Global Pediatrics 7 (2024) 100103

Contents lists available at ScienceDirect

Global Pediatrics

journal homepage: www.elsevier.com/locate/gpeds

Nutraceuticals for allergic diseases: A brief overview

Giorgio Ciprandi [a,*], Maria Angela Tosca [b]

[a] Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy
[b] Allergy Center, IRCCS Istituto Giannina Gaslini, Genoa, Italy

ARTICLE INFO

Keywords:
Allergy
Immune system
Type 2 inflammation
Nutraceuticals
Children

ABSTRACT

Allergic disorders are common diseases characterized by type 2 inflammation and typical symptoms. Although pharmacologic treatment can be effective, prolonged administration of drugs can be associated with adverse reactions and seldom reduction of effectiveness. Therefore, complementary medicine is widespread in clinical practice, mainly in pediatric settings, and pleasing to parents.

Nutraceuticals, such as "a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease," are commonly prescribed by pediatrics as well as self-prescription by parents. There is evidence that some components exert beneficial effects in allergic diseases. In this regard, the supplementation with some food supplements may significantly reduce symptom severity and functional parameters.

Some compounds, including micronutrients, vitamins, probiotics, herbal medicines, could positively and safely be used in children with allergic diseases as add-on or preventive remedies. Nutraceuticals should not substitute drugs.

Allergic diseases are extremely frequent and include allergic rhinitis (AR), the most common IgE-mediated disease, allergic asthma, food allergy, drug allergy, and allergy to insect venom.[1]

These disorders elicit a wide spectrum of clinical manifestations, ranging from the trivial itching to life-threatening anaphylactic shock.

Allergic diseases typically recognize a type 2 inflammation characterized by eosinophilic infiltrate of the nasal mucosa.[2] Type 2 immune response is sustained by a specific, functional, but potentially reversible defect of T regulatory cells.[3] This pathogenetic event was initially attributed to the hygiene hypothesis but has recently been reconsidered and renamed as the microbiota hypothesis.[4] In other words, gut and respiratory dysbiosis affect the maturation of the child's immune system, maintaining the type 2 polarization.[5] Actually, the mother to avoid a fetus rejection, as non-self, mounts a type 2 immune response; so, the newborn has a type 2 polarization that needs the immune system maturation to switch toward the physiologic type 1-oriented immunity.

In allergic subjects, the expansion of T helper 2 lymphocytes promotes the release of type 2 cytokines, such as interleukin four (IL-4), IL-5, and IL-13. These cytokines, on the one hand, induce the isotypic switch toward the IgE class and, on the other hand, promote eosinophilic inflammation.[6] As a result, allergic patients develop allergic inflammation when exposed to the causal allergen.[7] The type 2 inflammation persists until the allergic patient exposes him/herself to the causal allergen.[8]

These inflammatory events are relevant as type 2 inflammation causes and sustains the symptoms. The typical AR symptoms include nasal itching, sneezing, watery rhinorrhea, and nasal congestion, the typical asthma symptoms are wheezing, dyspnea, cough, and chest tightness, food allergy is pleiomorphic as well as venom and drug allergy.[9]

Anyway, these symptoms occur immediately after allergen exposure, the so-called early phase, and depend on the release of mediators, mainly histamine.[10] Thereafter, type 2 inflammation develops, giving rise to the development of other symptoms characteristic of allergic diseases, i.e., nasal and bronchial obstruction, impaired olfaction, urticaria, and systemic complaints.[11]

Also, some allergic patients experience mild fever as expression of a systemic inflammatory reaction; in fact, the old name of AR was hay fever.[12] In addition, allergic disorders significantly affect quality of life.[13,14] As a result, allergic diseases represent a relevant burden for the patient, family, and society.[15]

Notably, allergic patients frequently present comorbidities, including other allergic diseases (conjunctivitis, rhinitis, asthma, food allergy, and drug allergy) and frequent infections.[16]

* Corresponding author.
E-mail address: gio.cip@libero.it (G. Ciprandi).

https://doi.org/10.1016/j.gpeds.2023.100103
Received 8 December 2023; Accepted 17 December 2023
Available online 19 December 2023

In addition, allergic children frequently present a trajectory characterized by a progression of the allergic diseases. In this regard, patients with AR frequently present asthma as the two diseases constitute a unique medical condition named united airway disease.[17] Moreover, allergic diseases are commonly associated with other immunopathological disorders because of impaired immunity.[18]

Moreover, allergic patients present a defect of type 1 immunity, deputed to the defense against infection.[19] Accordingly, allergic children have more prolonged-lasting infections than non-allergic children.[20]

Considering all these aspects, it is clear that AR is a condition that should be considered and, therefore, requires appropriate management. In this regard, drugs represent a fundamental step in managing allergic patients. However, as allergic diseases are often chronic, or at least the symptoms may last for long periods, pharmacological therapy may induce side effects. This concept is particularly relevant in childhood. For this reason, the use of complementary therapies is frequently adopted by doctors and parents. Complementary therapies include may remedies; presently, we discuss the nutraceuticals.[21-24]

The term "nutraceutical" is a portmanteau of "nutrition" and "pharmaceutical." It has been coined to describe substances that possess health-promoting properties, and they are typically isolated from food sources and can be used as ingredients of enriched foods or food supplements. Therefore, nutraceuticals are products that combine the benefits of both nutrition and pharmaceuticals, as they are derived from food sources and provide health benefits beyond basic nutritional functions. These compounds have gained popularity for their potential to prevent, and manage various human diseases. Nutraceuticals can be classified into different categories based on their specific functions and applications in treating diseases. It's important to note that while some nutraceuticals may have positive health effects, they are not a substitute for conventional medical treatments.

Food supplements are defined as foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities.

The Table 1 synthetically summarizes the most common components used in clinical practice.

As above stated, nutraceuticals are not medications, thus, some relevant considerations have to be underlined. Nutraceuticals have no symptomatic effects and require long period to exert some benefits. Nutraceuticals must not substitute standard therapy, but they could be used as add-on treatment or preventive approach. Nutraceuticals can be used only respecting some rules.

First, these remedies should be safe and produced by serious companies. Namely, it is crucial know how any component is produced and managed. In particular, considering probiotics, the doctor should be prescribed only strains that have documented evidence about benefits and safety. The concept of probiotic is too generic and require adequate clarification.

Second, the dosage is a fundamental aspect: many multicomponent products contain minimal doses that does not guarantee any positive effect. This concept is mandatory: the doctor should prescribe products that contain adequate quantity of active ingredients.

Third, the duration of supplementation is another relevant aspect. Namely, food supplements may require long period to exert beneficial effects.

Consequently, the doctors may use nutraceuticals but they should inquire into the components, doses, and duration as well as for any pharmacological remedy.

In conclusion, nutraceuticals could be advantageous in managing allergic children. However, the doctors should prescribe food supplements choosing those products that have documented evidence of beneficial effects and safety.

Table 1
Synthetic list of the most common food supplements used in clinical practice.

Vitamins	Vitamin C, Vitamin D, Vitamin E, β-caroten
Polyphenols	Resveratrol, Catechins (green tea), Curcumin, Rosmarinic acid, Gingerol
ω−3 fatty acids	Fish oil, flaxseed oil
Probiotics	Lactobacilli, Bifidobacteria strains
Prebiotics	Inulin, FOS (fructo-olygosaccharides)
Postbiotics	Short chain fatty acids
Oligo-elements	Selenium, Zinc, Iron
Flavonoids	Quercitin, rutin, spirein
Immuno-modulants	Lactoferrin, Melatonin, Glucans

Funding

The present research had no funding.

CRediT authorship contribution statement

Giorgio Ciprandi: Conceptualization, Writing – original draft, Writing – review & editing. **Maria Angela Tosca:** Conceptualization, Supervision.

Declaration of Competing Interest

The authors have no conflict of interesting concerning the present article.

References

1.. Barr JG. Allergic rhinitis in children. *BMJ*. 2014;349:g4153.
2.. Meng Y, Wang C, Zhang L. Advances and novel developments in allergic rhinitis. *Allergy*. 2020;75(12):3069–3076.
3.. Zhang Y, Lan F, Zhang L. Update on pathomechanisms and treatments in allergic rhinitis. *Allergy*. 2022;77(11):3309–3319.
4.. Beikzadeh B. A deeper view of early life microbiota and hygiene hypothesis relationship: reducing the risk of allergic diseases is dependent on the permanent presence of good microbiota throughout life. *Int J Prev med*. 2023;14:22.
5.. Shao T, Hsu R, Rafizadeh DL, et al. The gut ecosystem and immune tolerance. *J Autoimmun*. 2023, 103114.
6.. Maspero J, Adir Y, Al-Ahmad M, et al. Type 2 inflammation in asthma and other airway diseases. *ERJ Open Res*. 2022;8(3):00576–02021.
7.. Ciprandi G, Cirillo I, Vizzaccaro A, Milanese M, Tosca MA. Nasal obstruction in patients with seasonal allergic rhinitis: relationships between allergic inflammation and nasal airflow. *Int Arch Allergy Immunol*. 2004;134(1):34–40.
8.. Ciprandi G, Buscaglia S, Pesce G, et al. Minimal persistent inflammation is present at mucosal level in patients with asymptomatic rhinitis and mite allergy. *J Allergy Clin Immunol*. 1995;96:971–979.
9.. Goniotakis I, Perikleous E, Fouzas S, Steiropoulos P, Paraskakis E. A clinical approach of allergic rhinitis in children. *Children*. 2023;10:1571.
10.. Wheatley LM, Togias A. Clinical practice. Allergic rhinitis. *N Engl J Med*. 2015;372 (5):456–463.
11.. Schuler Iv CF, Montejo JM. Allergic rhinitis in children and adolescents. *Immunol Allergy Clin North Am*. 2021;41(4):613–625.
12.. Ewan PW. Hay fever. A report of the Royal College of Physicians. *J R Coll Physicians Lond*. 1989;23(2):68–76.
13.. Brown T. Diagnosis and management of allergic rhinitis in children. *Pediatr Ann*. 2019;48(12):e485–e488.
14.. D'Elia C, Gozal D, Bruni O, Goudouris E, Meira E Cruz M. Allergic rhinitis and sleep disorders in children - coexistence and reciprocal interactions. *J Pediatr (Rio J)*. 2022;98(5):444–454.
15.. Bousquet J, Anto JM, Bachert C, et al. Allergic rhinitis. *Nat Rev Dis Primers*. 2020;6 (1):95.
16.. Bielory L, Delgado L, Katelaris CH, Leonardi A, Rosario N, Vichyanoud P. ICON: diagnosis and management of allergic conjunctivitis. *Ann Allergy Asthma Immunol*. 2020;124(2):118–134.
17.. Passalacqua G, Ciprandi G, Pasquali M, Guerra L, Canonica GW. An update on the asthma-rhinitis link. *Curr Opin Allergy Clin Immunol*. 2004;4(3):177–183.
18.. Cohen B. Allergic rhinitis. *Pediatr Rev*. 2023;44(10):537–550.
19.. Annunziato F, Romagnani C, Romagnani S. The 3 major types of innate and adaptive cell-mediated effector immunity. *J Allergy Clin Immunol*. 2015;135(3): 626–635.

20.. Ciprandi G, Tosca M. Continuous antihistamine treatment controls allergic inflammation and reduces respiratory morbidity in children with mite allergy. *Allergy*. 1999;54:358–365.
21.. Ciprandi G., Tosca M.A. Nutraceuticals and non-pharmacological remedies for managing patients with allergic rhinitis. Minerva Pediatr (Torino). (in press).
22.. Ciprandi G, Aragona SE, Drago L. La Mantia I. The nutraceuticals: a new therapeutic strategy in the management of digestive and respiratory disorders. *Acta Biomed*. 2019;90(7–S):5–7.
23.. Trincianti C, Tosca MA, Ciprandi G. Updates in the diagnosis and practical management of allergic rhinitis. *Expert Rev Clin Pharmacol*. 2023;16(7):669–676.
24.. Ciprandi G, Tosca MA, Drago L. Probiotics in asthma management: fiction or truth? *Expert Rev Clin Immunol*. 2023;19(5):457–460.