Adjunctive corticosteroids for acute bacterial meningitis in Africa – do we need more evidence?

Rob Heyderman
Rationale for Steroids - Pathogenesis of Bacterial Meningitis

- Immune activation
- Senescence
- Necrosis
- Apoptosis

↑BBBP
↓Blood Flow
Thrombosis

Neutrophils
Microglia
Astrocytes
Macrophages
Endothelium
Neurons

Bacterial products (PAMPs)
Cytokines
Chemokines
Reactive Oxygen Species
Eicosinoids
Dexamethasone as Adjunctive Therapy in Bacterial Meningitis

Matthijs Brouwer, Peter McIntyre, Kameshwar Prasad, Diederik van de Beek

The Cochrane Library, Issue 9, 2015; DOI: 10.1002/14651858

• 25 trials in acute bacterial meningitis (4121 participants)
  • 16 in children
  • 7 in adults
  • 2 children and adults

• 22 used dexamethasone; 3 used hydrocortisone or prednisone

• 9 were performed in low-income countries; 16 in high-income countries
Dexamethasone as Adjunctive Therapy in Bacterial Meningitis: MORTALITY

The Cochrane Library, Issue 9, 2015; DOI: 10.1002/14651858

<table>
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<tr>
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Total events = 367

Heterogeneity: Chi² = 28.68, df = 21 (P = 0.18); I² = 21%
Test for overall effect: Z = 1.80 (P = 0.07)

RR 0.90, 95% CI 0.80-1.01
Dexamethasone as Adjunctive Therapy in Bacterial Meningitis: sub-group analyses

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- **Reduced mortality** in *S. pneumoniae* meningitis (RR 0.84, 95% CI 0.72 to 0.98) **NOT** *H. influenzae* or *N. meningitidis* meningitis
- **Overall reduced severe hearing loss** in children with *H. influenzae* meningitis (RR 0.34, 95% CI 0.20-0.59) **NOT** non-*Haemophilus* meningitis
- **In high-income countries**
  - Reduced severe hearing loss (RR 0.51, 95% CI 0.35 to 0.73)
  - Any hearing loss (RR 0.58, 95% CI 0.45 to 0.73)
  - Short-term neurological sequelae (RR 0.64, 95% CI 0.48 to 0.85)
- **No beneficial effect in low-income countries**
The High Mortality for Childhood & Adult Meningitis in SSA

Dexi Mali

The New England Journal of Medicine
Volume 370, Number 2, February 2014

PLOS ONE

GLYCOLYSIS AND ACETOLYSIS AS A THERAPY TO AVOID THE OUTCOME OF BACTERIAL Meningitis in MICE CHILDREN

Levering & See-Dee

Levering & See-Dee

What is the evidence? We investigated the benefit of two candidate antibiotics in high-risk meningitis patients by comparing the outcomes of high-risk patients in two clinical trials. Patients were classified as high-risk if they were on steroids or intravenous antibiotics. In the first trial, the treatment group received high-risk antibiotics plus steroids, while the control group received only high-risk antibiotics. In the second trial, patients received high-risk antibiotics plus intravenous antibiotics, while the control group received only high-risk antibiotics.

Interpretation Although no tested regimen improved the final outcomes of these very ill children, the shorter course of b-lactam antibiotic infusions plus peracetic acid seemingly seemed warranted.

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RESEARCH ARTICLE

Goal directed therapy for suspected acute bacterial meningitis in adults and adolescents in sub-Saharan Africa

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The Survival Road for Bacterial Meningitis

- Carriage
- Invasion
- Clinical Disease

Survival
- No Sequelae

Survival
- Sequelae

Death
Is there sufficient **equipoise** in this highly vulnerable population?

- Are we trying to shortcut deficiencies in healthcare seeking, access healthcare and health systems?
- Will corticosteroids work in this setting?
- Could steroids be harmful (adverse event reporting has been selective)?
Adjunctive corticosteroids for acute bacterial meningitis in Africa – do we need more evidence?

VOTE

- Improve community recognition
- Improve access
- Health Systems interventions
- Identify novel targets & interventions

NO