Antimicrobial Stewardship Programme:
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Tidbits

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ASPIRES tidbits: IV to PO Antimicrobial Stepdown

By day 3 of therapy, 30-60% of patients on IV antibiotics can be stepped down to PO options.[1,2] Changing patients to PO medications reduces complications associated with IV therapy and allows earlier discharge from hospital. This reduces nosocomial infections, facilitates discharge, and allows sicker patients to use acute care beds. All patients who are eligible for PO stepdown should be stepped down.

Here are some considerations:

1. **Some antimicrobials are "bioequivalent," meaning IV offers no advantage over PO therapy**
   a. Azole antifungals (fluconazole, voriconazole)
   b. Clindamycin
   c. Linezolid
   d. Metronidazole
   e. Quinolones (ciprofloxacin, moxifloxacin)
   f. Trimethoprim-sulfamethoxazole

   Highly bioavailable drugs should always be given PO, unless the GI tract is not functioning whereby the IV route should be used (e.g. if the patient is not perfusing the bowel). A reasonable marker of good GI function is when patients are able to absorb enteral feeds.

2. **Some syndromes can be safely treated with PO therapy from the outset**
   Non-life threatening infections or those that are easy to cure (e.g. cellulitis, UTI) do not require IV therapy, even when the patient is admitted to hospital.[3,4] Use clinical judgment to identify patients who are at low risk for severe outcomes. For these patients, it is better to give PO antibiotics to avoid unnecessary complications with IV therapy.

3. **Some syndromes are best treated initially with IV therapy, but can then be stepped down to PO once the patient improves clinically**
   Patients admitted with a life-threatening infection that improves quickly, and where oral drugs can adequately cover suspected and identified pathogens are candidates for IV to PO conversion. This strategy has been studied in many clinical syndromes, including community-acquired pneumonia, intra-abdominal infections and urosepsis.[5] Criteria for IV to PO stepdown are as follows:
   a. Patient still requires antibiotic therapy
   b. Patient is clinically stable
   c. Patient tolerates PO medications and has no concerns regarding ability to absorb medication orally
   d. Patient's condition is improving (e.g. afebrile, WBC normalizing, organ failure resolving)

4. **Some antimicrobials are only available by IV route, but can be stepped down to other PO regimens that provide similar coverage**
   The PO stepdown regimen must provide coverage to adequately target both identified pathogens and those expected to be part of the clinical syndrome.

Examples of IV to PO stepdown to a regimen with similar coverage

IV Antibiotic	Possible PO Regimen	Considerations
Cefazolin	Cephalexin	
Ceftriaxone	Cefixime, cefuroxime, cefazolin	Choice depends on clinical syndrome being treated and susceptibilities
	Ciprofloxacin	
	Trimethoprim-sulfamethoxazole	
Ceftriaxone + metronidazole	Amoxicillin-clavulanic acid	Choice depends on clinical syndrome being treated and susceptibilities
	Ciprofloxacin + metronidazole	
	Clindamycin + ciprofloxacin	
Meropenem or impenem-cilastatin	Amoxicillin-clavulanic acid	Choice depends on clinical syndrome being treated and susceptibilities
	Amoxicillin-clavulanic acid + ciprofloxacin (if *Pseudomonas* coverage required)	
	Ciprofloxacin + metronidazole	
	Clindamycin + ciprofloxacin	
Pipercillin-tazobactam	Amoxicillin-clavulanic acid	Does not cover *Pseudomonas*
	Ciprofloxacin + metronidazole	Does not cover *Enterococcus*
	Clindamycin + ciprofloxacin	
Vancomycin	Trimethoprim-sulfamethoxazole, doxycycline, or clindamycin	For CA-MRSA, if organism tests susceptible

5. **Some antimicrobials are poorly absorbed by the PO route and should not be used for stepdown therapy**
   Drugs, such as cloxacillin and penicillin, have low bioavailability (oral absorption) and should only be used orally for mild infections.

6. **Some infections require IV therapy and should be treated with IV therapy for a minimum duration**
   Some infectious (such as febrile neutropenia, infective endocarditis, *S. aureus* bacteremia, etc.) may require IV therapy for the duration of treatment.

[1] Engel, Postma, Hulscher et al. Barriers to an early switch to oral antibiotic therapy in hospitalized patients with CAP. *European Respiratory Journal,* 2013;41:123-30.

[2] Van Niekerk, Venter, Boschmans. Implementation of Intravenous to Oral Antibiotic Switch Therapy Guidelines in the General Medical Wards of a Tertiary-level Hospital in South Africa. *J Antimicrob Chemother*, 2011;67:756-62.

[3] Aboltins, Hutchinson, Sinnappu et al. Oral versus parenteral antimicrobials for the treatment of cellulitis: a randomized non-inferiority trial. *J Antimicrob Chemother*, 2015;70(2):581-6.

[4] Pohl. Modes of administration of antibiotics for symptomatic severe urinary tract infections (review). *Cochrane database of Systematic reviews,* 2007;4(CD003237).

[5] Cairns. Implementation of Sequential Therapy Programmes – a Pharmacist's View. *Journal of Infection*, 1998;37(Sup 1):55-9.