

Oral hyposensitization in patients with contact dermatitis from *Parthenium hysterophorus*

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Parthenium hysterophorus is the commonest cause of airborne contact dermatitis in northern India. Treatment is mostly palliative and consists of repeated courses of antihistamines and topical and/or systemic corticosteroids. We have evaluated the effect of oral hyposensitization as an alternative therapeutic modality. In 70% of those patients who completed the study, there was a gradual improvement in their clinical status, as evident from a fall in their clinical severity score for eczema. 30% of patients had an exacerbation during the course of the study and hence hyposensitization in them was stopped. Patients tolerated therapy well and no significant side-effects were seen, except for abdominal pain, 'heartburn' and cheilitis.

Key words: *Parthenium hysterophorus*; oral hyposensitization; allergic contact dermatitis; plants; plant extracts. © Munksgaard, 2001.

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Parthenium hysterophorus, also known as congress grass or feverfew has become the commonest cause of airborne contact dermatitis in northern India (1, 2). As with other allergies, an ideal remedy would be complete removal of the allergen from the patient's environment (3), but this is usually not feasible in cases of allergic contact dermatitis from parthenium, due, in part, to the airborneness of the allergens and the ubiquity of the weed. Once induced, sensitivity to parthenium is lifelong and spontaneous cure very uncommon. Patients are subject to seasonal relapses, determined by the growth and flowering pattern of the weed, which is notoriously resistant to efforts at eradication (4, 5). The clinical picture may further be complicated by the development of photosensitivity (4, 6, 7). The treatment is palliative at best, consisting of antihistamines and topical corticosteroids to tide over each relapse. The end result is often a chronic eczema, difficult to manage and a frustrating problem for both the patient and the physician.

We considered oral hyposensitization, in patients with allergic contact dermatitis from parthenium, as an alternative to repeated courses of topical and systemic corticosteroids. There are, however, no established methods for hypo- or desensitization described in the literature for patients with parthenium dermatitis. We decided to evaluate the effect of oral administration of parthenium

extract on the clinical picture of the disease and the titre of contact hypersensitivity (TCH) (8).

Patients and Methods

24 subjects, known to be patch test positive to *Parthenium hysterophorus*, were enrolled in the study. Baseline investigations such as liver function tests, renal function tests, haematogram and a chest X-ray were done in all patients. Patch testing was done at the start of the study to assess the titre of contact hypersensitivity using aluminium chambers and increasing dilution(s) of parthenium extract. To record the clinical changes observed during the study, and in order to be objective, we used a modified form of the original psoriasis area severity index (PASI) (9). This score was calculated like the PASI (Table 1) and was recorded at the start of treatment (0 week) and at the end of the study (12 weeks) as the clinical severity score. The patients were asked for follow-up every 2 weeks. Ether extract of dried parthenium leaves was diluted in corn oil to make a stock solution of 1000 µg/ml. The 1st dilution used was 10,000 µg/ml. Oral hyposensitization was started with 1 dilution lower than the patient's own titre, determined after patch testing with serial dilutions. For example, if the patients TCH was 10^{-2} dilution, oral hyposensitization was started with an extract diluted 10^{-3} .

Table 1. Clinical severity scoring system

Score	0	1	2	3	4	5	6
%area involved	0	<10	10<30	30<50	50<70	70<90	90<100
Clinical signs:	none	slight	moderate	severe			
1. erythema and oedema							
2. vesico-pustules and crusts							
3. cracks and excoriations							
4. scaling and dryness							
5. lichenification							
Head (H)	Score			Trunk (T)	Score		
erythema and oedema	_____			erythema and oedema	_____		
vesico-pustules and crusts	_____			vesico-pustules and crusts	_____		
cracks and excoriations	_____			excoriation and cracking	_____		
scaling and dryness	_____			scaling and dryness	_____		
lichenification	_____			lichenification	_____		
sum	_____			sum	_____		
× area	_____			× area	_____		
× 0.1	_____			× 0.3	_____		
Lower limbs (LL)	Score			Upper limbs (UL)	Score		
erythema and oedema	_____			erythema and oedema	_____		
vesico-pustules and crusts	_____			vesico-pustules and crusts	_____		
cracks and excoriations	_____			excoriation and cracking	_____		
scaling and dryness	_____			scaling and dryness	_____		
lichenification	_____			lichenification	_____		
sum	_____			sum	_____		
× area	_____			× area	_____		
× 0.4	_____			× 0.2	_____		

Clinical severity score=sum of scores of (H) + (T) + (UL) + (LL).

Initially started with 5 drops/day, the dose was increased over a week, up to a maximum of 30 drops/day. The concentration of the extract used for hyposensitization was increased by 1 dilution every 4 weeks. The total duration of treatment was 12

weeks. Antihistamines were continued in all patients. Topical corticosteroids were used only after the 1st 2-weekly follow-up, if a patient insisted on being prescribed something for faster symptomatic relief.

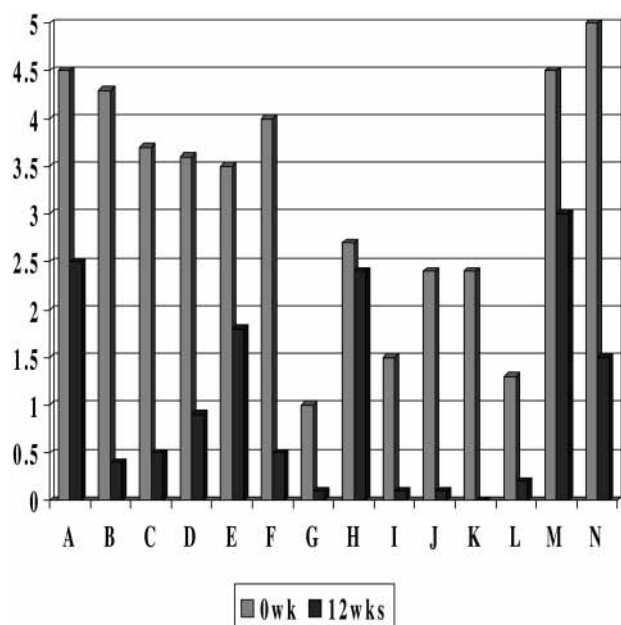


Fig. 1. Clinical severity score – pre and post hyposensitization

Results

24 patients were recruited for the study. Of these, 4 (16.7%) dropped out and only 20 (83.3%) completed the study. Of these, 13 (65.0%) were male and 7 (35.0%) female. Mean age of the patients was 51.5 years (range 38–70 years) and the mean duration of the disease was 6.0 years (range 4 months to 15 years). 6 patients (30.0%) experienced exacerbation during the course of the study, so hyposensitization in them was stopped. In the remaining 14 patients, there was a gradual fall in the mean clinical severity score after hyposensitization (Fig. 1). However, there was no significant change in the titre of contact hypersensitivity before and after treatment.

7 (50.0%) out of the 14 patients had a follow-up at 1 year. Exacerbation was observed in 4 (20.0%) patients within 3 weeks to 2 months of stopping parthenium hyposensitization. 3 (15.0%) patients were asymptomatic even after 1 year from stopping hyposensitization. Abdominal pain, 'heartburn' and cheilitis were the only side-effects seen: in 1

patient (5.0%) each. None of our patients had pruritus ani.

Discussion

Since the 1st report of contact dermatitis from *Parthenium hysterophorus* (10), over the last 3 decades, *Parthenium hysterophorus* has caused contact dermatitis of epidemic proportions in India (4, 5). The dermatitis is either due to direct handling of the plants or is an airborne contact dermatitis. The principal sensitizing allergens are sesquiterpene lactones, parthenin and ambrosin, concentrated in the trichomes of the plant. During the dry season, these are scattered by the wind and cause the airborne contact dermatitis (2).

Specific hyposensitization is the practice of administering gradually-increasing quantities of a specifically-relevant allergen to allergic patients until reaching a maintenance dose or loss of symptoms. It may be achieved by the oral, sublingual or parenteral route (3, 11). The most important hypothesis regarding the mechanism of hyposensitization is a switch from a Th2 into a Th1 reaction pattern in T-cell regulation (11). The exact mechanism of hyposensitization following oral administration remains unknown. It may be due to (i) macrophage inactivation, (ii) humoral inhibitory factors, (iii) depletion of specifically-reactive lymphocytes, (iv) blockade of receptors at effector lymphocytes, or (v) induction of antigen specific T-suppressor cells (3, 12).

Specific hyposensitization achieved by subcutaneous injections is the treatment of choice for patients with IgE-mediated allergies like seasonal or perennial allergic rhino-conjunctivitis, asthma or hymenoptera venom allergy (11). However, oral/sublingual hyposensitization is still not a routinely-accepted modality (11), though, having been well studied in patients with allergy to *Parietaria judaica* pollen and contact dermatitis from nickel (11, 13–16), it has also been used as a therapeutic modality in patients with rhus/urushiol dermatitis (17–19).

In the only case report of its kind, Srinivas et al. (20) tried oral hyposensitization in a patient with parthenium dermatitis using crushed leaves. The patient's symptoms, however, recurred on discontinuation of therapy. In our study, 66% of the patients had clinical improvement (as evident by a fall in their clinical severity score). Also, no significant side-effects were observed. Pruritus ani was surprisingly not a problem, unlike other studies on oral hypo-sensitization (18). 20% of our patients had exacerbation of the disease once hyposensitization was stopped.

Epstein et al. (18) observed a decrease in patch

test positivity after oral administration of urushiols. They observed optimal results in their patients with rhus/urushiol dermatitis when therapy was extended to 6 months. Similarly, Morris (15) demonstrated improvement of dermatitis in 85% of his patients with nickel allergy, along with a decrease in titre of hypersensitivity in all his patients, as evident from intradermal testing. In contrast, however, we did not find a significant difference in titre of contact hypersensitivity before and after parthenium hyposensitization in our patients.

Storrs et al. (21) used a mixture of Compositae oleoresins for hyposensitization and noticed improvement in 2 of their 4 patients, while Ikeda et al. (22) concluded that both oral and epicutaneous desensitization, used together, worked better than oral or epicutaneous administration of urushiols alone.

We know that a minute amount of antigen is capable of eliciting allergic contact dermatitis in a sensitized individual. (3) The presence of memory T-cells is however essential to eliciting a response. If an allergen is administered by the parenteral or oral route, the memory cells may be depleted by excess of this allergen/antigen in the circulation. This may, in turn, prevent the migration of memory cells to those sites in the skin where the sensitized individual is exposed to minute amounts of allergen. This probably explains how hyposensitization works and also why there is a need for continuous treatment.

In conclusion, we believe that probably increasing the duration of oral ingestion of parthenium extract may give a more measurable degree of hyposensitization, and further controlled studies on oral hyposensitization are urgently required to prove the efficacy of this therapeutic modality in patients with allergic contact dermatitis from *Parthenium hysterophorus*.

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