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ORIGINAL ARTICLE

Safety, tolerability and clinical efficacy of ultra-rush sublingual immunotherapy among patients suffering from allergic rhinitis☆

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Adverse reactions;
Tolerability;
Clinical efficacy

Abstract
Background: Conventional immunotherapy for allergy with 3–5 years of treatment period has poor compliance. Ultra-rush sublingual immunotherapy with a shorter period of treatment can have better compliance. There are very few studies on ultra-rush sublingual immunotherapy all over the world.
Objectives: (1) To determine allergen sensitivity among allergic rhinitis patients. (2) To assess safety, tolerability and clinical efficacy of ultra-rush sublingual immunotherapy.
Methods: The present study was conducted in Allergy clinic, KIMS Hospital & Research Centre, Bangalore, India from January 2010 to June 2011. After obtaining Institutional Ethics Committee approval, 40 allergic rhinitis patients (according to ARIA guidelines) in the 18–60 years age group who were positive for aeroallergens in skin prick test were recruited for ultra-rush sublingual immunotherapy (20 min initial phase and 4-month maintenance phase) and followed for 8 months with symptom and treatment diary.
Results: Out of 40 patients, the majority, 36 (90.00%) patients were sensitive to house dust mites. Six patients had seven immediate adverse reactions and seven patients had eight delayed adverse reactions. All subsided without medication or with symptomatic oral medications. All patients tolerated ultra-rush SLIT and there was significant decrease in both symptom-score and treatment received in these patients.
Conclusion: Ultra-rush SLIT regimen has excellent safety, tolerability and clinical efficacy among allergic rhinitis patients.

☆ A part of the data was presented in IAACON 2011 biennial conference, Bangalore, India on 14.8.2011 and was awarded the best paper in the same conference. Dr. Ruby Pawankar, Dr. Rossenwaller, Dr. Walter Canonica also attended the conference.

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Introduction

Allergen-specific immunotherapy is the only treatment modality available for allergic diseases with proven long-term benefits. The traditional subcutaneous route is burdened with the risk of severe adverse events. Sublingual immunotherapy is a novel method, patient friendly, easy to administer, has fewer adverse reactions and is of equal efficacy compared to subcutaneous route.[1] Sublingual immunotherapy (SLIT) regimens have traditionally an induction phase of updosing lasting approximately 2–3 weeks. Shorter regimens could simplify the administration and could be better accepted by patients, favouring their adherence to therapy.[2] A metaanalysis in 2005 showed that frequency of adverse effects associated with SLIT was not dose-dependent.[3] Local side effects are seen more frequently in the low dose groups, but no difference was seen in occurrence of systemic reactions.[4] Ultra-rush sublingual immunotherapy with a shorter period of treatment can have better compliance. Recently ultra-rush regimens with induction phases lasting less than 2 h have been tried.[5–9] These studies have demonstrated the safety and tolerability of ultra-rush regimens in a few randomised placebo-controlled trials performed with cypress pollen[5] and grass pollen[6,7] and also in some observational studies.[8,9] There are very few studies regarding the safety, tolerability and efficacy of ultra-rush sublingual immunotherapy all over the world, particularly in India. Nevertheless, additional and larger studies with other types of allergens are needed to further confirm the safety and efficacy of such regimens. Hence the present clinical trial was undertaken to study the safety, tolerability and clinical efficacy of ultra-rush sublingual immunotherapy among patients suffering from allergic rhinitis.

Objectives

1. To describe the socio-demographic profile of allergic rhinitis patients.
2. To determine the allergen sensitivity among patients suffering from allergic rhinitis.
3. To assess the safety and tolerability of ultra-rush sublingual immunotherapy based on adverse reactions.
4. To assess the clinical efficacy of ultra-rush sublingual immunotherapy using symptom diary and treatment diary.

Methods

The study was conducted in Allergy Clinic, Preventive Medicine Unit, Kempegowda Institute of Medical Sciences Hospital and Research Centre (KIMSH&RC), Bangalore from January 2010 to June 2011 for a period of 18 months. This is a non-randomised clinical trial carried out on 40 allergic rhinitis patients sensitive to aero allergens with sensitivity levels of grade 2 and above.

Calculation of sample size:

$n = 4pq/d^2$
p – Prevalence of allergic rhinitis[10] = 11%
$q = 1 - p$
With precision of 10%
$n = 4 \times 0.11 \times 0.89/(0.10)^2 = 39.16$
Approximately 40 patients

After obtaining the Institutional Ethical Clearance for the present study, individuals with clinical signs and symptoms of mild and moderate to severe persistent allergic rhinitis (as per ARIA guidelines[11–13]) were subjected to routine investigations such as Hb%, TC, DC, ESR and special investigations such as Modified Allergy Skin testing (Skin prick test), Absolute Eosinophil count, and Nasal smear for cytology.

Skin prick tests[14–16] were performed with 123 allergen extracts. The extracts included 19 pollens, 5 dusts, 2 dust mites, 10 fungi, 10 insects, 3 epithelia and 74 food allergens. Allergen extracts for skin prick tests were obtained from Creative Drug Industries, Navi Mumbai. Pollen antigens were selected based on the pollen calendar.

Individuals who were sensitive for aero allergens with sensitivity levels of grade 2 and above[17] in skin prick tests were included in the study and recruited for ultra-rush sublingual immunotherapy. Patients with autoimmune diseases, serious chronic inflammatory diseases, malignant disease, severe asthma, emphysema, bronchiectasis, pregnancy, ischaemic heart disease, high blood pressure, receiving immunosuppressive medications and beta-blockers, and suspicion of alcohol abuse were excluded.

Informed consent was obtained from each patient after informing about the nature and objectives of the study. The ultra-rush sublingual immunotherapy was given with an initial induction phase for 20 min followed by a maintenance phase for 4 months where the patient had to take the maximum dose of 2 ml (or tolerable dose) daily.

Customised vaccine kits (standardised allergen extract solutions) for ultra-rush SLIT were procured from Creative Drug Industries, Navi Mumbai based on the allergen sensitivity of the patients. The 20 min ultra-rush sublingual immunotherapy protocol for induction phase was followed as per Gammeri et al.[9] by converting the Allergoid Units standardised to w/v ratio/PNU estimation/biological activity test (according to the methodology of Allergo Pharma, West Germany), as shown in Table 1.

The induction phase was undertaken under medical supervision to monitor for any serious adverse events or life threatening anaphylactic reactions. The standardised allergen extract solutions were administered as sublingual drops and patients were instructed to keep the drops under the tongue for 2 min before swallowing. As per the dosing regimen which is summarised in Table 1, patients received the extracts at successive doses of 0.1, 0.3, 0.6, 1.0 and 2.0 ml of 1000 mcg/ml concentration solution (100, 300, 600, 1000 and 2000 Allergoid units respectively) with 5 min interval between each dose, for a total duration of 20 min, to reach the maximum dose of 2 ml (2000 AU) or up to the tolerable dose.

Blood pressure and pulse rate were measured before and after each dose. All adverse reactions occurring at each dose level (type of reaction, severity according to the