INTERNATIONAL DEVELOPMENT PLANNING REVIEW
ISSN:1474-6743 | E-ISSN:1478-3401

ADVANCES IN TREATMENT OF ASTHMA AMONG ADULTS: A SYSTEMATIC REVIEW

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Abstract

Background: Asthma is a chronic respiratory disease that significantly impacts the quality of life of millions of adults worldwide. Recent advancements in the treatment of asthma, including new medications, biologic therapies, inhalation devices, and management strategies, have the potential to enhance asthma control and reduce exacerbations. This systematic review aims to evaluate these advancements, focusing on their effectiveness, safety, and impact on patient outcomes.

Methods: A comprehensive search was conducted across multiple databases, including PubMed, Cochrane Library, Scopus, Embase, and Web of Science, for studies published from 2010 onwards. Eligible studies included randomized controlled trials (RCTs), cohort studies, case-control studies, and systematic reviews assessing the effectiveness and safety of innovative asthma treatments. Studies involving non-human subjects or pediatric populations were excluded. Data extraction was performed independently by two reviewers, and meta-analysis was conducted where applicable.

Results: The review identified several advancements in asthma treatment, including the introduction of biologic therapies such as monoclonal antibodies targeting specific inflammatory pathways, inhaled corticosteroid and long-acting beta-agonist (ICS/LABA) combination therapies, and the shift toward personalized treatment plans. Biologic therapies demonstrated significant improvements in reducing asthma exacerbations and improving lung function for severe asthma patients. However, challenges such as high costs and limited accessibility were noted. The review

also highlighted the importance of patient adherence to treatment regimens and proper inhaler technique in managing asthma effectively.
Conclusion: Recent advancements in asthma treatment, particularly biologics and personalized management strategies, have shown promising improvements in asthma control and quality of life. Despite these advancements, accessibility, adherence issues, and treatment costs remain significant barriers to optimal asthma management. A holistic, individualized approach to asthma care, integrating pharmacological interventions with patient education, is essential for achieving long-term control and improving patient outcomes.

Keywords: asthma treatment, biologic therapies, asthma management, inhaled corticosteroids, patient outcomes.

Introduction

Coping with massive volumes of information on an ever-increasing number of new equipment and medications is one of the greatest obstacles for anybody treating people with asthma. With so much data available, it may be challenging to determine which medication or treatment plan is best for a certain patient [1].
Systematic reviews have gained popularity during the last 20 years as a means for decision-makers to sift through mountains of data. The gold standard for these evaluations is to detail the steps taken to ensure objectivity and accuracy while minimizing bias [2-3]. A meta-analysis, which is the statistical synthesis of data from several studies to get a single estimate of an intervention's or healthcare situation's impact, may also be a component of these reviews [4]. Nevertheless, the majority of meta-analyses and systematic reviews that appear in peer-reviewed publications involve methodological flaws that might cast doubt on their reliability [5–12].
There have been some significant new efforts to raise the bar for the methodology used in meta-analyses and systematic reviews. When compared to reviews published in peer-reviewed publications, those produced by the enormous multinational organization known as the Cochrane Collaboration [11,13] seem to be more thorough and accurately documented [9, 14].
In the 2020 Update of articles published in the journals of the American Thoracic Society (ATS), we take a look back at recent advances in our knowledge of the causes, symptoms, and treatments for asthma, as well as related risk factors. The need of integrating achievements from many disciplines was emphasized in last year's Update in Asthma [15]. This will lead to a better understanding of epidemiological data, new ideas for successful prevention methods, and a shift in treatment emphasis towards the biological basis of asthma. Indeed, similar themes did emerge in 2020 throughout several fields of study.
Environmental exposures and pollution's effects on asthma's pathobiology, clinical manifestations, and developmental origins were among the most important. Factors such as sex, diet, obesity, and rhinovirus infection are implicated in the etiology and presentation of asthma, according to findings from both epidemiological and translational studies. With the decipherment of both new and old processes, the biology of airway epithelial cells and their connections to inflammation, mucosal immunity, and mucoobstruction became better understood. New information on what causes changes in the structure and function of the airway has improved our knowledge of how these variables impact the onset of symptoms and the efficacy of treatment.

Methods

Asthma is a chronic respiratory disease characterized by inflammation and narrowing of the airways, leading to symptoms such as wheezing, shortness of breath, chest tightness, and coughing.

The condition affected millions of adults worldwide, resulting in significant morbidity, reduced quality of life, and increased healthcare utilization. In recent years, numerous advancements in the treatment of asthma emerged, including new medications, biologic therapies, inhalation devices, and management strategies. These innovations had the potential to improve asthma control, reduce exacerbations, and enhance long-term outcomes for adult patients. This systematic review aimed to assess these advancements in asthma treatment, focusing on their effectiveness, safety, and impact on patient outcomes.

Review Question

The primary question addressed in this review was: What were the recent advances in the treatment of asthma among adults, with a focus on medication efficacy, safety, and overall patient outcomes?

Search Strategy

A comprehensive and systematic search was conducted in multiple well-established databases, including PubMed, Cochrane Library, Scopus, Embase, and Web of Science. The search was limited to studies published in English from 2010 onwards to ensure the inclusion of the most recent advancements. The search terms combined relevant keywords and MeSH terms related to asthma treatment, such as “asthma,” “adult asthma treatment,” “biologics in asthma,” “inhaled corticosteroids,” “asthma management,” “innovative asthma therapies,” and “clinical trials asthma treatment.” In addition to the database search, the reference lists of selected articles were hand-searched for any additional relevant studies.

Types of Studies to Be Included

The review included studies that investigated advancements in asthma treatment among adults. Eligible studies were randomized controlled trials (RCTs), cohort studies, case-control studies, and systematic reviews and meta-analyses. These types of studies provided reliable evidence regarding the effectiveness and safety of new asthma treatments. Observational studies focusing on treatment effects, safety, and long-term outcomes were also considered. Studies involving non-human subjects, pediatric populations, or studies not related to asthma treatment were excluded from the review.

Participants

The review focused on adults aged 18 years and older who had been diagnosed with asthma, regardless of disease severity or comorbidities. Both controlled and uncontrolled asthma populations were considered to capture a comprehensive view of the current treatment landscape. There were no restrictions based on gender, ethnicity, or other demographic factors, as long as asthma was the primary condition being treated in the study.

Search Keywords

The following search keywords and terms were used to identify relevant studies: "asthma treatment advancements," "adult asthma therapy," "biologics in asthma," "inhaler therapy in asthma," "asthma pharmacological interventions," "new asthma drugs," "asthma clinical trials," "innovative asthma therapies," "asthma treatment guidelines," and "asthma management strategies." These keywords ensured a broad and inclusive search for relevant studies related to recent treatment developments.

Study Selection Process

The selection of studies followed a rigorous and transparent process. Two independent reviewers initially screened the titles and abstracts of all identified studies for eligibility based on the inclusion criteria. Full-text articles were retrieved for studies that met the initial screening criteria.

The full-text articles were then reviewed independently by the same two reviewers. Any discrepancies in study inclusion were resolved through discussion, or by consulting a third reviewer if necessary. The study selection process was documented and reported using a PRISMA flow diagram to ensure transparency and reproducibility.

Outcomes

The systematic review assessed both primary and secondary outcomes. The primary outcomes included the effectiveness of treatments, measured by improvements in asthma control, lung function (e.g., forced expiratory volume in 1 second, FEV1), and reduction in asthma symptoms. Safety outcomes were assessed by identifying adverse events or side effects associated with the treatments, including complications from biologic therapies or corticosteroid use. Additionally, changes in quality of life were assessed using validated asthma-specific tools, such as the Asthma Control Test or the Asthma Quality of Life Questionnaire. Secondary outcomes included hospitalization rates due to asthma exacerbations, frequency and severity of asthma attacks, and long-term treatment outcomes such as sustained symptom control or remission.

Data Extraction and Coding

Data extraction was performed independently by two reviewers using a standardized extraction form. Relevant study details, such as author information, publication year, study design, sample size, participant characteristics, treatment interventions, and outcome measures, were extracted. Specifically, treatment details included information on the type of intervention (e.g., biologic agents, inhalers), dosage, and duration of treatment. The outcomes focused on the effectiveness of the treatment, safety profiles, and improvements in quality of life. Any disagreements in data extraction were resolved by consensus or with the help of a third reviewer. All extracted data were carefully coded and organized for further analysis.

Data Management

To ensure the accuracy and integrity of the data, all extracted information was stored in a secure and organized database, such as Excel or a systematic review software. Duplicate records were eliminated during the data management process, and each included study was thoroughly documented. Where applicable, a meta-analysis was conducted to synthesize the results and calculate pooled effect sizes. Any issues regarding data completeness or discrepancies in reporting were addressed during the data management process to ensure a high-quality review.

Results

The initial search identified a total of 1172 studies from PubMed, Embase, Cochrane Library, and CINAHL. There were 149 articles excluded due to their irrelevance. At the end of identification process, 1023 articles were screened. Of these, 332 full-text articles were reviewed, and 16 studies were eligible for inclusion in this systematic review (Figure 1).

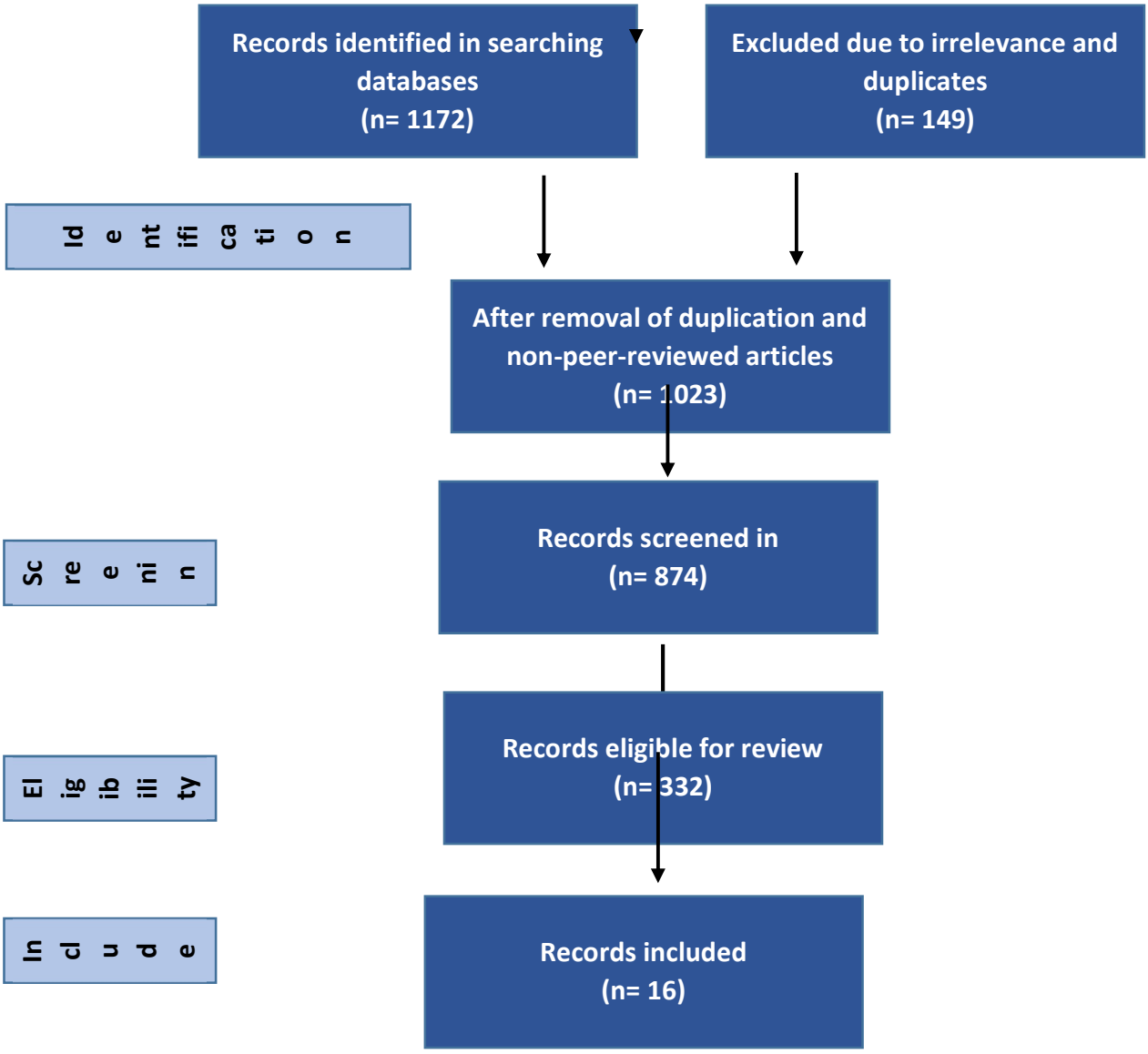

Figure 1: Flow chart of selection process

Controlling symptoms, preventing exacerbations, and minimizing the risk of permanent airflow restriction and asthma-related mortality are the goals of asthma treatment [16]. On a population level, control-based asthma care improves outcomes by adjusting medication depending on the presence of symptoms [16]. You may objectively track your asthma symptoms and control using one of many approved questionnaires that can be used serially. The Asthma Control Questionnaire (ACQ-5) and the Asthma Control Test (ACT) are two such examples. The second one asks the patient to rate their symptoms during the day and night, how much they are able to do, and how often they have used pain relievers in the last seven days using five different questions [17].

Because improper inhaler technique is common and affects optimum medication delivery, all patients should get training in right technique [18]. Every clinical review should also include an evaluation of symptoms, adherence, triggers, and optimizing comorbidities and risk factors as part

of personalized asthma therapy and standard of care [18]. There is a strong correlation between poor adherence to medication and unsatisfactory results [19]. Some practitioners may not have access to electronic inhaler monitors or prescription filling monitoring systems, which might provide a more reliable evaluation of adherence than self-reported adherence [19].

Pharmacological management

When a diagnosis of asthma is obtained, the first step in managing the condition is to start inhaled corticosteroids (ICS) [20].

Pharmacotherapy for asthma can be divided into three categories:

- Preventer medication, which controls symptoms, reduces risk of exacerbation and prevents the sequelae of chronic inflammation.
- Reliever medication, which is taken as required for symptoms.
- Add-on therapies, including biologic agents, for severe disease.

After the 2019 GINA guidelines were released, the way asthma is managed underwent a major shift. Due to substantial data showing that SABA-only therapy raises the risk of severe exacerbations and mortality from asthma, it is no longer advised to treat any adult with asthma with just SABA [21].

Initial therapy

When starting treatment, low-dose inhaled corticosteroid should be administered as required to the majority of individuals with moderate, infrequent symptoms [22]. Because of its faster start of action compared to other β2-agonists, formoterol is especially selected as the LABA in this case. When compared to as-needed SABA alone, as-needed ICS-formoterol decreased exacerbations in studies, and it may have benefits in treatment adherence when compared to continuous preventative therapy [23]. As an alternate starting treatment, a combination of a daily low-dose ICS preventer and SABA has been demonstrated to be more cost-effective, particularly in low-income areas, and to improve lung function and asthma control when compared to as-needed ICS-formoterol, with equivalent results regarding exacerbations [24]. The first line of treatment for individuals whose symptoms are severe enough to need a relief medicine more than twice a month is a daily low-dose ICS preventer [16].

Patients whose asthma symptoms first manifest as a severe exacerbation should be given a brief OCS treatment along with a long-term preventer that contains ICS. It is important to gradually increase the dosage of pharmacotherapy based on the patient's symptoms. Considerations like as budgetary constraints, patient expectations, and side effect monitoring are necessary for ensuring compliance. While using an inhaler once a day may increase compliance, it does not guarantee better clinical results [25].

Add-on pharmacotherapies

Stepping down

It is recommended to gradually decrease the dosage of ICS until the patient reaches a state of excellent control, as determined by monitoring symptoms and exacerbations. The patient should be informed to resume their old dosage if their symptoms worsen, and each decrease should be seen as a therapeutic trial [16].

Self-management education

Asthma self-management education should include the creation of a customized "Asthma Action Plan" for each patient, irrespective of the severity of their condition. This plan should explain in detail the signs of failing control or an exacerbation and how to cope with them. Peak flow values may be useful to include for certain patients, especially those who have trouble perceiving their

symptoms [16, 26]. Patients who received self-management instruction were 36% less likely to need hospitalization compared to those who did not [26].

Biologic drugs

Whether it's in a hospital environment, via a general practitioner, or even at home, biologic medicines for asthma target endotypical inflammatory pathways and are given as subcutaneous injections.

Anti-TSLP (tezepelumab)

Tezepelumab, an anti-TSLP monoclonal antibody, reduced exacerbations and improved lung function, asthma control and quality of life in moderate–severe asthma [27].

Anti–IL-33 (astegolimab)

Whether it's in a hospital environment, via a general practitioner, or even at home, biologic medicines for asthma target endotypical inflammatory pathways and are given as subcutaneous injections.

Bronchial thermoplasty

Some centers for severe asthma provide the option of bronchoscopy-assisted thermoablation, which targets the smooth muscle in the airways. Although the placebo group showed a significant response, bronchial thermoplasty (BT) enhanced symptom management and reduced exacerbations in certain trials [29]. The procedure's short-term side effects, such asthma aggravation, and its unclear long-term consequences keep BT in the spotlight. International guidelines do not endorse BT for any reason other than in the context of clinical trials and registry studies [30].

Immunotherapy

Immunotherapy, which involves reducing the IgE-mediated allergic reactions linked to asthma and rhinitis by administering an exogenous aeroallergen to which a patient has shown sensitization, either subcutaneously or sublingually (SLIT) [30], may be useful in some patients with allergic asthma. Asthma patients in Australia may benefit from registered treatments such as grass pollen SLIT and house dust mite SLIT [31–32], with the help of an allergy expert guiding the patient's treatment decision [30]. Even in people with well-controlled asthma, immunotherapy may exacerbate symptoms, therefore it should only be given to those under close medical monitoring [30].

Discussion

This systematic review sheds light on the significant advancements in asthma treatment, particularly in the areas of pharmacological management, biologic therapies, and self-management strategies. One of the key findings was the shift in asthma management following the 2019 GINA guidelines, which highlighted the risks associated with using short-acting beta-agonists (SABA) as monotherapy. This change emphasizes the importance of long-term control of asthma through inhaled corticosteroids (ICS) and the combination of ICS with long-acting beta-agonists (LABA) or formoterol as an effective strategy for reducing exacerbations. The findings also suggest that personalized treatment plans, including medication adherence and proper inhaler technique, play a crucial role in achieving optimal asthma control. However, despite the availability of more effective therapies, challenges such as patient non-adherence, improper inhaler use, and limited access to advanced therapies remain key obstacles to improving asthma outcomes.

The review also highlights the growing role of biologic therapies in the management of severe asthma, with monoclonal antibodies such as anti-TSLP and anti-IL-33 showing promising results in reducing exacerbations and improving lung function. These therapies target specific inflammatory pathways, offering new hope for patients with moderate to severe asthma who do

not respond well to conventional treatments. While biologic treatments demonstrate clear benefits, their high cost and limited accessibility pose significant challenges for widespread use, particularly in low-resource settings. Additionally, treatments like bronchial thermoplasty and immunotherapy were discussed, with bronchial thermoplasty showing potential for symptom relief but remaining controversial due to its uncertain long-term outcomes. The review emphasized the importance of a holistic, individualized approach to asthma management, integrating pharmacological treatments with patient education, self-management strategies, and careful monitoring to optimize care and minimize the burden of asthma on patients' quality of life.

The evaluation of trial data associated with asthma treatment options must be conducted using reliable and high-quality procedures. Wu et al. [33] examined 136 systematic reviews that fulfilled inclusion criteria; 8.8% were deemed high quality, while 61% were deemed critically low quality. The reviews focused on asthma treatments and were published between 2013 and 2019. The study's authors make some excellent points about how to make it better. For example, they suggest including a list of studies that weren't considered, being transparent about who paid for it, and registering the search protocol in PROSPERO (International Prospective Register of Systematic Reviews) while also explaining when they deviated from the protocol.

The effectiveness of the newly discovered T2-targeting biological therapy for severe asthma is without doubt [34], but there are still many unanswered clinical problems, such as whether or not these drugs can be utilized to alleviate acute exacerbations. The IL-5 receptor antagonist benralizumab decreased blood eosinophil cell counts within 4 hours following the first dosage, according to early studies by Moran and colleagues [35]. This decrease in blood eosinophil levels was better than therapy with the IL-5 antagonist mepolizumab at this early stage and was comparable to the effect magnitude seen with oral prednisolone treatment. These results add to the growing body of evidence from case reports that point to the potential usefulness of benralizumab as a therapy for severe asthma attacks [36–37]. A severe subtype of asthma, aspirin-exacerbated respiratory illness, is still difficult to treat. Recent research by Hayashi and colleagues provides strong support for the idea that omalizumab may be useful in treating this illness [38].

Omalizumab was discovered by the authors to lower urine leukotriene E2 and tetranor-PGDM (11,15-dioxo-9α-hydroxy-2,3,4,5-tetranorprostan-1,20-dioic acid), which are recognized indicators of aspirin sensitivity illness. Additionally, it was shown to dramatically improve asthma symptom ratings. An significant subgroup of asthma patients, those whose symptoms are worsened by aspirin, may have IgE as a therapeutic target because of its role in dysregulated mast cell activity [39]. Concerns about short-term consequences from bronchial thermoplasty contribute to the procedure's continued contentiousness. Performing fewer treatments is one strategy to reduce problems. To determine whether this method was feasible, a pilot research used hyperpolarized 129Xe MRI to identify which parts of the lungs had ventilation deficits and then treated those segments with bronchial thermoplasty. Compared to three treatments using conventional, unguided bronchial thermoplasty, this study showed that a single treatment guided by 129Xe MRI improved asthma symptom ratings just as much [40]. Based on these findings, 129Xe MRI-guided bronchial thermoplasty treatments may be able to achieve comparable therapeutic outcomes with a reduced number of operations.

When dealing with asthma, it is crucial to find novel bronchodilators since some people are resistant to β2-agonists. There is no longer any need to produce nitric oxide thanks to the development of new sGC (soluble guanylyl cyclase) agonists. These agonists increase the widening of airways, even in tissues that are not responsive to β-agonists [41]. Here is a fresh chance for asthma bronchodilator treatment, as there are sGC agonists for hypertension that have

been clinically authorized [42]. Preventing actin polymerization in ASM and disrupting force production is another novel approach to inhibiting ASM contraction [43]. ASM cells' ability to generate force was shown to be greatly reduced upon blocking a kinase known as Ste20-like kinase [44], which acts as a master regulator of actin polymerization. We need to verify whether these processes remain in the sick airway, but these novel possibilities for bronchodilation promotion are intriguing.

Conclusion

This systematic review identified 16 studies that met the inclusion criteria after a thorough search and screening process, involving 1172 articles from multiple databases. The review highlighted several key advancements in asthma treatment, including pharmacological strategies such as inhaled corticosteroids (ICS), long-acting beta-agonists (LABA), and biologic therapies. Notably, the 2019 GINA guidelines marked a significant shift in asthma management, emphasizing the avoidance of short-acting beta-agonists (SABA) as the sole treatment due to their associated risks. The findings suggested that a combination of ICS with formoterol or SABA could reduce exacerbations and improve asthma control, while daily low-dose ICS was recommended for individuals with moderate to severe symptoms. The review also underscored the importance of personalized treatment plans that incorporate patient adherence, proper inhaler technique, and comorbidity management.

Additionally, advancements in biologic treatments, such as anti-TSLP and anti-IL-33 monoclonal antibodies, were shown to effectively reduce exacerbations, improve lung function, and enhance quality of life for individuals with moderate to severe asthma. Bronchial thermoplasty, though providing short-term symptom relief, had uncertain long-term effects and was not recommended outside of clinical trials. Immunotherapy, particularly sublingual treatments for allergic asthma, demonstrated some benefits, but required careful monitoring due to potential exacerbations. The review concluded that the integration of these novel therapies, alongside robust self-management education and a personalized asthma action plan, could significantly improve patient outcomes and reduce asthma-related complications.

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