ARC Journal of Immunology and Vaccines
Volume 3, Issue 1, 2018, PP 12-15
www.arcjournals.org

Immunoprophylaxis of Respiratory Infections in Childhood

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Abstract: *The immune system of the infant and child differs from the immune system of the adults, denoting a slight physiological "deficit" which causes newborns to be more vulnerable to infections of the wide variety of pathogenic microorganisms. Increased incidence of bacterial respiratory infections together with the peculiarities of the childhood immune system recommend using of immunomodulators with the proven origin and consistent with the age of the child after performing a full clinical examination, and laboratory and immunological testing. Among immunomodulators used in childhood for immunoprophylaxis are agents containing inosine acedoben dimepranol, immunomodulators of bacterial origin, immunomodulators related to natural products, such as colostrum, echinacea, arabinogalactan, inositol, etc.*

In conclusion, the opinion of the most of specialists in clinical immunology is after the initial consultation and carried out immunoassays, when needed, to prescribe a plan for immunoprophylaxis consistent with the individual characteristics of each particular patient.

Keywords: *immunoprophylaxis, immune system in infants, immunomodulators, inosine acedoben dimepranol, bacterial components, colostrum, arabinogalactan*

1. Special Features of the Immune System in Children

The immune system of the infant and child differs both qualitatively and quantitatively from the immune system of the adults. The development of immune cells starts intrauterine, as T-lymphocytes form in the thymus, while B-lymphocytes, neutrophils, NK cells and other cell types - in the bone marrow [1]. A wide variety of cells is already formed at birth, even before a potential meeting with existing microorganisms in the environment. During fetal development B - lymphocytes do not produce antibodies (immunoglobulins), but instead immunoglobulin G (IgG), produced by the mother, crosses the placenta into the blood of the fetus and protects it passively from infections [1, 2].

Approximately up to 6 months after delivery, maternal IgG could be observed in the newborn. After this period, production of its own IgG molecules begins in an amount sufficient to provide humoral protection from various pathogens. Contrastly, mammalian immunoglobulins M and A (IgM and IgA) do not cross the placenta. They are produced only by the newborn [3]. Interestingly, by the end of the first year after birth, IgM levels reach 75% of those typical for the adults, and IgA levels - 20%. Moreover, normal IgA levels typical of a healthy adult are reached in the puberty [3]. The unique characteristic of IgA is its secretion in all secrets in respiratory, genitourinary and gastrointestinal systems - saliva, tears, sweat, milk, intestinal mucosa, bronchial secretions, prostatic fluid, etc. It is secreted at the basolateral sites of the epithelial cells in the mucosa and then it passes through the cells to be excreted in the intestinal lumen. One of the functions of IgA is to bind to the surface of various pathogenic micro-organisms and to prevent their attachment to mucosal epithelial cells [4].

At birth this slight physiological "deficit" of immunoglobulins and other components of the humoral immunity cause newborns to be more vulnerable to infections of the wide variety of pathogenic microorganisms, including bacteria, viruses, fungi, protozoa, etc [5]. Thus, the increased incidence of bacterial infections in children is mainly due to low production or decreased function of soluble immune factors, including immunoglobulins and antimicrobial peptides. Bacterial infections can also be due to reduced mobility of neutrophils or reduced production during stress [3]. The increased incidence of viral infections may

be due to the functional immaturity of NK, dendritic cells and T lymphocytes [3]. In conclusion, the earliest moments of human life are marked by a period of increased risk of developing infections [6]. For this reason, precautions and some specific immunotherapy are needed.

Another problem in childhood is the fact that there is a state of energy of the immune cell populations after viral infection, and particularly after varicella, infectious mononucleosis, influenza A, respiratory syncytial virus, rhinoviruses, rotaviruses, etc [3,5]. These facts together with the peculiarities of the childhood immune system recommend using immuno-modulators with the proven origin and consistent with the age of the child. This is crucial especially for children with more than 7-10 respiratory infections and more than 2 severe pneumonia per year.

2. Recommended Immune Testing Before Administration of Immune Prophylaxis Administration

Before proceeding to any kind of immune modulation therapy, it is recommended to perform a full clinical examination and laboratory testing, including specific immunological testing. The latter consists of the assessment of serum immunoglobulin levels and the number and percentages of the main lymphocytes subpopulations, as well as their functional status by testing for T-lymphocyte activation [7].

3. Types of Immunomodulating Drugs

3.1. Immunomodulators Used as Antiviral and/or Immunomodulatory Agents Containing Inosine Acedoben Dimepranol

These agents are characterized by proven immunomodulatory action [8]. They tend to reduce the number of recurrent respiratory infections and to reduce the frequency of exacerbations of the existing infections. When prescribed as antiviral drugs, it is necessary to start immediately with the appearance of the first symptoms and continue within 1-2 days after the symptoms have resolved (on average about 14 days) [8]. When they are prescribed as immunomodulators for recurrent (repeated or chronic) infectious conditions, the scheme is individual depending on the immune status of the patient. Moreover, the duration of treatment and dosing varies greatly. The main effect of this type of preparation, prescribed as immunomodulators, is to stimulate T-cell differentiation and increase the proliferation of proinflammatory cytokines such as interleukin-1, interleukin-2 and interferon-γ; also to increases the amount of secreted IgG, to potentiate the functions of NK cells, neutrophils, monocytes, as well as chemotaxis and phagocytosis in macrophages [9,10]. Studies indicate that using of products containing inosine acedoben dimepranol reduce the number of recurrent respiratory tract infections by 81.2% annually (5.31 times fewer infections), frequency of exacerbations of infections by 60.3% (2.52 times) and the number of antibiotic courses and other medicines by 93.5% (15.3 times), the duration of illness by 88.2% (8.44 times), as the overall clinical symptoms decrease by 72.5% (3.64 times) [11].

3.2. Immunomodulators of Bacterial Origin

Immunomodulators of bacterial origin are also used for the prevention of recurrent respiratory infections and infectious exacerbations of chronic bronchitis in children. This type of preparation contains lyophilized bacterial lysates of the most common respiratory infections such as Haemophilus influenzae (type b), Streptococcus pneumoniae (type 1, type 2, type 3 and type 47), Klebsiella pneumoniae, subsp. pneumoniae (2 strains), Klebsiella pneumoniae, subsp. ozaenae, Staphylococcus aureus (6 strains), Streptococcus pyogenes, Streptococcus viridans (3 strains), Neisseria (Branhaamella) catarrhalis (3 strains) [12].This type of preparation also has an immunomodulatory effect by stimulating T-helper cell type 1 (Th1) and B-lymphocytes for antibody synthesis. The use of this type of prophylaxis varies also and depends on the overall status of the particular child [13].

3.3. Immunomodulators Related to Natural Products

They contain colostrum, echinacea, arabinogalactan, inositol, thuja, sambucus, aloe vera, malva silvestris, etc [14]. The natural molecular complexes contained in them have a well-expressed immunomodulatory effect while simultaneously being non-toxic.

Colostrum is the liquid that is secreted by the mammary gland within the first three to four days after birth just before the onset of breast milk. It is rich in substances that support immune system functions such as proline, oligosaccharides, lactalbumin, lactoferrin,

vitamin D binding protein, and IgG, IgA, IgM [15]. The vitamin D binding protein promotes the activation of macrophages and the transport of active metabolites of vitamin D to the site of the local immune response. Colostrum also contains growth factors such as epidermal growth factor (EGF), insulin-like growth factor (IGF-1), transforming growth factors (TGFα, TGFb), platelet growth factor (PDGF), growth hormone (GH). Additionally, colostrum is rich in a large number of nutrients and bioactive ingredients - 46.7% proteins, 27.2% carbohydrates and 18% fats, vitamins A, B1, B2, B5, B6, B9, B12, C, E, beta-carotene, retinoic acid, sulfur, sodium, chromium, zinc, magnesium, calcium, iron, phosphorus and potassium. The multiform composition of the colostrum enhances the immune system by several mechanisms [16].

Colostrum is a major source of lactoferrin - a protein that is a part of the innate immunity in mammals, including humans. Lactoferrin has proven anti-viral activity through inhibition the entry of certain viruses in the cells. Lactoferrin possesses also antibacterial properties - bacteriostatic (inhibits bacterial growth through binding irons since all bacteria require iron for their development and formation of biofilm on the intestinal mucosa, which prevents the attachment of the bacterial cells) and bactericidal (by direct action on the bacterial wall leading to rapid release of lipopolysaccharides and osmotic shock of the bacterial cell) [17]. Lactoferrin has also shown to have antifungal and antiparasitic action, subject to the iron-binding properties.

Lactoferrinbinds improves the absorption of iron in the organism by transporting it to all the cells needed it. Thus, improving the bioavailability of the iron in the body, lactoferrin helps more quickly to cope with iron deficiency anemia [18].

Echinacea, the most widely used immunomodulator of plant origin in the world, has proven its effectiveness by reducing the severity and duration of illness by stimulating the immune system to cope with viral infections [14]. Echinacea also exhibits antibiotic properties.

Inositol exerts its role in preventing complications in respiratory diseases by promoting the development of the lungs and stabilization of surface lung lipids. It is involved in the composition of cell membranes as a building block for phospholipids [14].

Arabinogalactan is another natural product consisting of sugar galactose and arabinose. In addition to being a source of useful fiber for digestion, it is also an antibiotic that aids the colonization of 'good' bacteria in the intestine and, last but not least, it has an immunomodulating effect on the lymphoid tissues found in the digestive system. The immunomodulatory effect of arabinogalactan is associated with increased phagocytosis, lysosomal activity, production of cytokines such as TNFα, IL-6 by macrophages, activation of lymphocytes and stimulation NK cell cytotoxicity mainly by increasing interferon-γ production by immune cells [19]. This effect indirectly assists an organism in combating infectious agents encountered by the organism. Furthermore, the combination of arabinogalactan and echinacea act simultaneously to increase the production of properdin, which is involved in some specific immune responses of the organism, for example by absorbing phagocytes, thereby helping to actively deal with them [14].

In conclusion, the opinion of the most of specialists in clinical immunology is after the initial consultation and carried out immunoassays, when needed, to prescribe a plan for immunoprophylaxis consistent with the individual characteristics of each particular patient.

Schopenhauer said, "Nine-tenths of our happiness is based on health." Lets make sure our children are always happy.

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Citation: *Tsvetelina Velikova, Ekaterina Ivanova-Todorova. Immunoprophylaxis of Respiratory Infections in Childhood. ARC Journal of Immunology and Vaccines. 2018; 3(1): 12-15.*

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