Top Ten List in Antibiotic Policy in the ICU*

Emili Diaz, MD; and Jordi Rello, MD, PhD

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Abbreviations: VAP = ventilator-associated pneumonia; VRE = vancomycin-resistant enterococci

Strategies for Improving Antimicrobial Prescription


Over the last decade, the study of mortality in patients with ventilator-associated pneumonia (VAP) has raised a controversial question: whether the patient died of VAP or merely with VAP. Obviously, complications are a major risk in a patient with an infectious disease who does not receive treatment. Equally, if treatment is administered but the antibiotic choice is unsuitable, no beneficial influence on outcome is expected. Decreasing the rate of incorrect prescription is, however, not easy. One option that has demonstrated its reliability as an empirical treatment for ICU infections in recent years is rotation therapy. In this article, the authors report a decrease in the rate of inadequate treatment in previously scheduled empirical antibiotic use. Their multivariate analysis showed that level of severity (as determined by APACHE [acute physiology and chronic health evaluation] II score, the number of organ failures, and the use of vasopressors) and inadequate antimicrobial therapy were significant risk factors for mortality. The adjusted odds ratio of inadequate microbial therapy was 4.22.

This approach also produced a significant increase in nosocomial infections. The rate of VAP increased from 11.3% in period 1 to 14.0% in period 3 (p < 0.05), and the nosocomial bloodstream infection rate rose from 3.9% in period 1 to 6.8% in period 3 (p < 0.05). Further studies are needed to define which empirical antibiotic choice is optimal and to assess in more detail the role of rotation antibiotic therapy as a potential tool for improving outcome.


Antibiotic cycling proposes to reduce the antibiotic pressure that favors the emergence of resistance. The authors suggest that rotation antibiotic therapy not only reduces infections by multiresistant pathogens, but is also associated with lower mortality rates. The reduction in mortality seems to be related to a fall in infections by multiresistant pathogens, as the number of device-associated infections remained the same. With similar VAP episodes, the associated mortality rate for the rotation period was 18.6% compared with 33.8% (p = 0.04) for the control period. The authors provide a good description for the rotation period, but the picture of antibiotic policy during the control period is incomplete. Is rotation associated with more adequate treatment?

Strategies for Preventing Antimicrobial Resistance


Antimicrobial resistance is a problem that requires a multidisciplinary approach, including
measures to control antibiotic use and to control infection. Antibiotic control involves optimizing the choice and duration of empirical treatment and changing to the narrowest option when possible. It also aims to decrease the overuse of antibiotics for surgical prophylaxis. Infection control measures aim to heighten compliance with basic infection control techniques.

Following these principles, Murthy describes a way to prevent and reduce antimicrobial resistance in hospitals. First, the pathogen responsible at each institution must be identified. As Murthy explains, each problem pathogen has its own characteristics. Second, levels of compliance with basic strategies for infection control and antibiotic policy should be determined. Finally, the author recommends the implementation of infection control measures, focusing on compliance with antibiotic policy and educational programs. These measures require the support of the hospital administration and continuous feedback among clinicians, administrators, and all healthcare workers.


In this review, Karam and Heffner address a common problem in the ICU: the emergence of infections by multidrug-resistant pathogens. The first part of the article is a general appraisal of antibiotic resistance acquisition and prevention strategies. In the second part, the authors discuss the treatment of Gram-negative bacilli infections, which is now determined by the generation of β-lactamases, as follows: type 1 (with resistance to several β-lactams) or non-type 1 (with resistance not only to β-lactams). The authors then consider enterococcal infections, in particular vancomycin-resistant strains of pathogens. These infections provide an example of an infection that spreads rapidly under favorable conditions (eg, very high use of vancomycin in ICUs). In fact, the recommended approach is the reduction of vancomycin use. Finally, Karam and Heffner discuss Candida infections, which are now an emerging threat, especially because of the shift toward infections with species other than Candida albicans. The problem with Candida isolation in nonsterile products is establishing their pathogenic role.

This is a well-written article, of some five pages in length, which has some important considerations for clinicians, especially with regard to colonization and infection.

ANTIBIOTIC CYCLING AND SCHEDULED ANTIBIOTIC CHANGES


This article describes the authors’ experience with a change in antibiotic policy. As well as initiating a scheduled rotation therapy, they restricted the use of cefazidime and ciprofloxacin. Treatment with an antihypertensive drug is directed solely at the patient involved, but treatment with an anti-infectious agent may have consequences for all at-risk patients. As a result, it is difficult to establish exactly the impact of rotation therapy or of the restriction of two antibiotics on resistant pathogens. In the previous period, the association of cefazidime and ciprofloxacin was common as an empirical treatment, without de-escalation. Indeed, treatment duration was not established by antibiotic policy. Now, we have learned that the outcome of infection is not influenced by the length of treatment but is associated with the presence of antibiotic-resistant pathogens.

During the study period, the empirical antibiotic regimen was established on a monthly basis. The duration of the treatment for patients with microbiologically diagnosed VAP was 15 days, with 5 days of treatment with aminoglycosides, and de-escalation was started as soon as microbiologic studies were available.


This study shows that a relatively straightforward approach can be very effective in decreasing infections by multidrug-resistant pathogens. However, the impact of rotational therapy is not the only explanation for the lower rate of difficult-to-treat infections.

One of the most important findings of the scheduled rotation of antibiotics is the decrease in multidrug-resistant pathogens. In this article, the authors evaluated the impact of antibiotic rotational strategy on the acquisition of vancomycin-resistant enterococci (VRE). They concluded that antibiotic rotation with cefazidime and ciprofloxacin had no effect on enteric VRE acquisition among patients. The adjusted odds ratio was 1.03 (95% confidence interval, 0.51 to 2.08). In contrast, after logistic regression,
factors influencing VRE acquisition were related to enteral feeding, colonization pressure, and anaerobic therapy duration.

**Strategies for Antimicrobial Decolonization**


This interesting approach to assessing the impact of selective digestive decontamination on pneumonia and mortality among ICU patients is based on quality criteria. Van Nieuwenhoven et al observed an inverse association between the methodological quality score and the benefit of selective digestive decontamination on the incidence of pneumonia. This effect was not observed between selective digestive decontamination and mortality.

**Strategies for Restricting Antibiotic Use**


The best way to restrict antibiotic use is treat infectious diseases only. The problem begins when the diagnosis is unclear. In an attempt to solve this problem, the authors proposed initiating antibiotic treatment and then reassessing it 3 days later, after recording a pulmonary infection score. Patients with high scores were excluded and were treated as if they had pneumonia. Patients with a low likelihood of pulmonary infection (ie, low score) were randomized to receive either standard antibiotic therapy or a 3-day course of ciprofloxacin. Mortality and length of ICU stay did not differ between both comparative groups, but antimicrobial costs and antimicrobial resistance were lower in the interventional group. The most interesting aspect of this approach is its applicability in clinical practice. Antibiotic treatment should be started as soon as pneumonia is suspected and should be withdrawn if the diagnosis is not confirmed. This study discusses some relevant issues, such as the choice of the best antibiotic and whether or not a 3-day wait is required to decide whether an infiltrate that has disappeared was some type of pneumonia.

**Protocols and Guidelines**


The recent history of VAP can be divided into a number of different stages. First, attempts were made to identify the risk factors for VAP development. Then, the question of whether invasive or noninvasive tests should be used for etiologic diagnosis was discussed. Today, it is generally accepted that inadequate treatment increases mortality, and efforts are directed at ensuring that the initial antibiotic therapy is adequate.

This study has the following two strengths: the initiation of an antibiotic regimen within 12 h of a VAP diagnosis; and the local antibiotic policy based on continuous and updated microbiological data. With these guidelines, the rate of inadequate initial treatment was only 5.8%, whereas other authors have reported rates of around 30%. Significantly, there was no alteration in the mortality rate using this approach. The authors suggested that even a 1-week course of therapy is sufficient for VAP caused by pathogens that are not multi-resistant. In contrast, VAP caused by *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus* may require a longer period of treatment.


The Tarragona strategy is a 10-point, evidence-based practice guideline for the treatment of VAP. It has the following four basic principles: broad spectrum coverage with de-escalation if indicated; high and individualized doses based on location and pharmacodynamic features; immediate start of antimicrobial treatment; and choice of antimicrobial agent with regard to lung penetration. A key feature is the administration of appropriate antibiotic therapy as soon as possible. Underlying disease, local patterns of sensitivity, and pharmacodynamic characteristics all should be considered. The possibility of the presence of *P aeruginosa* in COPD patients or of the presence of methicillin-sensitive *S aureus* in patients who are in a coma remains highly probable. Other key features of the strategy are de-escalation, based on high-quality microbiological findings, and the decision not to treat colonization episodes. This policy favors a patient-based approach that is customized to local epidemiologic data instead of one that is based on following general guidelines.