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ARTIGO DE REVISÃO

NEONATAL IMMUNOTOLERANCE SYNDROME INDUCED BY MATERNAL MICROCHIMERISM: IMPLICATIONS FOR AUTOIMMUNE DISEASES IN CHILDHOOD

Síndrome de imunotolerância neonatal induzida por microquimerismo materno: implicações para doenças autoimunes na infância

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ABSTRACT

Maternal microchimerism-induced neonatal immunotolerance syndrome refers to the persistence of maternal cells in the newborn's body, a phenomenon that can impact the regulation of the infant immune system. During pregnancy, there is a bidirectional exchange of cells between mother and fetus, which can lead to a state of prolonged immune tolerance. Evidence suggests that this maternal cellular presence can both confer protection and increase susceptibility to autoimmune diseases in childhood, such as juvenile systemic lupus erythematosus, juvenile idiopathic arthritis and type 1 diabetes mellitus. Understanding the mechanisms involved in this process is essential to assessing its impact on childhood immune development. The aim of this study is to investigate the influence of maternal microchimerism on neonatal immunotolerance and its relationship with autoimmune diseases in childhood, analyzing the underlying immunological mechanisms and their clinical implications. This study is a literature review with a qualitative approach, investigating the impact of maternal microchimerism on immune tolerance and the development of pediatric autoimmune diseases. Articles published between 2020 and 2023 were analyzed, taking into account recent advances in the field. The studies analyzed indicate that maternal microchimerism can influence the neonatal immune response, promoting greater immune tolerance. This phenomenon can reduce the incidence of some inflammatory diseases, but also predispose to certain autoimmune diseases by altering the balance between tolerance mechanisms and immune activation. The presence of maternal cells in lymphoid and peripheral tissues can modulate the activity of regulatory T lymphocytes and the production of inflammatory cytokines, impacting the development of the infant immune system. Despite advances in understanding this phenomenon, the exact mechanisms and modulating factors are still under study. Therefore, neonatal immunotolerance induced by maternal microchimerism represents a relevant immunological factor in childhood, with a potential influence on protection or predisposition to autoimmune diseases. Although studies point to a regulatory role of maternal cells in the infant immune response, the complexity of this phenomenon requires further research to elucidate its clinical implications and identify possible therapeutic strategies for pediatric autoimmune diseases.

Keywords: Pediatrics, maternal microchimerism, autoimmune diseases in children.

RESUMO

A síndrome de imunotolerância neonatal induzida por microquimerismo materno refere-se à persistência de células maternas no corpo do recém-nascido, um fenômeno que pode impactar a regulação do sistema imunológico infantil. Durante a gravidez, há uma troca bidirecional de células entre a mãe e o feto, o que pode levar a um estado de tolerância imunológica prolongada. Evidências sugerem que essa presença celular materna pode conferir proteção e aumentar a suscetibilidade a doenças autoimunes na infância, como lúpus eritematoso sistêmico juvenil, artrite idiopática juvenil e diabetes mellitus tipo 1. Compreender os mecanismos envolvidos nesse processo é essencial para avaliar seu impacto no desenvolvimento imunológico infantil. O objetivo deste estudo é investigar a influência do microquimerismo materno na imunotolerância neonatal e sua relação com doenças autoimunes na infância, analisando os mecanismos imunológicos subjacentes e suas implicações clínicas. Este estudo é uma revisão de literatura com abordagem qualitativa, investigando o impacto do microquimerismo materno na tolerância imunológica e no desenvolvimento de doenças autoimunes pediátricas. Foram analisados artigos publicados entre 2020 e 2023, considerando os avanços recentes na área. Os estudos analisados indicam que o microquimerismo materno pode influenciar a resposta imune neonatal, promovendo maior tolerância imunológica. Esse fenômeno pode reduzir a incidência de algumas doenças inflamatórias, mas também predispor a certas doenças autoimunes, alterando o equilíbrio entre os mecanismos de tolerância e a ativação imunológica. A presença de células maternas em tecidos linfoides e periféricos pode modular a atividade de linfócitos T reguladores e a produção de citocinas inflamatórias, impactando o desenvolvimento do sistema imunológico infantil. Apesar dos avanços na compreensão desse fenômeno, os mecanismos exatos e os fatores moduladores ainda estão em estudo. Portanto, a imunotolerância neonatal induzida pelo microquimerismo materno representa um fator imunológico relevante na infância, com potencial influência na proteção ou predisposição a doenças autoimunes. Embora estudos apontem para um papel regulador das células maternas na resposta imune infantil, a complexidade desse fenômeno requer mais pesquisas para elucidar suas implicações clínicas e identificar possíveis estratégias terapêuticas para doenças autoimunes pediátricas.

Palavras-chave: Pediatria, microquimerismo materno, doenças autoimunes em crianças.

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INTRODUCTION

Neonatal immunotolerance is a fundamental phenomenon in the formation of the newborn's immune system, allowing the organism to differentiate its own structures from potential pathogens. This process is largely influenced by the presence of maternal cells in the fetus, a phenomenon known as maternal microchimerism. The transplacental transfer of maternal cells occurs during pregnancy and can persist in the infant's body for years, significantly affecting the development of the immune system and susceptibility to autoimmune diseases. Although this phenomenon is an essential mechanism for ensuring neonatal immune adaptation, recent research suggests that it may be related to a predisposition to autoimmune diseases in childhood, depending on the interaction between genetic and environmental factors (PARKER et al., 2020).

Maternal microchimerism can act in a paradoxical way: in some cases, it contributes to immune protection, promoting tolerance and reducing predisposition to exacerbated inflammatory reactions. However, studies show that this cellular presence can, under certain circumstances, lead to a state of immune hyperreactivity, triggering or exacerbating autoimmune diseases such as systemic lupus erythematosus (SLE), type 1 diabetes mellitus and juvenile idiopathic arthritis (CHIEN et al., 2022). This phenomenon occurs because maternal cells can be recognized as foreign by the newborn's body, leading to the activation of aberrant immune responses and the production of autoantibodies, a phenomenon characteristic of autoimmune diseases (MORRISON et al., 2023).

The influence of maternal microchimerism on neonatal immunity also raises important questions about the development of therapeutic and preventive strategies. Early identification of altered immunological patterns may allow for targeted therapeutic approaches, reducing the impact of autoimmune diseases from infancy. In addition, understanding the dynamics of this process opens up new perspectives on the role of pregnancy in modulating immunity throughout life and in transmitting maternal immunological characteristics to offspring (ROSSI et al., 2023).

Therefore, neonatal immunotolerance syndrome induced by maternal microchimerism represents an emerging field of immunology, with direct implications for understanding pediatric autoimmune diseases. Further research in this field could provide crucial information for the clinical management and prevention of these diseases, promoting advances in immunological and perinatal medicine. With the growing availability of new technologies for analyzing maternal-fetal interaction in the immunological context, it is expected that the coming years will bring a better understanding of the relevance of this phenomenon and its potential clinical applications (DAWE et al., 2021).

The aim of this study is to investigate the influence of maternal microchimerism on neonatal immunotolerance and its relationship with autoimmune diseases in childhood, analyzing the underlying immunological mechanisms and their clinical implications.

MATERIALS AND METHODS

This study is a literature review with a qualitative approach, investigating the impact of maternal microchimerism on immune tolerance and the development of pediatric autoimmune diseases. Articles published between 2020 and 2023 were analyzed, taking into account recent advances in the field.

- Guiding question:

What is the influence of maternal microchimerism on the development of the neonatal immune system and its possible relationship with autoimmune diseases in childhood?

- Inclusion criteria:

- Articles published between 2020 and 2023.

- Studies addressing maternal microchimerism, neonatal immune programming and pediatric autoimmune diseases.

- Publications available in full and indexed in PubMed, Scopus, Web of Science and SciELO.

- Works written in Portuguese, English or Spanish.

- Systematic reviews, clinical studies and experimental research relevant to the topic.

- Exclusion criteria:

- Studies from before 2020.

- Papers not available in full or without clinical relevance.

- Articles focused exclusively on microchimerism in adults with no relation to childhood immunity.

- Isolated case reports or studies without robust methodology.

- Boolean markers:

("Maternal microchimerism" AND "Neonatal immune tolerance") ("Microchimerism" OR "Fetal cell transfer") AND ("Autoimmune diseases in children") ("Pediatric immune programming" AND "Microchimerism").

Theoretical background

Maternal microchimerism is a phenomenon characterized by the transplacental transfer of maternal cells to the fetus, which can persist in the infant's body for long periods. This process occurs naturally during pregnancy and plays an essential role in regulating neonatal immunity. Recent studies indicate that the presence of these cells can contribute to the fetus' immunotolerance, promoting the acceptance of maternal antigens and reducing the incidence of severe immunological reactions at birth. In addition, this cellular interaction between mother

and child has been associated with the modulation of the innate and adaptive immune response, and is a determining factor in the development of the newborn's immunity (LARSON et al., 2022).

Although immunotolerance is a crucial process in avoiding maternal-fetal immune rejection, there is evidence that microchimerism can also predispose the individual to dysfunctional immune responses. Under certain conditions, maternal cells can be interpreted as "not their own" by the infant immune system, leading to the development of autoimmune reactions in childhood (KIMURA et al., 2021). Thus, the persistence of these cells may act as a risk factor for autoimmune diseases, making it essential to investigate their long-term effects.

The relationship between maternal microchimerism and pediatric autoimmune diseases has been increasingly explored in the scientific literature. Research indicates that children diagnosed with systemic lupus erythematosus (SLE), juvenile idiopathic arthritis and type 1 diabetes mellitus have a higher maternal cell load compared to healthy individuals, suggesting a possible role for these cells in triggering autoimmunity (RUIZ et al., 2020). This phenomenon may occur due to the activation of the immune system against maternal cells, generating an unregulated inflammatory response and the production of autoantibodies (MASON et al., 2021).

In the context of childhood SLE, for example, evidence indicates that the presence of maternal cells in the peripheral blood of affected children may be related to an exacerbated activation of the immune system. This process results in the formation of immune complexes and the activation of inflammatory pathways typical of the disease. Similarly, in type 1 diabetes mellitus, the persistence of pancreatic beta cells of maternal origin in children has been associated with the autoimmune destruction of these cells, leading to the progressive failure of insulin production (FERNÁNDEZ et al., 2023).

With the advance of research into maternal microchimerism, new therapeutic approaches are being investigated to reduce the impact of this phenomenon on the development of autoimmune diseases in childhood. Immunomodulatory strategies, such as the use of stem cell-based therapies and the induction of immune tolerance, have been explored as ways of minimizing the dysfunctional immune response associated with microchimerism (GARCÍA et al., 2022).

In addition, the early identification of children with a high maternal cell load may allow preventive interventions, such as continuous immunological monitoring and the adoption of dietary and pharmacological strategies to modulate the inflammatory response. An in-depth understanding of this phenomenon may also provide new perspectives for the clinical management of autoimmune diseases, helping to develop more effective and personalized therapeutic protocols for these patients (SANTOS et al., 2023).

Thus, neonatal immunotolerance syndrome induced by maternal microchimerism represents an emerging field of immunology, with direct implications for the understanding and treatment of pediatric autoimmune diseases. Further research in this area will enable significant advances in the identification of predisposing factors and the implementation of innovative preventive and therapeutic strategies for these conditions (OLIVEIRA et al., 2023).

CONCLUSION

It can be concluded that neonatal immunotolerance syndrome induced by maternal microchimerism represents an emerging field of immunology with direct implications for the development of autoimmune diseases in childhood. The persistence of maternal cells in the infant organism may play a dual role: on the one hand, contributing to immune regulation and, on the other, acting as a predisposing factor for dysfunctional autoimmune responses.

The relationship between maternal microchimerism and diseases such as systemic lupus erythematosus, juvenile idiopathic arthritis and type 1 diabetes mellitus reinforces the need for further investigation. The early identification of children with high maternal cell burden may be essential for the implementation of preventive and therapeutic strategies, reducing the impact of these conditions on patients' quality of life.

New therapeutic approaches, including immunomodulatory therapies and tolerance induction strategies, have been explored as potential interventions to minimize the adverse effects of this phenomenon. Advances in research into the interaction between microchimerism and the neonatal immune system could provide a better understanding of the mechanisms involved and contribute to the development of more effective and personalized treatments.

Understanding maternal microchimerism not only broadens our knowledge of neonatal immunotolerance, but also opens up new perspectives for the diagnosis, monitoring and management of autoimmune diseases in childhood. Further research in this area could bring significant advances to pediatric immunology, favoring more precise and effective approaches to the care of these children.

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Observação: os/(as) autores/(as) declaram não existir conflitos de interesses de qualquer natureza.