Nosocomial infections in the intensive care unit

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Abstract

Nosocomial infection in the intensive care unit (ICU) is associated with increased mortality, morbidity and length of stay. It is defined as infection that begins 48 hours after admission to hospital. The most common types are ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), urinary catheter-related infection and surgical site infection. The common pathogens include *Staphylococcus aureus, Pseudomonas aeruginosa, Candida* spp., *Escherichia coli* and *Klebsiella* spp. Antimicrobial resistance is generally increasing, and has emerged from selective pressure from antibiotic use and transmission via health workers. Prevention of infection can be achieved through good antimicrobial use and infection control, including hand hygiene. Grouped, easy to follow best practice activities called 'care bundles' have been developed to prevent VAP and CLABSI. Microbiological cultures are central to a rapid and accurate diagnosis, which improves outcomes and reduces resistance. The principles of treatment include early antimicrobial therapy (after appropriate specimens are taken) targeted to the local microbes, then de-escalation according to culture and susceptibility results. This article summarizes the pathogenesis, risk factors, microbiology, diagnosis, prevention and treatment of VAP, CLASI and nosocomial UTI in the adult ICU.

Keywords Catheter related infections; cross infection; intensive care; nosocomial infections; urinary tract infections; ventilator-associated pneumonia

Royal College of Anaesthetists CPD Matrix: 2C00, 2C03

Learning objectives

After reading this article, you should be able to:

- list the common pathogens that cause infections in the ICU
- discuss strategies used to prevent antimicrobial resistance in the ICU
- name the steps in the WHO '5 moments of hand hygiene' campaign
- discuss the risk factors for VAP, CLASBI and UTI in the ICU
- list the components of the care bundles for VAP and CLASBI

Introduction

Nosocomial infection (defined as onset more than 48 hours after hospital admission) in the intensive care unit (ICU) is associated with increased mortality, morbidity and length of stay. Prevalence rates of infection acquired in ICUs vary from 9% to 37% when assessed in Europe and the USA. Timely diagnosis, appropriate management and prevention improve patient outcomes and reduce antimicrobial resistance. The most common types are ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), urinary catheter-related infection and surgical site infection. Other types of nosocomial infection are also important, such as those in immunocompromised hosts and neonates, but beyond the scope of this article.

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Microbiology and resistance

Colonization of critically ill patients with nosocomial organisms usually occurs after 48–72 hours of admission; the most important pathogens are displayed in Table 1. The spectrum of nosocomial microorganisms is different from those in the community, with higher rates of resistant organisms. Antimicrobial resistance emerges in ICU because of:

- *evolution* of resistance in existing bacteria, through selective pressure from antibiotic use
- *nosocomial transmission* especially through contact with healthcare workers or via procedures.

Increasing incidence of resistant bacteria in ICUs is associated with poorer outcomes. These include: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE) and multi-drug resistant (MDR) Gram negatives. There is a longer time to receipt of effective therapy; and the agents used for treatment often have inferior efficacy, poor pharmacokinetics/pharmacodynamics or increased toxicity (e.g. vancomycin, linezolid, daptomycin, amikacin, colistin). More recently, studies describe success in controlling some types of resistant organisms (most notably reductions in MRSA, particularly attributed to better hand hygiene practices), but little impact on MDR Gram negative and fungal resistance. Inappropriate broad-spectrum antibiotic therapy increases the incidence of MDR organisms, and is also an independent risk factor for mortality.[1]

The emergence of resistant organisms tends to add to the total burden of infections, rather than substituting for the more sensitive organisms previously present. For example, as MRSA becomes endemic in a unit, the total number of staphylococcal infections increases; when MRSA is eliminated, the total number of staphylococcal infections reduces.

Diagnosis of nosocomial infection

Rapid and accurate diagnosis of nosocomial infection both improves patient outcomes and decreases selection pressure for resistance. It 'streamlines' patients into the most effective treatment, allowing rapid cessation of unnecessary antibiotics and minimizing unnecessary side effects. Correct timing is vital with

Common ICU nosocomial pathogens (EPIC II study)

Staphylococcus aureus	20%	Includes MRSA[a] (10%)
Pseudomonas aeruginosa	20%	
Candida	17%	
Escherichia coli	16%	
Klebsiella species	13%	
Enterococcus	11%	Includes VRE[b] (4%)
Staphylococcus epidermidis	10%	
Acinetobacter	9%	
Enterobacter	7%	

Important Gram negative resistance mechanisms include:

Extended-spectrum beta-lactamases (ESBLs): plasmid encoded genes that confer resistance to penicillins and extended-spectrum cephalosporins. Carbapenems are the treatment of choice.

AmpC-type beta-lactamases: Chromosomal or plasmid genes that are similar to ESBLs.

Metallo-beta-lactamases (MBLs): Confer resistance to carbapenems, inherent chromosomal (e.g *Stenotrophomonas maltophilia*) versus plasmid acquired (e.g. New Delhi metallo-beta-lactamases (NDM)). May be susceptible to colistin, tigecycline or fosfomycin. Combination therapy including a carbapenems (even if resistant) improves outcomes.

[a] Methicillin-resistant *Staphylococcus aureus*.
[b] Vancomycin-resistant *Enterococcus faecium*.

Table 1

all microbiologic tests: samples taken after new antibiotics are started rapidly lose sensitivity.

The single most useful microbiologic test in ICU is correctly performed blood cultures. A simple protocol is shown in Box 1.

General prevention measures

Nosocomial infections are reduced by good antibiotic use and strict infection control. Ongoing liaison between ICU, infectious diseases (or clinical microbiology) and pharmacy personnel is essential. This multidisciplinary approach is needed to develop local guidelines (preferably guided by local microbiology data), provide day-to-day advice, monitor usage and oversee control measures for broad-spectrum antimicrobials, and provide feedback to the ICU staff in a useful manner. Antimicrobial stewardship services can reduce broad-spectrum antibiotic usage, adverse antimicrobial events and MDR bacteria resistance rates, whilst improving antibiotic treatment in life-threatening bacterial infections, improve antibiotic dosing and shorten antibiotic durations without effecting patient outcome.[2] Elements of good antibiotic use in ICU are given in Box 2. The role of combination antibiotics in preventing resistance is controversial. It is usually necessary to use combination empiric therapy for sepsis to ensure adequate coverage of potential pathogens, but de-escalating to narrower cover once cultures results are known or the patient improves. Even pseudomonal infections do not require combination therapy once sensitivities are known, though some multidrug resistant organisms may have few alternatives to combination therapy. 'Cycling' antibiotic use is poorly studied, and not recommended.

Infection control minimizes cross transmission and prevents colonizing bacteria from causing infection. One of the key elements is *hand hygiene*, which prevents cross transmission of pathogens between patients by the hands of healthcare workers. It is estimated that over 30% of healthcare associated infections are preventable by hand hygiene. Multiple studies have shown a reduction in healthcare-associated infection rates, specifically reductions in MRSA and even elimination in some centres. The WHO has recommended '5 moments for hand hygiene' in healthcare settings, both resource rich and poor.[3] Alcohol-based hand-rubs should be used before touching a patient, before a procedure, after body fluid exposure, after touching a patient and after touching patient surroundings. Other aspects of infection control include surveillance for, and isolation of, patients with multi-resistant organisms. Alternative infection control measures such as chlorhexidine bathing and washcloths have in some cohorts demonstrated reductions in MDR bacteria colonization/infection and overall bacteraemia rates.[4,5]

Recent years have seen the widespread promotion of infection control 'care bundles'. These are groupings of 'best practices' that when applied together appear to result in greater improvement in outcomes, based on the philosophy that the 'total may be greater than the sum of the parts'. They are simple, logical (mostly, but evidence base can be variable) and easily evaluable (compliance

Effective diagnosis of nosocomial infection: taking blood cultures

- Take three sets *before* starting or changing antibiotics
- Fresh venepuncture, sterile technique (or from a new line inserted in an aseptic manner)
- Swab skin (70% alcohol with chlorhexidine), allow 30 seconds before venepuncture
- 10 ml per blood culture bottle
- No further BCs need be taken for 2–3 days unless clinical situation changes, or to demonstrate clearance of proven bacteraemia

Box 1

Good antibiotic use in ICU to reduce selection pressure for resistance

- Knowledge of local microbiological epidemiology to guide empiric therapy
- Prompt appropriate therapy for sepsis, including antifungals in higher risk patients
- Early source control, including changing of lines in a septic patient
- De-escalating broad-spectrum antibiotics early according to cultures and patient condition
- Using shorter duration of antibiotics overall, e.g. 5–7 days is adequate for most cases of VAP
- Appropriate dosing will both maximize cure rates and minimize selection of resistance. Unfortunately both under and over-dosing are common in the ICU setting

Box 2