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Improving Asthma Care in the Hospital: an Overview of Treatments and Quality Improvement Interventions for Children Hospitalized for Status Asthmaticus

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Opinion Statement

Asthma is one of the leading causes of pediatric hospitalization in the USA. This review summarizes evidence-based practices for inpatient pediatric asthma treatment, including routine care, care escalation, and discharge care, along with established and emerging inpatient quality improvement approaches. Intermittent inhaled beta agonists, systemic steroids, and, for patients with low oxygen saturation, supplemental oxygen remain the cornerstones of routine inpatient asthma care. Compared to nebulization, metered-dose inhaler delivery of intermittent beta agonist therapy is more effective and underused. Oral prednisone produces similar clinical outcomes and is more cost-effective when compared with

intravenous methylprednisolone. Standardized respiratory assessment scores should supplement clinical judgment in evaluating response to therapy. There are no studies that demonstrate the effectiveness of routine adjuvant anticholinergic therapy outside of the emergency room, though it may be effective in a subset of inpatients. Evidence for inpatient care escalation is limited. With respect to discharge care, simple provision of asthma care plans does not appear to reduce readmissions, though individually tailored asthma care plans remain a standard of discharge care, along with systemic steroids, beta agonists, and, when indicated, inhaled corticosteroids. To avoid medication access barriers for high-risk patients, clinicians can ensure that discharge medications are in-hand before the patient leaves the hospital. A number of quality improvement strategies have shown promise in the inpatient setting. Clinical pathways reduce length of stay and costs associated with care without an associated increase in readmissions. Inpatient family education programs can be effective but should incorporate multiple strategies, including individualized management strategies and post-discharge follow-up. Inpatient care also serves as a useful opportunity to assess home environmental risk and to refer high-risk families to outpatient and community resources.

Introduction

In the USA, asthma is the single most common chronic condition among children with an estimated 6.8 million affected by the disease [1]. Annually, there are approximately 150,000 asthma hospitalizations for children, making it a leading cause of hospital admission in the pediatric population [2]. Status asthmaticus refers to an acute exacerbation of asthma refractory to conventional therapy. Bronchial smooth muscle contraction, increased mucous production, and airway inflammation are the primary mechanisms of acute asthma exacerbations [3], and acute inpatient therapy is directed toward these components of its pathophysiology.

Despite these common mechanisms, it has become increasingly clear that asthma represents a heterogeneous collection of genotypes that appear phenotypically similar and often respond to similar therapy [4]. As a result, current management strategies for acute care rely upon long-standing therapeutic modalities [5••], and innovations in inpatient management often come in the form of augmenting and combining these approaches, as well as standardizing asthma care. In 1989, the National Institutes of Health convened the National Asthma Education and Prevention Program (NAEPP) to help standardize asthma definitions, disease control assessment, and management across care settings, including inpatient care. The NAEPP has published three reports; the most recent of which is the Expert Panel Report-3 (EPR-3) in 2007 [3].

In this review, we first highlight the evidence for common inpatient therapies delivered outside the intensive care unit (ICU) for status asthmaticus, including (1) routine care, (2) care escalation, and (3) discharge care (Fig. 1). We cite the primary literature wherever possible and refer to guidelines, such as the EPR-3, where evidence is limited. We then summarize recent literature on quality improvement efforts focused on inpatient care and highlight future opportunities for improving inpatient asthma therapy and outcomes.

Treatment

Routine Therapies

Inhaled Beta Agonists

Intermittent administration of inhaled beta agonists is a cornerstone of inpatient asthma therapy [3, 6, 7]. Inhaled beta agonists target the beta-2 receptors on smooth muscle in the pulmonary bronchioles leading to smooth muscle

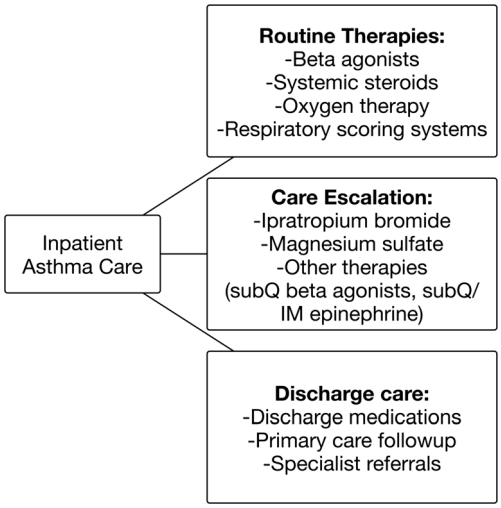

Fig. 1. Components of inpatient asthma care.

relaxation and bronchiolar dilatation. Frequency of administration of beta agonist treatment is determined by the severity of respiratory distress, a subjective determination that can be aided by validated respiratory scoring systems [8, 9]. For children receiving intermittent beta agonists, numerous studies from both the emergency room and inpatient setting suggest that delivery of beta agonists via metered dose inhalers is equivalent or superior to nebulization of medication with respect to improvement of pulmonary function parameters, clinical outcomes, and cost-effectiveness, even in children younger than five [10–13]. Despite this, available data suggest that MDI delivery devices are underutilized in routine inpatient therapy [6].

For children with more severe exacerbations, one small randomized trial evaluated the efficacy of hourly albuterol therapy compared with continuously aerosolized albuterol in the intensive care unit. This study demonstrated more rapid clinical improvement, shorter length of stay, and less respiratory therapy time by the bedside in the continuous albuterol group [14]. Although continuous administration of aerosolized beta agonists has traditionally been reserved for intermediate and intensive care settings [15], one recent single center study in the non-ICU setting demonstrated similar rates of adverse medication effects compared to intermittent therapy and relatively low rates of clinical deterioration with the appropriate clinical support infrastructure [16•, Class III].

Systemic Corticosteroids

Systemic corticosteroids are another cornerstone of inpatient asthma therapy. Steroids act through numerous pathways to suppress cellular inflammatory and allergic cascades. In addition to these effects, corticosteroids have been shown to reduce tolerance of smooth muscle to beta-2 agonists, producing a synergistic effect [17]. Multiple systematic reviews have demonstrated the effectiveness of systemic steroids in acute inpatient therapy [18, 19], yet there is less empirical evidence to guide specific clinical decisions regarding the route, type, and duration of administration of systemic corticosteroids in the inpatient setting. With respect to the route of administration, a randomized trial that compared oral prednisone

with intravenous methylprednisolone in 66 pediatric inpatients [20] demonstrated no significant differences in outcomes between the two therapies and patients who received oral prednisone actually required significantly fewer hours of oxygen therapy. For this reason, oral prednisone is recommended for use with inpatients due to its greater cost-effectiveness [20, 21].

With respect to duration and type of systemic steroid, there is less data to guide therapy. The EPR-3 recommendation for length of therapy for patients requiring hospitalization is 3 to 10 days, depending upon the severity of the exacerbation [3]. A single dose of dexamethasone, with a longer half-life, appears to be equally efficacious to the standard oral course of prednisone in children who present to the emergency department [22, 23] and offers potential cost savings [24]. However, there is insufficient evidence to assess the efficacy of dexamethasone versus prednisone for children whose exacerbation is severe enough to warrant hospitalization.

Oxygen Therapy

Oxygen is recommended to relieve hypoxemia in moderate to severe exacerbations [3]. Oxygen saturation is one of many indicators of a patient's clinical status, and while no studies have evaluated appropriate thresholds for oxygen therapy for inpatients, results of studies performed in the ED suggest that initial oxygen saturations less than 91 %, or lack of response to oxygen therapy, correlates with clinical outcomes [25, 26].

Continuation of Controller Medications

Guidelines recommend holding long-acting beta agonists during a hospitalization for acute asthma exacerbation [27]. Continuing inhaled corticosteroids likely provides negligible anti-inflammatory effects over systemic corticosteroids, but hospitalization may present an important opportunity to assess inhaler technique and encourage controller adherence habits.

Respiratory Scoring Algorithms

Several respiratory scoring algorithms are available to assist with severity assessment and treatment decisions. Well-validated algorithms include the Pediatric Asthma Severity Score (PASS) [8], a 6-point measure which assesses wheezing, retractions, and work of breathing, and the Pediatric Respiratory Assessment Measure (PRAM) [9], a 12-point score assessing suprasternal retractions, scalene contraction, air entry, wheezing, and oxygen saturation. The validation studies for these two scales were performed in the emergency department, where the scores correlated with hospital admission. Many institutions use derivatives of these scores to monitor response to therapy and guide treatment decisions in the inpatient setting.

Other commonly used scoring systems include the Modified Pulmonary Index Score (MPIS) and Pediatric Dyspnea Scale (PDS). The MPIS can be used to quantify the severity of illness in pediatric patient. MPIS is determined by assigning a score of 0 to 3 to each of the following categories: oxygen saturation, accessory muscle use, inspiratory-to-expiratory flow ratio, degree of wheezing, heart rate, and respiratory rate. A threshold of 12 is considered an indicator of severe exacerbation associated with increased oxygen requirement, ICU

admission, and longer length of stay [28]. The PDS can aid in discharge decision-making in hospitalized asthmatic children age 6 and over. The PDS utilizes a pictograph to assist children in answering "How much difficulty are you having breathing?" When assessed at the time of hospital discharge, an answer worse than "no trouble at all" or "a tiny bit" was a significant predictor of post-discharge relapse. The PDS performed better than FEV1, PEFR, or FENO in predicting relapse, activity limitation, and asthma-related quality of life outcomes 14 days after discharge [29].

Care Escalation

Ipratropium Bromide

Ipratropium bromide is an inhaled anticholinergic agent that acts at the muscarinic receptor resulting in bronchial smooth muscle relaxation. While a recent systematic review [30] demonstrated clear benefit of adjuvant ipratropium in addition to inhaled albuterol among children presenting to the emergency room, it has not been proven to be efficacious in the inpatient setting. Two inpatient focused studies directly addressed this question and found no significant difference between the ipratropium bromide treatment group and saline placebo in clinical outcomes, with one potential exception [31, 32]. The subgroup of patients in the treatment arm who were exposed to fewer than three ipratropium treatments in the ED experienced more rapid improvement in clinical severity score compared with the control group. This difference, however, was small and may lack clinical significance [32].

Magnesium Sulfate

Magnesium sulfate is another agent commonly used for enhanced bronchodilation. It acts by decreasing intracellular calcium by blocking its entry and release from the endoplasmic reticulum and by activating the sodium-calcium pumps. A number of studies support the safety of intravenous magnesium as an adjuvant therapy [33, 34]; these studies did not include non-ICU inpatient floors. In the emergency room setting, a systematic review and subsequent randomized controlled trial of inhaled magnesium for enhanced bronchodilation demonstrated limited efficacy [35, 36], while two meta-analyses have demonstrated more consistent effect of intravenous magnesium in preventing hospital admission [37, 38]. Given the evidence supporting its safety profile and efficacy in other settings, a dose of intravenous magnesium sulfate may be considered for inpatients who do not demonstrate sufficient response to inhaled beta agonists and systemic steroids.

Other Therapies

Few studies have assessed the efficacy or effectiveness of additional therapies for enhanced bronchodilation such as terbutaline (subcutaneous and intravenous) and epinephrine (intramuscular and subcutaneous). One study of epinephrine versus subcutaneous terbutaline found that the two drugs produced similar results, but noted that epinephrine was cheaper and resulted in greater improvement in respiratory rate compared to terbutaline [39]. However, the study

compared these medications as first-line therapies, not as adjuvants to standard therapy. Additional therapies such as ketamine, heliox, inhaled anesthetics, and enhanced airway support are rarely used outside of the intensive care unit and are beyond the scope of this review.

Discharge Care

Utilizing standardized discharge criteria can increase discharge efficiency and decrease length of stay [40•, Class III]. When determining if a child with asthma is ready for discharge, an objective assessment of clinical status should be completed. Additionally, the burden of the care (e.g., frequency of medications) should be manageable by the family at home.

Discharge Medications

Discharge medications should include bronchodilators and systemic steroids [3, 41••]. For children previously on inhaled corticosteroids, these medications should be continued or resumed at discharge. Hospitalization for asthma can be viewed as a sentinel event in the life of a child with asthma; therefore, initiation of inhaled steroids for those children not previously on them should be strongly considered [3]. Emerging evidence suggests that children assessed as having mild persistent asthma may not require daily inhaled steroids [42, 43], as was previously recommended. Daily use of inhaled steroids has been associated with a small but consistent finding of between 1 and 2 cm of diminished height following 2 years or more of treatment, which may persist into adulthood [44, 45]. This may be an important consideration for parents when discussing initiation or increased dosing of inhaled steroids. Younger children [46] and children with Medicaid [47] are less likely to be prescribed inhaled corticosteroids at discharge. Preferably, families should have the actual medications in hand at discharge, allowing the care team to address any potential barriers (such as insurance non-coverage or unexpectedly large copays) prior to discharge [48].

Asthma Care Plans

The EPR recommends an asthma care plan prior to discharge. Written asthma care plans have been shown to significantly improve outcomes in non-inpatient settings [49]. They provide a stepwise approach coordinating with the child's plan for chronic management and help children miss less school, have less nocturnal awakening, and improve symptom scores [50].

Outpatient Follow-up

The EPR-3 recommends that asthmatic children should follow up with a primary care physician 1–4 weeks post-discharge [3]. The follow-up appointment allows patients, physicians, and families to refine the asthma action plan, evaluate patient goal attainment, identify barriers to meeting activity goals, and identify potential treatment adjustments to prevent future exacerbations. Assistance with follow-up including transportation vouchers and appointment assistance significantly increases the likelihood that asthma patients will visit a primary care provider after an

emergency department visit [51]. Similarly, parents who perceive their child's exacerbation as being more severe are more likely to follow-up after an emergency department visit [52].

Guidelines suggest that referral to a specialist should be considered for any child hospitalized with a diagnosis of asthma [41••] but especially for patients with a history of life-threatening exacerbations or multiple hospitalizations [3].

Inpatient Care Quality

In the current health-care environment, establishing quality indicators and identifying interventions to improve patient outcomes have become priorities [53]. However, few studies have linked interventions aimed at improving the quality of inpatient asthma care with a corresponding improvement in patient outcomes. In this section, we highlight a number of the most common approaches to improving inpatient asthma care based on our review of the published literature and discuss a number of promising future care improvement approaches (Table 1).

In 2003, the Joint Commission established a collaborative working group that defined Children's Asthma Care (CAC) measures [7]. The measures are broken into three main components of inpatient hospital care: (1) CAC-1: use of bronchodilator/reliever medication, (2) CAC-2: use of systemic corticosteroids, and (3) CAC-3: completion of an asthma care plan prior to discharge. Approved in 2007, the measures were established for use as quality indicators of pediatric asthma hospitalizations.

Despite the widespread adoption of these CAC measures as national benchmarks and their use as publicly reported indicators of quality, there is conflicting evidence that adherence to these measures corresponds with improvement in patient outcomes. Two studies found compliance with CAC-3-improved readmission rates at 6 months and 90–180 days respectively, but both studies were limited by being single institution studies of readmissions and did not take into account the regional trends [54•, 55•, Class III]. In 2011, an administrative, cross-sectional study demonstrated nearly universal adoption of the CAC1 and CAC2 measures and that institutional-level adherence to the CAC-3 measure had no impact on subsequent ED utilization and hospitalization [56•, Class II]. These findings suggest the CAC1 and CAC2 measures may lack specificity in distinguishing better asthma care quality and that simply providing an asthma care plan at the time of discharge is not enough. How the plan is developed, discussed with, and used by the family may be critical factors in the plan's success.

Clinical Pathways

Outside the context of the CAC measures, there has been work on standardizing asthma care through clinical pathways. Specifically, clinical pathways have been used as an effective strategy to improve compliance with use of peak flow meters, spacers, and prescribing of controller medications at the time of discharge [57–60]. Clinical pathways have also been shown to decrease length of stay and, therefore, costs associated with hospitalization. Importantly, implementation of clinical pathways that have decreased the length of stay was not associated with an

Table 1. Studies of interventions to improve inpatient asthma care quality

Program	Author	Year	Participants	Study type	Primary results
Clinical pathways	Johnson et al. [57]	2000	*n*=110; 2–18 years	Randomized trial	Decreased length of stay, hospital charges, nebulized beta agonist use. No significant difference in 2-week readmission
	Kelly et al. [58]	2000	*n*=68; 2–18 years	Retrospective pre/post	Increased completion of patient education and prescription of controller medication, peak flow meter, and spacer. Decreased length of stay, hospital charges
	McDowell et al. [59]	1998	*n*=201; 1–18 years	Non-randomized prospective controlled trial	Decreased length of stay, hospital charges. No significant difference in 72-h readmission
	Wazeka et al. [60]	2001	*n*=1210; 2–18 years	Retrospective pre/post	Decreased length of stay, hospital charges. Two-week readmission rate of 0.02 % in clinical pathway patients (no control data)
Asthma-specific documentation templates	Beck et al. [61•]	2012	*n*=546; 2–16 years	Retrospective pre/post	Increased documentation of severity classification, utilization history, and environmental history
Family/staff education	Borgmeyer et al. [62]	2008	*n*=57; 9 months–17 years, 188 providers	Retrospective pre/post	Increased intern knowledge, positive family/staff feedback. No significant difference in length of stay, hospital charges, or readmission (time period undefined) between asthma nurse practitioners and interns
	Smith et al., [64]	2000	*n*=232; 2–16 years	Prospective pre/post	Increased provision of O_2 saturation checks, asthma management plans, and scheduling of primary care follow-up. No significant difference in administration of nebulized beta agonists, oral steroids, peak flow checks, inhaler technique assessments, or scheduling of inhospital follow-up
	Ng et al. [65]	2006	*n*=100; 2–15 years	Randomized trial	Decreased 3-month ED/hospital readmission. Increased drug compliance, parent satisfaction
Home environmental risk management	Beck et al. [67••]	2013	*n*=68 households, patients 1–16 years old	Retrospective pre/post	Inpatient doctors successfully referred 90 % of high-risk patients. Around 39 % of referrals completed hazard removal. Significant increase in home hazard communication among intervention households. No significant difference in symptom-free days in the last 2 weeks or Child Asthma Control Test score

increase in readmissions [57, 59, 60]. Asthma-specific documentation templates may augment inpatient clinical pathways by aiding clinicians in systematic assessment of asthma control and thus facilitate appropriate care planning [61•, Class III].

Inpatient Education Programs

A number of studies have reported on the use of the inpatient admission as an educational opportunity to be leveraged by a dedicated asthma educator for parents and patients. Most published programs use a dedicated nurse educator in providing educational programming for patients and families to improve asthma management knowledge at the point of discharge [62–64]. One randomized trial compared an enhanced bedside educational intervention that included a video, materials with pictures, skill assessment, and follow-up call to a basic bedside educational program. The group receiving enhanced bedside education had lower ED readmission and rehospitalization rates, as well as higher levels of parental satisfaction and medication adherence [65]. Another recent study suggests that inpatient education may need to go beyond asthma knowledge and also address medication adherence [66•, Class III].

Linking to Community Resources

A promising area of investigation recognizes inpatient admission as an opportunity to address the context of asthma control as it relates to environmental triggers in the home. One recent study formally evaluated the benefit of linking families to community-based resources at the point of discharge to help address social determinants of health negatively affecting asthma status in the home [67••, Class III]. Though the study did not report improvement in asthma-related outcomes, given the role that environmental factors play in asthma control, strong consideration should be given to the assimilation of these steps in care coordination as a best practice at the point of hospital discharge. Identification of environmental risks and linkage to community resources for high-risk inpatients is a key feature of a number of more broadly targeted asthma interventions [68–70].

Future Directions

As improvement of asthma patient outcomes continues to be a national priority, demand will build for effective interventions that improve hospital-based asthma outcomes. Given the constrained resources within health care, efforts to better define the methodology of risk stratification to allow for the prioritization of resources to patients more likely to have higher utilization rates will be a critical first step. Since hospitalization and rehospitalization rates are likely to be a measure of accountable care organization performance, tying inpatient care transition to outpatient follow-up will continue to be an important area of investigation, as it will improve post-discharge medication access. Interventions to improve post-hospitalization medication adherence using technology to maintain patient and family engagement should augment current strategies. Finally, enhancing relationships between inpatient care

coordinators, community resources, and health departments will help identify and intervene upon the social determinants of asthma care utilization in the home and community environment.

Compliance with Ethics Guidelines

Conflict of Interest

Dr. Chén C. Kenyon declares that he has no conflict of interest, Dr. Katherine A. Auger declares that she has no conflict of interest, Sarah A. Adams declares that she has no conflict of interest, Allison M. Loechtenfeldt declares that she has no conflict of interest, and Dr. James M. Moses declares that he has no conflict of interest.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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