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Published in:
Contact Dermatitis

DOI:
10.1111/cod.14197

Publication date:
2022

Document version:
Final published version

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Citation for published version (APA):

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Download date: 15. Sep. 2023
The benefit of late patch test readings in corticosteroid allergy

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KEYWORDS: allergic contact dermatitis, allergy, contact allergy, corticosteroid, hypersensitivity reactions, patch test, skin testing

Allergic contact dermatitis (ACD) to corticosteroids remains a diagnostic and therapeutic challenge for the clinicians. Patch testing is the golden diagnostic standard, which is recommended to be read twice, on day (D) 2, D3, or D4 and D7, although some skip the late reading. Previous studies suggest late reading of corticosteroids, but further data are needed. This retrospective study aims to investigate the benefit of day 7 readings.

1 | METHODS

We conducted a retrospective study of patients patch tested with corticosteroid allergens between January 1992 and December 2020 at the Department of Dermatology and Allergy Centre, Odense University Hospital, Denmark.

The patients were tested with TRUE Test® (SmartPractice® A/S, Hillerød, Denmark) and/or corticosteroid allergens in petrolatum or ethanol. In case of multiple patch tests, the last result was included. Patch tests were performed according to ESCD recommendations, with readings on D3/D4 and D7. Reactions designated as either +, ++ or +++ were positives. Follicular (F) and doubtful reactions (+) were registered and classified as negatives.

We defined “early” positive reactions as D3/4+, negative as D7- and “delayed” positive reactions as D3/4+ and D7 .

The Allergen database (journal no. 21/14482) and project (journal no. 21/27686) were approved by the Danish Data Protection Agency.

2 | RESULTS

A total of 10,746 patients were patch tested with corticosteroid allergens, with a total of 505 positive reactions in 201 patients (1.9%) (Table 1).

In total, 53.7% (271/505) were positive reactions on D3/4 and D7. We found 28.1% delayed positive patch test reactions (142/505) of which 26.1% (37) were evaluated doubtful at D3/4. The delayed positives showed primarily weak positive reactions (22.5%). In total, 18.2% (92/505) showed early positive reactions.

Looking at the TRUE Test® corticosteroids, 7% of sensitized to TRUE Test® corticosteroids were early positive. However, 21.8% of tixocortol-21-pivalate, 33.3% of budesonide and 38.5% of hydrocortisone-17-butyrate reactions were first registered on D7. The same pattern was found for tixocortol-21-pivalate and budesonide in petrolatum and hydrocortisone-17-butyrate in ethanol.

3 | DISCUSSION

A total of 28.1% of positive corticosteroids contact sensitizations would have been missed if only an early reading was performed. About 18.2% of sensitized were only found at D3/4 readings while 53.7% were found positive at both early and late readings.

Previous data on late reading of corticosteroid patch test are conflicting. In line with our results one study found 28.4% of corticosteroid sensitized were new D7 positives also in concordance with previous studies. However, very low number or even no new delayed positive reactions to corticosteroids have been reported from other clinics. Corticosteroids possess dual effects by allergenic and intrinsic immunological properties. The diagnostic patch test reading is challenged by non-allergic erythema due to locally induced vasoconstriction causing blanching and secondary vasodilatation as a steroid effect as well as the morphological “edge-effect” due to central relatively high concentration of corticosteroids inducing predominantly anti-inflammatory effect and peripheral allergic cutaneous manifestation. Variation in patch test...


<table>
<thead>
<tr>
<th>Allergen</th>
<th>Concentration</th>
<th>Reaction strength (n)</th>
<th>% of positive reactions</th>
<th>Early positives (D3/D4)</th>
<th>Total positives on D3/D4 or D7</th>
<th>Total positives on D3/D4 and D7</th>
<th>% of positive reactions</th>
<th>Delayed positives (D7)</th>
<th>% of positive reactions</th>
<th>Total</th>
<th>Reaction strength on D3/D4 (n)</th>
<th>Reaction strength on D7 (n)</th>
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<tbody>
<tr>
<td>TRUE Test® corticosteroid allergens (μg/cm²)</td>
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<td></td>
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<tr>
<td>Budesonide</td>
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<td>81</td>
<td>48</td>
<td>6</td>
<td>7.4</td>
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<td>33.3</td>
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<td>40</td>
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<td>7</td>
<td>7</td>
<td>17</td>
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<td>11</td>
<td>25.6</td>
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<td>1</td>
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<td>100</td>
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<tr>
<td>All corticosteroid allergens</td>
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<td>505</td>
<td>271</td>
<td>92</td>
<td>18.2%</td>
<td>“++: 62; “+++: 25; “++++: 5</td>
<td>142</td>
<td>28.1%</td>
<td>58</td>
<td>47</td>
<td>37</td>
<td>103</td>
</tr>
</tbody>
</table>

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*In ethanol.

*budesonide 0.1%, tixocortol-21-pivalate 1%, hydrocortisone 1%.
concentrations, materials, and diagnostic reading techniques might also explain the conflicting results.

This was a large retrospective study. One limitation was that patients being tested with corticosteroid in petrolatum/ethanol were suspected to have ACD to corticosteroids, thus risk of over-estimation of erythematous reactions, whereas TRUE Test corticosteroids were used as part of the baseline series in all patch tested patients including those without clinical suspicion of ACD to corticosteroids. We have no information on local treatment of strong reactions on D3/4, which could modify the result on D7.

Corticosteroid sensitization appears in about 2.7% of consecutively tested patients. This study emphasizes the importance of late patch test reading of corticosteroids in order to diagnose ACD to corticosteroids.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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How to cite this article: Svendsen SV, Mortz CG. The benefit of late patch test readings in corticosteroid allergy. Contact Dermatitis. 2022;1-3. doi:10.1111/cod.14197