

REVIEW

Inhaled corticosteroids in the management of bronchospasms in Pediatric Emergency Departments

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INTRODUCTION

Bronchospasms or asthma exacerbations are episodes characterized by inflammation, hyperresponsiveness and reversible airway obstruction, leading to shortness of breath, wheezing, coughing, and a feeling of tightness or chest pain, associated with decreased lung function.

Bronchospasms or asthma exacerbations are among the most frequent medical emergencies in pediatric practice and are a leading cause for consultation in Pediatric Emergency Departments. They are estimated to account for approximately 5% of pediatric emergency visits, increasing to nearly 15% during autumn and winter months due to their seasonal presentation pattern. A combination of infectious, allergic, environmental factors, emotional stress, and meteorological stimuli seem to underlie this seasonal pattern. These incidence peaks create significant pressure on Pediatric Emergency Departments and lead to an increased demand for specialized resources. Moreover, approximately 15% of patients require hospital admission, disrupting family dynamics and impacting the quality of life of affected children⁽¹⁾.

ASSESSMENT OF BRONCHOSPASM SEVERITY

In the initial evaluation of a patient with bronchospasms, accurately assessing the severity of the exacerbation is crucial to establish an appropriate treatment and care strategy. To this end, several clinical assessment scales have been developed in recent years to stratify the severity of airway obstruction and response to treatment. One of these is the

Pulmonary Score (PS) scale, a simple, widely used, and validated tool (Tables 1 and 2)^(1,2).

CURRENT MANAGEMENT OF BRONCHOSPASM IN PEDIATRIC EMERGENCY DEPARTMENTS

The current Clinical Practice Guidelines for treating bronchospasm in pediatric patients in the Emergency Department recommend as first-line treatment the use of short-acting β_2 -adrenergic agonists (salbutamol) in combination with anticholinergic drugs (ipratropium bromide), administered via nebulization or inhalation. In addition, systemic corticosteroids are recommended via oral or intravenous administration⁽¹⁻⁴⁾.

β_2 -adrenergic agonists

Short-acting inhaled β_2 -adrenergic agonists (the most widely used of which is salbutamol) are the first-line treatment. Their bronchodilating effect starts within a few seconds, peaks at 30 minutes, and has a half-life between 2 and 4 hours. They should preferably be administered with a pressurized inhaler and spacer, as this is as effective as the nebulized route, with fewer side effects and greater cost-effectiveness. Nebulized salbutamol is indicated in severe episodes with hypoxemia or in moderate episodes with significant respiratory distress. The doses used are usually well tolerated. The most common side effects include tremors, hyperactivity, vomiting, and tachycardia, which are generally mild. Repeated high doses may lead to hypokalemia and hyperglycemia, usually without clinical or electrocardiographic consequences.

Ipratropium bromide

Ipratropium bromide is an anticholinergic agent with a slower onset of bronchodilation compared to β_2 -adrenergic agonists, but with a longer duration of action. Co-administration of salbutamol and ipratropium bromide in moderate-to-severe bronchospasms results in a more rapid im-

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TABLE 1. Pulmonary Score for the clinical assessment of acute asthma episodes in children.

Score*	Respiratory rate		Wheezing	Accessory muscle use- Sternocleidomastoid***
	< 6 years	≥ 6 years		
0	< 30	< 20	No	No
1	31-45	21-35	Terminal expiration (stethoscope)	Mild increase
2	46-60	36-50	Entire expiration (stethoscope)	Increase
3	> 60	> 50	Inspiration and expiration, without stethoscope**	Maximal activity

*Score from 0 to 3 in each item (minimum 0, maximum 9). **If there is no wheezing and the activity of the sternocleidomastoid is increased, assign the wheezing item a score of 3. ***The use of accessory muscles refers only to the sternocleidomastoid, which is the only muscle that has been well correlated with the degree of obstruction.

Mild episode: 0-3 points; moderate episode: 4-6 points; severe episode: 7-9 points.

TABLE 2. Global assessment of the severity of asthma attacks in children by integrating the Pulmonary Score and oxygen saturation by pulse oximetry.

	Pulmonary score	Oxygen saturation by pulse oximetry
Mild	0-3	> 94%
Moderate	4-6	91-94%
Severe	7-9	< 91%

In case of discordance between the clinical score and the oxygen saturation, the one with the higher severity will be used.

provement of symptoms and respiratory function, leading to a decreased hospitalization rate. However, it has not been demonstrated that continued administration of ipratropium bromide beyond the initial three doses in the emergency department provides any additional benefit. Therefore, it is not recommended to maintain this treatment in hospitalized patients.

Systemic corticosteroids

Systemic corticosteroids are recommended early as an essential component of the treatment for bronchospasms, as they reduce inflammation and enhance the effects of bronchodilators. They have been demonstrated to prevent reconsultations, hospital admissions, and to decrease the total number of doses of β_2 -adrenergic agonists. As short cycles have been employed, no significant side effects have been observed. The effects typically start within 2-4 hours, with full action seen at 12-24 hours. They should be administered in moderate-to-severe episodes and considered in mild episodes with an inadequate response to bronchodilators or if the patient has a history of severe bronchospasms. The oral route is preferred because it is equally effective, rapid, less invasive, and more cost-effective than the intravenous route. Prednisone or prednisolone is the drug of choice and most commonly used. Dexamethasone has proven to be an effective and safe alternative, with a prolonged half-life allowing for a regimen of one or two doses. It does not show differences in admission rate, reconsultation, or persistence of symptoms after discharge. The intravenous route is reserved for more severe cases or in cases of oral intolerance, with methylprednisolone being the preferred drug.

CURRENT USE OF INHALED OR NEBULIZED CORTICOSTEROIDS IN ASTHMA PATIENTS

Inhaled corticosteroids for maintenance therapy in children with asthma

Inhaled glucocorticoids are the first-line maintenance therapy for children experiencing recurrent wheezing episodes or asthma. The effectiveness of daily inhaled glucocorticoids has been well established in improving clinical, functional, and bronchial inflammation parameters, enhancing quality of life, and reducing the risk of exacerbations and hospitalizations. In addition, inhaled glucocorticoids, at the usual doses, are safe drugs for the treatment of asthma in children⁽⁵⁾. Although inhaled corticosteroids are frequently used as maintenance therapy in children with persistent asthma, their use is not widespread in the Pediatric Emergency Department as their efficacy and clinical relevance in this setting where the clinical profile is acute has not yet been clarified.

Inhaled corticosteroids for asthma exacerbations in adults

It should be noted that the GEMA 5.3 guideline (Spanish Guide for the Management of Asthma; 2023)⁽⁵⁾ recommends the early administration of inhaled glucocorticoids within the first hour of care for adult patients experiencing moderate-to-severe asthma attacks, as they reduce the need for hospital admission. Additionally, the guideline suggest that combining inhaled glucocorticoids with systemic glucocorticoids results in an even greater decrease in the number of hospital admissions. The inhaled glucocorticoids used in adult patients include budesonide and fluticasone propionate. Budesonide can be administered via inhalation using a pressurized device and spacer at a dose of 800 μg (4 inhalations of 200 μg each puff) every 10-15 minutes, or via nebulization at a dose of 0.5 mg every 20 minutes during the first hour. Fluticasone propionate is administered via inhalation with a pressurized device and spacer at a dose of 500 μg (2 inhalations of 250 μg each puff) every 10-15 minutes. However, the same GEMA 5.3 guideline concludes that, in pediatric patients, there is insufficient evidence to recommend the use of inhaled or nebulized corticosteroids as an alternative or additional treatment to systemic corticosteroids for asthma attacks. Larger studies with improved

methodological quality, cost-effectiveness analysis, and safety assessments are needed.

POSSIBLE USE OF INHALED OR NEBULIZED CORTICOSTEROIDS FOR BRONCHOSPASMS IN THE PEDIATRIC EMERGENCY SETTING

Justification

Although the effectiveness of systemic corticosteroids in managing bronchospasm is well established, and their use represents the standard treatment for moderate-to-severe asthma exacerbations in Pediatric Emergency Departments, the slow onset of their action and the fact that many children still require hospital admission despite their administration remain concerns. Consequently, in recent years, research has focused on exploring new treatments, such as inhaled or nebulized corticosteroids, to optimize the management of these patients. Moreover, it should be taken into account that in the emergency department setting, most children with mild-to-moderate bronchospasms respond well to standard treatment. Therefore, it is the patients with severe bronchospasm who are most likely to benefit from a novel treatment approach.

What we know so far about the use of inhaled or nebulized corticosteroids for the management of bronchospasm

Previous studies support the use of nebulized corticosteroids in the acute setting based on the potential advantages they may provide: good tolerance to their use, fewer systemic side effects, rapid onset of action (1 to 2 hours after administration), and direct administration to the airways with local anti-inflammatory and vasoconstrictor effect contributing to the reduction of airway reactivity and edema. In addition, it is possible to administer corticosteroids and β 2-adrenergic agonists simultaneously in the same nebulization. However, we should be aware that the literature provides different and contradictory results on the use of nebulized corticosteroids for the management of bronchospasms. Several studies have demonstrated a beneficial effect of adding nebulized corticosteroids to standard short-acting β 2-adrenergic agonist therapy compared to placebo in reducing hospital admission rates⁽⁶⁻¹⁰⁾. However, few studies have investigated the potential additional benefits of nebulized corticosteroids in combination with systemic corticosteroids^(11,12). It should be noted that there is insufficient evidence to support the replacement of systemic corticosteroids with nebulized corticosteroids. Therefore, systemic corticosteroids should not be discontinued in patients with bronchospasm presenting to the Pediatric Emergency Department⁽¹³⁾. For these reasons, nebulized corticosteroids should be viewed as an adjunctive treatment rather than a substitute for systemic corticosteroids.

International Clinical Practice Guidelines

The GINA (Global Initiative for Asthma) Clinical Practice Guideline⁽¹⁴⁾, updated in 2023, indicates that the incorporation of inhaled corticosteroids into standard bronchospasm treatment (including the use of systemic corticosteroids)

does not appear to decrease the risk of hospitalization. However, it does reduce the length of stay in the Emergency Department and the scores on clinical asthma rating scales in pediatric patients. Nonetheless, the guideline concludes that the specific drug, dosage, and treatment duration remain unclear.

Similarly, in 2021, a consensus paper was published by experts in pediatric allergy and respiratory diseases in Thailand regarding the use of nebulized corticosteroids in children with asthma exacerbations⁽¹⁵⁾. Recommendations were made based on the review of published studies and clinical opinions. In accordance with the *Thai Pediatric Asthma Guideline*, they recommend the use of nebulized corticosteroids for treating all asthma exacerbations in children from 1 year of age. In addition to the standard treatment with short-acting β 2-adrenergic agonists and ipratropium bromide for mild-to-moderate asthma exacerbations, they recommend systemic corticosteroids or, alternatively, high doses of nebulized corticosteroids. They also suggest that nebulized corticosteroids may be more appropriate than systemic corticosteroids for this type of mild-to-moderate exacerbations. On the other hand, for severe asthma exacerbations, they recommend the combined use of systemic corticosteroids and high doses of nebulized corticosteroids, considering nebulized corticosteroids as a fast-acting adjunct to systemic corticosteroids.

Drug and dosage recommendations

In the literature, budesonide is proposed as the primary drug of choice, with nebulized fluticasone considered as an alternative. This choice is primarily based on the pharmacological properties of budesonide, which offer advantages over those of fluticasone. Budesonide exhibits faster absorption, greater water solubility, and longer deposition in the airways and lung tissues compared to fluticasone. In addition, budesonide is associated with a lower risk of pneumonia, which remains relatively consistent across all doses, whereas other corticosteroids such as fluticasone increase the risk of pneumonia in a dose-dependent manner. Finally, budesonide is associated with fewer systemic side effects than fluticasone⁽¹⁵⁾.

Regarding the dose and duration of nebulized corticosteroid treatment, studies indicate that a single dose is inadequate for managing asthma exacerbations. Repeated doses are necessary (i.e., administered in conjunction with the three standard treatment courses of nebulized short-acting β 2-adrenergic agonist bronchodilators) to be effective as add-on therapy to systemic corticosteroids in the setting of acute exacerbation⁽¹⁶⁾.

In the Thai consensus statement published by Direkwatanchai C et al⁽¹⁵⁾, recommendations are provided regarding the dosage of treatment. The authors recommend an appropriate dose of 0.5-1 mg of budesonide or fluticasone in each nebulization, emphasizing that the total daily dose of these corticosteroids should not exceed 2 mg. Concerning the nebulization regimen, they suggest administering the nebulized corticosteroid within the first hour of patient care in the hospital. It can be administered simultaneously in a mixture or sequentially after the short-acting bronchodilator dose. Each nebulized solution dose may be repeated every

20 minutes until completing three doses within the first hour of care.

Review of the current literature

Reviewing the literature of the last 4 years (2020- 2023), there are several articles on the use of inhaled or nebulized corticosteroids in the treatment of bronchospasm or asthma exacerbations in the pediatric emergency setting. Some of these publications are presented below.

In a meta-analysis, Sawanyawisuth K et al⁽¹⁷⁾ conclude that using inhaled corticosteroids as monotherapy in mild-to-moderate asthma exacerbations, and in combination with systemic corticosteroids in moderate-to-severe asthma exacerbations, could be beneficial in reducing the risk of hospitalization in pediatric patients.

Murphy et al⁽¹⁸⁾ conducted a systematic review that demonstrated that nebulized corticosteroids are at least as effective (non-inferior) as systemic corticosteroids in managing mild-to-moderate asthma exacerbations in patients under 5 years of age.

In another systematic review published by Ahmadi Afshar A et al⁽¹⁹⁾, several studies were analyzed to evaluate the impact of inhaled budesonide on hospitalization rate, changes in asthma clinical rating scale scores, and vital signs in children with asthma exacerbations. The results showed that, compared to placebo and systemic corticosteroids, the administration of inhaled budesonide decreased the risk of hospital admission, although the results were not statistically significant. On the other hand, compared to placebo and oral corticosteroids, no significant differences were found in terms of vital signs (heart rate, respiratory rate and oxygen saturation) after administration of inhaled budesonide.

In a systematic review, Castro-Rodriguez et al⁽²⁰⁾, reviewed different studies to evaluate the efficacy of inhaled corticosteroids added to systemic corticosteroids compared to systemic corticosteroids alone in children with asthma exacerbation. It was concluded that, compared to single administration of systemic corticosteroids, the addition of nebulized budesonide does not affect the admission rate, but does decrease hospital stay and significantly improves the score on clinical asthma rating scales in an emergency department setting.

Li CY et al⁽²¹⁾ published a meta-analysis that included various clinical trials aimed at evaluating hospital admission rates, the need for systemic corticosteroid use, length of hospital stay, and adverse events when adding inhaled budesonide to the standard treatment of moderate-to-severe bronchospasm in pediatric patients in the Emergency Department. The results indicated that children who received nebulized budesonide had a reduced risk of hospital admission and of requiring systemic corticosteroids compared to those who received a placebo. No differences were found in the length of hospital stay or in the risk of adverse events between the two groups.

To assess the impact of adding nebulized budesonide to salbutamol for the treatment of mild-to-moderate asthma exacerbations in pediatric patients compared to using nebulized salbutamol alone, Amir Najim Abood HA et al⁽²²⁾ conducted a clinical trial. The methodology involved determining the Pulmonary Score (PS) clinical rating scale score

upon arrival at the Emergency Department and then randomly assigning patients to two groups: group A (salbutamol group) or group B (budesonide plus salbutamol group). Subsequently, the PS score was calculated every 30 minutes. The results showed that, after 30 minutes, patients treated with the combination of nebulized budesonide and salbutamol had a significantly lower PS score than those treated with salbutamol alone. In addition, the mean length of stay in the emergency department was significantly shorter in patients treated with the combination of nebulized budesonide and salbutamol compared to the use of nebulized salbutamol monotherapy.

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