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Guiding principles of sublingual immunotherapy for allergic rhinitis in Japanese patients

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ABSTRACT

Objective: Sublingual immunotherapy (SLIT) appears to offer practical advantages for the treatment of allergic rhinitis (AR). Based on a review of the scientific literature, we present recommendations as guiding principles to administer SLIT safely.

Methods: Clinical questions concerning SLIT were prepared. Literature published between January 2003 and December 2012 was searched from PubMed, the Cochrane Library, and Japana Centra Revuo Medicina. Qualified studies were analyzed and the results were evaluated, consolidated, and codified. We answered 17 clinical questions and, based on this, presented evidence-based recommendations.

Results: Sublingual immunotherapy improved symptoms (e.g., quality of life [QOL]) and reduced medication scores in seasonal AR and perennial AR. Most SLIT-induced adverse effects were local oral reactions, although systemic adverse effects such as gastrointestinal symptoms, urticaria, and asthma are occasionally reported. There have been no reports of lethal anaphylactic reactions by SLIT. When SLIT is continued for 3–4 years, its effect persists long after discontinuation.

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Conclusion: A correct diagnosis of AR and sufficient informed consent from patients are required before initiating SLIT. Sublingual immunotherapy should be continued for 3 years or longer. The initial administration of SLIT during the uptitration of an allergen vaccine and the general condition of patients are critical for the safe performance of SLIT.

1. Introduction

Allergic rhinitis (AR) represents a global health care problem that greatly affects daily activity, work productivity, learning, sleep, and quality of life (QOL) in people of all ages [1]. Japanese cedar pollinosis (JCP) is a unique allergic disease not seen outside of Japan. A massive amount of pollen is dispersed in the spring. The disease affects many people in cities far from the source of the pollen because pollen travels long distances. The disease has high morbidity (35%) in the adult Japanese population and the prevalence of JCP is increasing [1,2].

Allergen-specific immunotherapy (IT) is recognized as the only curable treatment for AR. Subcutaneous immunotherapy (SCIT) has been used for treating AR in Japan. However, SCIT has several drawbacks such as the requirement for frequent hospital visits, injection site pain, and the risk of rare serious adverse drug reactions such as anaphylaxis [3]. Sublingual immunotherapy (SLIT) was developed to overcome these drawbacks and can be administered at home under a physician's direction. However, SLIT should be started after a correct diagnosis of AR and administered by the appropriate method [4,5].

Clinical trials have demonstrated the effectiveness of SLIT for patients with JCP [6,7]. National health insurance in Japan has covered SLIT for JCP since October 2014 and for house dust mite (HDM) since 2015. Based on research by the Japanese Rhinologic Society (JRS), the present guideline was prepared to provide accurate knowledge of SLIT and to contribute to the development of this therapy [8]. The JRS is an independent academic organization that receives no sponsorship or funding from specific organizations or businesses. Furthermore, the JRS has not obtained funds for the preparation of the present guidelines from any businesses, which include businesses representing the pharmaceutical industry.

2. Criteria for determining recommendation grades

This article discusses some clinical questions (CQs). Clinical questions were prepared with regard to the procedures, effects, adverse reactions, and mechanisms of SLIT. The literature published between January 2003 and December 2012 was searched for evidence using the databases of PubMed, the Cochrane Library, and the Japan Medical Abstracts Society (Web version 4). The principal search period was between October 2012 and June 2013 and the main search terms were "allergic rhinitis", "pollinosis", and "sublingual immunotherapy". Two people from the committee selected articles relevant to each CQ and collected information. The development committee then assessed and summarized the information and codified the findings, after achieving a consensus.

Level of evidence I–IV were determined, as follows: Ia, meta-analysis (with homogeneity) of randomized controlled trials; Ib, at least one randomized controlled trial; IIa, at least one well-designed, controlled study, but without randomization; IIb, at least one well-designed, quasi-experimental study; III, at least one well-designed, nonexperimental descriptive study (e.g., comparative studies, correlation studies, and case studies); and IV, expert committee reports, opinions, and/or experience of respected authorities. The recommendation levels of the Medical Information Distribution Service (MINDS) were adopted as follows: A, strong scientific evidence and implementation of the treatment is strongly recommended; B, scientific evidence and implementation of the treatment is recommended; C1: no scientific evidence, but implementation of the treatment is recommended; C2: no scientific evidence and implementation of the treatment is not recommended; and D: evidence suggests ineffectiveness or harm and implementation of the treatment is not recommended [3].

3. Indication and methods of SL IT

3.1. CQ1: does SLIT improve symptoms and QOL in patients with seasonal allergic rhinitis?

A meta-analysis of randomized placebo-controlled double-blind trials (RCTs) on the use of SLIT for seasonal allergic rhinitis (SAR) demonstrated that symptom scores and medication scores improved significantly in the active treatment group (Level Ia) [9], the symptoms of the active treatment group improved in all trials, and a significant effect was observed in 21 (58%) of 36 trials (Level Ia) [10], and that high efficacy rates were observed in adults and in patients who received preseason treatment of 12 weeks or longer before the pollen season (Level Ia) [11]. In 4 trials of 8 RCTs, disease-specific improvement in QOL was reported, which provided moderate evidence of efficacy for QOL by SLIT (Level Ia) [10]. In an RCT of JCP patients, SLIT for 3 months significantly improved symptoms and QOL during the pollen season (Level Ib) [6,7]. In an open-label study of children with JCP, SLIT for 2 months kept symptoms mild in all patients during the pollen season (Level III) [12].

The recommendation level is B. Sublingual immunotherapy improves symptoms and QOL in patients with SAR.

3.2. CQ2: does SLIT improve symptoms and QOL in patients with perennial allergic rhinitis caused by HDM?

In a meta-analysis of SLIT for HDM-induced perennial allergic rhinitis (PAR), nasal symptoms and medication scores significantly improved in the SLIT group (Level Ia)