OCCUPATIONAL AIRBORNE CONTACT DERMATITIS FROM PROTON PUMP INHIBITORS

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ABSTRACT
Proton Pump Inhibitors (PPI) are members of the benzimidazole family, and are commonly used in the treatment of acid-related disorders such as gastroesophageal reflux disease, peptic ulcer disease, associated Helicobacter pylori infection and Zollinger-Ellison syndrome, as they are potent inhibitors of gastric acid secretion. We report three cases of occupational airborne contact dermatitis from proton pump inhibitors (lansoprazole, omeprazole and pantoprazole) among workers in the pharmaceutical industry.

INTRODUCTION
Occupational exposure to active pharmaceutical ingredients can cause adverse health effects. Depending on the type of product and exposure, several occupational dermatoses have been described among workers in the pharmaceutical industry, including irritation, contact allergy, photosensitivity, urticaria, acne venerate, and less frequently, fixed drug eruptions, steroid-induced rosacea, and even toxic epidermal necrolysis.

Contact dermatitis from exposure to Proton Pump Inhibitors (PPI), such as lansoprazole, omeprazole and pantoprazole are quite uncommon. We report three cases of occupational airborne contact dermatitis from PPI.

Case Reports
The three cases correspond to male workers in the pharmaceutical industry between the ages of 33 and 49 and an exposure time ranging from 7 to 21 years. The time between the onset of clinical manifestations and diagnosis ranged was between 1 and 9 months. None of the workers had a prior history of atopy. Two were production workers and the other a maintenance worker. The clinical signs and symptoms would appear when they were in contact with PPI, and would decrease or disappear when not exposed to PPI.

Clinical manifestations in the production workers consisted of rashes involving the face, neck, and upper extremities. The maintenance worker presented with a facial rash and swelling of the eyelids.

All three cases responded to symptomatic treatment with oral corticosteroids. The main clinical features of the three patients are described in Table I (see next page), including sex, age, duration of exposure prior to clinical manifestation, work activity, offending drugs and clinical effects.

Both skin prick and patch testing were performed. Prick tests were performed at sub-irritant concentrations: lansoprazole (15 mg/1 ml of saline solution), omeprazole (40 mg/ml) and pantoprazole (20 mg/ml). Patch testing was done with Grupo Español Investigación Dermatitis de Contacto (GEIDC) standard series: lansoprazole (10%, 50%), omeprazole (0.1%, 0.5%, 1%) and pantoprazole (1%, 5%, 10%), all in saline solution. Results were read at 48 hours (D2) and 96 hours (D4) are described in Table II (see next page).

Prick tests and patch tests gave negative results in all 10 healthy controls. In all three cases, the prick test results were negative. Patch testing results were positive in one case for lansoprazole, other case for pantoprazole, the last...
case for lansoprazole, omeprazole and pantoprazole. They are described in Table II.

**DISCUSSION**

PPI are members of the benzimidazole family, and are commonly used in the treatment of acid-related disorders such as gastroesophageal reflux disease, peptic ulcer disease, associated *Helicobacter pylori* infection and Zollinger-Ellison syndrome, as they are potent inhibitors of gastric acid secretion.8

There are very few cases described of airborne occupational contact dermatitis from occupational exposure to PPI. In the case of omeprazole, Meding, 1986,4 reported the first two cases, Conde-Salazar et al, 20075 added two others, and Sanz-Gallen et al 2011 provided a fifth new case.6 Only one case each has been described in association with exposure to lansoprazole7 and pantoprazole.7

The addition of these three cases, one for each of these commonly used PPI, is important because it underscores their sensitising potential, which should be considered when describing the adverse effects of active pharmaceutical ingredients.9

**ACKNOWLEDGEMENTS**

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**Table I: Main features of the three cases of occupational airborne contact dermatitis caused by proton pump inhibitors**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Workplace exposure (years)</th>
<th>Job</th>
<th>Offending drug</th>
<th>Clinical effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Male</td>
<td>33</td>
<td>7</td>
<td>Production worker</td>
<td>Pantoprazole</td>
<td>Rash involving face, neck and hands</td>
</tr>
<tr>
<td>Case 2</td>
<td>Male</td>
<td>41</td>
<td>7</td>
<td>Maintenance worker</td>
<td>Lansoprazole</td>
<td>Rash in face, eyelid oedema</td>
</tr>
<tr>
<td>Case 3</td>
<td>Male</td>
<td>49</td>
<td>21</td>
<td>Production worker</td>
<td>Lansoprazole, Omeprazole and Pantoprazole</td>
<td>Rash involving face, neck and arms</td>
</tr>
</tbody>
</table>

**Table II: Patch testing results**

<table>
<thead>
<tr>
<th>Patch testing results</th>
<th>Case 1 (D2)</th>
<th>Case 1 (D4)</th>
<th>Case 2 (D2)</th>
<th>Case 2 (D4)</th>
<th>Case 3 (D2)</th>
<th>Case 3 (D4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (0.1%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Omeprazole (0.5%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Omeprazole (1%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lansoprazole (10%)</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Lansoprazole (50%)</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Pantoprazole (1%)</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Pantoprazole (5%)</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Pantoprazole (10%)</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>GEIDC standards series (*) patch</td>
<td>Nickel+++</td>
<td>Nickel+++</td>
<td>Cobalt+</td>
<td>Cobalt+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

(*) Sensitisation to cobalt, mercury and nickel were detected in cases 1 and 2, but not related to work activity. The slight positivity of mercury in cases 1 and 2 was probably caused by the extensive use of mercury and its compounds, such as antiseptic in topical medicines (mercurochrome, thimerosal), dental amalgam and preservative in cosmetics and shampoos.
REFERENCES

abstract winners

Dear colleagues,

Please join me in congratulating Roslynn on being awarded the best oral poster in the Occupational Allergy/Asthma section of the European Academy of Allergy and Clinical Immunology held in Copenhagen, Denmark 7-11 June 2014.

The poster was entitled: EXPOSURE-RESPONSE RELATIONSHIPS FOR WHEAT ALLERGEN EXPOSURE AND ASTHMA
Authors: Baatjies R, Meijster T, Heederik D, Jeebhay MF

Well done Roslynn Baatjies!

Prof Mohamed Jeebhay
Department of Occupational Medicine
UCT

Congratulations!