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Hydrocortisone in severe community-acquired pneumonia

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Ratings: *Methods*—4.5/5, *Usefulness*—4/5

Introduction

Background

Community acquired pneumonia (CAP) can lead to pulmonary and systemic inflammation that leads to impaired gas exchange, sepsis, and organ failure; resulting in an in-hospital mortality of 10–12%. Previous evidence showed potential benefit in using glucocorticoids to decrease inflammation in severe CAP in the intensive care unit (ICU).

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Objectives

Dequin and colleagues sought to evaluate whether early treatment with hydrocortisone reduces mortality at 28 days in patients with severe CAP.

Methods

Design

The CAPE-COD trial was a double blind, randomized, controlled, superiority trial.

Setting

This study was conducted in ICU and intermediate care units of 31 French centers.

Subjects

Patients (> 18 years) admitted to ICU or intermediate care with severe CAP.

Intervention

Hydrocortisone 200 mg IV daily for 4 or 7 days with a 4–7 day taper.

Comparator

Normal saline (placebo).

Outcomes

Primary outcome was mortality at 28 days. Secondary outcomes were mortality at 90 days, ICU length of stay, rate of mechanical ventilation, ventilator free days, initiation of vasopressors by day 28, vasopressor free days, P:F ratio change,

Table 1 Primary and select secondary outcome results

Outcome	Hydrocortisone (%)	Placebo (%)	HR for hydrocortisone vs placebo (95% CI)	ARR for hydrocortisone vs placebo (95% CI)	*P*-Value
Death by day 28	6.2	11.9		5.6% (1.7%–9.6%)	0.006
Death by day 90	9.3	14.7		5.4% (0.8%–9.9%)	
Intubation by day 28	18.0	29.5	0.59 (0.40–0.86)		
Vasopressor by day 28	15.3	25.0	0.59 (0.43–0.82)		

Sequential Organ Failure Assessment (SOFA) score, and quality of life at 90 days on a SF-36 scale.

Results

The study included 795 patients in a modified intention to treat analysis (n = 400 for hydrocortisone and $n = 395$ in placebo). The proportion of patients with underlying COPD was 21.5% in the hydrocortisone and 26.6% in the placebo group. The mean age, rate of mechanical ventilation, baseline SOFA score, baseline laboratory markers, and timing of treatment were similar between the groups. The primary and selected secondary outcomes, along with the relative risk results are presented in Table 1. Statistically significant results are bolded.

Appraisal

Strengths

- Patient centered outcomes
- Minimal loss to follow-up
- Large sample size across 31 centres

Limitations

- Trial was stopped early despite not reaching predetermined alpha risk threshold; the resulting smaller sample size could lead to decreased precision of the treatment effect
- No standardization of antimicrobials or microbiologic confirmation of pneumonia
- Strict inclusion criteria and exclusion of patients in shock leading to lower than anticipated mortality and limiting generalizability, especially in ED populations

Context

Severe CAP can lead to significant pulmonary and systemic inflammation. Previous studies have shown evidence for steroids reducing mortality in adults with severe pneumonia but not non-severe pneumonia [1]. Recently, the RECOVERY trial has shown a mortality benefit when administering dexamethasone to patients requiring oxygen with COVID-19 infections to help with the significant inflammatory organ injury [2]. However, a recent similar randomized control study did not show any significant differences for severe CAP in the ICU when using methylprednisolone and including patients in septic shock [3]. Current critical care guidelines still vary on the recommendation of corticosteroid in severe CAP.

Local ICU physician Dr. Hendin, agrees there is a benefit for steroids in inflammatory conditions such as pneumonia. This is seen in previous literature in relation to acute respiratory distress syndrome, COVID-19, and septic shock. However, steroid choice, specific indication, and optimal usage for CAP is yet to be determined.

Bottom line

There is a mortality benefit for corticosteroids in severe CAP and should be considered after initiation of standard of care therapies such as antibiotics, fluids, and supportive care. This is especially important for patients in ED's that may not reach ICU-level care within 24 h. Physicians should be cautious about applying the results to ED specific populations in the initial phase of resuscitation given the narrow inclusion criteria.

Declarations

Conflicts of interest There are no conflicts of interests for any authors.

References

1. Stern A, Skalsky K, Avni T, Carrara E, Leibovici L, Paul M. Corticosteroids for pneumonia. Cochrane Database Syst Rev. 2017. https://doi.org/10.1002/14651858.CD007720.pub3. (**PMID: 29236286, PMCID: PMC6486210**).
2. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T,

Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, Landray MJ. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384(8):693–704. https://doi.org/10.1056/NEJMoa2021436. (**Epub 2020 Jul 17 PMID: 32678530, PMCID: PMC7383595**).

3. Meduri GU, Shih MC, Bridges L, Martin TJ, El-Solh A, Seam N, Davis-Karim A, Umberger R, Anzueto A, Sriram P, Lan C, Restrepo MI, Guardiola JJ, Buck T, Johnson DP, Suffredini A, Bell WA, Lin J, Zhao L, Uyeda L, Nielsen L, Huang GD, ESCAPe Study Group. Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 2022;48(8):1009–23. https://doi.org/10.1007/s00134-022-06684-3. (**Epub 2022 May 13 PMID: 35723686, PMCID: PMC9208259**).