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ASSOCIATION BETWEEN RHINOVIRUS AND RESPIRATORY SYNCYTIAL VIRUS (RSV) LINKED TO ASTHMA EXACERBATION IN PEDIATRIC PATIENTS

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Abstract: The following text addresses asthma as a global challenge in children's health, highlighting its prevalence and impacts on quality of life. Discusses the diagnostic complexity due to overlapping symptoms with other infections. Emphasizes the significant association between viral infections, such as RSV and rhinovirus, and the development, persistence, and exacerbations of asthma in children. The need to understand risk factors and underlying mechanisms is highlighted to inform specific preventive and therapeutic strategies in the pediatric age group.
Keywords: Otorhinolaryngology. Pediatrics. Rhinovirus.

INTRODUCTION

Asthma, as the most prevalent chronic condition in children, is emerging as a global public health challenge. Its manifestation translates into persistent inflammation of the airways, resulting from complex interactions between inflammatory cells, mediators and structural components of the respiratory system. When manifesting itself in an impactful way, this condition has a direct impact on children's quality of life, manifesting fundamental symptoms such as wheezing, accelerated breathing, chest tightness and coughing, with the most intense crises being linked to variations in expiratory flow. The symptomatological overlap with other recurrent infections in childhood creates diagnostic complexities, compromising the implementation of adequate treatment. Given the significant prevalence of asthma, especially among young people, and the adverse impacts on quality of life, understanding the risk factors and underlying mechanisms is crucial to preventing its development.

At the heart of asthma, multiple infectious agents play preponderant roles, highlighting the significant association between viral infections and the onset of symptoms such

as wheezing and asthma in children. Among the main viral strains that trigger wheezing in babies and children are respiratory syncytial virus (RSV), rhinovirus (RVH), human metapneumovirus (hMPV), bocavirus and influenza virus, with special emphasis on RSV and RVH as preponderant pathogens. Historically underestimated due to their connection to harmless colds, these viruses, in addition to their significant incidence, especially in winter, are correlated with the highest rates of morbidity and mortality in children under 5 years of age. Studies corroborate its significant contribution to the development, persistence and exacerbations of asthma in previously infected children and adolescents.

The solidification of the correlation between the manifestation of asthma in children and previous viral infections, especially RVH and RSV, finds robust support in the scientific community, based on several studies and clinical trials. However, the pathophysiological mechanisms underlying this close relationship still require complete elucidation, incorporating possible local, systemic or genetic determinants.

A thorough understanding of the interaction between respiratory viral infections and the increased risk of developing asthma in the pediatric age group is imperative, outlining the formulation of preventive protocols and specific therapeutic strategies.

GOAL

To establish a correlation between asthma exacerbation attacks and rhinovirus and Respiratory Syncytial Virus.

METHODOLOGY

The present work consists of a literary review that sought to address results found in research on the topic in question, whether in a comprehensive, orderly or systematic way. To carry out the work, the following steps were followed:

1) Selection of corresponding themes;
2) Selection of samples found and used;
3) Analysis of the characteristics of the original research;
4) Analysis of the results obtained;
5) Carrying out the review.

The databases of scientific literature and techniques used in carrying out the review were Google Scholar, Scientific Electronic Library Online (SciELO), Virtual Health Library, Latin American and Caribbean Literature in Health Sciences (LILACS), in English and Portuguese.

Thus, the present work seeks not only to analyze the pneumatological interface, but also to highlight the various contents on the topic in question, aiming to shed light on an educational path, establishing the correlation to pediatric patients and factors involving the respective disease.

DEVELOPMENT

Asthma, a chronic inflammatory condition, induces structural changes and hyperreactivity in the airways. Symptoms such as coughing, wheezing, dyspnea and chest tightness reflect the characteristic bronchial narrowing. The inflammatory process, eminently complex, involves the infiltration of diverse cells, including neutrophils, eosinophils and degranulated mast cells. This inflammatory response triggers events such as bronchial vasodilation, loss of epithelial integrity, thickening of the basement membrane, goblet cell hyperplasia and luminal reduction with accumulation of mucus.

These changes, initially observed in mild

asthmatic exacerbations, become more pronounced in severe forms. Eosinophilic infiltration, combined with the activation of Th2 lymphocytes and mast cell degranulation, results in the release of interleukins (IL-4, IL-5 and IL-13), highlighting IL-4 in the specific production of immunoglobulin E. Free radicals' oxygen, histamine, prostaglandins, and leukotrienes are additional components that contribute to the inflammatory scenario.

The complex interaction between genetic elements and environmental factors is intrinsically linked to the development and exacerbation of asthma. This interrelationship triggers variations in airflow, manifested by bronchial muscle contraction, edema, mucosal desquamation, accumulation of mucus and deposition of cellular debris. This condition, if left untreated, can progress to severe respiratory symptoms, including dyspnea and, in extreme cases, death. The temporal course reveals distinctive structural changes, characterizing airway remodeling, with muscular hypertrophy, thickening of the basement membrane and development of fibrosis.

The diagnosis of this complex clinical entity is fundamentally clinical, with viable confirmation through techniques such as spirometry and bronchial provocation testing. This integrated approach is imperative for a comprehensive understanding of asthma, outlining therapeutic and preventive strategies that are essential in academic and clinical settings.

The Respiratory Syncytial Virus (RSV) stands out as the main causative agent of respiratory infections, especially in pediatrics, increasing the risk of progression to more serious clinical conditions, hospitalization and bronchial inflammation. In RSV infection, the recognition of viral RNA by pattern identification receptors, including Toll-like receptors, triggers the activation of nuclear factors, inducing the production of INF-B, initiating the cascade of IFN-a, CXCL8 and IFN- 1, resulting in an intense inflammatory process.

This virus, characterized by its negative-strand RNA, envelope and belonging to the Paramyxoviridae family, during airway involvement, promotes the activation of B lymphocytes and CD8+ T cells, playing pro-inflammatory roles that accentuate the inflammatory process. Deficiency in IFN-γ production compromises IFN-γ-dependent viral clearance, causing T-helper 1 dysfunction. Acute RSV bronchiolitis imbalances Th1 and Th2 cytokines in airway secretions from peripheral blood mononuclear cells (PBMCs).

Furthermore, the inflammation triggered by the virus results in the release of mediators such as TNF-a, eotaxin, interleukins IL-1a, IL-1B, IL-6 and IL-8, as well as chemokines, intensifying airway damage. RSV presents a significant risk due to its cytopathic activity amplified by an intense and deficient immune response of the organism, resulting in significant local inflammation, epithelial damage and desquamation, with increased mucus production and severe bronchial obstruction.

Intense viral replication, readily established in the epithelial cells of the respiratory tract, causes necrosis of the bronchial epithelium, edema, recruitment of defense cells and bronchoconstriction. These complex interactions underscore the potential severity of RSV and its implications for the airways.

Exploring the human rhinovirus (RVH) in more depth, this pathogen emerges as the predominant agent in respiratory infections, especially in the pediatric age group, and has the potential to evolve into more serious clinical conditions, culminating in hospitalization and showing manifestations of bronchial inflammation. In the context of RSV infection, recognition of viral RNA by

pattern-identifying receptors, including Toll-like receptors, triggers the activation of nuclear factor, stimulating the production of INF-B and initiating the cascade of events involving IFN-B. a, CXCL8 and INF-1, resulting in a vigorous inflammatory process.

RSV, an enveloped negative-strand RNA virus belonging to the Paramyxoviridae family, during the progression of airway invasion, promotes the activation of B lymphocytes and CD8+ T cells, playing pro-inflammatory roles that accentuate the inflammatory course of the infection. Dysfunction in IFN-γ production, with reduction in IFN-γ-dependent viral clearance, induces a disturbance in the balance of Th1 and Th2 cytokines in airway secretions, the latter being triggered by acute RSV bronchiolitis, as observed in mononuclear cells peripheral blood cells (PBMCs).

The inflammation triggered by RSV releases mediators, such as TNF-a, eotaxin, interleukins IL-1a, IL-1B, IL-6 and IL-8, in addition to chemokines, intensifying airway damage. The marked cytopathic activity of RSV, amplified by an intense and unbalanced immune response, results in significant local inflammation, triggering epithelial damage and desquamation, with exacerbated mucus production and severe bronchial obstruction. Robust viral replication, easily established in the epithelial cells of the respiratory tract, culminates in necrosis of the bronchial epithelium, edema, recruitment of defense cells and bronchoconstriction.

When addressing RVH, it is the predominant causative agent of colds and is directly correlated with asthma exacerbations in childhood. The key RVH receptor, intercellular adhesion molecule 1 (ICAM-1), physiologically interacts with antigen-1, associated with leukocyte function, triggering the recruitment, migration and activation of immune cells at sites of local inflammation. Increased expression of ICAM-1, a result of previous allergic sensitization, facilitates the adhesion and establishment of viral cells, while RVH infection itself further intensifies this expression, exacerbating the inflammatory response to allergens and perpetuating a continuous inflammatory cycle.

In addition to the prominent increase in ICAM-1 expression, RVH infection triggers the release of several inflammatory mediators, including IL-6, IL-8, TNF-a, IL-B, RANTES and GM-CSF, triggering an inflammatory process of considerable relevance. The intricate mechanisms of RVH infection, in their interaction and influence on asthma exacerbations, are intrinsically linked to the early manifestation of differentiated immunological functions and airway inflammation. RVHs, by inducing recurrent infections, characterized by limited cytotoxicity, when present, through the activation of airway cells and the release of pro-inflammatory mediators, result in recurrent or persistent bronchial hyperreactivity in predisposed individuals. This dynamic complexity highlights the significant contribution of RVH to asthmatic complications, highlighting its influence on the recurrence and persistence of symptoms.

Returning to the context of asthma, allergic sensitization and respiratory tract infections of viral origin, accompanied by wheezing, emerge as preponderant risk factors for the emergence of this condition in childhood. Practically all episodes of wheezing during the first years of life coincide with viral respiratory infections, often linked to Human Rhinovirus (RVH) and Respiratory Syncytial Virus (RSV).

The connection between RSV infection and recurrent asthmatic wheezing, as well as the increased risk of developing asthma, is widely recognized, although the underlying pathophysiological mechanisms are not clearly established. These mechanisms orbit

around two central hypotheses:

1. Respiratory syncytial virus acts as an indicator of childhood susceptibility to the development of wheezing and asthma.

2. The pathogen plays a role as a trigger for recurrent wheezing, regardless of the child's predisposition to asthma.

Children with hypersensitivity to common allergens, bronchial hyperresponsiveness and physiological and anatomical changes in the airways are more likely to develop recurrent wheezing in response to RSV-induced respiratory infections. Furthermore, the presence of susceptible genes associated with the development of bronchial inflammation is also a relevant consideration. In addition to the existence of susceptibility genes likely to be associated with the development of bronchial inflammation, they are divided into:

Airway mucosal response;

Innate immune response;

Adaptive immune response;

Allergic response.

The Respiratory Syncytial Virus (RSV) replicates in the tissues lining the airways and in type I pneumocytes, triggering an infection that causes an intense inflammatory process. This amplified process results in increased viscosity, mucus secretion, and significant bronchial obstruction. The comprehensive inflammatory process of the airways causes injuries and damage to the respiratory epithelium, allowing substances to enter the tissues. This, in turn, facilitates sensitization to allergens or the stimulation of irritant receptors, contributing to a greater incidence of wheezing episodes. This is not directly related to the child's greater susceptibility to developing asthma, but rather to the greater likelihood of the condition occurring due to damage and injuries to the respiratory epithelium.

The close correlation between asthma and Human Rhinovirus (RVH) reaches the point where the C variant of RVH is frequently associated with asthma exacerbations. The mechanism underlying the link between atopy and RVH infection, exemplified by the increased expression of ICAM-1 (intercellular adhesion molecule 1 - main RVH receptor) in atopic individuals, favors:

- More serious cases of infection;
- Greater response mediated by T helper 2 (Th2) cells, suppressing Th1 responses, such as IFN-gamma, a component of the non-specific defense mechanism against viral infections;
- Disruption of airway epithelium due to allergic inflammation, pollution and recurrent infections, promoting RVH adhesion and replication.

Anatomical-physiological changes, such as a decrease in the diameter of the airways and the subsequent reduction in lung capacity, together with cellular and immunological mechanisms, are predisposing elements for episodes of wheezing triggered by the Human Rhinovirus (RVH) in children.

Finally, it is crucial to highlight that Respiratory Syncytial Virus (RSV) acts more as an instigator of asthma, while RVH plays the role of trigger, recognizing atopy as a facilitator. Prematurity and early chronological age are identified as risk factors for the development of serious infections caused by RSV.

The infection is associated with extensive epithelial damage in the airways and the overexpression of neurogenic inflammation, resulting in long-lasting bronchial hyperreactivity. RVH infection is favored by atopy and induces the occurrence of recurrent infections, characterized by minimal cytotoxicity, release of mediators by structural and inflammatory cells in the airways, in addition to inducing long-lasting bronchial hyperreactivity.

CONCLUSION

The text addresses the complex mechanisms involved in RVH and RSV infection, highlighting their influence on the genesis and worsening of wheezing and asthma in children. The relationship between these viruses, genetic predisposition and lesions in the respiratory epithelium increases susceptibility to asthma, prompting relevant considerations for primary prevention. Targeting therapies for allergic sensitization and viral respiratory diseases shows promise, although further studies are needed to establish the precise relationship.

Regarding prevention factors, the most important are the elimination of predispositions, prenatal care, adequate home environment and hygiene, regular physical activity and the promising vaccination, especially against RVH. However, these treatments are in the development stages, requiring more investment and studies to ensure an effective and safe vaccine for children, allowing for efficient public health intervention.

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