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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 receiving epinephrine.¹

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 (PN) and tree nut (TN) OFCs.

Methods: Retrospective review of OFCs eliciting objective reactions to BE, BM, E, M, PN, and TN performed at Nationwide Children's Hospital between 6/1/2017 and 6/1/2019. $p \leq 0.05$ was considered statistically-significant.

Results

37.5% of 163 BE/BM OFCs elicited objective allergic reactions.
88 BE/BM OFCs were tolerated; 23 were inconclusive due to refusal to ingest the target dose.

Table 1. Demographics

	BE, BM n=53	E, M n=39	PN, TN n=82	P Value
Median age at OFC in months (IQR)	24 (11-149)	38 (8-187)	20 (6-137)	0.03*
Male	69%	68%	57%	0.24
Eczema	77%	56%	73%	0.06
Intermittent asthma	21%	26%	13%	0.23
Persistent asthma	21%	18%	17%	0.77
Allergic rhinitis &/or conjunctivitis	8%	18%	28%	0.023*
Multiple food allergies	77%	62%	48%	<0.01*
Median skin prick wheal diameter to the OFC food in mm (IQR)	6 (4-20)	4 (0-10)	5 (2-17)	N/A**
Median sIgE to the OFC food in kU/L (IQR)	16.4 (3.1-100)	1.9 (1.7-36.2)	1.5 (0.6-8.1)	N/A**

*Significant difference between BE/BM and PN/TN by Kruskal-Wallis and Dunn's post-hoc test (median age) or Pearson's chi-squared and Holm Sidak post-hoc analysis (categorical variables).

†Significant difference between BE/BM and E/M by Kruskal-Wallis/ and Dunn's post-hoc test.

**Not compared since interpretation is food-specific and reproducible predictive values for BE/BM are lacking.

Results

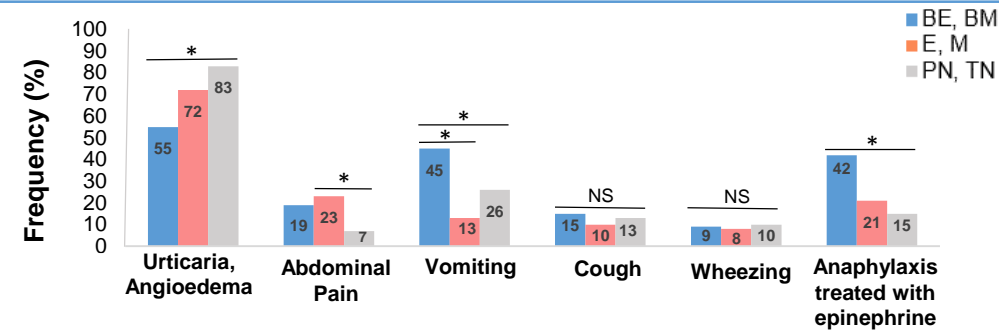


Fig. 1) Frequency of clinical signs and symptoms elicited during OFCs
Evaluated by Pearson's chi-squared test. Significant pairwise comparisons identified by Holm-Sidak post-hoc analysis.
*Adjusted $p < 0.05$ NS: not significant

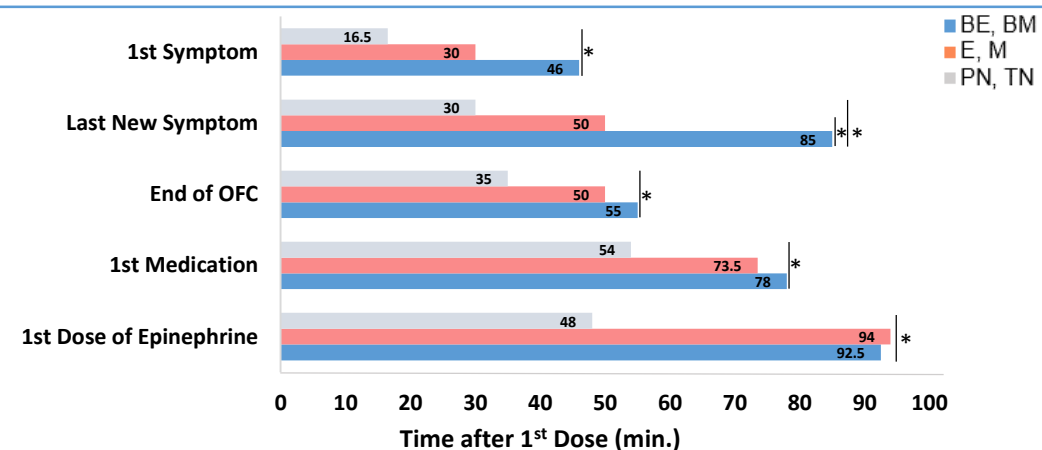


Fig. 2) Temporal characteristics of OFCs provoking allergic reactions
Evaluated by Kruskal Wallis test. Significant pairwise comparisons identified by Dunn's post-hoc analysis.
* $p < 0.01$

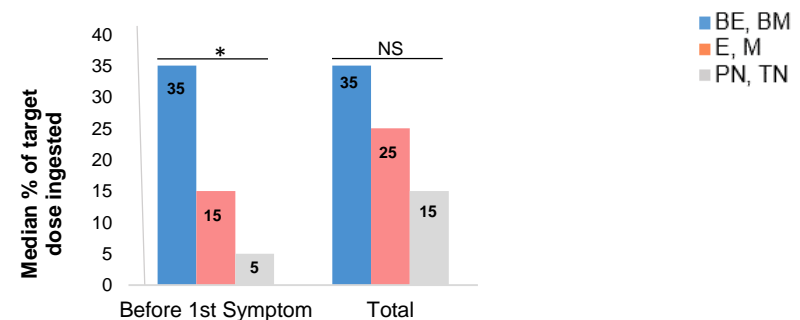


Fig. 3) Eliciting and total doses consumed during OFCs
Evaluated by Kruskal Wallis test. Significant pairwise comparisons identified by Dunn's post-hoc analysis.
* $p < 0.01$ NS: not significant

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 ≥ 60 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

- Leonard SA, Caubet JC, Kim JS, Groetch M, Nowak-Wegrzyn A. Baked milk and egg-containing diet in the management of milk and egg allergies. *J Allergy Clin Immunol Pract* 2015;3(1):13-26.
- Chapman JA, Bernstein L, Lee RE, Oppenheimer J, Nicklas RA, Portnoy JM et al. Food allergy: a practice parameter. *J Allergy Clin Immunol* 2006;96:S1-S68.