

Clinical Questions #7

Editor's note: This is the seventh installment in a series of "Clinical Questions." Readers are presented with a case and clinical question. An evidence-based answer is provided on a later page. The answer includes how the evidence was found and evaluated.

Systemic corticosteroid dosing for acute asthma: Is higher better?

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Patient

A 20-year-old man with asthma and allergic rhinitis is brought to the emergency department by emergency medical services. He is found to be in respiratory failure and requires emergent endotracheal intubation. He had 3-4 days of viral upper respiratory infection symptoms prior to his presentation. He has a history of non-adherence with his medical regimen for moderate persistent asthma.

Clinical Question

In adults with severe acute asthma requiring hospitalization, are high-dose systemic (oral, intramuscular, or intravenous) corticosteroids more effective than lower-dose regimens in decreasing mortality or length of hospital stay?

How and where could you locate evidence to answer this question?

How would you treat this patient?

Turn the page for one possible approach.

Authors are with the University of Wisconsin Hospital and Clinics. Doctor Ehlenbach is chief medical resident, and will be beginning a pulmonary/critical care fellowship at the University of Washington this year. Doctor Feldstein is an academic hospitalist. He is also an assistant professor in the Department of Medicine at the University of Wisconsin-Madison.

Suggested Approach for Clinical Question #7

Search Strategy

1. Cochrane Database of Systematic Reviews (4th Quarter 2005) using Ovid interface:
 - a. “acute asthma or asthma exacerbation”
 - b. “corticosteroids or glucocorticoids or prednisone or hydrocortisone or methylprednisolone or dexamethasone”
 - c. “high-dose”
 - d. combine (a) and (b) and (c)
 - e. 41 matches, 1 that applied to our clinical question: Manser R, Reid D, Abramson M. “Corticosteroids for acute severe asthma in hospitalised patients.” The last search for this review was in September 2002.
2. All years of MEDLINE (1966 to November Week 2 2005)
 - a. “acute asthma or asthma exacerbation” (keyword)
 - b. “exp steroids” (exploded MeSH heading)
 - c. “random” (keyword; used to limit the results to randomized trials)
 - d. combine (a) and (b) and (c)
 - e. limit (d) to Humans, English Language, Year 2002-2006 (year 2002 chosen since the last search for the meta-analysis found in #1 was performed in that year)
 - f. 34 matches, none applicable to our clinical question

Study Characteristics

- Systematic review and meta-analysis of randomized controlled trials (last updated July 2005, with last search performed in September 2002)
- Objective to determine whether higher doses of systemic corticosteroids (oral, intravenous, or intramuscular) are more effective than lower doses in the management of patients with acute severe asthma requiring hospital admission
- Divided treatment into 3 levels of steroid dosing
 - o low (≤ 80 mg/day methylprednisolone or equivalent)
 - o medium (≥ 80 mg/day and ≤ 360 mg/day)
 - o high (≥ 360 mg/day)
- The primary outcome was data from pulmonary function tests (PFTs)
- Secondary outcomes included clinical outcomes (length of stay), other physiologic data, symptom scores, and side effects

Validity of Evidence

- Posed a focused clinical question regarding therapy
- Included randomized controlled trials (RCTs) from the Cochrane Airways Review Group Register, from primary authors and experts, and bibliographies from studies, reviews, and texts
 - o Search strategy is discussed in detail and appears exhaustive
- Methodological quality of studies assessed by 2 independent reviewers using the Jadad scoring system; trial authors were contacted to provide additional information regarding the methodology of their studies
- No statistical heterogeneity detected for any pooled outcomes

Results

- Search Results
 - o Nine RCTs met inclusion criteria, with a total of 344 patients

- o Only 6 of the trials provided sufficient data for meta-analysis
- o Inter-reviewer reliability ranged from good to perfect
- o Seven of the 9 trials were of good methodological quality with a Jadad score ≥ 3
- Pooled Results
 - o Two studies reported length of stay (LOS).
 - No statistical difference between low or medium versus high dose
 - 95% confidence intervals spanned a 4-hour reduction in LOS for high dose to a 21-hour reduction in LOS for low dose
 - o PFTs at 24, 48, and 72 hours
 - No clinically important or statistically significant differences between varying doses of corticosteroids (L versus M, M versus H and L versus H)
 - o No deaths in the 9 studies
 - o None of the studies included mechanically ventilated or intensive care unit (ICU) patients
 - o One study evaluated symptom scores, and found no statistical difference between groups at 24 hours or 12 days

Applying the Evidence to the Patient

- Systemic corticosteroids at low, medium, or high dose are feasible therapies for this patient
- Our patient required endotracheal intubation, mechanical ventilation, and ICU management
 - o No patients with respiratory failure or other indications for ICU admission were included in any of the trials

Summary

This systematic review by Manser et al is a high-quality meta-analysis of small, reasonable-quality randomized controlled trials. Previous studies have proven the benefit of systemic corticosteroids in acute asthma, but optimal dosing remains unknown. In this review, higher dose systemic corticosteroids showed no significant improvements in any of the outcomes measured. This is an important result, since many of the short-term side effects of corticosteroids appear to be dose-dependent. However, the results should be interpreted with caution, since the review included a small number of studies and the total number of patients was small. None of the trials in this meta-analysis included intubated or ICU patients, but the disease process is essentially the same regardless of severity, so extrapolation to the patient in question is reasonable. There is a need for larger studies in this area to determine the appropriate doses of systemic steroids in severe acute asthma exacerbations.

Conclusion

There does not appear to be any therapeutic benefit of steroid doses greater than methylprednisolone 80 mg IV per day (or equivalent). The patient should be treated with this dosing regimen.

References

1. Manser R, Reid D, Abramson M. Corticosteroids for acute severe asthma in hospitalised patients. Cochrane Airways Group, Cochrane Database of Systematic Reviews.

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