May 2020

Enterobacteriaceae Bacteremia of Urinary Source

If uncomplicated:

- Step down to a high bioavilability PO agent as soon as afebrile and hemodynamically stable for 48 hours (usually day 3 or 4) and treat for **total 7 days**.
  - **TMP/SMX** is preferred to fluroquinolones as it has a lower C diff infection risk.
  - **Amoxicillin-clavulanate** is reasonable as it has been shown to be comparable to fluroquinolones and TMP/SMX.

Cotrimoxazole (TMP/SMX) dosing:

UTI – 1 DS tab (TMP 160mg/SMX 800mg) PO BID

Gram-negative sepsis – 10mg/kg TMP IV/PO per day, divided BID to QID, see below table.

Gram-negative sepsis			
Actual Body Weight	**CrCl > 50ml/min**	**CrCl 30-50 ml/min**	**CrCl 10-30ml/min**
< 45 kg	consult pharmacist		
45-59 kg	1.5 DS PO BID	1 DS PO BID	1 DS PO BID
60-74 kg	2 DS PO BID	1.5 DS PO BID	1 DS PO BID
75-89 kg	2.5 DS PO BID	2 DS PO BID	1.5 DS PO BID
90-100 kg	3 DS PO BID	2 DS PO BID	1.5 DS PO BID
> 100 kg	consult pharmacist		

Cotrimoxazole pseudo-AKI: the trimethorprim component competes with creatinine excretion. Expect to see 15-35% rise in SCr in 3 days. This is reversible with therapy discontinuation. (J Int Med 1999l246:247-52; TDM 1987;9:161-5)

Cotrimoxazole induced hyperkalemia: the trimethorprim component inhibits potassium excretion via sodium channel blockade. This rarely leads to serum K > 5.5. (Case Rep Emerg Med. 2012; 2012: 815907.)

Fluoroquinolones carry many **black box warnings** in addition to QT prolongation and CDI risk: Aortic dissections, tendon rupture, peripheral neuropathy, delirium, etc.

Question? Call 604-417-8921
https://my.vch.ca/dept-project/Antimicrobial-Stewardship-Programme-ASPIRES

Antimicrobial Stewardship Programme:
Innovation, Research, Education, and Safety
Quality and Patient Safety, Vancouver Coastal Health

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Duration: 7 days vs. 14 days

Seven versus 14 days of antibiotic therapy for uncomplicated gram-negative bacteremia: A non-inferiority randomized controlled trial. Clin Infect Dis, 2019;69(7):1091–8

- Mainly E coli and Klebsiella spp of urinary source
- Afebrile and hemodynamically stable for ≥48 hours on day 7
- Antibiotic choice and time to PO stepdown at MRP discretion
- Outcome – not significant:
  - **90-day all-cause mortality** 12% vs 11%
  - **Readmission** 39% vs 43%
  - **Relapse of bacteremia** 2.6% vs 2.7%

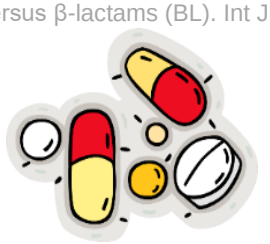
Route: PO stepdown vs. IV only

Association of 30-day mortality with oral step-down vs continued intravenous therapy in patients hospitalized with Enterobacteriaceae bacteremia. JAMA Intern Med 2019; 179:316–23.

- Mainly E coli and Klebsiella spp of urinary source
- Median 3 days of IV therapy prior to PO stepdown
- Outcome - not significant:
  - **30-day mortality** 13.1% vs 13.4%
- Outcome - significant:
  - **Length of stay** 5 days vs 7 days; p<0.001

PO Drug Agent: Fluroquinolones vs. β-lactams

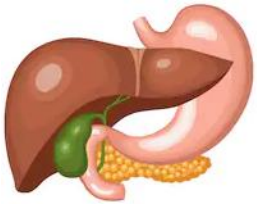
Retrospective analysis comparing oral stepdown therapy for Enterobacteriaceae bloodstream infections: fluoroquinolones (FQ) versus β-lactams (BL). Int J Antimicrob Agents 2018; 51:687–92.



- Mainly E coli and Klebsiella spp of urinary source
- Median IV duration 3 days, Median total duration 14 days (IQR 11-15)
- Outcomes - not significant:
  - **Clinical success** 86.9% vs 87.1% (no new-onset sepsis, temp >38C, WBC >12, hypotension requiring pressors)
  - **Infection-related 30-day re-admission** 4.8% vs 5%

PO Drug Bioavailability: Low vs. High

Low-bioavailability versus high-bioavailability oral antibiotics for the definitive treatment of Enterobacteriaceae bacteremia from suspected urine source in hospitalized veterans. Abstract presented at: 2–6 October 2019; Washington, DC.



- All urinary source with predominantly E coli, Klebsiella, and Proteus spp
- 24% urinary retention/obstruction/structural abnormality, 18% urologic procedure within 90 days, 13% prostate Ca
- Median PO stepdown on treatment day 4, Median treatment duration 14 days
- Outcomes - not significant:
  - **30-day all-cause mortality** 3% vs 2.6%
  - **Recurrent bacteremia within 30 days** 1.5% vs 0.4%, (95% CI 0.46-22.8)

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Innovation, Research, Education, and Safety
Quality and Patient Safety, Vancouver Coastal Health

ASPIRES smart prescribing

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