Hydrocortisone in Community Acquired Pneumonia

Subjects: Health Policy & Services
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Summary of Key Findings Oxygenation and Respiratory Outcomes: Hydrocortisone significantly improved oxygenation (PaO_2/FiO_2 ratio) and increased the number of mechanical ventilation-free days. This suggests that hydrocortisone could be beneficial in enhancing respiratory outcomes. Reduction in Major Complications: There was a notable reduction in the incidence of major complications, including delayed septic shock and MODS, among patients treated with hydrocortisone. Mortality: ICU, hospital, and 60-day mortality were significantly lower in the hydrocortisone group, indicating a potential survival benefit. Length of Stay and Ventilation Duration: Patients in the hydrocortisone group had shorter ICU stays, hospital stays, and duration on mechanical ventilation, supporting its efficacy in reducing the burden of intensive care needs. Safety Profile: Although complications like ARDS, ventilator-associated pneumonia, and acute renal failure were monitored, there were no significant increases in these adverse events with hydrocortisone. This supports its safety profile in the ICU setting.

pneumonia Cape Cod Hydrocortisone

1. Introduction

Variable	Confalonieri 2012	Nafae 2013	Cape Cod 2023
Mortality Outcomes			
ICU Mortality	7/23 (30%) Placebo, 0/23 (0%) Hydrocortisone	Not reported	Not reported
28-day Mortality	Not reported	Not reported	47/395 (11.9%) Placebo, 25/400 (6.2%) Hydrocortisone
60-day Mortality	8/23 (35%) Placebo, 0/23 (0%) Hydrocortisone	Not reported	Not reported
Hospital Mortality	7/23 (30%) Placebo, 0/23 (0%) Hydrocortisone	6/20 (30%) Placebo, 4/60 (6.7%) Hydrocortisone	Not reported
Mechanical Ventilation			
Need for Mechanical Ventilation	15/23 (65%) Placebo, 6/23 (26%)	5/20 (25%) Placebo, 8/60 (13.3%)	65/220 (29.5%) Placebo, 40/222 (18%)

	Hydrocortisone	Hydrocortisone	Hydrocortisone
Mechanical Ventilation-Free Days	0 (0-6) Placebo, 4 (0-7) Hydrocortisone	Not reported	Not reported
Duration of Mechanical Ventilation	10 (2-44) days Placebo, 4 (1-27) days Hydrocortisone	12-22 days Placebo, 5-24 days Hydrocortisone	Not reported
PaO_2/FiO_2 Ratio			
Baseline PaO_2/FiO_2 Ratio	237 ± 92 Placebo, 332 ± 80 Hydrocortisone	319.4 ± 54.3 Placebo, 343.9 ± 51.6 Hydrocortisone	Not reported
PaO_2/FiO_2 Improvement ≥ 100	8/23 (35%) Placebo, 20/23 (87%) Hydrocortisone	Not reported	Not reported
Inflammatory Markers			
CRP (mg/L) - Baseline	34 (0–225) Placebo, 18 (0–44) Hydrocortisone	95.4 ± 45.64 Placebo, 91.3 ± 39.96 Hydrocortisone	Not reported
CRP (mg/L) - Reduction	Not reported	43.7 ± 46.2 Placebo, 16.3 ± 18.9 Hydrocortisone	Not reported
ESR (mm/hr)	Not reported	81.7 ± 6 Placebo, 79.9 ± 9.7 Hydrocortisone	Not reported
Length of Stay			
ICU Stay (days)	18 (3–45) Placebo, 10 (4–33) Hydrocortisone	6.3 ± 8.2 Placebo, 3.1 ± 4.9 Hydrocortisone	Not reported
Total Hospital Stay (days)	21 (3–72) Placebo, 13 (10–53) Hydrocortisone	16.5 ± 2.24 Placebo, 9.27 ± 2.4 Hydrocortisone	Not reported
Safety and Complications			
Delayed Septic Shock	10/23 (52%) Placebo, 0/23 (0%) Hydrocortisone	Not reported	Not reported
ARDS	4/23 (17%) Placebo, 0/23 (0%) Hydrocortisone	6/20 (30%) Placebo, 4/60 (6.7%) Hydrocortisone	Not reported
Nosocomial Infection	4/23 (18%) Placebo, 0/23 (0%) Hydrocortisone	Not reported	44/395 (11.1%) Placebo, 39/400 (9.8%)

			Hydrocortisone
Gastrointestinal Bleeding	1/23 (4%) Placebo, 1/23 (4%) Hydrocortisone	1/20 (5%) Placebo, 1/60 (1.6%) Hydrocortisone	13/395 (3.3%) Placebo, 9/400 (2.2%) Hydrocortisone
Hypokalemia	Not reported	5/20 (25%) Placebo, 35/60 (58.3%) Hydrocortisone	Not reported
Uncontrolled Diabetes (glucose > 250 mg/dL)	Not reported	8/20 (40%) Placebo, 19/60 (31.7%) Hydrocortisone	Not reported
Blood Chemistry and Hematology			
WBC (·10^3/cm)	Not reported	17 ± 4.5 Placebo, 17.8 ± 4.5 Hydrocortisone	Not reported
Hematocrit (%)	Not reported	28.9 ± 2.7 Placebo, 30 ± 4.2 Hydrocortisone	Not reported
BUN (mg/dL)	Not reported	41.8 ± 19.5 Placebo, 31.6 ± 14.2 Hydrocortisone	Not reported
Creatinine (mg/dL)	Not reported	1.5 ± 0.8 Placebo, 1.14 ± 0.5 Hydrocortisone	Not reported
Sodium Level (Na, mEq/L)	Not reported	130.1 ± 3.71 Placebo, 131.9 ± 6 Hydrocortisone	Not reported
Potassium Level (K, mEq/L)	Not reported	3.63 ± 0.44 Placebo, 3.6 ± 0.46 Hydrocortisone	Not reported

[1][2][3][4][5] Table1. Common Variables and Results Across [6], Nafae 2013, and Cape Cod 2023.

2. Meta-Analysis Table for Key Parameters and Outcomes

Parameter/Outcome	Placebo	Hydrocortisone	p-Value	Interpretation
Demographics				
Male/Female	15/8	17/6	0.53	No significant difference in gender distribution
Age, years	66.6 ± 14.7	60.4 ± 17.3	0.20	No significant age difference
Smoking Habit	See subgroup analysis	See subgroup analysis	NS	Not significantly different

Parameter/Outcome	Placebo	Hydrocortisone	p-Value	Interpretation
Severity Scores				
APACHE II Score	18.2 ± 4.0	17.2 ± 4.1	0.39	No significant difference in severity
MODS Score	1.2 ± 0.4	1.2 ± 0.5	0.75	No significant difference
Vital Signs and Laboratory Values				
Temperature (°C)	38.2 ± 1.2	38.3 ± 0.9	0.76	No significant difference
WBC Count ($\times 10^9$/L)	13.9 ± 5.1	13.4 ± 5.5	0.73	No significant difference
PaO_2/FiO_2 Ratio	178 ± 58	141 ± 49	0.03	Significant difference; lower in hydrocortisone group
$PaO_2/FiO_2 \leq 200$	13 (57%)	21 (91%)	0.02	Significant; worse oxygenation in hydrocortisone group
CRP (mg/dL)	29 (6–200)	55 (14–349)	0.04	Significant; higher CRP in hydrocortisone group
Respiratory Support and Ventilation				
On Mechanical Ventilation	19 (83%)	15 (65%)	0.18	Not significant
Mechanical Ventilation-Free Days	0 (0–6)	4 (0–7)	0.01	Significant; more vent-free days in hydrocortisone
PaO_2/FiO_2 Ratio (after treatment)	237 ± 92	332 ± 80	0.0008	Significant improvement with hydrocortisone
PaO_2/FiO_2 Improvement ≥ 100	8 (35%)	20 (87%)	0.0007	Significant improvement in oxygenation
Chest Radiograph and MODS				
Chest Radiograph Score	2.6 ± 1.3	1.1 ± 0.7	< 0.0001	Significant improvement with hydrocortisone
Improvement in Chest Radiograph Score	5 (22%)	21 (91%)	< 0.0001	Significant improvement with hydrocortisone
Patients with MODS	16 (70%)	8 (35%)	0.02	Significant reduction in MODS with hydrocortisone

Parameter/Outcome	Placebo	Hydrocortisone	p-Value	Interpretation
Shock and Complications				
Delayed Septic Shock by Day 8	9 (43%)	0 (0%)	0.001	Significant reduction in delayed septic shock
New ARDS by Day 8	3 (13%)	0 (0%)	0.23	Not significant
Major Complications				
Major Complications	18 (78%)	6 (26%)	< 0.001	Significant reduction in complications
Delayed Septic Shock	10 (52%)	0 (0%)	< 0.001	Significant reduction with hydrocortisone
Shock Not Related to Sepsis	2 (9%)	0 (0%)	0.5	Not significant
ARDS	4 (17%)	0 (0%)	0.11	Not significant
Nosocomial Infection	4 (18%)	0 (0%)	0.11	Not significant
Ventilator-Associated Pneumonia	3 (13%)	0 (0%)	0.23	Not significant
Acute Renal Failure	3 (13%)	0 (0%)	0.23	Not significant
Mortality and Survival				
ICU Mortality	7 (30%)	0 (0%)	0.009	Significant reduction in ICU mortality
Hospital Mortality	7 (30%)	0 (0%)	0.009	Significant reduction in hospital mortality
60-day Mortality	8 (38%)	0 (0%)	0.001	Significant reduction in 60-day mortality
Length of Stay and Mechanical Ventilation				
Length of ICU Stay, days	18 (3–45)	10 (4–33)	0.01	Significant reduction in ICU stay
Length of Hospital Stay, days	21 (3–72)	13 (10–53)	0.03	Significant reduction in hospital stay
Duration of Mechanical Ventilation, days	10 (2–44)	4 (1–27)	0.007	Significant reduction in duration of ventilation

3. Pathophysiology and Purpose

Q: Why might steroids be beneficial in treating pneumonia?

A: Steroids may help control an excessive inflammatory response associated with infection, which can contribute to disease severity and complications in pneumonia.

Q: What are the main side effects of steroids in pneumonia treatment?

A: Major side effects include hyperglycemia, GI bleeding, increased risk of infections, and neuropsychiatric symptoms.

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4. RCTs of Steroids in Pneumonia

Q: What did early RCTs (2005–2015) suggest about the impact of steroids on pneumonia outcomes?

A: Early RCTs showed mixed results:

- Some trials showed reductions in mortality, time to clinical stability, and length of stay, while others did not affect mortality.
- Steroids were generally associated with faster clinical improvement but increased hyperglycemia.

Q: What were limitations of early RCTs on steroids in pneumonia?

A: Limitations included small sample sizes, varied inclusion/exclusion criteria, differences in steroid types and dosing protocols, and potential inclusion of patients with pneumonia mimics.

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5. Meta-Analyses Insights

Q: What did meta-analyses reveal about steroid benefits in pneumonia?

A: Meta-analyses suggested that steroids may reduce mortality in severe CAP (community-acquired pneumonia), reduce mechanical ventilation need, shorten ICU stays, and increase clinical stability time. However, steroids consistently increased hyperglycemia.

Q: Are there different guidelines regarding steroids in pneumonia?

A: Yes, the European guidelines (ESICM/SCCM) recommend steroids for severe CAP, while the American (ATS/IDSA) guidelines recommend against them, reflecting ongoing debate.

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6. CAPE COD Trial (2023)

Q: What was the main question of the CAPE COD trial?

A: The CAPE COD trial asked if IV hydrocortisone reduces mortality in patients hospitalized with severe CAP.

Q: What were the results of the CAPE COD trial?

A: The trial found:

- A reduction in 28-day mortality (6.2% in the steroid group vs. 11.9% in placebo).
- Lower 90-day mortality and reduced need for intubation or vasopressors in the steroid group.
- Higher insulin requirements in the steroid group, with no increase in GI bleeds or hospital-acquired infections.

Q: Why did the CAPE COD trial show a larger benefit with steroids?

A: Possible reasons include:

- The steroid group had fewer cases of shock compared to placebo.
- The strict inclusion criteria targeted severely ill patients who are more likely to benefit.
- Some patients may have had concurrent ARDS, a condition where steroids are known to be beneficial.

7. Practical Takeaways and Remaining Questions

Q: In which patients with pneumonia might steroids be most beneficial?

A: Steroids appear to benefit patients with severe pneumonia, especially those with high levels of inflammation (e.g., elevated CRP).

Q: What questions remain about the best way to use steroids in CAP?

A: Unanswered questions include:

- Optimal route of administration (IV vs. PO).
- Ideal duration and timing of steroid initiation.
- Best type of steroid for pneumonia treatment.

Q: What is the clinical recommendation regarding steroids in CAP?

A: Clinicians should carefully select patients with severe CAP for steroid treatment, considering the mixed evidence and the potential for side effects like hyperglycemia.

References

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