

PREGLED LITERATURE – REVIEW ARTICLE

How good is early introduction of complementary food?

Rano uvođenje mešovite hrane – da ili ne?

Naire Sansotta¹, Diego Peroni²

¹ Department of Paediatrics, University of Verona, Verona, Italy

² Department of Paediatrics, University of Ferrara, Ferrara, Italy

Summary Timing of first exposure to solid foods for children has been changed over the last 40 years. In the 1970s, there was growing evidence supporting an association between timing of weaning and the increasing prevalence of allergic diseases. Many studies recommended delaying solids after 6 months of age based on the concept that introducing solids too early could play a role in food allergy. Conversely, through the last years, several studies have investigated whether delay in timing of solid food introduction after 6 months of age could determine food allergy instead of preventing it. Furthermore if an early weaning could have more favorable results than postponing it. This review discusses the current guidelines about the optimal timing of introduction of solids in children.

Key words: allergy, complementary food, child

Sažetak U poslednjih 40 godina, preporuke za uvođenje solidne hrane u prvoj godini života dece, su promenjene. Sedamdesetih godina prošlog veka, rano uvođenje mešovite hrane povezano je sa porastom alergijskih bolesti kod dece. Mnogi naučnici su podržali koncept kasnijeg uvođenja solidne hrane, nakon šestog meseca života, sa ciljem prevencije razvoja nutritivne alergije. Međutim, poslednjih godina, istraživanja su pokazala suportan koncept, to jest da uvođenje solidne hrane nakon šestog meseca života, olakšava razvoj nutritivne alergije, umesto da je prevenira, što znači da bi rano uvođenje mešovite čvrste hrane imalo koristan efekat. Ovaj članak obrađuje aktuelne kliničke vodiče sa temom optimalnog uvođenja solidne hrane kod dece.

Cljučne reči: alergija, ishrana, deca

Introduction

Food allergy and allergic diseases are commonly encountered in many countries, affecting 6-8% of children (1) and there is a great interest in understanding the reasons for the rising prevalence of the allergic disorders (2).

The prevalence of food allergy is highest in infants and toddlers, with 2.5% of infants suffering from cow's milk allergy, while other allergens such as egg, nuts, soya, wheat and fish/shellfish are also common (3).

In the 1970s, there has been a progressive and dramatic delay in timing of first exposure to solid foods for all children until after 6 months of age based on the hypothesis of reducing the prevalence of food allergy. But these recommendations do not appear to have been successful in preventing food allergy (4).

Recently, with advances in allergy research, a more active approach to managing food allergy is being adopted. This approach includes first of all, early dietary introduction of potentially allergenic foods that are tolerated (5).

In fact, with a better understanding of the immune system, it is now clear that delays in timing of introduction of allergenic foods may have actively contributed to the rising prevalence of food allergy in conjunction with other environmental and genetic factors (2).

We reviewed emerging literature and present the current clinical revised guidelines published in the UK and US about timing of introduction (both for high risk infants but also for the general population) aiming to provide a true evidence base in infant feeding process.

OLD recommendations

In the 1970s some studies have been published showing an increased risk for eczema and possibly asthma in babies who were introduced to solid foods very early. First of all, in a 10-year longitudinal study, Ferguson et al. observed that very early exposure (before four months of life) to a varied solid food diet may predispose susceptible children to recurrent or chronic eczema (6).

In a randomized, controlled trial, Zeiger et al. reported that early (before fourth month) combined maternal and

infant allergen avoidance of food antigens significantly reduced the risk of eczema in children of atopic parents (7). Later, a joint statement by the European Society for Paediatric Allergology and Clinical Immunology (ESPACI) Committee on hypoallergenic formulas and by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition Weaning and allergy prevention (ESPGHAN) Committee on nutrition advised postponing the introduction of solid foods to infants beyond six months of age to prevent atopic diseases (8).

Furthermore, a position statement from the American Academy of Paediatrics (AAP) recommended withholding cow's milk until the age of one year, eggs until the age of two years, and peanuts, tree nuts and fish until the age of three years, particularly in high risk children (9).

In 2001, the World Health Organization limited their recommendations and proposed exclusive breastfeeding for the first six months of life and the introduction of solids only thereafter, even in not-at-risk infants (10).

And even a more recent consensus document from the American College of Allergy, Asthma, and Immunology, emphasizing the need for specific practical guidelines for parents and health professionals, suggested that in high-risk infants the introduction of dairy products should be delayed until 12 months of age, eggs until 24 months and peanuts, tree nuts, fish and seafood (fishes and shellfish) until three years of age (11).

New concepts

There have been dramatic changes in evidence for timing of first exposure to solid foods for children over the last years. Different prospective studies have failed to demonstrate an association between early introduction of complementary foods and either eczema or food allergy. Conversely, an increased risk of atopic dermatitis, eczema and allergic sensitisation (with or without symptoms) has been associated with delayed introduction of eggs, milk, cereals and other solids (12,13,14).

In two birth cohort studies, Zutavern et al. found an increased risk of eczema and atopic dermatitis related to the late introduction of eggs, milk, vegetables and meat products. There was a statistically significant increased risk of eczema in relation to the late introduction of these foods (15,16).

Poole et al. analyzing children who were first exposed to cereals after six months of age concluded that they had an increased risk of wheat allergy compared to children who were first exposed to cereals before six months of age (17). Similarly, Nwaru et al. showed that allergic sensitisation to any food allergens was associated with the late introduction of potatoes, oats, rye, meat, fish and eggs (beyond four months of age). Similarly, sensitisation to any inhalant allergens was associated with the late introduction of potatoes, oats, rye, meat and fish (18).

What about peanut? Du Toit et al. demonstrated that despite precise guidelines recommending avoidance of peanuts during infancy, which are strictly applied in the

United Kingdom, Australia and North America, peanut allergy continues to increase in these countries; whereas this sensitisation is decreasing among children from Israel. Since the median consumption of peanut products in Israel for infants aged 8-14 months is 7,1 g/month, and 0 g/month in the UK ($p < 0,01$), it is fascinating to hypothesize that early introduction of peanuts during infancy, rather than strict avoidance, would prevent the development of peanut allergy (19).

Venter et al. showed that peanut sensitisation and reported allergy in children born in 1994-1996 increased from 1989 but seems to have stabilised or slightly decreased since the late 1990s, although not significantly (1).

Amin et al. in a cohort of patients diagnosed with "food allergy" from 2003 to 2008 demonstrated that the percentage of peanut allergic children in 2008 was slightly larger than in 2003 but this difference was not statistically significant (20).

Recently, The Learning Early about Peanut Allergy (LEAP) randomized, open label controlled trial has been published. The authors enrolled 640 children aged 4- 10 months at high risk of peanut allergy (defined as a history of egg allergy or severe eczema), without current peanut allergy (SPT < 4mm on study entry and no history of reaction to peanut) in order to examine the effect of early peanut consumption on peanut allergy. Infants were randomized to either regular consumption of peanut protein (2g in three serves per week) or peanut avoidance and the prevalence of peanut allergy in the two groups was assessed and compared at 5 years of age. They concluded that peanut consumption was associated with an 86% reduction in peanut allergy at 60 months of age in SPT negative cohort and 70% in SPT positive cohort. At 60 months, the mean diameter of wheals and peanut specific IgE titers were higher in the peanut avoidance group than in the consumption group. Furthermore, the peanut consumption group showed a significantly greater and earlier increase in levels of peanut specific IgG and IgG4. Early sustained consumption of peanut products was associated with a substantial and significant decrease in the development of peanut allergy in high risk infants (21).

Nowdays: "Work in progress"

Several intervention studies currently in progress could have the potential role to clarify the link between timing of infant feeding and food allergy.

After LEAP study, just published, in UK the EAT study is ongoing to examine the effect of early consumption of a range of potentially allergenic foods on IgE-mediated allergy to any of these foods. The EAT study will involve 2 500 infants with mothers recruited during pregnancy. The intervention arm will introduce six potentially allergenic foods into the infants' diets prior to 6 months of age (cow's milk, egg, wheat, sesame, fish and peanut). The control arm will follow standard UK government advice (exclusive breastfeeding until 6 months of age and no introduction of

allergenic foods – egg, wheat, peanuts, tree nuts, seeds, fish and shellfish - before 6 months of age). The outcomes examined will be IgE-mediated food allergy to the six intervention foods between 1 and 3 years of age (22).

In Germany, the Hen's Egg Allergy Prevention (HEAP) study will involve 800 children, randomized to receive either hen's egg or a placebo at 4–6 months of age, with the effect on egg allergy measured at 12 months of age (23).

There are three important ongoing studies into the prevention of food allergy in Australia: STAR (Solids Timing for Allergy Research), STEP (Starting Time for Egg Proteins) and BEAT (Beating Egg Allergy) studies. They will include about 1900 high-moderate and intermediate risk with or without eczema randomized to receive egg powder or a placebo (rice powder) from 4 to 6.5 months of age aiming at determining the development of egg allergy or sensitization at 12 months (24).

Early results from the STAR trial indicate that a high proportion of high risk infants with eczema already have sensitization to foods as well as clinical reactivity prior to the introduction of solid foods at 4 to 5 months of age indicating the possible need for interventions prior to the introduction to solid foods to prevent food allergy(25).

Conclusions

There is no convincing scientific evidence that avoidance or delayed introduction of potentially allergenic foods, such as fish and eggs, reduces allergies either in infants considered at increased risk for the development of allergy, or even in those not considered to be at increased risk.

Conversely, there is strong evidence stating that delaying the introduction of certain foods may actually increase (rather than decrease) the prevalence of allergic diseases.

It is important to review current guidelines about timing of solid food introduction in different countries and provide a true evidence base to inform public health practice such as infant feeding guidelines.

References:

1. Venter C, Hasan Arshad S, Grundy J, et al. Time trends in the prevalence of peanut allergy: three cohorts of children from the same geographical location in the UK. *Allergy* 2010;65:103–8
2. Szajewska H. Early nutritional strategies for preventing allergic disease. *Isr Med Assoc J.* 2012 Jan;14(1):58-62.
3. Sicherer SH, Sampson H. Food allergy. *J Allergy Clin Immunol* 2010;125 (Suppl 2): S116–25.
4. Koplin JJ., Allen KJ. Optimal timing for solids introduction – why are the guidelines always changing? *Clinical & Experimental Allergy*, 43, 826–834.
5. Anagnostou K, Stiefel G, Brough H, du Toit G, Lack G, Fox AT. Active management of food allergy: an emerging concept *Arch Dis Child.* 2015 Apr;100(4):386-90.
6. Fergusson DM, Horwood LJ, Shannon FT. Early solid food feeding and recurrent childhood eczema: a 10-year longitudinal study. *Paediatrics.* 1990;86:541-6
7. Zeiger RS, Heller S, Mellon MH, Forsythe AB, O'Connor RD, Hamburger RN, et al. Effect of combined maternal and infant allergen avoidance on development of atopy in early infancy: a randomized study. *J Allergy Clin Immunol.* 1989;84:72-89.
8. Host A, Koletzko B, Dreborg S, Muraro A, Wahn U, Aggett P, et al. Dietary products used in infants for treatment and prevention of food allergy. Joint Statement of the European Society for Paediatric Allergology and Clinical Immunology (ESPACI) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. *Arch Dis Child.* 1999;81:80-4.
9. American Academy of Paediatrics. Committee on Nutrition. Hypoallergenic infant formulas. *Paediatrics.* 2000;106:346-9
10. The Optimal Duration of exclusive breastfeeding: report of an Expert consultation. Geneva. http://www.who.int/nutrition/publications/optimal_duration_of_exclusive_breastfeeding_report_eng.pdf
11. Fiocchi A, Assa'ad A, Bahna S, Adverse Reactions to Foods Committee; American College of Allergy. Asthma and Immunology Food Allergy and the introduction of solid foods to infants: a consensus document. *Ann Allergy Asthma Immunol.* 2006;97:10-20.
12. Zutavern A, von Mutius E, Harris J, Mills P, Moffatt S, White C, et al. The introduction of solids in relation to asthma and eczema. *Arch Dis Child.* 2004;89:303-8.
13. Snijders BE, Thijs C, van Ree R, van den Brandt PA. Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study. *Paediatrics.* 2008;122:e115-22.
14. Sariachvili M, Droste J, Dom S, Wieringa M, Hagendorens M, Stevens W, et al. Early exposure to solid foods and the development of eczema in children up to 4 years of age. *Pediatr Allergy Immunol.* 2010;21:74-81.
15. Zutavern A, Brockow I, Schaaf B, von Berg A, Diez U, Borte M, et al., LISA Study Group. Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA. *Paediatrics.* 2008;121:e44-52.
16. Zutavern A, Brockow I, Schaaf B, Bolte G, von Berg A, Diez U, et al. Timing of solid food introduction in relation to atopic dermatitis and atopic sensitization: results from a prospective birth cohort study. *Paediatrics.* 2006;117:401-11.
17. Poole JA, Barriga K, Leung DY, Hoffman M, Eisenbarth GS, Rewers M, et al. Timing of initial exposure to cereal grains and the risk of wheat allergy. *Paediatrics.* 2006;117:2175-82.
18. Nwaru BI, Erkkola M, Ahonen S, Kaila M, Haapala AM, Kronberg- Kippilä C, et al. Age at the introduction of solid foods during the first year and allergic sensitization at age 5 years. *Paediatrics.* 2010;125:50-9
19. Du toit G, Katz Y, Sasieni P, Meshel D, Maleki SJ, Fisher HR, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol.* 2008;122:984-91.
20. Amin JA, Davis MC. Changes in prevalence and characteristics of IgE-mediated food allergies in children referred to a tertiary care center in 2003 and 2008. *Allergy Asthma Proc.* 2012;33:95-101
21. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, Brough HA, Phippard D, Basting M, Feeney M, Turcanu V, Sever ML, Gomez Lorenzo M, Plaut M, Lack G;

LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med.* 2015 Feb 26;372(9):803-13.

22. Lack G, Perkin M, Flohr C, <http://www.eatstudy.co.uk>

23. http://www.charite-ppi.de/aktuelles/klinische_studien/huehnereiallergie_praeventionsstudie

24. Fleischer DM, Spergel JM, Assa'ad AH, Pongratic JA. Primary prevention of allergic disease through nutritional interventions. *J Allergy Clin Immunol.* 2013;1:29–36.

25. Metcalfe J, Prescott SL, Palmer DJ. Randomized controlled trials investigating the role of allergen exposure in food allergy: where are we now? *Curr Opin Allergy Clin Immunol.* 2013;13:296–305

Primljeno/Received: 27. 11. 2015.

Prihvaćeno/Accepted: 30. 11. 2015.

Copyright © 2015. Uruženje za preventivnu pedijatriju Srbije

Correspondance to:

Diego Peroni

Associate Professor of Pediatrics

University of Ferrara, Ferrara, Italy

perodiego@gmail.com