

## Clinical Progress Note: Care of Children Hospitalized for Acute Asthma Exacerbation

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Since the last National Heart, Lung, and Blood Institute's (NHLBI) guidelines that were released in 2007, additional evidence has emerged in several areas of asthma care.<sup>1</sup> To provide a concise clinical update relevant to the practice of pediatric hospital medicine, we searched PubMed for asthma publications in the last 10 years with a particular focus on articles published in the last 5 years. We used a validated pediatric search filter to identify pediatric studies, MeSH term for "Asthma," and the following terms: "Clinical Pathways," "Clinical Protocols," "Dexamethasone," and "Albuterol." From these articles, we identified three areas of emerging evidence supporting practice change relative to the inpatient care of children with asthma, which are summarized in this brief review. This clinical practice update covers the emerging evidence supporting dexamethasone use for acute asthma exacerbations, the shift away from nebulized albuterol toward metered dose inhaler (MDI) albuterol, and the utility of asthma clinical pathways.

### DEXAMETHASONE VS PREDNISONE FOR ACUTE ASTHMA EXACERBATIONS

In the last decade, emergency departments (EDs) have increasingly prescribed dexamethasone over prednisone because it is noninferior and has a superior side-effect profile, including less vomiting.<sup>2</sup> However, the evidence for dexamethasone use in hospitalized children lagged behind ED practice change. This led to uncertainty among pediatric hospitalists regarding the most appropriate oral steroid to use, particularly for children who received dexamethasone in the ED prior to admission.<sup>3</sup>

Several studies have been published to address this gap in the literature. In 2015 Parikh et al. published a multicenter retrospective cohort study of dexamethasone vs prednisone among hospitalized children using the Pediatric Health Information Systems (PHIS) database.<sup>4</sup> The authors compared 1,166 patients who received dexamethasone only with a propensity-matched cohort of 1,284 patients receiving only prednisone/prednisolone. Outcomes included the proportion with a length of stay (LOS) greater than 3 days, all-cause readmission at 7 and 30

days, and cost of admission. A greater proportion of patients receiving prednisone/prednisolone had a LOS greater than 3 days when compared with those in the dexamethasone cohort. There were no significant differences in all cause 7- or 30-day readmission. The dexamethasone cohort had statistically significantly lower costs. The authors concluded that dexamethasone may be a viable alternative to prednisone/prednisolone for children admitted for acute asthma exacerbation not requiring admission to the pediatric intensive care unit (PICU).

In 2019, Tyler et al. published a single-center, retrospective, cohort study that used interrupted time series analysis to evaluate outcomes for inpatients with asthma before and after an ED's protocol was changed to dexamethasone.<sup>5</sup> Outcomes analyzed included LOS, hospital charges, and PICU transfer rates. The study included 1,015 subjects over a 36-month period. In the post-protocol change group, 65% of the subjects received dexamethasone only while 28% received a combination of dexamethasone and prednisone/prednisolone. The authors found no immediate significant differences in LOS, ICU transfers, or charges after the protocol change. However, they did see an overall 10% increased rate of PICU transfers in the period following the protocol change, a trend that could have been caused by difficult-to-measure differences in severity of patients before and after the protocol change. If the increase in PICU transfer rate was temporally associated with the ED protocol change, an immediate change in rate would be expected, and this was not seen. The authors speculated that dexamethasone may be inferior to prednisone for inpatients with the highest severity of asthma.

Combined with the practical benefit of dexamethasone's shorter treatment course and decreased vomiting,<sup>2</sup> these two studies support the use of dexamethasone in the inpatient setting for patients who don't require ICU level care. A feasibility trial to determine noninferiority of dexamethasone vs prednisone is currently enrolling, according to clinicaltrials.gov.

### NEBULIZED VS METERED-DOSE INHALER ALBUTEROL FOR ACUTE ASTHMA EXACERBATIONS

The 2007 NHLBI guidelines are clear that short-acting beta-2 agonists (SABA), delivered via nebulization or metered-dose inhaler (MDI) with a valved holding chamber (VHC), along with systemic steroids, should be the primary treatment in pediatric acute asthma exacerbations.<sup>1</sup> The guidelines caution that nebulization therapy might be needed for patients who are ineffective in using MDIs because of age, level of agitation, or severity of

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asthma symptoms. Specific recommendations for management in the inpatient setting are brief but note that inpatient medication administration and care should mirror ED management strategies.<sup>1</sup> Specific in-hospital management recommendations regarding nebulization vs MDI are not addressed.

A Cochrane Review by Cates et al. assessed pediatric and adult randomized trials comparing SABA delivery via MDI-VHC with that via nebulization.<sup>6</sup> The analysis included 39 trials with a total of 729 adults and 1,897 children. Six of the included trials were conducted in an inpatient setting (207 enrolled children in these studies). The authors found that mechanism of SABA delivery did not affect ED admission rates or significantly influence other markers of treatment response (peak flow and forced expiratory volumes). In children, MDI-VHC use was associated with shorter ED length of stay, as well as a decreased frequency of common SABA side effects (ie, tachycardia and tremor). This review cites several areas in which research is needed, including MDI use in severe asthma exacerbations. This population often falls outside pediatric hospitalists' scope of practice because these patients often require ICU-level care.

A recent systematic review of pediatric acute asthma management strategies by Castro-Rodriguez et al. found that using MDI-VHC to deliver SABA was superior to using nebulization as measured by decreased ED admission rates and ED length of stay, improved asthma clinical scores, and reduced SABA side effects.<sup>7</sup> A 2016 prospective randomized trial of MDI-VHC vs nebulization in preschool-aged children presenting to an ED with asthma or virally mediated wheeze found that the SABA delivered via MDI-VHC was at least as effective as that delivered via nebulization.<sup>8</sup>

International asthma management guidelines more strongly recommend MDI-only treatment for pediatric patients admitted with moderate asthma.<sup>9</sup> Despite this guidance, and the literature supporting transition in inpatient settings to bronchodilator administration via MDI, there are several barriers to exclusive MDI use in the inpatient setting. As mentioned by Cates et al., a recognized challenge in MDI-VHC adoption is overcoming the "nebulizer culture" in treating pediatric acute asthma symptoms.<sup>6</sup> Perhaps not surprisingly, Press et al., in a retrospective secondary analysis of 25 institutions managing adults and children with acute asthma symptoms, found that 32% of all pediatric patients assessed received only nebulized SABA treatments during their hospitalization.<sup>10</sup> Transitioning from nebulized albuterol to exclusively MDI-VHC albuterol will require significant systems changes.

## UTILITY OF CLINICAL PATHWAYS

Clinical pathways operationalize practice guidelines and provide guidance on the treatments, testing, and management of an illness. Use of pediatric asthma pathways has increased steadily in the past decade, with one study of over 300 hospitals finding that, between 2005 to 2015, pathway implementation increased from 27% to 86%.<sup>11</sup> This expanded use has coincided with a proliferation of publications evaluating the effects of these pathways. A systematic review examining the implementation and impact of asthma protocols identified

over 100 articles published between 1986 and 2010, with the majority published after 2005.<sup>12</sup> The study found implementation of guidelines through an asthma pathway generally improved patient care and provider performance regardless of implementation method.

Since that review, Kaiser et al. investigated the effects of pathway implementation at 42 children's hospitals.<sup>13</sup> They used interrupted time series to determine the effect of pathway implementation on LOS. Secondary outcomes included cost, use of bronchodilators, antibiotic use, and 30-day readmissions. This study found pathway implementation was associated with an 8.8% decrease in LOS and 3% decrease in hospital costs while increasing bronchodilator administration and decreasing antibiotic exposure. To determine the factors that allowed successful implementation of asthma pathways (as determined by reduction in LOS), Kaiser et al. performed qualitative interviews of key stakeholders at high- and low-performing hospitals.<sup>14</sup> The most successful hospitals all used rigorous data-driven quality-improvement methodologies, set shared goals with key stakeholders, integrated the pathway into their electronic medical record, allowed nurses and respiratory therapists to titrate albuterol frequency, and engaged hospital leadership to secure needed resources.

Although in each of these studies, pathway implementation led to improvements in the acute management of patients, there was no reduction in pediatric asthma readmissions at 30 days.<sup>12,13</sup> A meta-analysis of asthma-related quality improvement interventions also did not find an association between pathway implementation alone and decreased readmissions or ED revisits.<sup>15</sup> The lack of improvement in these metrics may have been caused by the tendency for pathways to focus on the acute asthma management and lack of focus on chronic asthma severity. Asthma admissions are an opportunity for full evaluation of disease severity, allergen exposures, and education on medication and spacer technique. Refinement of pathways with a focus on chronic control and on transition from hospital to home may move the needle on decreasing the long-term morbidity of pediatric asthma.

## CONCLUSION

Current evidence suggests pediatric hospitalists should consider transitioning from prednisolone/prednisone to dexamethasone and from nebulized albuterol delivery to MDI albuterol delivery for children admitted for acute asthma exacerbation who do not require ICU-level care. Implementing asthma clinical pathways that use rigorous quality improvement methods is an effective approach to adopt these and other evidence-based practice changes.

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