Review: Corticosteroids reduce mechanical ventilation and ARDS in inpatients with community-acquired pneumonia

Siemieniuk RA, Meade MO, Alonso-Coello P, et al. ***Corticosteroid therapy for patients hospitalized with community-acquired pneumonia: a systematic review and meta-analysis.*** *Ann Intern Med. 2015;163:519-28.*

Clinical impact ratings: HO ★★★★★★☆ ID ★★★★★★☆ PM ★★★★★★☆

Question

In hospitalized patients with community-acquired pneumonia (CAP), what is the efficacy of corticosteroids?

Review scope

Included studies compared oral or IV corticosteroids with placebo in adults hospitalized with CAP. Studies of patients with ventilator-associated pneumonia, aspiration pneumonia, *Pneumocystis jirovecii* pneumonia, or chronic obstructive pulmonary disease were excluded. Studies had to report ≥ 1 relevant outcome, including mortality, mechanical ventilation, intensive care unit (ICU) admission, acute respiratory distress syndrome (ARDS), duration of hospitalization, and time to clinical stability.

Review methods

MEDLINE, EMBASE/Excerpta Medica, Cochrane Central Register of Controlled Trials (2010 to May 2015); Google Scholar; and reference lists were searched for randomized controlled trials (RCTs). Articles included in a previous Cochrane review* were included. 13 RCTs (n = 2005) (mean or median age 36 to 74 y, 48% to 74% men when reported), ranging in size from 30 to 784 patients, met the selection criteria. Corticosteroids assessed were hydrocortisone (6 RCTs), prednisolone (3 RCTs), methylprednisolone (2 RCTs), dexamethasone (1 RCT), and prednisone (1 RCT). Follow-up duration ranged from in-hospital to 60 days. Risk for bias was low in 5 trials (70% of patients).

Main results

Meta-analysis showed that corticosteroids did not reduce mortality compared with placebo overall (Table); subgroup analyses showed that corticosteroids reduced mortality in trials enrolling patients with more severe pneumonia (relative risk [RR] 0.39, 95% CI 0.20 to 0.77) but not in trials of patients with less severe pneumonia (RR 1.00, CI 0.79 to 1.26) (P = 0.010 for interaction). Corticosteroids reduced risk for mechanical ventilation and ARDS, but not ICU admission (Table). Corticosteroids reduced duration of hospitalization (mean difference 1.00 d, CI 0.21 to 1.79 in 3 trials [n = 1288] at low risk for bias) and time to clinical stability (mean difference 1.22 d, CI 0.35 to 2.08). Corticosteroids increased risk for hyperglycemia (Table) but not gastrointestinal hemorrhage, severe neuropsychiatric complications, or rehospitalization.

Conclusion

In adults hospitalized with community-acquired pneumonia, corticosteroids reduce length of stay, mechanical ventilation, and ARDS but increase hyperglycemia.

**Chen Y, Li K, Pu H, Wu T. Corticosteroids for pneumonia. Cochrane Database Syst Rev. 2011;(3):CD007720.*

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Commentary

The excellent synthesis by Siemieniuk and colleagues integrates disparate studies and challenges the status quo by suggesting the use of steroids in CAP. The Infectious Diseases Society of America/American Thoracic Society guidelines (1), updated in 2007, do not recommend use of steroids for CAP. However, mechanistic studies of C-reactive protein, interleukin-10, and other inflammatory biomarkers indicate a benefit of steroids in CAP (2). Improvements in time to clinical stability and hospital length of stay could have a profound effect on both patient outcomes and the economics of this common disease.

Meta-analysis and interpretation of the results of the trials included in the review are confounded by their heterogeneous populations (e.g., proportion of patients with COPD or at increased risk for corticosteroid adverse events), methodologies, and outcomes. Patients with severe CAP may benefit most from steroids based on increased event rates and small absolute risk reductions. However, with different definitions of severe CAP and steroid doses assessed in small populations, how do we select the patient population and dose?

The ADRENAL and ESCAPe trials are currently assessing the efficacy of steroids in 3800 patients with sepsis and 1450 patients with severe CAP, respectively, and will finish data collection in 2016 (3, 4). We should await the pooled results of these trials before we change national standards of care. In high-risk patients with severe CAP, clinicians may consider use of 0.5 mg/kg of prednisone for 5 days based on a low grade of evidence.

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Corticosteroids vs placebo in adults hospitalized with community-acquired pneumonia†

Outcomes	Number of trials (n)	Weighted event rates		In-hospital to 60 d	
		Corticosteroids	Placebo	RRR (95% CI)	NNT (CI)
Mortality	12 (1974)	5.3%	7.9%	33% (−1 to 55)	Not significant
Mechanical ventilation	5 (1060)	2.6%	5.7%	55% (21 to 74)	32 (24 to 84)‡
Intensive care unit admission	3 (950)	5.2%	7.6%	31% (−3 to 54)	Not significant
Acute respiratory distress syndrome	4 (945)	0.7%	3.0%	76% (44 to 90)	45 (38 to 77)‡
				RRI (CI)	NNH (CI)
Hyperglycemia	6 (1534)	13%	8.7%	49% (1 to 119)	24 (10 to 1154)

†Abbreviations defined in Glossary. Weighted corticosteroid event rate, RRR, RRI, NNT, NNH, and CI calculated from control event rates and risk ratios in article using a random-effects model.

‡Note: The authors report NNTs of about 20 for mechanical ventilation and acute respiratory distress syndrome, using risks from patients not treated with corticosteroids in large observational studies.

References

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2. **Annane D.** Corticosteroids and pneumonia: time to change practice. Lancet. 2015;385:1484-5.
3. ADjunctive corticosteroid trEatment IN criticAlly ilL Patients with Septic Shock (ADRENAL). ClinicalTrials.gov NCT01448109.
4. Extended Steroid in CAP(e)(ESCAPe). VA Clinical Study Protocol #574. ClinicalTrials.gov NCT01283009.