Can dexamethasone be useful in community-acquired pneumonia?

Paola Fracasso · Giorgio Costantino ·

On behalf of Gruppo di Autoformazione Metodologica (GrAM)

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Background

Community-acquired pneumonia is a common and potentially serious illness. While pneumonia mortality decreased sharply after the introduction of antibiotics in the 40s, since 1950, the overall acute in-hospital mortality has remained stable or increased [1, 2]. Adjunctive therapy for community-acquired pneumonia could help to reduce the severity of the disease. In pneumonia, produced pulmonary cytokines are needed to control and eliminate the primary infection. However, organ dysfunction can result from a systemic inflammatory response [3]. Therefore, a balanced cytokine response needs to be sufficient to control the local infection yet not be excessive, to prevent systemic effects. An ideal therapeutic intervention should reduce the systemic complications of the inflammatory response without affecting the resolution of local inflammation [4, 5]. Corticosteroids are very powerful inhibitors of inflammation. They switch off genes that encode proinflammatory cytokines and switch on genes that encode anti-inflammatory cytokines. Treatment with low-dose corticosteroids down-regulates proinflammatory cytokine transcription, which prevents an extended cytokine response, and might accelerate the resolution of systemic and pulmonary inflammation in the early phase of community-acquired pneumonia [3–5]. Despite concern about immunosuppression, glucocorticoid treatment in low-to-moderate doses is beneficial

and safe for a wide variety of infections and in severe sepsis [1, 6]. However, it is still unclear whether the addition of steroids provides clinical benefit in patients with community-acquired pneumonia.

Summary

Meijvis et al. [3] randomized in a double-blind, placebo-controlled trial 304 adult patients with confirmed community-acquired pneumonia, who presented to the emergency departments (EDs) of two teaching hospitals in the Netherlands, to receive 5 mg of intravenous dexamethasone once a day (151 patients) or placebo (153 patients) for 4 days from admission in addition to antibiotic treatment. Patients were ineligible if they were immunocompromised, needed immediate transfer to an intensive care unit, or were already receiving corticosteroids or immunosuppressive drugs. They find a reduced length of hospital stay (primary outcome) in patients treated with dexamethasone. Median length of stay was 6.5 days (IQR 5.0–9.0) in the dexamethasone group compared with 7.5 days (5.3–11.5) in the placebo group (95% CI of difference in medians 0–2 days; $p = 0.0480$). Of interest 143 (47%) of the 304 enrolled patients had pneumonia of pneumonia severity index class 4–5 (79 [52%] patients in the dexamethasone group and 64 [42%] controls). In-hospital mortality and severe adverse events were infrequent, and rates did not differ between groups (in-hospital mortality 5% in both groups). More patients in the dexamethasone group had hyperglycaemia (44%) compared with controls (23%) ($p < 0.0001$). The authors conclude that dexamethasone can reduce the length of hospital stay when added to antibiotic treatment in non-immunocompromised patients with community-acquired pneumonia.

P. Fracasso
Azienda Ospedaliera San Paolo, Università degli Studi di Milano, Milan, Italy

G. Costantino (✉)
Medicina Interna II, Azienda Ospedaliera L. Sacco, Università degli Studi di Milano, Via GB Grassi 74, 20157 Milan, Italy
e-mail: giorgic@libero.it

Strengths of the study

- The study addresses a relevant clinical problem.
- It is based on a strong pathophysiologic substrate.

Weakness of the study

- Length of hospital stay cannot be considered a hard endpoint, and it is doubtful if 1 day less of hospital stay can be considered a clinically relevant result. However, the choice of a clinically relevant endpoint, such as mortality, would have necessitated the enrollment of a huge number of patients.

Question marks

- The mean time of the switch to oral antibiotics was similar in the two groups (5.0 days $\pm$ 4.2 in the dexamethasone group and 5.1 days $\pm$ 3.5 in the placebo group). The discrepancy between a similar mean time of switching to oral therapy and a different median length of hospital stay in the dexamethasone and control groups is singular. In fact international guidelines suggest a switch to oral therapy when “patients are hemodynamically stable and improving clinically, are able to ingest medications, have a normally functioning gastrointestinal tract” along with a recommendation to discharge the patients as soon as they are clinically stable, have no other active medical problems, and have a safe environment for continued care, reporting that “inpatient observation while receiving oral antibiotic therapy is not necessary” [7].
- It would be interesting to get more information about the hyperglycemic effects of dexamethasone (how many patients are involved, what glycemic values). Since hyperglycemia has been linked to mortality in the acute setting, this adverse reaction is worrisome [8].

Sponsorship

Not reported.

Clinical bottom line

Dexamethasone may be useful as adjunctive treatment in community-acquired pneumonia. Benefits of corticosteroids should be weighed against their potential side effects, such as hyperglycemia. More studies with clinically relevant endpoints are needed before this treatment can be recommended. In the meanwhile, steroids during infection may be used with less fear.

Conflict of interest None.

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