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REVIEW OF DEXAMETHASONE AND PREDNISONE FOR ACUTE ASTHMA EXACERBATIONS IN PEDIATRIC PATIENTS

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Abstract:

Asthma exacerbations are the main cause of hospitalizations among children. Corticosteroids are crucial for treating asthma exacerbations. The majority of current corticosteroid therapy regimens for hospitalized children with asthma exacerbation involve a 5-day course of prednisone or prednisolone. We searched electronic medical databases for all pertinent research published through the end of 2022. Systemic corticosteroids enhance the condition of hospitalized children with acute asthma. Among the potential benefits include an earlier discharge and fewer relapses. At this time, inhaled or nebulized corticosteroids cannot be recommended as an alternative to systemic steroids. Dexamethasone has been proposed as an alternative to prednisone/prednisolone for young children with acute asthma exacerbations.

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INTRODUCTION:

>6 million children in the United States have asthma, making it the most prevalent chronic childhood condition [1,2]. Asthma accounted for 2% of all ambulatory care and emergency department (ED) visits by patients younger than 18 years old [3]. Asthma is characterized by airway edema, bronchoconstriction, and airway hyperresponsiveness. In addition to bronchodilators, corticosteroids are crucial to the treatment of acute asthma exacerbations. They reduce inflammation systemically, decrease mucus formation, and augment the actions of -agonists [2]. National and international guidelines [2,3] recommend early administration of systemic corticosteroids for moderate or severe exacerbations and for mild exacerbations that do not react immediately and completely to short-acting -agonists. The severity of the disease fluctuates over time, and episodes of aggravation frequently necessitate emergency department (ED) management [4].

The major goal of treatment for acute asthma exacerbations [5] is the rapid reversal of bronchospasm and the lowering of airway inflammation. Oral corticosteroids are extraordinarily efficient for symptom relief in children [6]. Inhaled 2-agonists are the first-line treatment for acute asthma exacerbations in children, according to the 2019 British recommendations for the Management of Asthma. Also advised is the early use of oral steroid therapy, with prednisone being the medication of choice [7]. Despite treatment, 5–25% of patients experience relapses, and many require hospitalization to manage repeated exacerbations [8]. Relapse after prednisone medication has been linked to various reasons, including the drug's unpleasant bitter taste, adverse effects such as vomiting, and its multi-dose regimen of 3–5 days, which may decrease patient compliance [9].

Numerous trials [5,9] have analyzed the role of dexamethasone in an effort to increase patient compliance and decrease relapse rates. Initial studies examining a single intramuscular (IM) dosage of dexamethasone found it to be equally efficacious as a 3–5-day prednisone course (10,11). Studies subsequently compared a 1- or 2-day oral dexamethasone treatment to a 3–5-day oral prednisone regimen [5,12]. Oral formulations are preferable for pediatric since they cause less pain. As of April 2016, two meta-analyses have examined oral dexamethasone and prednisone for severe asthma exacerbations in children [4,5].

DISCUSSION:

Diagnosis of bronchial asthma among children:

For children under 6 years old, for whom conventional pulmonary function testing is not feasible, the diagnosis of asthma is based on a typical pattern of symptoms (cough with wheezing or dyspnea that typically varies in severity over time), response to therapy (immediately after administration of a bronchodilator or, more importantly, over time after initiation of anti-inflammatory therapy), and absence of "warning signs" that suggest an alternative diagnosis. 85% of children can be accurately diagnosed with asthma using minimal clinical information, according to statistics from primary care [14].

Parents and health care workers may confuse wheeze with noisy breathing produced by retained upper airway secretions that the kid has not learnt to swallow or is unable to swallow; this is especially common in infants and children with significant developmental delay. In individuals with moderate asthma-like symptoms, it may be difficult to distinguish cough or congestion typical of a viral cold from mild asthma; in such cases, a trial of medication is frequently beneficial. In asthma, excessive mucus production is a crucial factor in airway blockage. The presence of crackles or radiographic indications of atelectasis can be caused by mucus plugging. These characteristics frequently lead to an inaccurate diagnosis of "bronchitis" or pneumonia in patients with viral respiratory tract illness and fever. Underappreciated asthma, which may be the underlying cause of "recurrent pneumonia" in up to 92% of pediatric cases [15,16], is the most prevalent cause of recurrent "bronchitis" or pneumonia in children.

Current asthma medications are highly successful, and a lack of response to adequately dosed therapy should initiate a search for inadequate adherence, faulty inhaler technique, or an other diagnosis [13]. The Australian asthma guidelines emphasize the significance of ruling out other diseases when wet cough is the primary symptom and when shortness of breath or wheezing are absent, especially among indigenous children where other diagnoses such as bronchiectasis are common. Bronchiectasis appears to be more prevalent among First Nations and Inuit children in Canada [17,18], particularly if they have a history of severe illness of the lower respiratory tract during early childhood.

Table 1: Other diagnoses to consider in young children with asthma-like symptoms

Clinical finding	Potential diagnosis
Failure to thrive, steatorrhea	Cystic fibrosis
Frequent, persistent or unusual infections	Immunodeficiency
Chronic rhinitis and severe recurrent otitis media, with or without situs inversus	Primary ciliary dyskinesia
Severe regurgitation or vomiting	Gastroesophageal reflux
Persistent wheezing	Fixed obstructive lesion of the airway (e.g., vascular ring, hilar adenopathy, aspirated foreign body)
Heart murmur or known congenital heart disease	Wheezing caused by congestive heart failure
Noisy breathing caused by retained upper airway secretions, aspiration	Swallowing disorder (particularly if the child has an underlying neurologic disorder or developmental delay)

The injection of systemic corticosteroids is crucial for the treatment of children exhibiting symptoms consistent with severe asthma exacerbations (CSs). Systemic CSs decrease the need for hospitalization and the risk of relapse following first treatment, and may also promote early hospital departure [19]. Some centers already utilize a brief course of dexamethasone for the treatment of asthma in hospitalized patients. However, while results are encouraging for outpatients, there is no evidence to support this practice for hospitalized patients. The majority of current CS regimens for hospitalized children with asthma exacerbation consist of a 5-day course of prednisone or prednisolone.

There is evidence that 2 days of once-daily dexamethasone is at least as beneficial as 5 days of prednisone in avoiding asthma relapse in outpatient children [20]. Moreover, individuals who receive dexamethasone are considerably less likely to vomit in the emergency department (ED) and even after leaving home [20]. Preliminary cost estimates indicate that dexamethasone may save as least $3,500 per 100 patients when compared to standard prednisone or prednisolone treatment [21].

Prednisone is only available as a pill or a compounded suspension in Canada, which restricts its use due to difficulties in swallowing and accessibility. Prednisolone is associated with poor palatability and considerable vomiting compared to dexamethasone [22]. Poor compliance is associated with both prednisone and prednisolone. Prednisone and prednisolone are synthesized using the same formulas, and hence have the same flavor. One study found compliance with 5 days of prednisone for pediatric asthma to be as low as 64% [23].

Systemic corticosteroids alleviate symptoms and airway obstruction, increase oxygenation, and reduce the likelihood of emergency room admission [24]. Therefore, these medications should be considered part of the initial treatment for all asthma exacerbations except the mildest [25]. Only children with recurrent vomiting or very severe sickness (score of 8 or higher on the Preschool Respiratory Assessment Measure [see the section "Initial management in the emergency department" in this article]) should receive intravenous therapy. Because the anti-inflammatory impact of corticosteroids takes several hours to manifest, these drugs should be administered as soon as feasible following the child's admission in the emergency room. The recommended dose of oral prednisolone or prednisone is 1–2 mg/kg (60 mg/dose maximum) taken daily for 5–7 days [24]. Tapering is not required for short (even 10-day) therapeutic courses [26]. Dexamethasone syrup has a longer physiologic half-life than prednisone; consequently, a 2-day course of this medicine at 0.15 mg/kg may be as efficacious as a 5-day course of prednisone. Patients with mild to moderate exacerbations may respond similarly to a single dose of dexamethasone 0.6 mg/kg [27,28]. Inhaled corticosteroids are less efficient than oral corticosteroids during acute exacerbations in children, and hence systemic corticosteroids should be utilized for stabilization [29,30,31].

Due to the fact that dexamethasone is a strong glucocorticoid with a lengthy half-life, concerns have been raised about its ability to inhibit the adrenal glands. 14 days after receiving a single dose of dexamethasone or 5 days of oral prednisone, there was no significant difference in adrenal function [23].

While systemic corticosteroids tend to improve certain outcomes, there has been inadequate study on nebulised drugs, thus definitive conclusions regarding their use cannot be drawn at this time. Due to the

exclusion of patients requiring critical care or status asthmaticus from the included studies, the results cannot be generalized to such patients. Patients receiving regular oral corticosteroids were not included in any of the investigations, therefore the results may not be applicable to these patients. Some people with chronic asthma have been reported to require relatively large oral maintenance doses of corticosteroids, whereas others are categorized as steroid-resistant. Therefore, these results may not apply to certain patient subgroups [15,27].

Oral and intravenous groups can be distinguished amongst the research comparing systemic steroids to placebo. In the comparison of oral corticosteroids, three studies evaluated the effect of a single prednisolone dose [21]. Clearly, these patients were healthy enough to withstand medication, therefore it was anticipated that a single dose would suffice to manage their exacerbation. Prednisolone is reported to exert its effects within one-fourth of an hour and to have a physiological half-life of 12 to 30 hours [31]. Consequently, it is probable that any benefits of this regimen would be observed early and subsequently disappear within the first day. All intravenous trials administered repeated doses for the duration of the patient's hospital stay, sustaining a continuous steroid impact. Intravenous drugs are independent of the severity or compliance of the patient. There are greater costs, risks, and discomfort associated with this type of therapy; however, given the comparisons between studies and the small number of patients involved, no definitive conclusions can be drawn regarding the comparative efficacy of the two routes of systemic corticosteroid administration. In hospital, only one study has compared nebulized medication to oral treatment [29,30,31].

Others have documented this poor outcome of acute asthma attacks in children, attributing the significant morbidity to inadequate patient follow-up in the outpatient setting or inefficient usage of asthma controller medicines. Consistent with previous research, roughly 40% of patients exhibited with persistent asthma symptoms at enrollment. Although these individuals are more likely to develop severe exacerbations, fewer than one-fourth of them receive frequent maintenance medication. Identifying individuals with chronic asthma and optimizing the usage and adherence to controller medicines [32,33] require increased effort.

Several features of the inclusion criteria ought to be discussed. Children aged >2 years with a history of atopy and a first wheezing episode were included in the trial, as were children aged 12 months to 2 years who had responded to b2-agonist medication in previous wheezing episodes. In these individuals, the diagnosis of asthma is questionable, and they may have a poorer response to corticosteroids, but they are often treated according to established guidelines for asthma therapy in the emergency department. According to earlier research, both dexamethasone and prednisone/prednisolone were equally successful in treating these patients. A further point of concern is that the shorter course of treatment with dexamethasone may necessitate the administration of additional doses, a feature that has been linked to clinicians' conventional preference for prednisone [33,34]. Intriguingly, patients in both groups who got additional steroid dosages had a worse short-term prognosis than the entire trial population, but there were no significant differences between dexamethasone and prednisone/prednisolone. This subset of patients' families reporting a less favorable outcome would likely prompt primary care pediatricians to recommend further steroid dosages. Dexamethasone is also more palatable than prednisolone among youngsters arriving to the emergency department with asthma exacerbations. Due to its concentration, however, the liquid formulation of dexamethasone requires a large volume [35].

CONCLUSION:

Asthma is characterized by airway edema, bronchoconstriction, and airway hyperresponsiveness. In addition to bronchodilators, corticosteroids are crucial to the treatment of acute asthma exacerbations. They reduce inflammation systemically, decrease mucus formation, and augment the actions of -agonists. National and international standards recommend the early use of systemic corticosteroids for moderate or severe exacerbations, as well as mild exacerbations that do not react immediately and completely to short-acting -agonists. Current treatment protocols involve oral prednisone or prednisolone once or twice daily for five days. As an analogous treatment, oral (PO) or intramuscular (IM) dexamethasone has been proposed. Possible benefits include a longer half-life necessitating a shorter course, increased compliance with a single dosage, and a reduction in vomiting with dexamethasone.

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