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A Review on Choice of Inhaled Corticosteroids in Exacerbation of Asthma

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Abstract **Review Article**

Background: Asthma is a chronic inflammatory condition that significantly affects patients' quality of life and poses a substantial healthcare burden. Inhaled corticosteroids (ICS) are a primary treatment modality, yet variations in treatment objectives between patients and healthcare providers necessitate a collaborative approach to asthma management. ***Objective*:** This review aims to evaluate the efficacy and safety of different ICS formulations and combination therapies in managing asthma and to identify optimal treatment strategies that align with both clinical guidelines and patient preferences. ***Methodology***: A systematic search of the MEDLINE database was conducted to identify studies published from 2019 to the present, focusing on the safety and efficacy of ICS in asthma therapy. Out of 106 initial results, 11 studies (including controlled and randomized controlled trials) met the inclusion criteria for review. ***Results***: The analysis revealed that the timely administration of ICS can significantly reduce emergency room visits and hospitalizations during acute exacerbations. Studies highlighted the comparative advantages of various ICS, such as fluticasone furoate's enhanced airway protection and the effectiveness of self-titration strategies in managing symptoms. Combination therapies involving ICS improved asthma control and lung function, particularly in patients with moderate to severe asthma and those with asthma-COPD overlap. ***Implications***: The findings underscore the importance of individualized ICS therapy, suggesting that tailored treatment regimens can enhance clinical outcomes and patient adherence. Integrating patient feedback into treatment decisions is essential for optimizing asthma management strategies.

Keywords: Inhaled, Corticosteroids, Asthma, COPD.

INTRODUCTION

Asthma is a chronic inflammatory condition that causes burst-ups (exacerbations) and imposes a massive burden on individuals. Inhaled corticosteroids (ICSs) are a keystone of asthma conservation therapy [1]. ICSs apply profound anti-inflammatory effects through the activation/ suppression of multifold transcriptional networks [2], multiple inquests have displayed that treatment with ICS reduces symptoms, improves lung function, controls asthma, and prevents exacerbations [3-5]. The first asthma management recommendations were first released by Australia and New Zealand in the mid-1980s. The Canadian Thoracic Society (CTS), the British Thoracic Society, the National Asthma Education and Prevention Program (NAEPP), and the Global Initiative for Asthma (GINA) have all released guidelines that can be used and shared since then [6]. An organized approach is the establishment of asthma treatment. Control-based individual care entails an iterative cycle of evaluation (symptoms, risk agents, etc.), treatment revision (pharmacological, non-pharmacological, and treatment of adjustable risk factors), and reaction assessment (symptoms, side effects, exacerbations, etc.). Numerous multinational guidelines for asthma remedies promote corticosteroids, whether inhaled or systemic, as the most effective treatment for asthma in grown-ups and children [7]. Because of their anti-inflammatory qualities, corticosteroids are useful in reducing the underlying inflammatory process in the airways and managing asthma symptoms. Cases with chronic persistent asthma are treated primarily with inhaled corticosteroids [8]. In light of the possibility that individuals and physicians may have different intentions, it's important to consider patients' choices and believe that successful asthma management arises from a collaboration between the patient and the healthcare provider [7].

METHODS

MEDLINE database was searched to identify studies that were designed to investigate the best choice of Inhaled corticosteroids, comparing the safety and efficacy of different ICS, combination therapies, and treatment effects of ICS for asthma patients. The study published from 2019 to date is reviewed. Out of 106 results available in the form of free full texts and abstracts, using keywords of Inhaled corticosteroids, and asthma, eleven studies were found suitable for this review. The article types included were controlled trials and randomized controlled trials.

Effect of ICS on Asthma Patients

Research has indicated that the administration of inhaled and systemic corticosteroids during the initial hour of an acute asthma exacerbation can reduce the duration of stay in the emergency room and the hospitalization rate [9].

Peter Daley-Yates *et al*., conducted a placebo-controlled randomized cross over study to compare the airway potency, systemic activity, and therapeutic index of three inhaled corticosteroids—fluticasone furoate, fluticasone propionate, and budesonide—that differ in terms of their glucocorticoid receptor binding affinity, physicochemical properties, and pharmacokinetic features. The results of the study demonstrated that FF, as compared to FP or BUD, can offer greater protection against airway hyperresponsiveness with less systemic activity [10].

Baggott C *et al*., conducted a pre-specified analysis from a randomized controlled trial for the self-titration of inhaled corticosteroid and β2-agonist in response to symptoms in mild asthma. For 52 weeks, the participants were randomly assigned 1: 1 to maintenance budesonide (200 Turbuhaler, one actuation twice a day) or as-needed budesonide–formoterol (200/6 μg Turbuhaler, one actuation) and as-needed terbutaline (250 μg, two actuations). The study inhalers of 110 participants were equipped with electronic monitors that recorded the date and time of each actuation. The usage patterns of β2-agonists and ICS were important outcome measures. It was determined that one actuation of budesonide–formoterol was comparable to two terbutaline actuations as a bronchodilator dosage. They discovered that, when linked to increased overall usage of as-needed β2-agonist, the timing of ICS dose when self-titrated to β2-agonist use is more significant than total ICS dose in lowering the risk of severe exacerbation in moderate asthma [11].

As a prodrug, ciclesonide is activated by bronchial esterases at the site of action, which is the lining fluid and bronchial cells of the bronchus. These change ciclesonide into desisobutyryl ciclesonide, which binds to the glucocorticoid receptor 100 times more strongly than ciclesonide does [12]. Demétrius Tierno Martins *et al*., conducted a study on 58 patients with moderate or severe asthma who were divided into two groups randomly for the study. One group received 500 mg of intravenous hydrocortisone plus an identical placebo to ciclesonide (hydrocortisone + placebo) over four hours, while the other group received 1440 mcg of inhaled ciclesonide plus the same placebo to hydrocortisone (ciclesonide + placebo). Fenoterol hydrobromide and ipratropium bromide, two short-acting bronchodilators, were given to each group. They came to the conclusion that inhaled ciclesonide improved both clinical and spirometric parameters and was equally effective in managing acute asthma exacerbations as systemic hydrocortisone [13].

Comparison of ICS

The recommended first-line therapy for persistent asthma is a combination of long-acting β2-agonists (LABA) and inhaled corticosteroids [14-16]. Maciej Kupczyk *et al*., conducted another randomized, multicenter, non-inferiority, phase IV clinical study on a new formulation of fluticasone propionate/salmeterol in a metered-dose inhaler (MDI HFA) that allows for the reduction of a daily dose of corticosteroid and provides optimal asthma control. The study group (treated for 12 weeks with fluticasone propionate/salmeterol MDI HFA) or the control group (treated for 12 weeks with fluticasone propionate/salmeterol DPI) of adults with asthma (n = 231) were assigned at random. During four study visits, a variety of factors were evaluated, including lung function, physical activity, short-acting β2-agonist (SABA) use, asthma symptoms, exacerbations, and overall health. The results demonstrated that fluticasone propionate/salmeterol (250 μg/50 μg, twice daily) MDI HFA provides the best asthma control and is not worse than fluticasone propionate/salmeterol (500 μg/50 μg, twice daily) DPI [17].

Susumu Fukahori *et al*., used to know the added effect features of Formoterol Co-Inhalation and Tulobuterol Patch on Budesonide Inhalation in geriatric cases with Asthma. It involved 18 outpatients who were treated for mild to moderate bronchial asthma with intermediate ICS dosages and who visited the hospital. They were randomly assigned (9 cases per group) to either the BUD+ TUL group (BUD 200 mcg: 2 inhalations twice daily + TUL 2 mg daily) or the FBC group (BUD/FOR 160/4.5 mg, 2 inhalations twice daily). The comparison was conducted in parallel with 2 arms over 12 weeks. The Asthma Control Questionnaire, mini-Asthma Quality of Life Questionnaire (mini-AQLQ), peak expiratory flow, forced expiratory volume, impulse oscillometry, fractional exhaled nitric oxide (FeNO), and incidence of adverse events were compared. The patch was better at delivering the medication due to its altered formulation, but the inhaled combination was believed to improve respiratory function more effectively [18].

Clinicians frequently employ inhaled glucocorticoids to treat and prevent wheezing attacks. Research now in existence suggests that the optimal initial treatment for preschool-aged children who are at risk of asthma should be long-term inhaled corticosteroid therapy [19-22]. Lu Li *et al*., explored and compared the clinical control of three atomized inhalation budesonide (BUD) regimens for Chinese preschool children with recurrent wheezing. The three regimens—the daily BUD atomized inhalation regimen, the intermittent high-dose atomized BUD inhalation regimen, and the intermittent medium-dose atomized BUD inhalation regimen—have comparable control abilities and can greatly enhance the clinical control of recurrent wheezing preschoolers with positive mAPI [23].

Oliver Kornmann *et al*., conducted a phase III, multicentre, randomised, double-blind, double-dummy and parallel group study to assess the efficacy and safety of low-dose IND/MF 150/80 µg once daily (o.d.) versus MF 200 µg o.d. in adult and adolescent cases with poorly controlled asthma The findings lend evidence to the use of low-dose IND/MF 150/80 µg o.d. as a prospective treatment for patients with asthma that is not well controlled in adults and adolescents [24].

The ease and enhanced patient adherence come with a single device that contains a fixed-dose combination of LABA, LAMA, and ICS once daily [25, 26]. Christian Gessner *et al*., did a randomized, Phase IIIb, non-inferiority study on a fixed-dose combination of indacaterol/glycopyrronium/mometasone furoate once-daily versus salmeterol/fluticasone twice-daily plus tiotropium once-daily in patients with uncontrolled asthma. When compared to SAL/FLU high dose plus TIO, IND/GLY/MF high-dose o.d. improved lung function, asthma control, and overall health. In contrast, IND/GLY/MF medium-dose demonstrated similar efficacy but at a lower steroid dosage [27].

Fang Yi *et al*., directed a study on the effects of treatment with montelukast only, budesonide/ formoterol alone, and a blend of both in cough variant asthma. In cases with CVA, the antitussive effect and anti-eosinophilic airway inflammation were analogous, and the effectiveness of montelukast only, budesonide/ formoterol alone, and a combination of both in diminishing cough reflex sensitivity and refining cough symptoms as well as eosinophilic airway inflammation was observed [28].

As a practical and efficient treatment for obstructive airway illnesses, triple therapy with inhaled corticosteroids (ICS), long-acting muscarinic antagonists (LAMA), and long-acting β2 agonists (LABA) have gained popularity in clinical practice [29, 30]. Nineteen patients with ACO participated in a 12-week open-label, randomized, cross-over pilot trial to examine the impact of triple therapy with glycopyrrolate (GLY) 50 µg/day on budesonide/formoterol fumarate (BUD/FORM) 640/18 µg/day conducted by Yoshihisa Ishiura [31] *et al*., Lung function metrics, especially IC, improve with triple therapy using BUD/GLY/FORM, suggesting that triple therapy has potential benefits as a routine treatment for ACO. When used in conjunction with GINA standards, FeNO can help adult asthma patients receive a correct daily dose of ICS was stated by Tung Truong-Thanh [32] *et al*.,

CONCLUSION

This review of recent studies highlights significant advancements in the understanding of inhaled corticosteroids (ICS) and their role in asthma management. Across the reviewed studies, various ICS formulations, dosages, and combination therapies were evaluated, demonstrating a spectrum of effectiveness in controlling asthma symptoms, reducing exacerbations, and improving overall lung function. The findings underscore the potential benefits of tailored ICS therapies, such as the use of fluticasone furoate for enhanced airway protection with minimal systemic activity and the effective management of asthma through self-titration strategies. Additionally, combination treatments involving ICS and bronchodilators were shown to improve clinical outcomes, particularly in more severe cases of asthma and related conditions like asthma-COPD overlap (ACO). These insights contribute to a more nuanced approach to asthma treatment, emphasizing the importance of individualized therapy based on specific patient needs and the characteristics of different ICS formulations.

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