Patch test results in patients with suspected allergic contact dermatitis: a study from Mashhad, Iran and a review of literature

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INTRODUCTION

A wide range of reactions are possible when the skin comes in contact with different exogenous agents, including hyper and hypopigmentation, acne, urticaria, atrophy, phototoxic and photoallergic reactions and eczema. Eczema might be either allergic (20%) or irritant (80%) 1. Allergic

Background: The standard patch test is known as the most reliable test to identify and confirm causative agents of allergic contact dermatitis (ACD). Previous studies have shown that the prevalence of specific allergens varies by geographic area. The results of patch test in patients visiting our dermatology clinics with suspected ACD were prospectively investigated and compared with those reported in the literature of Iran.

Method: We performed the European Standard Series patch test produced by Almiral Hermal GmbH, containing 28 allergens in a group of 100 patients (55 females and 45 males) with suspected ACD who were referred to Emam Reza and Ghaem Hospitals, Mashhad, in 2010-2011. The tests were read after 2 and 4 days.

Result: Fifty-four percent of the patients had 1 or more positive reactions of which 65% were relevant to current or past dermatitis. Positive reactions were due to 12 allergens. The most frequent allergens were nickel sulfate (25%) and potassium dichromate (25%), followed by cobalt chloride (15%), thiuram mix (11%), para tertiary butylphenol formaldehyde resin (5%), fragrance mix II (3%), para-phenylenediamine free base (3%), colophony (1%), wood alcohols (1%), mercapto mix (1%), budesonide (1%), and sequiterpene lactone mix (1%). The positive reaction to nickel was significantly more common in women (p<0.001). Men showed significantly more positive reactions to chrome (p<0.001). According to the localization of ACD, hands, as the most common site, were involved in 59 (59%) cases, followed by the feet in 28 (28%) cases.

Conclusion: Nickel sulfate and potassium dichromate are the most common allergens in Iran. As the causative agents of contact dermatitis are different in various geographic areas, modifying standard patch test series in each region with regard to its allergen prevalence might be a reasonable and cost effective approach for more appropriate preventive measures and therapeutic strategies.

Keywords: allergic contact dermatitis, allergen, eczema, patch test
contact dermatitis is a hypersensitivity reaction to an exogenous agent which occurs in a short time after contact with an allergen. Acute phase lesions consist of erythematous or scaly plaques, and vesicles or bullae may occur in contact areas in severe cases. Meticulous history taking and physical examination, although of indisputable importance in recognizing etiologic agents, are not often conclusive due to the versatility of the causative agents. The patch test remains the most reliable method in verifying the diagnosis and recognition of the etiologic agent in allergic contact dermatitis reactions. So far, in the majority of studies, nickel has been reported to be the most common allergen.

In many occasions, the diagnosis of allergic contact dermatitis is of considerable importance; for example, in a worker who is sensitive to potassium dichromate, most routine preventive measures to lower the contact rate are generally unavailing, and a change in carrier might be the only effectual approach to avoid contact with chrome salts. Patients with allergic contact dermatitis encounter many difficulties in their daily activities, because their quality of life is very easily affected by contact with environmental provocative agents. In most occasions, the patient is unable to recognize a certain reacting agent, which potentially leads to psychosocial and economic problems to the patient and its community due to frequent dermatologist visits and prolonged treatment courses. The appropriate use of the patch test, which is a non-invasive diagnostic measure, might be very helpful in this setting. Since no other investigation has been performed in the Province of Khorasan Razavi to identify the relative prevalence of allergens, we sought to define a schema of it in order to provide a background for future more comprehensive studies.

PATIENTS AND METHODS

Prospectively, 105 consecutive patients suspected of ACD attending Emam Reza and Ghaem Hospitals in Mashhad were patch tested during 2010 and 2011. Inclusion criteria were as follows:

1. Clinical diagnosis of ACD
2. Informed consent
3. No history of receiving systemic steroids (equivalent to 15 mg prednisolone or more), or topical application of large amounts (potentially equivalent to 15 mg prednisolone per day) at the test site within 2 previous weeks.
4. No history of receiving immunosuppressive medications within the above mentioned interval.
5. No substantial exposure to sunlight in the previous month.

Five enrollees were excluded from the study because they met the exclusion criteria; three patients did not attend the predetermined sessions, and elastic tapes were prematurely peeled off in two patients. Finally, 100 patients were included in statistical analysis.

Patients were advised to take a bath on the day before the test. At the time of attendance, patients were given a comprehensive explanation about the indications of the test and its routine steps. A written informed consent was obtained from each participant, and they were requested to avoid taking a bath, physical exercises, sweating, and lying on the back until the tapes were in place. A questionnaire including demographic information and clinical findings was recorded for each patient.

Then, 28 allergen substances provided in the European Standard Series manufactured by Almiral Hermal GmbH were applied using Finn chamber on the patient’s upper back and the test site was marked by indelible ink. After two days, the tapes were removed, the test site was examined and photographed, and the results were recorded in a check list. The second examination was performed on the 4th day, and the same routine was applied. The patch test reactions were recorded and interpreted according to the international contact dermatitis research group criteria.

Demographic information, and clinical and test data were analyzed using SPSS 11.5. Patient characteristics were provided as descriptive statistic indices. Analytic studies were performed with Mann-Whitney U test and Kruskal-Wallis tests. Furthermore, differences in proportions were investigated by Chi square test. P<0.05 was considered statistically significant.

RESULTS

One hundred patients (55 women, 45 men) aged 3.5 to 73 years were studied (Mean age=33.97±12.44
years. Important demographic characteristics of the patients according to the MOHLFA index are shown in Table 1. The duration of the disease was 1-240 months (mean: 43.74±51.92 months). Moreover, 22% of the patients had a personal history of atopy whereas 30% had a family history of atopy. In addition, 54% of the patients had at least one positive reaction while 46% had none. Among the reactors, 27% displayed reaction to one, 19% to two, 5% to three, and 3% to four substances. Overall, 92 positive reactions were demonstrated to allergens. The most common reactions were to nickel sulfate and potassium dichromate (Table 2).

Distribution of positive reactions to allergen according to sex is demonstrated in Table 2. The prevalence of allergy to potassium dichromate and thiuram mix was higher in men and allergy to nickel sulfate was significantly higher in women (P<0.001). In age group analysis, potassium dichromate was found to be significantly more prevalent in patients aged 15-35 years. Considering the localization of dermatitis, a significant relevancy was found between hand involvement and positive reactions to potassium dichromate (P<0.001), thiuram mix (P=0.002), and nickel sulfate (P=0.035). Regarding the relevancy of positive reactions, 60 cases (65%) of positive reactions were found to be relevant to present or past skin disease, most commonly with thiuram mix (81.8%), potassium dichromate (80%), nickel sulfate (68%), para-phenylenediamine (66%), cobalt chloride (60%), and P-TBPF (60%). During this study, only one case of angry back occurred following patch testing whose provocative agent was thiuram mix, and remitted after topical corticosteroid use.

DISCUSSION

Allergic contact dermatitis is a hypersensitivity reaction to an exogenous agent occurring after contact with allergen substance. History and physical examination, although of remarkable importance, are inconclusive in definitive diagnosis because of the diversity of allergens in the environment 2. So far, patch test is known to be the most reliable test to diagnose allergic contact dermatitis and identify its etiologic agent 3. Previous studies have clarified that early diagnosis of allergic contact dermatitis by patch test would lead to a better quality of life, increased treatment responsiveness, and lowered treatment expenses. Moreover, identifying the etiologic agent and avoiding it, might prevent progression toward chronic non-remittable stages of the disease 8. We found ten previous studies in Iran which were similar to our study. Their findings are shown in Table 3 along with the data of the current survey.

Considering the site of involvement, the hands

<table>
<thead>
<tr>
<th>Index</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M (Male)</td>
<td>55 (55%)</td>
</tr>
<tr>
<td>O (Occupation)</td>
<td>35 (35%)</td>
</tr>
<tr>
<td>A (Atopic dermatitis)</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>H (Hand involvement)</td>
<td>59 (59%)</td>
</tr>
<tr>
<td>L (Leg involvement)</td>
<td>35 (35%)</td>
</tr>
<tr>
<td>F (Face involvement)</td>
<td>27 (27%)</td>
</tr>
<tr>
<td>A (Age&gt;40)</td>
<td>28 (28%)</td>
</tr>
</tbody>
</table>

Table 1. Demographic characteristics of the patients according to the MOHLFA index

<table>
<thead>
<tr>
<th>Allergens</th>
<th>Patients with positive reactions n (%)</th>
<th>Men n (% for each allergen)</th>
<th>Women n (% for each allergen)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium dichromate</td>
<td>25 (25%)</td>
<td>24 (96%)</td>
<td>1 (4%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Thiuram mix</td>
<td>11 (11%)</td>
<td>11 (100%)</td>
<td>0 (0%)</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Fragrance II</td>
<td>3 (3%)</td>
<td>2 (66.7%)</td>
<td>1 (33.3%)</td>
<td>P=1.00</td>
</tr>
<tr>
<td>Cobalt chloride</td>
<td>15 (15%)</td>
<td>8 (53.3%)</td>
<td>7 (46.7%)</td>
<td>P=1.00</td>
</tr>
<tr>
<td>Para-phenylenediamine free base</td>
<td>3 (3%)</td>
<td>3 (100%)</td>
<td>0 (0%)</td>
<td>P=0.25</td>
</tr>
<tr>
<td>Colophonhy</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
<td>P=0.45</td>
</tr>
<tr>
<td>Wool alcohols</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
<td>P=0.45</td>
</tr>
<tr>
<td>Mercapto mix</td>
<td>1 (1%)</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
<td>P=1.00</td>
</tr>
<tr>
<td>Budesonide</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
<td>P=0.45</td>
</tr>
<tr>
<td>Para tertiary butylphenol formaldehyde resin</td>
<td>5 (5%)</td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>P=0.17</td>
</tr>
<tr>
<td>Nickel sulphate</td>
<td>25 (25%)</td>
<td>4 (16%)</td>
<td>21 (84%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Sequiterpene lactone mix</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
<td>P=0.45</td>
</tr>
</tbody>
</table>

P values of <0.05 were considered statistically significant.
Table 3. Significant features of patch test studies conducted in Iran.

<table>
<thead>
<tr>
<th>Study</th>
<th>Region (city)</th>
<th>Number of patients</th>
<th>Diagnosis</th>
<th>Age (Mean ± SD) (years)</th>
<th>Female/Male ratio</th>
<th>Patch test allergens (Number of substances)</th>
<th>Positive reaction (%)</th>
<th>Number of positive allergens</th>
<th>The most common allergens (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taheri et al</td>
<td>Mashhad</td>
<td>100</td>
<td>ACD</td>
<td>33.97±12.44</td>
<td>0.82</td>
<td>European standard series (28)</td>
<td>54</td>
<td>12</td>
<td>Nickel sulfate and potassium dichromate (25)</td>
</tr>
<tr>
<td>Nasiri et al</td>
<td>Tehran</td>
<td>223</td>
<td>ACD or AD</td>
<td>31±12</td>
<td>NA</td>
<td>European standard series (24)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Golchi et al</td>
<td>Rasht</td>
<td>100</td>
<td>CD or AD</td>
<td>30.67±10.85</td>
<td>2.85</td>
<td>European standard series (24)</td>
<td>36</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Davoodi et al</td>
<td>Tehran</td>
<td>222</td>
<td>CD or AD</td>
<td>33.5±13.8</td>
<td>1.99</td>
<td>European standard series (24)</td>
<td>65.3</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Shamsadini et al</td>
<td>Kerman</td>
<td>125</td>
<td>CD or AD</td>
<td>NA</td>
<td>1.23</td>
<td>European standard series (24)</td>
<td>52.8</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Firooz et al</td>
<td>Kerman Rasht</td>
<td>401</td>
<td>CD or AD</td>
<td>31.06±11.56</td>
<td>1.50</td>
<td>European standard series (24)</td>
<td>43.8</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Niforoosh zadeh et al</td>
<td>Ahvaz</td>
<td>100</td>
<td>HD</td>
<td>30.8±11.8</td>
<td>NA</td>
<td>European standard series (28)</td>
<td>32</td>
<td>13</td>
<td>Nickel sulfate (13.5)</td>
</tr>
<tr>
<td>Toosi et al</td>
<td>Kerman</td>
<td>100</td>
<td>CD or AD</td>
<td>32.7±13.1</td>
<td>2.22</td>
<td>European standard series (23)</td>
<td>86</td>
<td>24</td>
<td>Nickel sulfate (20)</td>
</tr>
<tr>
<td>Kashani et al</td>
<td>Esfahan</td>
<td>250</td>
<td>CD or AD</td>
<td>31.5±12.6</td>
<td>3.16</td>
<td>Allergen screening series (DKG) (28)</td>
<td>50.4</td>
<td>5</td>
<td>Fragrance mix I (27.5)</td>
</tr>
<tr>
<td>Firooz et al</td>
<td>Tehran</td>
<td>1137</td>
<td>HD</td>
<td>31.5±12.6</td>
<td>2</td>
<td>Nickel sulfate, potassium dichromate, Cobalt chloride</td>
<td>7.2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Khatami et al</td>
<td>Tehran</td>
<td>1137</td>
<td>HD</td>
<td>31.5±12.6</td>
<td>2</td>
<td></td>
<td>27.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACD: Allergic contact dermatitis, AD: Atopic dermatitis, CD: Contact dermatitis, OD: Other dermatitis, NA: Non applicable
have been found to be the most commonly involved site in the current (59%) and other Iranian studies 2,6,17. This finding has been consistent with the results of studies from other parts of the world 18,19. In a cross-sectional study by Mortz et al. in Denmark, a statistically significant relationship was found between allergic contact dermatitis and hand eczema 20.

In the current study, 54 patients (54%) showed at least one positive reaction. Different studies conducted in Iran have reported different percentages ranging from 32 to 86%. The percentage was reported 43.5% in a study by Lazarov et al. from Israel 4, 69.3% in a study performed by Wetter et al. from US 21, 51.16% in a study conducted by Akasya –Hillenbrand from Turkey 22, 59.7% in an investigation conducted by Wongiyabovorn et al. from Thailand 3, 63.5% in a study by Machovcova et al. from Czech Republic 5, and 57% in a study by Marks et al. from North America 23. At least one positive reaction was found in 50 to 92.5% of the studies 24.

In our study and a study conducted by Shamseddini et al. from Iran 11, women showed significantly higher rates of nickel sensitivity. Holness et al. mentioned a tendency toward equality of sex prevalence in more recent years, probably related to the public trends of body piercing in both sexes 25. In the current study, a significantly different prevalence was observed between men and women in this regard due to the low prevalence of body piercing in Iranian men. On the other hand, in our study and the study performed by Shamseddini from Iran, dichromate potassium sensitivity was reported more commonly in men, which is probably due to their occupational exposure. In this study, nickel sensitivity was found to be significantly different between the age groups (p=0.011), and the highest prevalence was reported in the age group of 15-35 years (16 cases, 64%). Similarly, Firooz et al. reported a significant relationship between nickel sensitivity and age younger than 40 years 12.

In our study, nickel sulfate and potassium dichromate, each positive in 25 (25%) cases, were identified as the most common allergens. Similar results reported in another study by Nilforoushzadeh et al. in Iran 13, whereas nickel sulfate has been identified as the most common allergen followed by potassium dichromate in other studies from Iran and many other countries 3,5,22. On the other hand, in a study from India, potassium dichromate was the most common allergen (26%) followed by nickel sulfate (18%), which was attributed to the presence of potassium dichromate in detergents and cement 24. In addition, Boonchai et al. from Thailand reported potassium dichromate (27%) and nickel sulfate (26.6%) as the two most common allergens and concluded that the prevalence of allergens varied in different geographical locations 26. The relatively higher percentage of potassium dichromate sensitivity in our study can be explained by this varied prevalence and the higher number of construction workers (33%) in our study, which was the most common occupation in our patients. These patients showed a high rate of potassium dichromate sensitivity (61%) since they are in close contact with cement and tile.

In our study, other substances causing positive reaction were cobalt chloride, thiuram mix, P-TBPF, fragrance mix, para-phenylenediamine, colophony, wood alcohol, mercapto mix, budesonide, and sequiterpene lactone mix. Of special note is the lower reported prevalence of sensitivity to fragrance mix in the current study (3%) when compared to other similar studies. Davoodi et al. reported a prevalence of 13.6% in Iran 10, Lazarov et al. reported a prevalence of 7.1% in Israel 4, Wongpiyabovorn et al. reported a prevalence of 14.3% in Thailand 3, and Kuljanac et al. reported a prevalence of 9.4% in Croatia 27. The difference can be explained by the less use of perfume and cosmetics in patients visiting our clinic.

With respect to relevancy, in this study, 60 positive reactions (65%) were considered relevant to dermatitis in the patients with thiuram mix being the most commonly relevant allergen (81.8%), which is similar to the results of a study performed by Marks et al. from America (84% relevant) 23. In this study potassium dichromate (80%), nickel sulfate (68%), para-phenylenediamine (66%), cobalt chloride (60%) and P-TBPF (60%) were found to be clinically relevant to the disease course while the rest of the allergens were not. However, Marks et al. reported a range of relevancy from 45% (thimerosal) to 84% (thiuram mix) 23. The differences may be related to the higher number of patients in the study performed by Marks (3549) than our study (100). Akasya-Hillenbrand et al.
reported a relevancy of 96.2% for carbamix, 95.2% for thiuram mix, 78.1% for potassium dichromate, and 37.5% for nickel 22.

With respect to the studies conducted in Iran, nickel sulfate and potassium dichromate are the most common allergens causing allergic contact dermatitis. Comparison of the results of similar studies in Iran shows a considerable overlap between allergens causing positive reactions all around the world that might reflect the usefulness of the standard patch test in different geographical areas. On the other hand, a considerable diversity is evident in the relative frequency of allergens in these studies. Use of a more limited substitute for the standard patch test series in many areas of the world might be a more affordable and cost effective screening measure.

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Patch test in allergic contact dermatitis


