Maternal Prenatal Use of Reflux Medication and the Development of Food Protein-Induced Allergic Proctocolitis in Offspring

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Abstract

Rationale: Recent studies have linked exposure to prenatal acid suppressive medications with the development of allergic diseases early in life, but associations with food-protein-induced allergic proctocolitis (FPIAP) have not been well-studied. We hoped to evaluate the association between FPIAP and prenatal exposure to acid suppressive medication.

Methods: The Gastrointestinal Microbiome and Allergic Proctocolitis (GMAP) Study is an ongoing prospective observational cohort study of 1003 healthy newborn infants enrolled at their first well visit. Mothers disclosed whether they took acid suppressive medications during pregnancy in a comprehensive initial visit questionnaire administered at study enrolment and prior to the development of FPIAP. The diagnosis of FPIAP was made by the treating pediatrician. Investigators reviewed each case to confirm prespecified inclusion criteria, including documented gross or occult blood in the stool. Associations were tested using univariable and multivariable logistic regression.

Results: Of 903 infants that were analyzed, 153 (17%) were identified as cases. 67 mothers (7%) took a histamine-2 receptor antagonist and 113 mothers (13%) took a calcium carbonate antacid during pregnancy. FPIAP was associated with prenatal exposure to calcium carbonate antacids (OR 2.56, 95%CI [1.64, 3.98], p<.001) but not associated with prenatal exposure to a H2 blocker (OR 1.60, 95%CI [.89, 2.89], p=.12). This association between prenatal calcium carbonate antacid exposure and FPIAP remained significant after adjusting for sex, race, maternal proton pump inhibitor and H2 blocker use, and relevant family history. Results also remained significant using a stricter FPIAP diagnosis criteria requiring gross blood or mucus in stool.

Conclusion: We found a novel association between prenatal exposure to calcium carbonate antacids and FPIAP development in offspring. More research should be conducted to explore this potential association.

Key Findings

- Prenatal calcium carbonate antacid but not H2 blocker use significantly associated with FPIAP development
- No association between prenatal reflux medication and IgE-mediated food allergy
- Further study needed to better understand the relationship between prenatal reflux medication and FPIAP development

Table 1. GMAP Study Population Demographics

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Median Age (months)</th>
<th>17 Weeks</th>
<th>30 Weeks</th>
<th>40 Weeks</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants with FPIAP (n=153)</td>
<td>153</td>
<td>36 (30-43)</td>
<td>15 (12-19)</td>
<td>17 (13-19)</td>
<td>17 (13-19)</td>
<td>1.60 (1.16-2.16)</td>
</tr>
<tr>
<td>Infants without FPIAP (n=350)</td>
<td>350</td>
<td>36 (30-43)</td>
<td>15 (12-19)</td>
<td>17 (13-19)</td>
<td>17 (13-19)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
</tbody>
</table>

* Significant difference (p value < .05)

Table 2. Associations Between Prenatal Reflux Medication and Food Allergic Manifestations

<table>
<thead>
<tr>
<th>Medication</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Carbonate Antacid</td>
<td>2.56</td>
<td>1.64-3.98</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>H2 Receptor Antagonist</td>
<td>1.60</td>
<td>.89-2.89</td>
<td>.12</td>
</tr>
</tbody>
</table>

*The asterisk refers to P value < .05 calculated with binomial logistic regression.

Figure 1. GMAP Study Consort Diagram

Figure 2. Association between FPIAP Development and Prenatal Reflux Medication

References

Martin et al, JACI: In Practice, 2020

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