

Is There a Safe and Cost-Effective Method for Early Egg Introduction?

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Practice Options from Beyond Our Pages focuses on identifying, critiquing, and placing into context research studies published in other journals that have the potential to change our clinical practices. It is written by Allergy-Immunology Fellows partnered with faculty members, and does not require an invitation for submission. This feature is coordinated by Editorial Board members Matthew Rank, MD and Julie Wang, MD.

REFERENCE

Shaker M, Verma K, Greenhawt M. The health and economic outcomes of early egg introduction strategies. *Allergy* 2018;73:2214-23.

BACKGROUND

Although early introduction of allergenic foods in order to prevent allergy is convincing for peanut, the data for egg are less so. In the United States, there are currently no recommendations for early egg introduction (EEI). United Kingdom and Australia have published recommendations about introducing cooked egg around 6 months without any testing regardless of the infant's atopy.¹⁻³ This study aimed to quantify health care utility and resultant costs associated with different egg introduction strategies in US infants with early-onset eczema.

METHODS

Shaker et al devise a model using a computer-based mathematical simulation and Markov modeling while taking into account the probabilistic risk of egg reactions and/or tolerance. In summary, a user inputs information on types of patients, sets the time advance, and the probability of transitioning from one health state to the next.⁴

Here they applied different data to the total number of US infants from the 2016 census estimated to have eczema at 5 months of age. The egg introduction strategies analyzed in this study are: (1) EEI of baked egg at 6 months without screening; (2) skin prick test (SPT) screening by an allergist before egg introduction; (3) egg white serum-specific IgE (sIgE) testing only by the primary care doctor (sIgE > 0.35 kU/L was considered egg allergy); and (4) delayed introductions (>12 months old without screening). The outcomes were tracked over a 20-year period and patients could presumably be

either egg tolerant, egg allergic, egg avoidant, egg allergic then tolerant or egg tolerant then allergic.

One of the models used in the simulation was the Japanese prevention of egg allergy in high-risk infants with eczema (PETIT) trial,⁵ which enrolled infants with eczema at 4 to 5 months of age (similar to the Learning Early About Peanut Allergy [LEAP] cohort)⁶ to randomly receive baked egg or placebo to evaluate EEI in at-risk infants. The EEI group received 50 mg of daily baked egg from 6 to 9 months of age; then the dose was increased to 250 mg daily from 9 to 12 months of age. The primary outcome was oral food challenge results to 32 g of baked egg at 12 months of age.

Another input data used in the current study was a prevalence of 24% of positive SPT to egg white based on the Martin et al study.⁷ Additional factors inputted from various studies included the rate of inadvertent egg-allergic reactions, food-allergic fatality, annual tolerance rate, costs of testing, allergy consultation, or epinephrine autoinjector prescriptions. All information was analyzed to assess the overall cost of EEI via multiple interventions and presumed outcomes.

RESULTS

EEI at 6 months without screening was less costly with less egg allergy prevalence than screening or delayed introduction, regardless of atopy history for cooked egg but also for raw egg when the rate of reactions was lowered (otherwise, the preferred method was delayed introduction for raw pasteurized egg) (Table 1). The costliest strategy was screening in the primary care setting using sIgE, which also resulted in the highest egg allergy diagnoses.

Next, a sensitivity analysis showed that for both low and high egg allergy prevalence, a no screening method was less costly. When the probability of an allergic reaction to baked egg exceeded 24.8%, screening, specifically SPT, became the preferred (less costly) method.

CRITICAL APPRAISE

This study brings important information on the topic of egg introduction in US infants with eczema; however, using input data from multiple studies of different cohorts may potentially have limitations that we would like to discuss. Specifically, the PETIT trial⁵ is based in Japan where the prevalence of egg allergy (2.6%) is higher than that in the United States (1.7%)⁸ and might reflect variable nutritional and food introduction habits (eg, baked egg vs raw/slight cooked egg consumption) in Japan

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TABLE I. Sensitivity analysis of cost per child and overall egg allergy rates with different screening methods

Introduction strategy	Cooked egg		Raw egg	
	Percentage egg allergic at 20 y	Incremental cost per subject (\$)	Percentage egg allergic at 20 y	Incremental cost per subject (\$)
EEl; no screening	2.5	557	15.2	3345
EEl if SPT negative	9.5	2791	15.1	4013
Office challenge if SPT positive	9.1	2736	14.7	3959
EEl if sIgE negative	21	4737	25.9	5713
No screening; delayed introduction	12	2645		

EEl, Early egg introduction; SPT, skin prick test.

and the United States, which were not accounted for in the current analysis. In addition, the PETIT trial used very low doses of egg protein that could potentially reflect the desensitization effect rather than prevention.

Secondly, the rate of positive SPT is set up at 24%, and in the original Martin et al study,⁷ this refers to children less than 1 years old with eczema identified as egg sensitized by either positive egg SPT (≥ 2 mm) and/or sIgE ≥ 0.35 kU/L. Therefore, the rate of positive SPT in children with eczema is not known, and it is unclear how this might have affected the interaction with other variables and the overall results.

Another limitation is that to assess the implications of egg allergy screening solely through blood testing, any value of egg white sIgE >0.35 kU/L was considered egg allergy. Not surprisingly, this strategy led to higher rates of egg allergy diagnoses. We do not know if the results would have been different if the commonly accepted egg white sIgE cutoffs to define egg allergy (sIgE ≥ 2 kU/L if <2 years old)⁹ would have been used.

Another important aspect is that delayed introduction was the preferred method for raw egg when the relative egg allergy risk reported in the literature was inputted. However, the fact that the preferred method became early introduction without screening when the allergy risk was decreased shows that more clinical data is needed to comment on the introduction strategies for raw versus cooked egg. The importance of clinical trials in food allergies relies also on the fact that a similar Markov analysis on peanut introduction showed that the most favorable outcome was the early introduction without screening regardless of risk factors¹⁰; nevertheless, this differs from the current guidelines taken from the LEAP study.⁶

RECOMMENDATION

This study attempts to convey through data analysis that EEI at 6 months in US infants with eczema without any prescreening is the method that results in less egg allergy diagnosis prevalence and lower overall health costs. However, with the available

information at this time on EEI and the multitude of variables that are taken into consideration in a Markov analysis, we believe that real-life prospective studies with both raw and cooked egg are necessary before an official recommendation is made. At that time, a cost analysis might be an interesting addition to the available data.

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