Delayed Anaphylaxis to Baked Egg and Baked Milk Oral Food Challenges

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Background
Oral food challenges (OFCs) to baked egg (BE) and baked milk (BM) are frequently performed in clinical practice. Previous studies reported anaphylaxis frequencies ranging from 14-35% of BE/BM OFCs which elicited objective reactions, with 6-35% of patients experiencing epinephrine. Characteristics of reactions to BE and BM during OFCs compared to other food allergens have not been previously described.

Objective & Methods
Objective: Compare the differences between clinical reactions to BE/BM OFCs, cooked egg (E) fresh cow's milk (M) OFCs, and peanut (P) and tree nut (T) OFCs.
Methods: Retrospective review of OFCs eliciting objective reactions to BE, BM, E, M, P, and TN performed at Nationwide Children’s Hospital between 6/1/2017 and 6/1/2019. P < 0.05 was considered statistically-significant.

Results
Table 1. Demographics

<table>
<thead>
<tr>
<th></th>
<th>BE, BM</th>
<th>E, M</th>
<th>P, TN</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at OFC in months (IQR)</td>
<td>24 (11-149)</td>
<td>38 (8-187)</td>
<td>20 (6-137)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Male</td>
<td>69%</td>
<td>68%</td>
<td>57%</td>
<td>0.24</td>
</tr>
<tr>
<td>Eczema</td>
<td>77%</td>
<td>56%</td>
<td>73%</td>
<td>0.06</td>
</tr>
<tr>
<td>Intermittent asthma</td>
<td>21%</td>
<td>26%</td>
<td>13%</td>
<td>0.23</td>
</tr>
<tr>
<td>Persistent asthma</td>
<td>21%</td>
<td>18%</td>
<td>17%</td>
<td>0.77</td>
</tr>
<tr>
<td>Allergic rhinitis &amp;/or conjunctivitis</td>
<td>8%</td>
<td>18%</td>
<td>28%</td>
<td>0.023*</td>
</tr>
<tr>
<td>Multiple food allergies</td>
<td>77%</td>
<td>62%</td>
<td>48%</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Median skin prick wheel diameter to the OFC food in mm (IQR)</td>
<td>6 (4-20)</td>
<td>4 (0-10)</td>
<td>5 (2-17)</td>
<td>N/A**</td>
</tr>
<tr>
<td>Median % of target dose ingested (IQR)</td>
<td>16.4 (3.1-100)</td>
<td>1.9 (1.7-36.2)</td>
<td>1.5 (0.6-8.1)</td>
<td>N/A**</td>
</tr>
</tbody>
</table>

**Significant difference between BE/BM and P/N/T by Kruskall Wallis and Dunn’s post-hoc test (median age) or Pearson’s chi-squared and Holm-Sidak post-hoc analysis (categorical variable).**

*Significant difference between BE/BM and E/M by Kruskall Wallis and Dunn’s post-hoc test.

Significant pairwise comparisons identified by Dunn’s post-hoc analysis. *p < 0.01.

Fig. 1) Frequency of clinical signs and symptoms elicited during OFCs

Fig. 2) Temporal characteristics of OFCs provoking allergic reactions

Fig. 3) Eliciting and total doses consumed during OFCs

Delayed reactions to BE/BM OFCs were common. 25% of patients who reacted to BE/BM OFCs developed new symptoms ≥60 min. after the end of the challenge, compared to 2.5% of other OFCs (p < 0.01).

Anaphylaxis occurred ≥50 min. after the challenge ended in 5 BE OFCs (9.4%), compared to 1 cooked egg OFC (0.8%, p < 0.01). Challenges were originally terminated for abdominal pain and vomiting.

1 biphasic anaphylactic reaction to BE occurred.

Hypotension (n=4) and hypoxemia (n=2) were observed exclusively during BE/BM OFCs.

No OFCs caused allergic reactions after discharge to home, long-term morbidity, or death.

Summary
Compared to reactions to other foods, allergic reactions to baked egg and baked milk elicited during OFCs were:

- *More likely to cause gastrointestinal symptoms without cutaneous manifestations*
- *Severe*
- *Delayed*

Conclusions
The high incidence of delayed anaphylaxis to BE and BM could be an inherent property of the antigen, related to higher eliciting doses, or secondary to delayed recognition of reactions lacking cutaneous manifestations.

Clinicians may consider these unique characteristics of reactions to baked egg and baked milk when conducting OFCs to optimize safety.

References