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ORIGINAL ARTICLE

Risk of adverse IgE-mediate reaction at the first egg ingestion in children with atopic dermatitis. Results of a case-control study

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Abstract
Background: Studies have reported that children with atopic dermatitis (AD) have a high risk of adverse reactions at first egg ingestion.
Methods: We enrolled 79 children with AD retrospectively and 45 children without AD (control group) prospectively, who had never eaten egg. All children underwent skin prick tests (SPT) with commercial extracts and prick by prick with natural food (raw and boiled egg). Oral food challenge (OFC) was performed in SPT positive patients.
Results: Sixty-six percent (52/79) of AD group and 11% (5/45) of Control group had at least one positive SPT ($p < 0.001$), Relative Risk (RR) = 5.9 and Odds Ratio = 15.4. Of the 46/52 sensitised children in the AD group, 36 children ate egg for the first time in hospital during an OFC and 10 children ate egg at home because of their parents' choice, with 19/46 (41%) resulting in allergic reactions to raw and/or boiled egg. Four/five sensitised children in the control group underwent OFC and three of them (75%) showed an allergic reaction to raw, but not boiled egg. Thirty percent (14/46) of AD group had a systemic reaction vs. 25% (1/4) of Control group.
Conclusion: A child with AD has a RR of sensitisation to egg six times higher than a child without AD, before the first known ingestion. We propose to test sensitisation to egg in every child with AD who has never eaten egg, and to perform OFC in those with positive SPT in hospital setting.

Introduction

Studies have reported that children with atopic dermatitis (AD) have a higher risk of adverse reactions at the first egg ingestion.[1–4] Caffarelli et al.[1] studied 21 infants (19 with AD) affected by IgE-mediated food allergy (FA) and 12 infants (control group) with non IgE-mediated FA. Sixty-two percent of patients in the active group and 8% in the control group had immediate reactions to oral food challenge (OFC) with boiled egg ($p < 0.01$), one patient had anaphylactic shock. Monti et al.[2] enrolled 107 children with AD (66 boys, 41 girls), aged 1–19 months; skin prick test (SPT) resulted positive in 63% of them. The egg OFC was conducted with raw

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egg at age 12–24 months, and resulted positive in 72/107 children (67.3%). Adverse reactions were observed in 48% of children with mild AD, 77% with moderate AD and 80% with severe AD. Seven percent of patients underwent anaphylactic reactions (5/72), 3/72 children with severe AD, 2/72 with mild/moderate AD. De Boisseau et al.[3] studied 30 children with AD and IgE positive for egg, 24/30 children ate egg for the first time at a mean age of 30 ± 9 months, and 18 presented adverse reaction. Dieguez et al.[4] studied 104 cow's milk-allergic children (60% with AD); IgE for egg and OFC were performed at the age of 14 months, 65/104 (62.5%) resulted sensitised and 38/65 (76% with AD) allergic to egg; egg allergy was diagnosed in 22% (10/44) of children with IgE-mediate cow's milk allergy and without AD. Recent studies which tested the cooked egg tolerance in children allergic or sensitised to egg[5,6] showed that adverse reaction at the ingestion of baked cake with egg was possible in patients with AD who had never eaten it. In children who presented specific IgE and had never eaten the suspected trigger food, some position papers[7–9] suggested to perform OFC in the hospital setting. The authors gave this suggestion even for children with AD who had never eaten egg.[8] This indication is quite expensive because of the economic and human resources employed and, to confirm the appropriateness of this indication, it is necessary to consider a control population (without AD or food allergy). There are no case-control studies available at the moment in this field.

We aimed to quantify the risk of sensitisation and allergy to egg in children with AD (first aim) by enrolling a group of healthy children without AD and without known food allergy – control group –, we tested their sensitisation and allergy to egg, and we compared these data to those obtained in a group of paediatric patients with AD. Moreover, since we know that the reactivity to raw egg is higher than that to heated egg,[10] we tested both reactivities in our population (second aim).

Material and methods

Inclusion criteria

The study was performed in the Paediatric Department and Paediatric Allergy Day-Case Unit at Agostino Gemelli Hospital of Rome. Children with AD, with no limit of age, were retrospectively enrolled from June 2010 to June 2011 (AD group). AD was defined mild, moderate or severe according to the holistic assessment.[11] Children of AD group were referred to our Paediatric Department by a family paediatrician, or taken to the Unit by their parents due to suspected food allergy. We prospectively enrolled from June 2011 to September 2011 healthy children referred to the General Paediatric Department of Agostino Gemelli Hospital of Rome for health supervisions (control group).

Each time a paediatrician established that children of both groups had never eaten egg before, even as an ingredient of a manufactured meal (such as biscuits, cakes, ice creams, sauces, pasta, meatballs). We excluded from the study children suffering from chronic illnesses, treated with immunosuppressor in the last four months or antihistaminic drugs in the last four weeks, or those who refused to consent.

The study was approved by Agostino Gemelli Hospital' Ethics Committee.

Skin prick test

SPT were performed with: 1) raw egg (mixed albumen and yolk), 2) boiled (for 10 min) albumen and yolk separately, and 3) commercial extracts of albumen and yolk (Lofarma, Milan, Italy). Histamine (Lofarma, Milan, Italy 10 mg/ml) was used as positive control and saline as negative control. Reactions occurring within 15 min were analysed, and SPT were positive if mean diameter of the wheal was at least 3 mm bigger than negative control.

Oral food challenge

An open OFC with raw egg was performed in those children with positive SPT to raw egg, using a whole egg with sugar. The meal was given in six increasing doses (one drop, 3 drops, 1 ml, 3 ml, 10 ml, 30 ml) every 20 mins. An open OFC with boiled egg was performed in those children with positive SPT to boiled egg, using a whole boiled egg (chopped and mixed with salt), starting with one gram and doubling the dose every 20 min until reaching one whole egg.

In case of subjective symptoms (oral itching, nausea, abdominal pain) or mild objective ones (a single episode of vomit, few urticaria wheals, few sneezes, mild ocular hyperaemia) OFC was not stopped and the dose causing symptoms administrated again and then slightly increased. OFC was considered positive and stopped in case of objective symptoms and/or serious, persistent, reproducible ones.[12] OFC was considered negative in the absence of adverse reactions within two hours after the last dose. Reactions were defined systemic if they were anaphylactic, according to Sampson et al.,[13] or generalised, corresponding to old definition of mild or moderate anaphylactic reactions.[14]

Statistical analysis

Statistical analysis was performed using the Statistics program for biomedical disciplines – Stanton Glanz version 5.0. Chi-squared test was used to compare sensitised patients with patients allergic to egg proteins.

Results

Seventy-nine children were enrolled in the AD group and 45 in the Control Group. Population characteristics are described in Table 1. Regarding the AD group, the reason for office visits has never been the difficulty of the symptomatic treatment of eczema, but the evaluation of a possible causal relationship with an allergy; so our children with AD are not different, for their severity, from those of the general population of children with AD. Although some children had an advanced age, a careful medical history could be ruled out that they had ever eaten the egg, which in Italy is considered as very allergenic, especially in children with AD. No child had known food allergies (IgE- and non IgE-mediated) at the time of recruitment. No subjects had to be excluded because they had recently received or were receiving antihistamines