

To prevent the allergic disease: the dream of the allergist

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Summary. Allergen avoidance, allergen immunotherapy, IgE antagonists, biological medications, prevention and treatment of respiratory infections, probiotics, adapted formula, vitamins, and oligo-elements have been investigated as strategies in the prevention of allergic diseases. Promising findings were obtained. To prevent allergic diseases could be a dream that will be soon realized in clinical practice. (www.actabiomedica.it)

Key words: allergy, children, prevention, treatments

Allergic diseases represent a compelling burden in the human health as the prevalence is about 40% of the general population and will rapidly arrive at 50% (1,2). Therefore, to prevent allergic diseases is an urgent problem to solve.

Scholastically, prevention may be primary, such as to prevent the onset of allergy, secondary, such as to prevent the development of the natural course, and tertiary, such as to prevent the worsening of the complications.

Of course, this topic is enormously extended and continuously in progress as well as the debate is strenuously arguing. Consistently, the number of publications on this topic is almost 40,000 at present, but it is constantly growing (3).

Therefore, a complete and exhaustive review of the matter falls outside of the aim of the current article. Actually, we would present the most relevant issues consistent with the studies published on the current Supplement.

It is well known that allergic diseases, including allergic rhinitis and asthma, are a major cause of morbidity and lost scholar attendance in childhood. Despite the tremendous burden of these disorders, the scientific community is still struggling to find an effective means of prevention. Obviously, the contribution of genetics to the development of atopy can-

not be altered, but environmental changes as well as pharmacotherapy have been investigated as modifiable risk factors. Many trials to date have been effective only for subjects with well-defined characteristics. This may depend on the heterogeneity of allergic disease spectrum, with a variety of triggers, phenotypes and endotypes. Thus, an intervention to prevent allergy and asthma, including the allergic march, will greatly improve quality of life for a multitude of patients and could decrease healthcare expenditures. Moreover, the strong epidemiologic and pathophysiologic association between allergic rhinitis (AR) and asthma defined the concept of ‘united airways disease’ or ‘respiratory allergy’, implying that allergy, in its widest sense, underlies this clinical syndrome. Progression from AR to asthma is frequent and part of the “atopic march” and has been also named as “asthma march”. Since pediatric immune response is more adaptable and therefore may be more amenable to treatment, interventions at early childhood are characterized by a higher chance to affect the natural course of allergy. Although current treatments are quite effective in relieving allergy symptoms, it has proven much more difficult to modify the progression of the disease. Much more promising is the field of allergen-specific immunotherapy, there is evidence that it is really a disease-modifying treatment. In addition, newer or emerging, possibly more

effective or more targeted interventions are promising in the preventive sense. In this regard, the most promising compounds are: adapted milks, probiotics, vitamins, oligo-elements, and phytotherapy.

There is increasing evidence that highlights the importance of the gut microbiota in health and diseases, mainly concerning allergy. Recently, it has been reported the importance of the “window of opportunity” in the early life, during which interventions modifying the intestinal microbiota may induce long-term effects (4). In fact, the neonate’s gut microbiota composition and metabolism could therefore exert an essential role in preventing allergy. Breastfeeding shapes the gut microbiota in early life, both directly by exposure of the neonate to the maternal milk microbiota and indirectly, via substances present in the maternal milk able to influence the bacterial growth and metabolism, including oligosaccharides, secretory IgA, and anti-microbial factors. The potential of maternal milk to modulate the offspring’s early gut microbiota is a promising tool for allergy prevention at present.

Moreover, there is a high interest in the role of probiotics for the prevention and treatment of allergic diseases, as clear evidence showed that the risk of developing allergy may be associated with a dysbiosis of the gut microbiome (5). The research is ongoing and some studies demonstrated the possible benefits of probiotics, with poor or no risk. Actually, these studies suggested a realistic promise in probiotic use for the prevention or treatment of allergy. However, there is the need of further studies that point out the efficacy, the optimal dosing, and the specific strains really effective.

Vitamin D has a crucial role in the regulation of bone metabolism, particularly during pediatric age, mainly concerning the bone mass acquisition. In addition, it has been recently evidenced that vitamin D may, directly or indirectly, regulate up to 1250 genes, displaying several activities. Vitamin D may be involved in the pathogenesis of several disorders, including infections, allergy, and autoimmunity. However, a recent meta-analysis, identifying 1932 articles, selected only one RCT and four NRS as eligible for analysis (6). Very low certainty in the body of evidence across examined studies suggests that vitamin D supplementation for pregnant women, breastfeeding women, and infants may not decrease the risk of developing

allergic diseases such as atopic dermatitis (in pregnant women), allergic rhinitis (in pregnant women and infants), asthma and/or wheezing (in pregnant women, breastfeeding women, and infants), or food allergies (in pregnant women). Therefore, limited information was available addressing primary prevention of allergic diseases after vitamin D supplementation, and its potential impact still remains uncertain. Therefore, vitamin D deficiency may affect many acute and chronic diseases. In Italy, vitamin D deficiency is common in both children and adolescents. In this regard, an expert panel provided a practical approach to vitamin D supplementation for infants, children, and adolescents (7).

Phytotherapy, such as the use of herbal medicine in clinical practice, has a millennial tradition, but only recently real evidence of its effectiveness is providing. Documented mechanisms of action and proved clinical benefit are accumulating (8-10). Therefore, phytotherapy has acquired the dignity of a conventional therapy as documented by a series of randomized controlled trials.

On the basis of this background, the studies reported in the current Supplement may represent a further proof that also non-pharmacological treatments may exert relevant benefits in the wide area of prevention, including the use of symptomatic therapy, the effect on infections, and the decline of lung function.

The first study investigated the potential capacity exerted by the nutraceutical Lertal® in the secondary prevention of antihistaminic use. The results showed that the nutraceutical truly reduced the use of antihistamines in children with allergic rhinoconjunctivitis. This outcome has a clinical relevance as it is well known that antihistamines exert a symptomatic activity that shortly disappear after its suspension (11), also after a long-lasting course (12). Therefore, the role of antihistamines in the treatment of allergic rhinitis should be considered as a symptomatic approach because this pharmacological class is not disease modifying. In this regard, sparing antihistamines could be an objective of the management of allergic rhinitis. The study demonstrated that the nutraceutical halved the consume of antihistamines; thus, this finding suggested that a course of nutraceutical, lasting for 8-16 weeks, may prevent the antihistaminic use. This fact has a relevance both from a pharmacoeconomic point

of view and a safety one. This result is depending on the activity exerted by the single components of the products that can exert anti-inflammatory and immune-modulating effects.

The second study evaluated the possibility of obtaining a secondary prevention in children with allergic rhinoconjunctivitis. There is evidence that subjects with allergic rhinitis may suffer from asthma over time: this occurrence has been named “asthma march”, such as the progression of allergic disease from the nose to the bronchi (13). In this regard, the assessment of lung function performing a spirometry is a very fruitful tool to early detection of initial bronchial impairment in patients with allergic rhinitis. Namely, the evaluation of the middle airways, such as the mid expiratory flow, has been demonstrated a good predictor of the progression from rhinitis to asthma (14). The nutraceutical significantly increased the value of MEF₅₀. Even though there is no evidence that a single course could really prevent the asthma onset, a significant increase of MEF₅₀ could mean that it might delay or avoid bronchial impairment if the nutraceutical is used for long period.

The last study investigated the possibility of achieving a tertiary prevention in children with allergic rhinoconjunctivitis, such as to reduce the number of respiratory infections. Allergic disorders are characterized by a pronounced susceptibility to contract infections (15). This characteristic depends on the type 2 inflammation, such as the functional defect of T helper 1 cells, deputed to fight infections (16). Moreover, the accumulation of type 2 inflammatory cells promotes pathogens growth (17). The study showed that a nutraceutical course significantly affected the number of respiratory infections during a one-year follow-up. This result has different clinical impacts. First, a reduction of respiratory infections in childhood has important advantage concerning the quality of life of the family, the scholar (and working for parents) attendance, and the use of antibiotics and symptomatic drugs. Second, preventing respiratory infections is important as they are the most risk factors for wheezing and asthma in childhood (18,19). Therefore, this study added new information about the possibility to tertiary prevention in allergic children. This topic is particularly attracting as recently discussed in a systematic review (20).

In conclusion, the real prevention of allergic disorders does still remain a dream in the drawer, but there are convincing premise and documented evidence that it could be soon realized in some situations. The way has been paved and fruits are about to be gathered.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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