UCSF Medical Center

Antimicrobial Management for Critically Ill Patients

POLICY 133.23
Patient Care
Antimicrobial Management for Critically Ill Patients

P&T Approved Nov, 2004
EMB Approved Jan 25, 2005

Office of Origin: Infectious Diseases Management Program

I. PURPOSE

The purpose of this policy is to outline recommendations for the optimal use of antimicrobial therapy and to reduce/prevent resistance through misuse of antimicrobial agents.

II. REFERENCES

Not applicable.

III. DEFINITIONS

Not applicable.

IV. POLICY

A. The following are clinical practices to ensure proper management of antimicrobials in the critically ill patients (see Appendix A for more details):

1. **Combination therapy for gram-negative infection will be reserved for neutropenia or serious pseudomonal infection** (pneumonia, meningitis, endocarditis). Monotherapy shall be used in the treatment of presumed or documented gram-negative infection. In the absence of neutropenia or documented pseudomonal infection, 2-drug coverage will be narrowed to monotherapy in 3-5 days. If continuation of 2-drug coverage is desired and the patient is not neutropenic and/or with documented pseudomonal infection, approval by infectious diseases is required.
2. **Vancomycin will only be used for maximum of 3-5 days in the absence of beta-lactam allergy or certain gram-positive infections [methicillin-resistant staphylococci *(S. aureus, coagulase-negative staphylococcus*), and ampicillin-resistant enterococcus.)]** If continuation of vancomycin is desired in the absence of a beta-lactam allergy or gram-positive infections as above, approval by infectious diseases is required.
3. **Empiric use of cefepime, meropenem, or imipenem may be continued for a maximum of 3-5 days in the absence of resistant gram-negative infection.** Those patients without documented infection due to these organisms will have therapy discontinued or switched to more narrow spectrum coverage. For 3rd generation cephalosporin- or piperacillin-tazobactam-resistant isolates, these agents appropriately can be continued. If continuation of cefepime, meropenem or imipenem is desired and no organism has been isolated, approval by infectious diseases is required.
4. **Empiric use of clindamycin or metronidazole added to a beta-lactamase inhibitor or carbapenem will be avoided.** The exceptions may include: Metronidazole can be added to beta-lactamase inhibitor

combinations or carbapenem for the treatment of C. difficile and clindamycin can be added to beta-lactamase inhibitor combinations in the empirical treatment of necrotizing fasciitis.

5. **All adult critical care antimicrobials orders will be in accordance to UCSF Medical Center "Antimicrobial Dosing Guidelines."** The infectious diseases team in consultation with critical care team will review all these orders for appropriateness and make recommendations to the primary teams.

6. **All antibacterials and antifungals continued beyond 7 days will be reviewed for appropriateness.** This is to reduce or eliminate the chance for superinfection due to resistant gram-positive and gram-negative bacteria and fungus. The infectious diseases team in consultation with critical care team will review all these orders for appropriateness and make recommendations to the primary teams. In those instances in which the use of the given agent(s) is deemed inappropriate, infectious diseases discussion with the primary team will take place to clarify appropriateness of use. Direct discussion between the primary team and the infectious diseases fellow or infectious diseases attending will be required and infectious disease approval will be required for continuation of antimicrobial therapy.

B. While the policy is centered upon the patients in the critical care units, it may apply to non-acute floor patients as well.

V. PROCEDURES

A. Combination-Drug Therapy for Gram-negative Infection

1. **Background:** Early studies suggested reduced mortality with combination antibacterial therapy in the treatment of serious pseudomonal infection, specifically bacteremia. However, these earlier studies were primarily based upon combinations of older, less potent drugs, e.g. aminoglycosides and carbenicillin (or ticarcillin). The more recent investigations have not confirmed this reduction in mortality associated with combination. The most recent data suggest combination therapy may be appropriate for 72 hours specifically for Pseudomonas aeruginosa and then tailored to monotherapy; neutropenic patients similarly may benefit from combination antibacterials. With the exception of these two indications, 2-drug coverage is not superior to monotherapy.

2. **Procedure:** With the exception of neutropenia or serious pseudomonal infection (pneumonia, meningitis, endocarditis), monotherapy shall be used in the treatment of presumed or documented gram-negative infection. In the absence of neutropenia or documented pseudomonal infection, 2-drug coverage will be narrowed to monotherapy in 3-5 days. If

continuation of 2-drug coverage is desired and the patient is not neutropenic and/or with documented pseudomonal infection, approval by infectious diseases is required.

B. Vancomycin

1. **Current Policy/Background:** As per current policy, vancomycin will be allowed a maximum of 3-5 days with the following exceptions:

   a. Significant beta-lactam allergy

   b. Documented infection due to methicillin-resistant staphylococci (S. aureus, coagulase-negative staphylococcus), ampicillin-resistant enterococcus

   If continuation of vancomycin is desired in the absence of a beta-lactam allergy or gram-positive infections as above, approval by infectious diseases is required.

C. Cefepime/Imipenem/Meropenem

1. **Background:** Historically, cefepime, imipenem, and meropenem represent the last line of antibacterials versus multidrug-resistant gram-negative organisms.

2. **Procedure:** In the absence of resistant gram-negative infection, cefepime, meropenem or imipenem empirically can be continued a maximum of 3-5 days. Those patients with no documented infection due to these organisms will have therapy discontinued or switched to more narrow spectrum coverage. For 3rd generation cephalosporin- or piperacillin-tazobactam-resistant isolates, these agents appropriately can be continued. If continuation of cefipime, meropenem or imipenem is desired and no organism has been isolated, approval by infectious diseases will be required.

D. Double anaerobic coverage:

1. **Background:** The addition of clindamycin or metronidazole to beta-lactam-inhibitor (BLI) combinations does not expand the anaerobic antibacterial coverage of BLIs. The one exception is the use of metronidazole in the treatment of C. difficile colitis in a patient receiving a BLI for a concurrent infection. 99-100% of all isolates of B. fragilis are inhibited by BLI; in contrast, cefotetan inhibits only 80-90% of isolates, thus, the addition of metronidazole may be reasonable in certain intra-abdominal or pelvic infections. While the addition of metronidazole to cefotetan may be considered for established infection, the combination has no role in surgical antibiotic prophylaxis; cefotetan monotherapy is adequate in this indication. It is well described that antianaerobic agents

predispose to VRE colonization and infection. Consequently, they should not be used without a clear indication.

2. **Procedure:** Metronidazole (or clindamycin) is not recommended in combination with BLI in the treatment of anaerobic infection and will be discontinued when this combination is ordered. Metronidazole can be added to beta-lactamase inhibitor combinations for the treatment of C. difficile and clindamycin can be added to beta-lactamase inhibitor combinations in the empirical treatment of necrotizing fasciitis.

E. Antimicrobial Dosing

1. **Background:** For the last decade, recommendations for the dosing of antimicrobials have been developed based upon the Antibiotic Advisory Subcommittee of the Pharmacy & Therapeutics Committee. Critical care patients are particularly complicated in light of concomitant liver and/or renal insufficiency, multiple modes of dialysis and altered body composition.

2. **Procedure:** In consultation with infectious diseases and/or critical care, all antimicrobial doses will be reviewed. In those instances in which dosage change is necessary, the dose will be appropriately changed.

F. Review of Appropriateness of Any Antimicrobial (Antibacterial and Antifungal) continued for > 7 days

1. **Background:** Continuation of long-term antibacterials or antifungals is associated with superinfection due to resistant gram positive and gram-negative bacteria and fungus.

2. **Procedure:** In consultation with infectious diseases and/or critical care, all antimicrobials continued > 7 days will be reviewed. In those instances in which the use of the given agent(s) is deemed inappropriate, infectious diseases discussion with the primary team will take place to clarify appropriateness of use. Direct discussion between the primary team and the infectious diseases fellow or infectious diseases attending will be required and infectious disease approval will be required for continuation of antimicrobial therapy.

VI. RESPONSIBILITY

Questions about the implementation of this policy should be directed to the Chair,