reports have demonstrated rare drug-induced neuropsychiatric events such as aggression, depression, suicidal thinking, and behavior.[57,58] Also Montelukast is more expensive than oral antihistamines and is not recommended as primary therapy for patients with AR. ARIA recommends that clinicians should not offer LTRAs as primary therapy for patients with AR but may use it with oral antihistamines. This group of drugs has recently been introduced into the Nigerian market. However, there is no clinical data on its efficacy among Nigerian patients with allergic rhinitis.

INTRANASAL CORTICOSTEROIDS
The development of corticosteroids that could be administered topically and avoid systemic adverse effects started in the 1960s. Dexamethasone phosphate and Beclomethasone phosphate were the initial products that were effective with topical administration. However, it was found that these drugs showed high plasma levels and thus posed a risk of systemic adverse effects. The new generation of intranasal corticosteroids (INS) was introduced in 1973.[59] These were found to be effective in the control of the nasal symptoms of allergic rhinitis but with low systemic bioavailability. These include Beclomethasone dipropionate (Beconase®), Budesonide (Rhinocort®), Flunisolide (Nasalide®), Triamcinolone acetonide (Nasacort®), Fluticasone propionate (Flixonase®), Mometasone furoate (Nasonex®) and more recently Fluticasone furoate (Avamys®). They are improvements in the earlier intranasal corticosteroids however there is variation in their potency and systemic bioavailability. Their potency is dependent on pharmacokinetic factors such as concentration in the nasal mucosa, degree of affinity for the glucocorticoid receptors, absorption profile into the systemic circulation, metabolism by the liver and elimination.[60]

Concentration in the nasal mucosa is dependent on the lipophilic nature of the drugs. The more lipophilic drugs tend to penetrate the nasal mucosa more readily.[61] Mometasone furoate, Fluticasone furoate and Fluticasone propionate are most lipophilic and are also less absorbed into the systemic circulation. However, for all the intranasal corticosteroids, 70 – 80% of the administered drug is propelled into the nasopharynx and swallowed. They are absorbed in the gastrointestinal tract are rapidly metabolized in the liver to inactive forms. This accounts for the low systemic bioavailability of the drugs resulting in low risk of systemic adverse effects.[60–62]

Mechanism of Action
The mode of action of intranasal corticosteroids (INCS) is complex.[59] However, it has been recognized that their

potency is related to their high affinity to bind with the glucocorticoid receptors.[63] The receptors exist in the nasal epithelial cells and many cells in the body.[64] Studies have demonstrated that a major mechanism is that glucocorticoids exert their action through interaction with intracellular glucocorticoid receptors.[61,63] The glucocorticoids (GC) are small, lipophilic molecules which are readily trapped by the nasal mucous. They diffuse across the cell membrane into the cell cytoplasm, where they bind with the intracellular glucocorticoid receptor (GR) in the cytoplasm. The cytoplasmic GR has been shown to exist normally in an inactive form stabilized by a heat shock protein (hsp).[65] Molecular studies have demonstrated that the binding of glucocorticoids with the glucocorticoid receptor dissociates the hsps.[66,67] The resulting GC – GR complex translocate into the cell nucleus where it acts by modifying gene transcription which inhibits the production of pro inflammatory cytokines. The GC – GR complex also act by interacting directly with cytoplasmic transcriptional factors.[68,69] There is also evidence that intranasal glucocorticoids induce the T regulatory cells towards reduction of elaboration of Th2 cells and cytokines.[70,71] These mechanisms activate the production of anti-inflammatory gene expression and inhibit inflammatory gene expression. This promotes the expression of anti-inflammatory enzymes, receptors, cytokines, adhesion molecules, and chemokines. The resultant effect is reduction in inflammatory cell recruitment and survival.[73]

At cellular level, the activity of mast cells such FcεR expression, cytokine production and mediator release is inhibited and apoptosis of eosinophils is induced. Also it has been shown that class-switching to IgE in the nasal mucosa is inhibited.[61] This mechanism of action explains many of the effects of intranasal corticosteroids on rhinitis symptoms, but does not fully explain the effect in reduction of the early-phase characteristic symptoms of itching, sneezing, and rhinorrhea. It has been postulated that this is due to reduction in the number of nasal mucosal mast cells, basophils and eosinophils. This leads to reduction in histamine release especially if this drug is administered before allergen exposure.[67,72,73] Further studies are needed to verify this hypothesis as this may strengthen the evidence for potential prophylactic use of intranasal corticosteroid.

Adverse effects
The main side effects with the use of intranasal steroids are mainly local effects on the nasal mucosa. These are sensations of nasal dryness, nasal stinging, and burning which have been reported to occur in 5% to 10% of patients. Epistaxis is a side effect which has been shown to occur in about 5% of patients. Septal perforation is a rare occurrence and is best prevented by directing the spray toward the inferior turbinate rather than the septum.[60,62,74,75] Intranasal corticosteroids have been shown to devoid of systemic side effects because of the pharmacodynamics.[60–62,74,75] With use of these drugs in

children, there has been concern on the potential side effect on growth. Thus, measure of the hypothalamic pituitary- adrenal (HPA) axis function is being assessed as biologic markers of this side effect in children. These studies involve the use of tests that assess basal and dynamic functions. Data from these studies suggest that intranasal corticosteroids have minimal effects on the HPA axis.[76,77] A study in Nigeria showed the efficacy and safety of Beclomethasone dipropionate.[75] Fluticasone propionate (Flixonase) and Fluticasone furoate (Avamys) are now widely available in the Nigeria market. The use of topical nasal corticosteroids has advanced the treatment of allergic rhinitis by reducing nasal mucosal inflammation resulting in good symptom control. However, many patients are concerned about the safety of steroids, making patient education an important aspect of this therapeutic approach to ensure compliance.[78] Compared with the antihistamines and anti-leukotrienes, intranasal corticosteroids have been demonstrated by numerous studies to be superior in reducing overall nasal symptom score and nasal blockage. ARIA recommendation is for its use in moderate to severe allergic rhinitis whether intermittent or severe. It may also be used with oral H1 antihistamines.

OPHTHALMIC PREPARATIONS
Ophthalmic preparations are available as H1 receptor antihistamines, mast-cell stabilizers, and anti-inflammatory drugs. These medications can be considered in patients who have ophthalmic symptoms that are not effectively managed by oral antihistamines or intranasal corticosteroids.

IMMUNOTHERAPY
Immunotherapy involves the administration of progressively increasing doses of specific allergen extracts to a patient with the aim of inducing immune tolerance to the specific allergen. The concept was first documented by Noon in 1911 following his successful use of injections of increasing doses of ragweed allergen extract to treat hay fever.[79] Initially, the exact mechanism of this mode of treatment was not clearly understood. However, over the past 20years several research efforts have led to major advances in understanding the molecular and cellular mechanisms.

Mechanism of action of Allergen Specific Immunotherapy (ASIT)
Studies have shown that the induction of peripheral T cell tolerance is the hallmark of immunotherapy.[80] Multiple mechanisms have been shown to be involved in the control allergic inflammation.[81] Allergen Specific Immunotherapy (ASIT) causes a change in the balance of the T cell types involved in immune processes with reduction in T helper 2 (Th2) cells, increase in T helper 1 (Th1) cells, increase in the naturally occurring T regulatory (FOXP3 Treg) cells and stimulation of production of the inducible T regulatory (Tr I). It has been shown that the T-regulatory cells (T-regs) inhibit

Th2 responses directly by cell - contact and through secretion of inhibitory cytokines such as Interleukin 10 (IL-10) and transforming growth factor b (TGF-b). IL-10 has been shown to induce the isotype switching of immunoglobulin production from IgE to IgG4 while TGFβ mediates switching from IgE to IgA with the resultant reduction in IgE levels. This causes a significant down regulation of allergic responses. IgG4 has also been shown to inhibit allergen induced IgE dependent mediator release.[82–84] The overall effect of these actions is a long term reduction in serum allergen specific IgE levels and induction of peripheral resistance to the specific allergen.

Clinically, there are now two methods of treatment with allergen specific immunotherapy. These are subcutaneous immunotherapy (SCIT) and the sublingual immunotherapy (SLIT).[85,86] Various clinical studies have shown that with appropriate use, these treatment methods are effective in the long term relief of allergic symptoms.[87–89] They also provide a high potential for cure. However, for effective treatment, the specific allergen or allergens which trigger the inflammation need to be identified. Therefore patients will need to have skin prick tests performed on them. Careful selection of patients who will benefit from the treatment is paramount and they need to be adequately briefed on the process. Immunotherapy has been shown to be safe provided that adequate precautions are taken.[90,91]

Subcutaneous immunotherapy is used for patients who are willing, motivated and will adhere to the instructions on the procedure. The indication for immunotherapy is moderate to severe intermittent or persistent allergic rhinitis in which allergen avoidance is difficult or impossible and there is failure of symptom control with pharmacotherapy. It is also more useful in patients with a limited spectrum of allergies. The contraindications are co-existent uncontrolled asthma, patients on medication with beta blockers, patients with other medical/immunological diseases and patients who may not be able to comply with the immunotherapy treatment protocol.[92] Subcutaneous immunotherapy involves weekly subcutaneous injections of increasing concentrations of allergen extracts for 8 to 16 weeks (build-up or induction phase) until a maintenance dose is reached. This is followed by a monthly maintenance dose of same concentration for a period of 3 to 5 years.93. There is also the cluster up-dosing schedule.[94] It is important to assess the patient for the presence of any local or systemic adverse reaction at each visit for injections and adequate facilities to treat anaphylaxis.[95] This immunotherapy technique is rigorous, painstaking and cumbersome for many patients.

The Sublingual immunotherapy was developed as a non-injection technique. Sublingual immunotherapy (SLIT) involves the use of drops of allergen extracts or allergen tablets placed under the tongue and retained for 2 minutes before swallowing. This has been shown to be a safe and favorable route. Randomized, placebo controlled and double blinded clinical trials have shown that it is efficacious and long lasting. It has been shown to be effective for all nasal and ocular symptoms. Moreover, it is equally effective in poly sensitized compared to mono sensitized patients and in those with or without associated seasonal asthma.[96] Sublingual immunotherapy has been shown to be well tolerated and can be used by the patient at home after full instructions and counselling on the use.[96,97] This non – injection technique reduces hospital visits and is more patient friendly. Adverse effects reported are usually minor local oral itching, burning sensations and lip / tongue swelling which tends to be self - limiting. However, these symptoms have been occasionally reported to be severe enough to result in discontinuation of use. Systemic adverse reaction of anaphylaxis is rare.[96] ARIA recommends Immunotherapy for moderate / severe persistent allergic rhinitis. In Nigeria, there is paucity of data on the use of immunotherapy in the treatment of allergic rhinitis.

CONCLUSION
The treatment of allergic rhinitis is multifaceted and each of the methods of treatment is usually not optimal in many patients. There are many factors that will guide the treatment of choice especially in sub Saharan Africa. The ARIA guidelines is very useful, however due to peculiarities in various parts of the world, other guidelines have been developed. These are mainly in the developed countries. It is apparent that combination of the modes of treatment will tend to yield better outcomes in patients. This again is dependent on disease type and severity. Due to non-availability of appropriate diagnostic tools especially allergen extracts that are specific in developing countries, specific allergen avoidance measures and immunotherapy are difficult to utilize. Thus pharmacotherapy remains the main stay of management of allergic rhinitis in sub Saharan Africa. The use of oral antihistamines and intranasal glucocorticoids either as monotherapy or combination therapy is the norm. There is the need for more randomized controlled studies to provide data in sub Saharan Africa on the efficacy and safety profile of the treatment regimens. These will provide the basis for systematic review and meta-analysis studies that will enable the development of clinical practice guidelines. There is also the urgent need to produce allergen extracts that are specific for the region to aid adequate diagnosis and pave the way for allergen specific immunotherapy. Symptomatic relief and improved quality of life can be achieved for most patients who have allergic rhinitis by avoiding the inciting allergen and using pharmacotherapy appropriately. When these methods of medical management fail, further evaluation by an allergy specialist and consideration for allergy immunotherapy may be beneficial.

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