

Parthenium dermatitis: is parthenolide an effective choice for patch testing?

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Summary

Background. Patch test positivity to parthenolide was observed less often than expected in strongly suspected cases of parthenium dermatitis after Chemotechnique Diagnostics (Sweden) replaced parthenium extract with parthenolide (0.5% pet.) by itself while marketing its Indian baseline series for patch testing.

Objective. The study was performed to find whether parthenolide detects parthenium contact sensitivity more effectively than parthenium extract in patients clinically presenting with classic parthenium dermatitis.

Material and methods. One hundred consecutive patients with suspected parthenium dermatitis were patch tested prospectively with the Indian baseline series, parthenium extract (1% aq.) and parthenolide (0.5% pet.) between July 2011 and April 2012.

Results. Only 37 of 100 patients with suspected parthenium dermatitis (male/female ratio of 20:17) reacted to parthenium extract (32 patients), parthenolide (17 patients), or both (12 patients). Reactions to parthenium extract were generally stronger than reactions to parthenolide.

Conclusion. Patch testing with parthenolide (0.5% pet.) detects fewer cases of suspected parthenium dermatitis than patch testing with parthenium extract (1% aq.).

Key words: airborne contact dermatitis; parthenin; parthenium dermatitis; parthenium extract; *Parthenium hysterophorus*; parthenolide; patch testing.

Patch testing either with parthenium extract or with sesquiterpene lactones (SQLs) has been the standard diagnostic method in clinically suspected cases of parthenium dermatitis. Both parthenolide (0.1% pet.) and SQL mix (0.1% pet.), a mixture of alantolactone, dehydrocostus lactone, and costunolide, are included for patch testing in most plant series. Patch test positivity

to parthenolide was observed less often in our contact dermatitis clinic (unpublished data) than expected in strongly suspected cases of parthenium dermatitis after Chemotechnique Diagnostics (Vellinge, Sweden) replaced its parthenium extract with parthenolide in the Indian baseline series marketed during 2010–2011. These observations prompted this study, with the objective of determining whether parthenolide is able to detect cases more effectively than parthenium extract in patients clinically presenting with classic parthenium dermatitis.

Materials and Methods

The study comprised 100 consecutive patients aged ≥ 18 years and clinically suspected of having parthenium dermatitis. They were patch tested with the

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Indian baseline series, parthenium extract (1% aq.) and parthenolide (0.5% pet.) between July 2011 and April 2012, after written/informed consent had been obtained. Pregnant or lactating women, patients with acute dermatitis and patients taking prednisolone (≥ 20 mg daily) were excluded. Patch testing was performed with Finn Chambers[®], parthenium extract (1% aq.) and the Indian baseline series containing parthenolide (0.5% pet.) from Chemotechnique Diagnostics (www.chemotechnique.se), marketed in India by Systopic India Ltd (New Delhi, India). For parthenium extract, mature and healthy-looking whole *Parthenium hysterophorus* plants growing locally (identified with the help of the Department of Botany, Punjab University, Chandigarh, India) were selected for the preparation of aqueous extract, as described previously (1). Briefly, after gentle washing with distilled water to remove surface contaminants, the selected plants were air dried in the shade at room temperature. The dried material was pulverized, weighed, mixed with six times the volume of distilled water (5 g of powder in 30 ml of distilled water) in a light-protected glass container, and left at room temperature, with frequent shaking. After 24 hr of extraction, the mixture was filtered through Whatman no. 1 filter paper (Whatman International Ltd, Maidstone, UK). The filtrate, that is, the crude (100%) extract, was stored in air-tight, amber-coloured glass bottles at 4°C (replaced each month with fresh stock solution), and dispensed as 1% aq. for patch testing. The patch tests were applied on the upper back, and the patients returned for reading of results after both 48 hr (D2) and 72 hr (D3). The results were graded according to the International Contact Dermatitis Research Group criteria (2). Reactions persisting on D3 were considered to be positive for final analysis.

Results

Only 37 of 100 patients (male/female ratio of 20:17) aged between 18 and 63 years showed positive reactions to parthenium extract [32 (86%) patients], parthenolide [17 (46%) patients], or both [12 (32%) patients] (Table 1). In the majority of patients, parthenium extract elicited stronger positive reactions (3+ in 10 and 2+ in 15), than parthenolide (3+ in 2 and 2+ in 8). One patient developed an angry back. Various clinical patterns of these patch test-positive parthenium dermatitis cases were noted: airborne contact dermatitis (ABCD) in 20 (54%), acrofacial dermatitis in 6 (16%), and acral dermatitis in 5 (14%). Other patterns (facial dermatitis, lichenoid dermatitis, flexural dermatitis, face and trunk dermatitis and exfoliative dermatitis in 1 case each) were noted in the other 6 (17%) patients.

Discussion

P. hysterophorus (common names: parthenium, wild feverfew, carrot weed, and congress grass) belongs to the Compositae family of plants. The weed has high sensitizing potential, causing sensitivity in as many as 56% of occupationally exposed persons without causing apparent dermatitis. It has caused allergic contact dermatitis in nearly epidemic proportions in India among all populations since its accidental introduction in 1950s along with shipments of American wheat. In the United States, the ABCD caused by members of the Compositae, including *P. hysterophorus*, is described as 'weed dermatitis', and in Australia it is described as 'Australian bush dermatitis' (3, 4). Parthenium dermatitis has also been reported in Pakistan and among returning travellers in Europe (5, 6). The exposure occurs chiefly via direct contact with plants, airborne pollens, and dry/friable plant particles, including SQL-rich trichomes. The various dermatitis patterns noted in our patients have been described previously in most series, the classic and the commonest being ABCD, followed by acral (hand and foot) dermatitis, hand dermatitis, and exfoliative dermatitis (7).

Parthenin, hymenin, ambrosin, hysterothrin, tetraeneurin-A, dihydroisoparthenin and coronopilin are the main sensitizing SQLs in different populations of parthenium plants (8, 9). The trichomes on leaves and the capitulum have the highest concentrations of these SQLs, constituting almost 8% of plant's dry weight (10). The SQL mix (alantolactone in particular) included in most 'plant series' is known to give unsatisfactory patch test results in parthenium dermatitis (11). The SQL parthenolide is a crystalline substance in its pure form (melting point of 115°C), and is soluble in many organic solvents but only slightly soluble in water. In an impure state (in admixture with other SQLs present in the plant), it forms an oleoresin. It is considered to be the principal allergenic SQL in feverfew (*Tanacetum parthenium*), and is present throughout the plant and pollen, making up 0.3–1% of the plant's dry weight (3, 12, 13). Parthenolide and volatile monoterpenes [α -pinene, camphene, limonene, *p*-cymene, (*E*)-chrysanthanol, (*E*)-chrysanthenyl, camphor, γ -terpinene, and (*E*)- β -ocimene] are considered to be major allergens for contact dermatitis induced by European ragweed (*Ambrosia* spp.) and feverfew (*T. parthenium*) (3). Cross-reactions between *T. parthenium* and several other Compositae plants and their SQLs (*Achillea millefolium*, *Aster*, *Helianthus annuus*, *Leucanthemum vulgare*, *Tanacetum vulgare*, etc.) also occur frequently (14). However, the significance of the sensitizing potential of parthenolide with regard to monoterpenes released from the plant

Table 1. Parthenium dermatitis and patch test results from parthenolide and parthenium extract during the year 2011–2012

Patient no.	Age (years)/sex	Clinical diagnosis in 37 patients who showed positive patch test reactions to parthenolide, parthenium extract, or both (n = 100)	Patch test results at D3	
			Parthenolide (0.5% pet.)	Parthenium (1% aq.)
1	60/F	ABCD	2+	–
2	18/M	Lichenoid dermatitis	1+	–
3	55/F	ABCD	1+	–
4	38/M	ABCD	1+	–
5	62/F	ABCD	2+	–
6	32/M	Acrofacial dermatitis	–	3+
7	62/M	Acrofacial dermatitis	–	3+
8	45/M	Acrofacial dermatitis	–	3+
9	41/F	ABCD	–	2+
10	65/M	ABCD	–	1+
11	72/M	Acral dermatitis	–	1+
12	60/M	Acral dermatitis	–	2+
13	53/F	Hand and abdomen dermatitis	–	2+
14	56/M	ABCD	–	3+
15	65/M	Acrofacial dermatitis	–	3+
16	56/M	ABCD	–	2+
17	42/F	Exfoliative dermatitis	–	2+
18	48/F	ABCD	–	1+
19	67/M	Acrofacial dermatitis	–	2+
20	53/F	Flexural dermatitis	–	2+
21	32/F	Acral dermatitis	–	2+
22	59/F	Facial dermatitis	–	2+
23	43/F	ABCD	–	1+
24	55/M	ABCD	–	3+ (ulceration)
25	42/F	Acral dermatitis	–	2+
26	62/F	ABCD	2+	3+
27	56/M	ABCD	2+	3+
28	40/F	Acrofacial dermatitis	1+	1+
29	39/F	Facial dermatitis	Angry back phenomenon	
30	68/M	ABCD, photoaggravation	3+	3+
31	60/M	ABCD	2+	2+
32	50/F	ABCD	2+	2+
33	70/F	ABCD–CAD	1+	1+
34	59/M	Acral dermatitis	2+	2+
35	60/M	ABCD	1+	3+
36	50/M	ABCD	2+	2+
37	62/M	ABCD, photoaggravation	3+	2+

ABCD, airborne contact dermatitis; CAD, chronic actinic dermatitis; F, female; M, male.

remains a subject of controversy (15, 16). Parthenolide alone gave positive reactions in only 36% of our patients, whereas parthenium extract alone gave positive reactions in 86%. Thirty-two per cent of our patients showed positive reactions to both parthenium extract and parthenolide, indicating that some patients with sensitivity to parthenium extract may also react to parthenolide. The possible reasons for this could be that they were previously sensitized to other plants

containing parthenolide (sunflower/*T. parthenium*), or that there was a cross-reaction with one or more of the sensitizing SQLs in *P. hysterophorus*. The least likely, but not impossible, explanation is that *P. hysterophorus* also contains hitherto undetected parthenolide, but this needs confirmation by its isolation and analytical testing. It is of concern that Chemotechnique Diagnostics replaced parthenium extract with parthenolide in the Indian baseline series for diagnosing parthenium dermatitis,

given that *P. hystrophorus* has not been reported to contain parthenolide; or perhaps *T. parthenium* (feverfew) was confused with wild feverfew, another name for *P. hystrophorus* (4). We feel that parthenium extract prepared from *P. hystrophorus* growing locally should be an essential component of any standard (plant) patch test series. This is especially important in view of morphological differences and variations in SQL chemistry between individual parthenium populations (8, 9). Moreover, it is not uncommon for there to be positive patch test results with the whole parthenium plant and negative results with parthenin alone (17). Better designed studies will perhaps help to resolve these difficulties.

Although an acetone extract of parthenium is reportedly more sensitive than an aqueous extract (18), the extracts in organic solvents tend to become concentrated with time because of evaporation, and this can ultimately affect patch test results. The oleoresins of parthenium are moderately soluble in water as well (19), and it is easier to prepare an aqueous extract than to isolate and purify SQL constituents for patch testing. However, aqueous extracts deteriorate and lose their antigenic properties in a short period of time (19), and therefore need to be frequently replenished with fresh stock solution. The risk of active sensitization or irritant reactions from crude parthenium extract is a concern, but this was not observed in this study.

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