Comparative Analysis of New Therapeutic Approaches in the Management and Outcomes of Pediatric Asthma

Abstract

Background: Asthma continues to lead to significant health issues and deaths worldwide, and there has been little progress in treatment outcomes over the past ten years, even though treatment costs have risen.

Literature Review: This literature review explores emerging therapeutic approaches for managing pediatric asthma, focusing on monoclonal antibody treatments, inhaled corticosteroids, long-acting muscarinic antagonists (LAMAs), macrolides, vitamin D supplementation, and innovative devices like temperature-controlled laminar airflow (TLA) and electronic monitoring tools. Monoclonal antibodies, such as omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab, have shown significant efficacy in reducing asthma exacerbations, improving asthma control, and enhancing quality of life in pediatric populations. Omalizumab notably reduces asthma flare-ups and corticosteroid use, while mepolizumab and benralizumab have demonstrated benefits in severe eosinophilic asthma. Dupilumab and tezepelumab offer broader benefits across asthma phenotypes, substantially improving exacerbation rates and lung function. Inhaled corticosteroids remain the cornerstone of asthma management, though they require careful use to prevent tachyphylaxis. Tiotropium, a LAMA, has emerged as a promising add-on therapy, particularly for patients with poorly controlled asthma. Additionally, macrolide antibiotics and vitamin D supplementation have demonstrated the potential to reduce exacerbations and improve symptom control in certain asthma subsets. Innovative devices such as TLA and electronic monitoring tools offer significant advancements in personalized asthma management by reducing allergen exposure and improving medication adherence.

Conclusion: Recent advancements in pediatric asthma treatment, including monoclonal antibodies, inhaled corticosteroids, non-pharmacological devices, long-acting muscarinic antagonists (LAMAs), macrolides, vitamin D supplementation have shown significant improvements in asthma control and quality of life. These therapies offer personalized

approaches, particularly for children with severe asthma or specific inflammatory phenotypes. Ongoing research is essential to optimize their long-term safety, efficacy, and application across diverse populations.

1. Introduction

Asthma is a complex condition that involves ongoing inflammation in the airways(1). It includes symptoms like wheezing, difficulty breathing, a feeling of tightness in the chest, and coughing, which may vary over time in intensity, frequency, and occurrence(1). According to estimates from the World Health Organization, asthma impacted 262 million people and led to 455,000 deaths globally in 2019(2, 3). Given the current trends, it's anticipated that this number will hit 400 million by 2045(4). Asthma is an extremely prevalent persistent illness in children and is the main reason for them missing school, going to the Emergency Department, and being hospitalized(5).Asthma in children is one of the top 20 conditions globally when looking at disability-adjusted life years(6).

Climate change and the increase in carbon dioxide levels promote pollen growth, which is linked to higher rates of asthma in children(7). Currently, 11%–14% of children aged 5 years and older around the world report having asthma symptoms, and it's estimated that 44% of these cases are linked to environmental exposure(8). Environmental factors including dampness, air pollution, indoor mold, andtobacco smokemake asthma worse in children(9).

Asthma is a long-term inflammatory condition of the airways that involves increased sensitivity, both sudden and ongoing tightening of the airways, swelling, and the buildup of mucus(10). Asthma's inflammatory aspect includes various cell types, such as epithelial cells, mast cells, T lymphocytes, eosinophils, and neutrophilsalong with their biological products(10). Most asthma patients can achieve good long-term control with a combination of reliever therapy and controller therapy(10). Many children who have asthma usually experience mild or moderate symptoms(11). They can manage their condition well by avoiding triggers and using medications like inhaled corticosteroids short-acting inhaled b2-receptor agonists (SABA), and sometimes adding leukotriene receptor antagonists and long-acting b2-agonists when necessary(11). Even so, around 2–5% of children with asthma still experience uncontrolled symptoms, even when they are on the highest doses of standard medications, which means they need extra biological treatments(12).

Recently, there have been a lot of new therapeutic tools for pediatric asthma, which is great for both mild and severe cases. This review aims to summarize the latest developments in asthma management and outcomes, particularly highlighting new strategies for treating pediatric asthma.

2. Literature Review

2.1. Monoclonal Antibody Treatment

Omalizumab is the first humanized monoclonal antibody that targets IgE, and it has been studied a lot for moderate-to-severe allergic asthma(13). A study that looked at 2168 children with asthma found that omalizumab really helped reduce asthma flare-ups (risk ratio 0.52) and decreased the need for inhaled as well as oral corticosteroids, which led to better asthma control and improved quality of life(13). Real-life studies also confirmed these outcomes, showing that there were lower rates of exacerbations and less need for steroids(14, 15). In these studies, Omalizumab was mostly well tolerated, showing only mild side effects such as pain at the injection site, and there was no obvious increased risk of cancer(14, 15)..

Mepolizumab, which targets IL-5, has been found to be effective in treating severe eosinophilic asthma(16). The MENSA Phase 3 study showed that there was a 53% decrease in asthma exacerbations and better lung function for adults as well as children (16). A Phase 2 study showed that in children aged 6-17 years, there was a 27% reduction in exacerbations, but there weren't any significant improvements in asthma control or lung function (17). The safety profiles observed in children matched those found in adults, and there were no new safety issues that came up. The results indicate that mepolizumab could be a useful add-on treatment for children with severe eosinophilic asthma, but we still need more information about its long-term safety and effectiveness.

Benralizumab, which targets the IL-5 receptor α chain, has shown notable effectiveness in decreasing asthma exacerbations in cases of severe eosinophilic asthma(18). In Phase 3 trials, benralizumab was found to lower exacerbation rates when compared to a placebo, especially in patients who had blood eosinophil counts of 300 cells/μL or more(19, 20). Even though research in adolescents has shown some inconsistent findings, long-term follow-ups indicated that there are low rates of exacerbation with ongoing use in both children and adolescent groups(20). Benralizumab was mostly well tolerated, and there were no significant safety issues found in the

pediatric group(20). At the same time, dupilumab, which targets IL-4 receptors, has been demonstrated to decrease severe asthma flare-ups and enhance lung function in children experiencing type 2 inflammation(21). The VOYAGE trial showed that dupilumab helped reduce exacerbations and improve asthma control in children, and it also had a good safety profile(22, 23). Lastly, tezepelumab, a drug that inhibits thymic stromal lymphopoietin (TSLP), has shown the potential to decrease asthma exacerbations and enhance asthma control in different asthma phenotypes(24). The NAVIGATOR trial showed that tezepelumab substantially decreased annual exacerbation rates in children when compared to placebo(24). The treatment was generally well accepted, with some mild side effects such as joint pain and sore throat(25)

2.2.Inhaled corticosteroids

Asthma is an inflammatory condition, so it needs to be treated with anti-inflammatory agents, like inhaled corticosteroids(26). Starting treatment early with inhaled corticosteroids leads to better results, a lower chance of asthma flare-ups, and a decreased risk of death related to asthma in children (26). So, it still needs to be demonstrated if starting (or delaying) anti-inflammatory treatment changes the progression of the disease(26). It's really important to understand that using short-acting β2-agonists regularly can cause tachyphylaxis, which means the receptors become tolerant quickly. This can lead to rebound bronchoconstriction, a decreased response to these medications, and even more reactions to allergens and inflammation(27).

2.3.Long-Acting Muscarinic Antagonist

Tiotropium is a muscarinic antagonist that is widely used to manage chronic obstructive pulmonary disease(28). Acetylcholine, a neurotransmitter, is released by parasympathetic nerves in the lungs, leading to several responses, including the release of proinflammatory mediators from the airway epithelial pathways, increased mucus secretion, contraction of airway smooth muscles and enhancement of ciliary beat frequency(28). This also stimulates vasodilation and fibroblast proliferation. Tiotropium effectively binds to M1, M2, and M3 cholinergic receptors but has a slower dissociation from M1 and M3 receptors, contributing to its prolonged bronchodilatory effects(29). It is typically administered once daily, as its effects last up to 35 hours, with peak efficacy occurring within 60 minutes of administration(29).Clinical trials indicate that using tiotropium Respimat™ as an add-on therapy to inhaled corticosteroids can lead to better lung function in patients who have poorly controlled asthma(30).. Tiotropium

could be a helpful and new add-on treatment choice, particularly for patients who do not achieve enough asthma control with moderate-to-high ICS, with or without the administration of LABA(30).The results from the extensive clinical trial program involving adolescents and children with varying levels of asthma severity show that tiotropium Respimat® is an effective and well-tolerated bronchodilator when used alongside inhaled corticosteroids, leading to better lung function(29).

2.4.Macrolides antibiotics

Macrolide antibiotics help decrease the frequency of exacerbations in bronchiectasis through their antibiotic properties or their ability to reduce inflammation(31). Brusselle et al. pointed out that macrolide antibiotics might only be beneficial for adults who have non-eosinophilic inflammation. A current investigation by Gibson and its colleagues involving 420 children with moderate or severe asthma found that oral azithromycin reduced the occurrence of moderate flare-ups of asthma(32).

2.5.Vitamin D Supplements

There's a lot of interest in how taking vitamin D might help lower the risk of asthma flare-ups and improve control of asthma symptoms. One theory to explain how vitamin D works is that its combination of antimicrobial, antiviral, and anti-inflammatory properties might lower the exacerbation risks, which are frequently triggered by respiratory infections. Research indicates that children with asthma have been found to have insufficient vitamin D levels in different environments(33). Children with lower vitamin D levels tend to have poorer asthma control, reduced lung function, and a higher risk of exacerbations(34). Therefore, taking vitamin D can be beneficial. As a previous meta-analysis involving individuals with mostly moderate asthma indicates that vitamin D may help lower the risk of severe asthma exacerbations and reduce the need for healthcare services(35).

2.6.Temperature-Controlled Laminar Airflow (TLA) Devices And Electronic Monitoring Tools

Temperature-controlled laminar Airflow (TLA) devices and electronic monitoring tools have shown important advantages in controlling asthma(36, 37). The TLA device helps reduce allergen exposure while sleeping by providing cooled, filtered air from above. It has been shown

to improve asthma-specific quality of life in patients, particularly in those with more severe asthma(36, 37). In a year-long study, people with poorly managed asthma experienced notable improvements in their symptoms and sleep quality. At the same time, electronic monitoring devices that keep track of medication adherence and provide real-time feedback have been shown to be effective in improving asthma control(37). Research has repeatedly indicated that these devices enhance adherence rates, frequently achieving the 75-80% level needed for improved asthma management, particularly in challenging cases(37).

3. Conclusion

In conclusion, recent advancements in pediatric asthma management have introduced promising therapeutic approaches, including monoclonal antibodies and non-pharmacological devices, which significantly improve asthma control. Biologics targeting IgE, IL-5, IL-4/IL-13, and TSLP have shown marked reductions in asthma exacerbations and improvements in lung function and quality of life, especially for children with severe asthma or those with type 2 inflammation. Additionally, treatments like tiotropium, when used as an add-on to inhaled corticosteroids, have demonstrated effectiveness in enhancing asthma control. Non-pharmacological interventions, such as temperature-controlled laminar airflow (TLA) devices and electronic monitoring tools, have proven beneficial in reducing allergen exposure and improving adherence, key factors in managing asthma. These developments represent a significant step forward in personalized asthma care, though ongoing research is essential to optimize treatment strategies and ensure long-term safety and efficacy in diverse pediatric populations.

4. References

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