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OMALIZUMAB IN CHILDREN OVER 12 YEARS OLD - EFFECTIVENESS AND CLINICAL CONSIDERATIONS IN ASTHMA AND ATOPIC DERMATITIS: A LITERATURE REVIEW

Nicolas Francisco Silva
Universidade de Vassouras
Vassouras - Rio de Janeiro
http://lattes.cnpq.br/3634607339139597

Natalia Barreto de Sousa
Universidade de Vassouras
Vassouras- Rio de Janeiro
http://lattes.cnpq.br/4593315918843827

Abstract: Omalizumab is a humanized monoclonal antibody used to treat allergic conditions, such as moderate to severe allergic asthma and chronic spontaneous urticaria. It specifically acts on immunoglobulin E (IgE), an important mediator of the allergic response. 245 articles were analyzed in the PubMed, LILACS and SciELO databases, resulting in 23 articles selected following inclusion and exclusion criteria. The included articles were published in the last 10 years and addressed the efficacy and clinical considerations of omalizumab in asthma and atopic dermatitis. Studies have demonstrated its effectiveness in controlling asthma, especially in severe and difficult-to-control cases, reducing exacerbations and improving quality of life. In children, omalizumab has been shown to be a promising therapeutic option for severe uncontrolled asthma, significantly reducing exacerbations and improving disease control. In addition to asthma, omalizumab has also been studied in atopic dermatitis, demonstrating a reduction in symptoms and an improvement in quality of life. However, its use is not free from side effects, such as reactions at the injection site and increased risk of respiratory infections, and it is important to carefully evaluate the benefits and risks for each patient. In conclusion, omalizumab represents a valuable therapeutic option for children and adolescents with severe allergic asthma and atopic dermatitis, offering an innovative approach to treating allergic conditions.
Keywords: Omalizumab; anti-IgE; child.

INTRODUCTION

Omalizumab is a humanized monoclonal antibody developed to treat allergic conditions such as moderate to severe allergic asthma and chronic spontaneous urticaria. This therapy represents an innovative approach to treating allergic diseases, specifically targeting immunoglobulin E (IgE), an important mediator of the allergic response. (BUSSE W, et al. 2013) (HANANIA NA, et al. 2021).

Asthma is one of the conditions in which omalizumab has been studied extensively, especially in severe and difficult-to-control cases, where it has been shown to reduce exacerbations and improve disease control. Furthermore, studies have shown that asthma in children is often undertreated and poorly controlled, even with optimal therapies such as high doses of inhaled corticosteroids plus long-acting β2-agonists, leukotriene receptor antagonists, or theophylline. Uncontrolled severe asthma in this age group can result in significant risks, such as frequent exacerbations, hospitalizations, compromised lung function and negative impacts on quality of life. (TEACH SJ, et al. 2015) (CHEN T, et al. 2017).

Studies have shown that omalizumab has emerged as a promising therapeutic option for children with severe, uncontrolled asthma. As an IgE antagonist, omalizumab interrupts the allergic cascade, reducing the binding of IgE to its receptors on mast cells and basophils, resulting in less release of inflammatory mediators and, consequently, less airway inflammation (IYENGAR SR, et al. 2013), (JOHANSSON SGO, et al. 2018).

In children, studies have shown that omalizumab can significantly reduce asthma exacerbations, improve disease control and, consequently, quality of life. In addition to asthma, omalizumab has also been studied in other allergic conditions, such as atopic dermatitis (AD). AD is a chronic inflammatory

skin disease common in children, with a significant impact on quality of life and a considerable economic and psychosocial burden. Studies indicate that IgE plays an important role in the pathophysiology of AD, and high levels of IgE are associated with more severe forms of the disease. In this context, omalizumab has been studied as a therapeutic option for severe cases of AD, aiming to reduce IgE levels and, thus, alleviate the symptoms of the disease (CHAPMAN KR, et al. 2019).

The effectiveness of omalizumab in children with asthma and other allergic conditions has been well documented, with studies demonstrating significant improvements in quality of life and disease control. However, it is important to highlight that omalizumab is not without side effects and must be used with caution, especially in children. Adverse effects such as injection site reactions, severe allergic reactions, and increased risk of respiratory infections have been reported in some studies. Therefore, the decision to prescribe omalizumab in children must be carefully evaluated, considering the potential benefits and risks for each patient (JOHANSSON SGO, et al. 2018).

In summary, omalizumab represents a valuable therapeutic option for children with allergic conditions, such as asthma and atopic dermatitis, especially in severe and difficult-to-control cases. Its specific mechanism of action, targeting IgE, offers an innovative approach to treating these diseases, with consistent evidence of efficacy in reducing exacerbations and improving disease control. However, the benefits of omalizumab must be weighed against its potential side effects, and its use in children must be carefully considered and monitored (CASALE TB, et al. 2018), (HANANIA NA, et al. 2021).

METHODS

This is an integrative literature review study, carried out in the National Library of Medicine (PubMed), Scientific Electronic Library Online (SciELO) and Latin American and Caribbean Literature in Health Sciences (LILACS) information banks. The search for articles was carried out using the following descriptors: Omalizumab; anti-IgE; child, considering the Boolean operator "AND" between the respective words. The following steps were carried out: establishment of the theme; definition of eligibility parameters; definition of admission and exclusion requirements; verification of publications in databases; examination of the information found; analysis of the studies found and presentation of the results. Articles published in the last 10 years (2013 - 2023), in English and Portuguese, and articles such as clinical trials, randomized clinical studies and newspaper articles were included. The exclusion criteria were articles that added other information to the central topic and those that did not specifically address the efficacy and clinical considerations of omalizumab in asthma and atopic dermatitis.

RESULTS

Given the association of descriptors used, a total of 245 works was analyzed, 240 were selected from the PubMed database, 5 from the LILACS database and 0 from the SciELO database. Using the inclusion criteria: articles published in the last 10 years (2013-2023), resulted in a total of 148 articles. Then, articles of the type clinical trial, randomized controlled clinical trial or newspaper articles were added as inclusion criteria, totaling 23 articles. Articles in Portuguese or English were selected, resulting in 23 articles and then the full and free text option was added, totaling 23 articles.

After reading the abstracts, those that did not fit the topic covered or that were duplicates were excluded, totaling 21 articles, as illustrated in Figure 1.

DISCUSSION

Patients with atopic asthma often experience persistent symptoms and exacerbations despite normal lung function. Poor control or exacerbation of asthma often leads to the need for intervention with oral corticosteroids. Factors that contribute to loss of control include exposure to allergens and/or respiratory infection. Omalizumab, a recombinant humanized monoclonal antibody that selectively binds free IgE, is indicated for patients (≥12 years) with moderate to severe allergic asthma inadequately controlled with inhaled corticosteroids. In a 24-week, double-blind, placebo-controlled, multicenter study, the efficacy of omalizumab was evaluated in patients aged 12 to 75 years with atopic asthma who were symptomatic despite normal lung function. Although the primary outcome of reducing asthma exacerbation rates was not statistically significant, there was a 27% reduction with omalizumab versus placebo. Subgroup analysis showed a 59% reduction in exacerbation rates in patients with elevated eosinophil counts. Omalizumab may benefit patients with symptomatic asthma and normal lung function, particularly those with elevated eosinophil counts, suggesting eosinophil counts as a potential biomarker for predicting omalizumab treatment outcomes (BUSSE W, et al. 2013).

Omalizumab, which is an anti-IgE therapy, modulates immune responses beyond immediate hypersensitivity. It reduces the proliferation of allergen-specific T cells and the expression of Th2 cytokines, suggesting a role in regulating antigen-specific T cell responses. In children with severe atopic dermatitis (AD), omalizumab effectively reduced the levels of free IgE and key molecules involved in the pathogenesis of AD, such as TSLP, TARC, OX40L and IL-9. These findings support further investigation of the effects of omalizumab on antigen-specific T cells and its potential as a treatment for AD (IYENGAR SR, et al. 2013)

Models were developed to describe the relationships between serum free IgE and asthma-relevant outcomes: FEV1 and FeNO. Omalizumab significantly reduced free IgE levels, with a mean IC50 of 19.8 ng/ml for FEV1 and EC50 of 19.7 ng/ml for FeNO, indicating that free IgE levels below 23-28 ng/ml may improve lung function and reduce airway inflammation. Interindividual variability was high, suggesting that target free IgE levels may vary between individuals (ZHU R, ZHENG Y, et al. 2013).

One approach, trialing the seasonal addition of omalizumab to standard therapy, significantly reduced asthma exacerbations during the fall, especially benefiting patients with recent exacerbations. There was no significant difference between omalizumab and augmentation of inhaled corticosteroids in preventing exacerbations, but omalizumab was more effective in patients with recent exacerbations. These results highlight the importance of careful patient selection for treatment with seasonal omalizumab (TEACH SJ, et al. 2015).

Another demonstration of omalizumab improved treatment adherence in patients with difficult-to-control asthma and poor adherence to inhaled corticosteroids. Additionally, it significantly reduced the need for prednisone for asthma exacerbations, decreased emergency room visits, and improved adenosine PC20 (a test used to assess airway reactivity in patients with asthma), indicating a reduction in airway inflammation. The treatment was well tolerated, with few serious side effects.

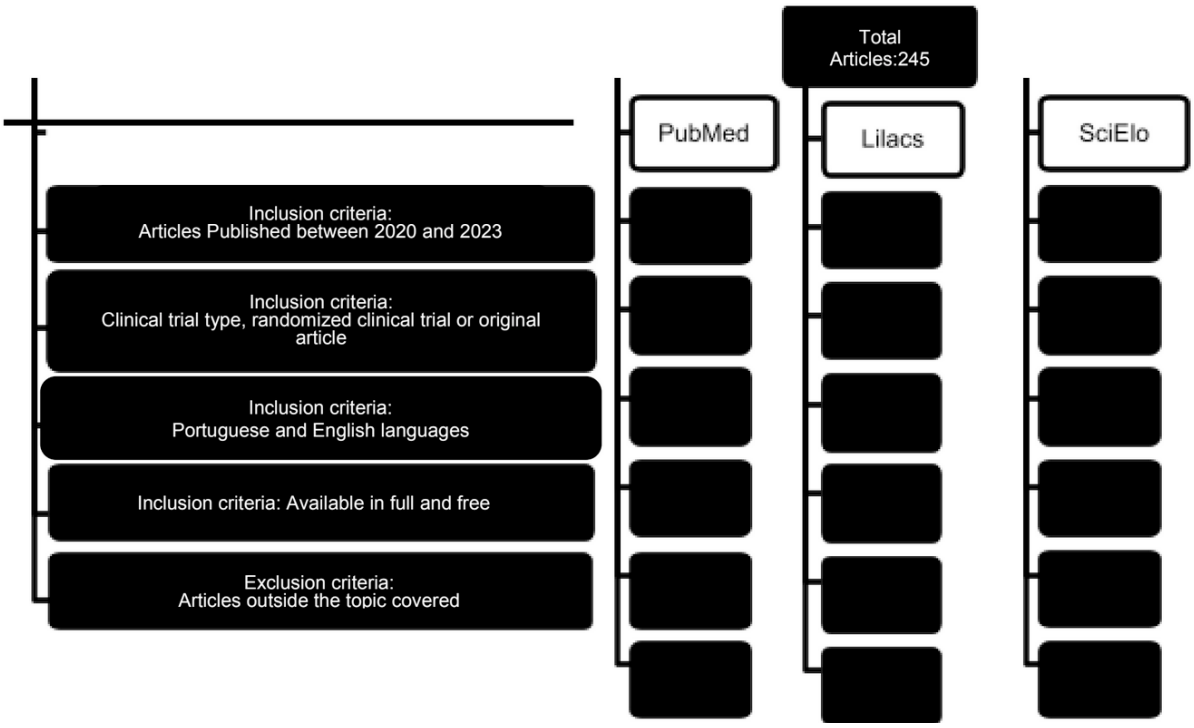

FIGURE 1: Flowchart for identifying articles in PubMed, LILACS and SciELO.

Source: Authors (2024)

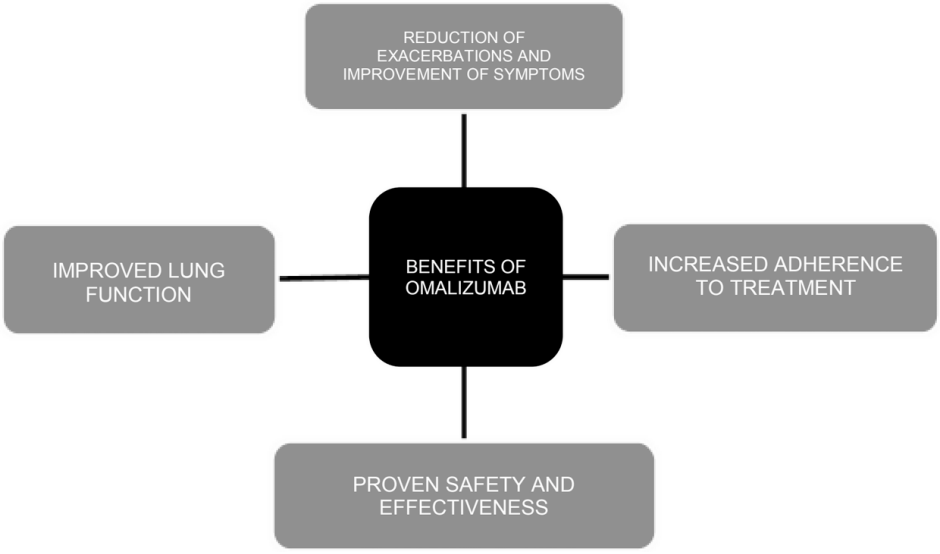

FIGURE 2: Summary of the most found results according to the articles analyzed.

Source: Authors (2024)

Omalizumab can be considered as additional therapy for patients with very poor control asthma and poor adherence to inhaled corticosteroids (HENDELES L, et al. 2015)

The review of omalizumab dosage allowed the frequency of administration to be reduced, improving adherence and reducing costs for patients with severe asthma. Predictive models have shown that doubling the dose and dosing every 4 weeks maintains efficacy and safety. Omalizumab acts mainly by suppressing free IgE, improving asthma symptoms. Dosage changes do not significantly affect the efficacy or safety of treatment. This dosage adjustment may be a valuable alternative for patients with asthma and atopic dermatitis who face adherence and cost challenges. These findings reinforce the importance of considering not only clinical efficacy, but also practical and economic factors when choosing treatment for these conditions, always seeking a balance between clinical benefit and accessibility (LOWE PJ, et al. 2015).

The safety of omalizumab was evaluated in patients with moderate to severe allergic asthma, finding no association with an increased risk of malignancy. The study followed patients for about 5 years and included individuals with a history of cancer or a high risk of cancer. Analyzes showed no significant differences in the risk of malignancy between the groups of patients who received omalizumab and those who did not. The most common types of cancer were compatible with the incidence in the general population. Although the study has limitations, such as the inability to detect significant increases in the rates of specific types of cancer, the results provide evidence that omalizumab is safe in relation to the risk of malignancy (LONG A, et al. 2015).

Omalizumab has demonstrated significant efficacy in reducing seasonal asthma exacerbations, especially in patients sensitized to cockroach allergen. This medication has also shown benefits in reducing asthma symptoms and exacerbations in children and adolescents, with effects observed in the first weeks of treatment and maintained over time. It has been suggested that omalizumab may be effective in different stages of asthma and in different age groups, children aged 6 to 12 years and older adolescents over the age of 12 years. These groups showed similar benefits from the use of omalizumab in the treatment of persistent allergic asthma, with certain subgroups of patients being more likely to benefit. These results contribute to the understanding of the use of omalizumab in the treatment of persistent allergic asthma in children and adolescents, providing important thoughts for the selection and individualization of therapy (SORKNESS CA, et al.2014).

An article of great importance, investigated the safety, efficacy and pharmacological effects of omalizumab in children with severe uncontrolled asthma. Nearly 90% of patients received treatment for ≥104 weeks, with significant improvements in asthma control and quality of life. Discontinuation of treatment resulted in worsening of symptoms, indicating the continued importance of omalizumab. The safety profile was similar to previous studies, with few additional concerns. Prolonged treatment showed no loss of efficacy or increased risks. The study suggests that omalizumab may have disease-modulating effects, reducing IgE production and keeping asthma under control after stopping treatment. Omalizumab was well tolerated and effective as complementary therapy in children with severe allergic asthma, without evidence of increased risks or loss of efficacy with prolonged exposure (ODAJIMA H, et al. 2017).

In the same sense, omalizumab in patients with severe and moderate asthma

demonstrated a significant reduction in exacerbations and improvements in ACT scores after 12 months of treatment. Patients with elevated biomarker levels showed greater improvement in asthma symptoms, and the majority of patients uncontrolled at the start of the study achieved asthma control at the end. The treatment was effective across several biomarker values, although the clinical relevance of the improvement in FEV1 is uncertain. Multivariate analysis suggests that men and patients with positive allergen-specific IgE test results may respond better to treatment. Variability in IgE levels did not appear to affect the efficacy of omalizumab. In summary, omalizumab has been shown to be effective and safe for the treatment of moderate to severe asthma, especially in patients with elevated biomarkers (CASALE TB, et al. 2018).

It is important to highlight that omalizumab is an effective treatment for this condition, acting by binding to free circulating IgE, thus reducing the amount of IgE available to bind to inflammatory cells. Studies have shown that allergic sensitivity can be determined by CD-sens, a marker that correlates with bronchial allergic sensitivity. In a clinical study, 28% of patients became CD-sens negative after 16 weeks of treatment, and an increase in dose resulted in success in another 20% of patients. However, although there was a decrease in IgE-mediated inflammation, there was no conclusive improvement in clinical parameters after 16 weeks of treatment. The efficacy of omalizumab appears to be influenced by the size of the IgE-ab fraction, indicating the need to consider this factor before starting treatment (JOHANSSON SGO, et al. 2018).

Several studies have shown a reduction in exacerbation rates and improved lung function in patients with allergic asthma. Improvements in lung function were observed as early as week 4 of treatment. Omalizumab was more effective in reducing exacerbations in patients with high reversible bronchodilation (BDR), regardless of airway obstruction (FAO) status, but was not more effective than placebo in patients with low BDR. Improvements in lung function were observed mainly in FAO- patients with elevated BDR. The results suggest that the response to omalizumab may be influenced by underlying mechanisms such as acute inflammation and structural changes in the airways. This study provides valuable insights into the effectiveness of omalizumab in different subgroups of patients with allergic asthma (HANANIA NA, et al. 2021)

In summary, omalizumab has demonstrated to be an effective and safe therapeutic option for the treatment of allergic asthma and atopic dermatitis, especially in patients with elevated biomarkers. Its disease-modulating effects, reducing exacerbations and improving quality of life were consistent in reviewed clinical studies. Individualization of therapy, considering IgE levels and other biomarkers, is essential to maximize the benefits of omalizumab in these patients. Further studies are needed to further elucidate its mechanisms of action and potential clinical applications.

CONCLUSION

Omalizumab therapy represents an innovative and effective approach to treating allergic conditions such as allergic asthma and atopic dermatitis. This humanized monoclonal antibody targets immunoglobulin E (IgE), a key mediator of the allergic response, providing significant benefits in patients with severe asthma and severe atopic dermatitis. Over the years, several studies have corroborated its efficacy and safety, especially in children and adolescents, filling an important gap in the treatment of serious and difficult-to-control allergic conditions. Allergic asthma, in particular, represents a significant challenge, with children often undergoing aggressive

therapies and yet experiencing persistent symptoms. Omalizumab appears as a promising therapeutic option, reducing exacerbations, improving disease control and, consequently, quality of life. Its ability to modulate the allergic response, reducing the release of inflammatory mediators and airway inflammation, has been fundamental to these benefits.

In addition to asthma, omalizumab has also shown efficacy in the treatment of severe atopic dermatitis, reducing IgE levels and alleviating the symptoms of the disease. Its specific action on free IgE has a direct impact on the pathogenesis of atopic dermatitis, offering a new approach in the treatment of this complex condition. It is important to highlight that, despite the benefits of omalizumab, it is not free from side effects, such as reactions at the injection site and increased risk of respiratory infections. Therefore, the decision to prescribe omalizumab must be carefully evaluated, considering the potential benefits and risks for each patient. In conclusion, omalizumab represents a valuable therapeutic option for children and adolescents with severe allergic asthma and atopic dermatitis, providing significant improvements in disease control and quality of life. Its specific mechanism of action on IgE offers an innovative approach in the treatment of allergic conditions, highlighting its importance in the current therapeutic arsenal. However, more studies are needed to fully elucidate its mechanisms of action and potential clinical applications, always aiming for maximum benefit for patients.

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