

LETTER TO THE EDITOR

**COMPARISON BETWEEN CONTINUOUS OR INTERMITTENT SCHEDULES OF
SUBLINGUAL IMMUNOTHERAPY FOR HOUSE DUST MITES: EFFECTS ON
COMPLIANCE, PATIENTS' SATISFACTION, QUALITY OF LIFE AND SAFETY**

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Sublingual immunotherapy (SLIT) is indicated in the treatment of allergic rhinitis and asthma. However, an issue scantily investigated is the patient's satisfaction and the consequent compliance. This study is aimed at evaluating the possible differences of SLIT administered continuously or intermittently on several parameters: clinical efficacy, Quality of Life (QoL), satisfaction, compliance and safety. Forty allergic patients were treated for 12 months. The treatment was carried out by sublingual administration of an allergen extract of a 50% mixture of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* at 10 and 300 IR/ml concentrations. Patients were randomly treated continuously or intermittently (i.e. 2 month treatment alternate to 2 month suspension). Both schedules were significantly effective in reducing allergic symptoms and improving QoL. Compliance and satisfaction were good in both groups. Local and systemic reactions were few, self-resolving, and mild in both schedules. Intergroup analysis did not reveal any difference between the two groups regarding these parameters. In conclusion, this preliminary study provides the evidence that also intermittent SLIT is as effective and safe as traditional continuous treatment. In addition, compliance and satisfaction are super-imposable in the two groups.

Allergen specific immunotherapy (SIT) can be considered as a "vaccine" for allergic diseases (1). SIT is able to act as an immune modifier (2), and to influence the natural history of the disease. Subcutaneous immunotherapy (SCIT) is still the most common route of administration, but entails the risk of anaphylaxis (3). This has led to the development of sublingual immunotherapy (SLIT),

which shows a high-quality profile regarding safety and efficacy, when an adequate dose is administered (4). Numerous studies on SLIT support these data, both in adults and children (5-6). A main issue of SLIT is the compliance that is related to the daily need for SLIT also during the maintenance phase. This issue makes the development of easier schedules, such as an intermittent treatment, useful.

Key words: sublingual immunotherapy, mites, continuous schedule, intermittent schedule, clinical efficacy, compliance, safety

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The aim of our study is to evaluate satisfaction and compliance related to different schedules of SLIT: continuous versus intermittent administration. The equivalence of efficacy and safety of the two schedules was also evaluated.

MATERIALS AND METHODS

Patients aged between 5 and 50 years with perennial allergic rhinitis (PAR) due to sensitization to dust mites (HDM) were included in the study. Exclusion criteria were sensitization to cockroach, moulds, animal epithelia and *Parietaria* pollen, and common contraindications to immunotherapy. Subjects were randomized into two groups, according to SLIT schedule: the conventional schedule with maintenance dose three times per week, and the new one with maintenance treatment carried out with courses of two month duration, with daily administration, alternated with periods of suspension of the same duration. The treatment lasted one year, including a build-up phase of 11 days (equal for the two schedules). SLIT was performed by giving an allergen extract containing a 50% mixture of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (Staloral 300, Stallerg enes, Antony, France) at 10 and 300 IR/ml concentrations. Treatment with symptomatic

drugs, including cetirizine, loratadine, nedocromil eye drops, fluticasone nasal and bronchial inhaler, and formoterol inhaler were allowed. Patients were allocated to continuous or intermittent treatment according to randomization tables. The study was conducted according to the updated version of the Helsinki declaration and to good clinical practice. The Ethic Committees of each center approved the protocol. The following criteria were evaluated: 1) *Compliance* by the rate of withdrawal in every group. The correct assumption of SLIT was verified by measuring the residual content in ml in the recovered vials; 2) *Patient's satisfaction* by a standardized questionnaire; 3) *Quality of life* by the Juniper questionnaire RQLQ (7); 4) *Clinical effectiveness* by the score of allergic symptoms and by drug consumption, as recorded in clinical diaries. In addition, a Visual Analogical Score (VAS) was administered; 5) *Safety* information was registered on an apposite form for adverse events. Differences between the two treatment groups for every parameter were assessed with non-parametric tests, considering significant a p value <0.05.

RESULTS

Forty patients were enrolled, 20 per group. Six patients (3 per group) stopped the study for personal

Table I. Changes in assessed parameters in the two treatment groups.

Parameter	Continuous SLIT (17 pts)		Intermittent SLIT (17 pts)		P value
Compliance (no SLIT-related withdrawal)	17/17 (100%)		16/17 (94%)		n.s.
Total compliance (no missing doses)	11/17 (65%)		12/17 (70.5%)		n.s.
Satisfaction	15/17 (88%)		15/17 (88%)		n.s.
Quality of life	Baseline 9.82±5.43	Final visit 5.76±4.76	Baseline 11.29±3.7	Final visit 8.29±2.69	n.s.
Difference (P value)	0.0004		0.008		
Symptom/medication score	Baseline 23.8±15.01	Final visit 13.4±10.1	Baseline 20.8±9.18	Final visit 15.3±8.78	n.s.
Difference (P value)	0.0001		0.036		
VAS	Baseline 4.84±2.59	Final visit 7.41±2.02	Baseline 5.67±1.91	Final visit 6.46±1.71	n.s.
Difference (P value)	0.01		n.s.		
Local reactions (oral, gastrointestinal)	3/17 (17.6%)		4/17 (23.5%)		n.s.
Systemic reactions (rhinitis, conjunctivitis)	2/17 (11.8%)		4/17 (23.5%)		n.s.

reasons, unrelated to treatment. The duration of immunotherapy was homogeneous in the two groups. The cumulative doses received with the two methods were equal, corresponding to 34.560 IR (1.75 mg of Der p1 and 4.32 mg of Der f 1) for continuous, and 40.320 IR (2.01 mg of Der p1 and 5.04 mg of Der f 2) for intermittent SLIT, respectively. Table I shows the results obtained for each parameter.

DISCUSSION

In recent years SLIT received clear demonstrations of effectiveness and safety in the treatment of rhinitis and asthma caused by aeroallergens (4-6, 8). However SLIT requires, also during maintenance, daily or frequent administrations (differently from SCIT), and that may lead to early withdrawal. This makes compliance a pivotal issue, particularly in perennial allergies such as rhinitis and asthma due to sensitization to HDM.

Few studies have focused on compliance to SLIT (9-10). A survey conducted by telephone interviews to 86 patients receiving SLIT in sublingual tablets estimated an adherence rate of about 97% (9), while a study on a much larger population gave different results (10). In fact, a treatment withdrawal before completion was reported in 9.5% in hospital setting and in 38.8% in private offices. This focuses the attention on the relationship between the patient and the physician during the course of SLIT. Moreover, one may argue that a less demanding commitment for patients to perform the treatment could improve the compliance, and this is the major aim of the present study. The results provide evidence that both continuous and intermittent schedules have a good profile of compliance and satisfaction, being of comparable effectiveness in improving allergic symptoms and quality of life related to allergic diseases. This suggests that when the patient is adequately followed, the type of schedule has little importance. However, an important observation regards safety, which was super-imposable in both groups, which demonstrates that after two months of suspension, the treatment can be safely re-assumed with no need of dose reduction, and this has practical utility in routine administration of SLIT.

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