Isotretinoin in Severe Peanut- and Soy-Allergic Patients: Is it Safe or Not?

Denorme P*, Schrijvers R2*, Van Hoeyveld E1, Verfaillie S3, Bullens D2*, Morren MA1, Breynaert C2,3

1University Hospitals Leuven, Department of Dermatology, Leuven, Belgium
2KU Leuven Department of Microbiology, Immunology and Transplantation, Allergy and Clinical Immunology Research Group, Leuven, Belgium
3University Hospitals Leuven, Department of General Internal Medicine, Allergy and Clinical Immunology, Leuven, Belgium.


Isotretinoin is contraindicated in patients with peanut allergy, soy allergy, or both. We present a case of successful oral challenge with isotretinoin in a patient with both primary peanut and soy allergy and suggest a stepwise work-up.

A 25-year-old man with severe acne and a history of allergic asthma, rhinoconjunctivitis, and allergic reactions to peanut in childhood was referred to the allergy department by his dermatologist to evaluate the safety of isotretinoin. The prescribing information leaflet states that isotretinoin is contraindicated in patients with known soybean or peanut allergy, owing to the risk of potential cross-reactivity. All oral isotretinoin formulations in Belgium contain soybean oil. However, data about the safety of isotretinoin in patients with potential severe peanut and/or soybean allergy are scarce [1-4].

The patient had avoided peanuts and soybean products since childhood because of several allergic reactions involving facial swelling, itching, and dyspnea immediately after eating peanuts or food containing peanut or peanut oil. He had never experienced reactions to soy, although a careful dietary history suggested absence of exposure to soy-containing food. An allergy work-up was performed. Skin prick tests (SPTs) were positive for peanut extract (4+) and soy milk (4+). Specific IgE (sIgE, ImmunoCAP ThermoFisher/Phadia) to the crude extract of peanut and the stable 2S-albumin seed storage protein of Ara h 2, which is associated with systemic reactions to peanut [5], was >100 kU/L in both cases. sIgE for the other seed storage proteins of peanut (Ara h 1 and Ara h 3) was also detected (respectively >100 kU/L and 36.30 kU/L), with no relevant sensitization to Bet v 1 or lipid...
transfer protein (Ara h 8 and Ara h 9, respectively, 0.12 kU/L and 0.16 kU/L). sIgE for the crude extract of soy, the stable seed storage proteins of soy (Gly m 5 and Gly m 6, which are associated with severe allergic reactions [6]), and the Bet v 1–cross-reactive allergen Gly m 4, were respectively 6.82 kU/L, 12.70 kU/L, and <0.10 kU/L (normal <0.10 kU/L); total IgE was 915 kU/L. SPTs with the capsule and content of 3 isotretinoin-containing products available in Belgium (Isosupra, Isotretinoine EG, and Roaccutane), all containing soybean oil, were negative. A subsequent open oral challenge with Isotretinoine EG (0.01-0.1-1-10-20-100%, cumulative dose of 131.11% [13.11 mg]) was negative. Given the oil content of the capsule, we dissolved the drug in hot milk in order to be able to perform an updosing protocol. After this successful challenge, long-term treatment with isotretinoin was successfully initiated.

Peanut and soy are phylogenetically and antigenetically related and share several homologous proteins. Patients with severe peanut allergy are also at risk of developing severe reactions to soy [7]. Soybean oil still contains soy proteins; therefore, isotretinoin, which contains soybean oil, is contraindicated in patients with known soybean or peanut allergy, owing to the risk of potential cross-reactivity. However, it has been demonstrated that the allergenicity of proteins in soybean oil is reduced with regard to soybean allergy [8]. The only case of potential anaphylaxis after a first dose of isotretinoin was reported in a patient with minor sensitization to soybean (Gly m 4 1.38 kUA/L) [9]. However, it remains arguable whether isotretinoin was the culprit of the reaction: the 27-year-old patient, with known cashew nut allergy, developed facial swelling only 12 hours after the first dose of isotretinoin and was able to continue the treatment for 3 days. The authors report successful initiation of treatment with isotretinoin in 4 patients with negative SPT and sIgE results for soybean.

Only 3 cases of successful oral provocation with isotretinoin in peanut allergic patients have been reported, and low sIgE results for soybean (0.39 kU/L) was detected in only 1 case, although the patient did not report allergic reactions to soy and was not avoiding soy in his diet (Table) [1-3]. Spierings et al [4] report the successful introduction of isotretinoin in 6 patients with known severe peanut allergy, although they do not report the results of component-specific IgE [4]. Challenge testing in the hospital yielded negative results.

We present an oral challenge strategy for isotretinoin based on increasing doses that is feasible in high-risk patients with severe soybean allergy, peanut allergy, or both. The summary of product characteristics states that oral isotretinoin is contraindicated in patients with known soybean or peanut allergy. Therefore, we suggest, as do other authors, that there is probably only a theoretical risk for allergic reactions to isotretinoin, even in patients with severe primary peanut and/or soybean allergy [10].

Based on our results and previous case reports, we suggest the following steps before initiation of isotretinoin in patients with potential soybean and/or peanut allergy:

1. Establish a correct diagnosis of soybean and/or peanut allergy.
2. In the case of Bet v 1–associated soybean and/or peanut allergy, isotretinoin can be started safely at home without precautions.
3. In the case of (severe) primary soybean and/or peanut allergy, depending on the potential risk and need for the regimen, a first intake under medical supervision can be performed with a 1-hour observation period. In high-risk patients and children, oral challenge with isotretinoin dissolved in hot milk can be performed in a hospital setting, as described in the present case.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentations

These data were presented at a National Meeting of the Belgian Society of Allergy and Clinical Immunology on November 25th, 2017.

Table. Published Cases of Oral Provocation With Isotretinoin in Patients With Soybean and/or Peanut Allergy

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin prick testing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPT peanut</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>SPT soy</td>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>SPT isotretinoin</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Specific IgE (ImmunoCAP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total IgE (kU/L)</td>
<td>959</td>
<td>817</td>
<td>4229</td>
</tr>
<tr>
<td>Peanut (kU/L)</td>
<td>3.93</td>
<td>NR</td>
<td>35.7</td>
</tr>
<tr>
<td>Ara h 2 (kU/L)</td>
<td>0.72</td>
<td>4.12</td>
<td>7.97</td>
</tr>
<tr>
<td>Ara h 8 (kU/L)</td>
<td>NR</td>
<td>9.74</td>
<td>3.72</td>
</tr>
<tr>
<td>Soy (kU/L)</td>
<td>&lt;0.35</td>
<td>NR</td>
<td>0.39</td>
</tr>
<tr>
<td>Gly m 5 (kU/L)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gly m 6 (kU/L)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Oral challenge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Abbreviations. NR, not reported; SPT, skin prick test.

References

Allergens Are Not Detected in the Bronchoalveolar Lavage Fluid of Patients Undergoing Fiberoptic Bronchoscopy

Rueda M1, López-Matas MA2, Agustí C3, Lucena C3, Carnés J2, Valero A3,4
1 Allergology Service, Hospital Quirónsalud, Barcelona, Spain
2 R&D Department, Laboratorios LETI S.L.U., Tres Cantos, Madrid, Spain
3 Neumology and Allergy Service, Hospital Clinic, Barcelona, Spain
4 Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Centro de Investigaciones Biomédicas en Red de Enfermedades Respiratorias (CIBERES), Barcelona, Spain

doi: 10.18176/jiaci.0353

Key words: Bronchoalveolar lavage. Allergen. Mass spectrometry. Monoclonal Antibodies. Small airway.


Allergen sources range in size from 0.28 to 0.40 mm for mites, 2 to 500 µm for molds, and 2 to 200 μm for pollens. Early studies suggested that given their large size, aeroallergenic sources were unable to reach the lower airways [1]. The nose filtering system retains particles larger than 10 μm, and only fine or ultrafine particles reach distal bronchioles (diameter 1-5 µm) [2,3]. However, it has been demonstrated that grass pollen allergens are released as breathable aerosols, the atmosphere contains allergen-carrying, plant-derived, paucimicronic particles (2-5 µm) [4], and small spores and fragments of mold spores can reach the lower airways [5].

Ferguson et al [6] identified the major allergen from Dermatophagoides pteronyssinus (Der p 1) in the small airways of allergic patients. The authors assessed the link between environmental exposure to mites and the presence of the allergen in bronchoalveolar lavage (BAL) fluid in 9 patients sensitized to D pteronyssinus.

Horvath et al [7] studied deposition of inhaled pollens in the airway using computer simulation. Their results suggested that pollen particles (0.5-20 μm) may deposit more efficiently in the asthmatic lung than in the healthy lung, especially in the bronchial region.

The aim of our study was to examine the possible presence of major allergens from mites, pollen, and molds in BAL fluid collected from patients undergoing fiberoptic bronchoscopy.

We performed an observational descriptive study. BAL samples were obtained from patients undergoing fiberoptic bronchoscopy (hospitalized and outpatients) over 1 year. Indications for fiberoptic bronchoscopy included hemoptysis, chronic cough, and upper airway assessment. Patients with...