

NOSOCOMIAL INFECTIONS - AN OVERVIEW

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ABSTRACT

With increasing use of antimicrobial agents and advance in lifesaving medical practices which expose the patients for invasive procedures, are associated with the ever increasing of nosocomial infection. Despite an effort in hospital infection control measures, health care associated infections are associated with significant morbidity and mortality adding additional health care expenditure which may leads to an economic crisis. The problem is further complicated with the emergence of difficult to treat multidrug resistant (MDR) microorganism in the hospital environment. Virtually every pathogen has the potential to cause infection in hospitalized patients but only limited number of both gram positive and gram negative bacteria are responsible for the majority of nosocomial infection. Among them *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and Enterococci takes the leading. Many intrinsic and extrinsic factors predispose hospitalized patients for these pathogens. Hospital-acquired infection can be prevented to a large extent by implementing three sets of precautions: (1) standard safety precautions, (2) transmission-based precautions and (3) special precautions. Many antimicrobial agents are available today and antibiotic therapy should theoretically be chosen when the infecting organism and its susceptibility has been established in a given infection.

Keywords: Nosocomial infection, pathogens, antibiotics.

INTRODUCTION

Hospital acquired infections are infections that are neither present nor incubating when a patient enters hospital. About nine per cent of inpatients have a hospital acquired infection at any one time, equivalent to at least 100,000 infections a year. Their effects vary from discomfort for the patient to prolonged or permanent disability and a small proportion of patient deaths each year are primarily attributable to hospital acquired infections. With recent changes in health care delivery, the concept of "nosocomial infections" has sometimes been expanded to include other "health care-associated infections," including infections acquired in institutions other than acute-care facilities (e.g. nursing homes); infections acquired during hospitalization but not identified until after discharge; and infections acquired through outpatient care such as day surgery, dialysis, or home parenteral therapy.¹

The most frequent types of infection are urinary-tract infection, surgical-wound infection, pneumonia, and bloodstream infection (Table 1). These infections follow interventions necessary for patient care, but which impair normal defenses. At least 80 percent of nosocomial urinary infections are attributable to the use of an indwelling urethral catheter. Surgical-wound infection follows interference with the skin barrier, and is associated with the intensity of bacterial contamination of the wound at surgery. Nosocomial pneumonia occurs most frequently in intensive-care-unit patients with endotracheal intubation on mechanical ventilation—the endotracheal tube bypasses normal defenses of the upper airway. Finally, primary nosocomial bloodstream infection occurs virtually only with the use of indwelling central vascular catheters, and correlates directly with the duration of catheterization.²

Infections Site	Incidence	
	All patients	Device-related
Urinary tract infection	2.34/100 admissions	5.3-10.5/1,000 catheter days
Surgical site infection	4.6-8.2/1,000 discharges	2.1-7.1% of wounds
Pneumonia	0.5-1.0/100 admissions	9-47% ventilated patients 1-3%/ventilator day
Central vascular line	-	1.4% of central catheters 1.7/1,000 catheter day

Impact of nosocomial infections

Hospital-acquired infections add to functional disability and emotional stress of the patient and may, in some cases, lead to disabling conditions that reduce the quality of life. Nosocomial infections are also one of the leading causes of death. The economic costs are considerable. The increased length of stay for infected patients is the greatest contributor to cost. Prolonged stay not only increases direct costs to patients or payers but also indirect costs due to lost work. The increased use of drugs, the need for isolation, and the use of additional laboratory and other diagnostic studies also contribute to costs. Hospital-acquired infections add to the imbalance between resource allocation for primary and secondary health care by diverting scarce funds to the management of potentially preventable conditions.

The advancing age of patients admitted to healthcare settings, the greater prevalence of chronic diseases among admitted patients, and the increased use of diagnostic and therapeutic procedures which affect the host defences will provide continuing pressure on nosocomial infections in the future. Organisms causing nosocomial infections can be transmitted to the community through discharged patients, staff, and visitors. If organisms are multiresistant, they may cause significant disease in the community³.

EPIDEMIOLOGY

The study of nosocomial infections includes understanding the causes of these infections, the characteristics of the patients who become infected, and how often these infections occur. By identifying the characteristics of patients who are at highest risk for infection, we can more effectively direct and prioritize our prevention and control efforts. It also permits us to follow closely the trends of infections that are increasing in incidence, e.g., bloodstream infections.

The epidemiology of nosocomial infections has been affected by the introduction of the prospective payment system, which changed the economics of health care delivery in the United

States. The patients admitted to hospitals now differ from those admitted only a few years ago. More surgical operations are being performed in outpatient settings, and when patients are admitted to the hospital, they are more seriously ill or require sophisticated, and sometimes high-risk, procedures that can be performed only on inpatients. Paradoxically, they are usually discharged from the hospital earlier, and their care is usually continued at home or in skilled-nursing facilities. With increasing average severity of illness among hospitalized patients, the infection rate is also expected to increase. The task of monitoring the infection rate is complicated by the difficulty of detecting infections in patients following discharge from the hospital. Postdischarge surveillance for certain infection sites may be necessary for a quality surveillance system and is being urged by some experts.⁴

SOURCES OF NOSOCOMIAL INFECTION

- *Endogenous*: It is caused by microorganisms from patient's own flora
- *Exogenous*: It is caused by microorganisms acquired by exposure to another patient, hospital personnel, visitor, medical devices and/or hospital environment.

Factors predisposing to nosocomial infection:

They are as follows:

- Susceptible host (advanced age, immunosuppression, malnutrition and incapacitation)
- Inanimate hospital environment comprising of soiled linen, biomedical waste, used equipments and instruments congenial for microbial growth.
- Invasive diagnostic and therapeutic procedures and long surgical procedures.
- An interplay between these factors culminates in NI.⁵

CHANGES IN MICROBIAL FLORA

The distribution of pathogens responsible for NI has changed over the years. The introduction of penicillin, which heralded the antibiotic era

banished cases of severe sepsis mainly caused by *S. aureus*. Then as Staphylococci became beta-lactamase producers, beta-lactamase stable compounds controlled them. Then methicillin-resistant *S. aureus* (MRSA) and Gram-negative bacilli emerged as agents responsible for NI. More recent surveys have indicated the reemergence of Gram-positive cocci including coagulase-positive Staphylococci, coagulase-negative Staphylococci (C-NS) and Streptococci, whereas incidence of *E. coli* and *K. pneumoniae* has decreased from 23% to 16% and from 7% to 5% respectively. In addition, all surveys report the increasing or simultaneous persistence of *P. aeruginosa*, *Acinetobacter spp.* and emergence of newer nosocomial Gram-negative organisms such as *B. cepacia* and *S. maltophilia*.⁵

Factors that predispose to nosocomial infections

- Related to underlying health status
- Advanced age
- Malnutrition
- Alcoholism
- Heavy smoking
- Chronic lung disease
- Diabetes
- Related to acute disease process
- Surgery
- Trauma
- Burns
- Related to invasive procedures
- Endotracheal or nasal intubation
- Extracorporeal renal support
- Surgical drains
- Nasogastric tube
- Tracheostomy
- Urinary catheter
- Related to treatment
- Blood transfusion
- Recent antimicrobial therapy
- Immunosuppressive treatments
- Stress-ulcer prophylaxis

- Recumbent position
- Parenteral nutrition and length of stay.

TYPES OF NOSOCOMIAL INFECTION

Though any organ system may be involved, but four infections are most common as external device is put or a breach in the integrity of skin is involved. These are:

1. Catheter-associated urinary tract infection (CAUTI).
2. Ventilator-associated pneumonia (VAP).
3. Central line-associated blood stream infection (CLABSI).
4. Surgical site infection (SSI) and skin and soft-tissue infections (SSTI).

DISTRIBUTION OF PATHOGENS IN SPECIFIC SITES

In CAUTI, *E. coli*, *Klebsiella spp.*, *Proteus spp.* and *Streptococcus faecalis* predominate while in VAP, *P. aeruginosa* and *S. aureus* are the leading pathogens. In SSI, SSTI and burns, *Staphylococci* and *Enterococci* are the leading pathogens respectively.³

INFECTION CONTROL

They organize education for staff, develop local infection control policies and provide advice and guidance as part of a programme of work including surveillance and audit. Effective infection control programs rely on an extensive knowledge of the local epidemiology of pathogens and the provision of a monitoring system that recognizes the emergence of antibiotic-resistant bacteria.^{5,11}

PREVENTION STRATEGIES

Hospital-acquired infection can be prevented to a large extent by implementing three sets of precautions: (1) standard safety precautions, (2) transmission-based precautions and (3) special precautions.

General measures		Nosocomial pneumonia	Bloodstream infection	Surgical wound infections
Personnel	Educational programmes: hand-washing, gloves, gowns, etc.: control of infections at risk for healthcare workers: Immunisation	Maintenance, disinfection of respiratory equipment (endotracheal tubes, suctioning devices, ventilators, etc): careful use of invasive exploratory	Careful manipulation of catheters: aseptic technique for insertion; search for source of bacteraemia (infection focol)	Preparation of operative team (surgical gloves, gowns, masks, etc.)
Patient	Patient isolation: single room for high risk patients: antibiotic prophylaxis: controversial, specific conditions (neutropenic, burn patients): SDD: controversial, topical treatments for colonised sites	Oropharyngeal decontamination: treatment of nosocomial sinusitis: local antibiotics (aerosols): gastric alkalinisation: semi-recumbent position: care of enteral nutrition	Duration of catheterisation, changed at appropriate intervals : adjusting for severity of underlying disease: blood cultures with best techniques (automated) for rapid identification of pathogens: SDD limits translocation and endotoxin release	Wound classification (clean, clean-contaminated, dirty): minimise preoperation stay: suitable skin preparation, hair removal: antibiotic prophylaxis
Treatment	Optimal use of antibiotics, control of antibiotic use (antimicrobial use audits)			
Environmental infection measures	Hospital noscomial surveillance: close cooperation with microbiology: computerised systems in surveillance and fast transmission of data: proper elimination of medical waste	Surveillance of air conditioning humidities, hot water nebulisers (Legionella): isolation precautions: isolation guidelines	Hospital and intensive care unit surveillance (epidemiology): disposable catheters, close cooperation with microbiology	Limiting source of exogenous contamination: excellent surgical technique, limiting "dead space" exposing wound: proper wound dressing
Administration	Infection Control Committee: (regulatory restriction policies (hospital organisations, formularly) : guidelines for guidelines, prevention: consensus consensus conferences: application conferences) of guidelines			Sterilization and suitable disinfection measures for reusable equipment: disposable instruments whenever possible: disposal regulations
Miscellaneous	Hospital design engineers for suitable structure of wards, rooms, specific isolation units and health care facilities. Close cooperation between authorities, microbiologists, infections diseases			

STRATEGIES FOR MANAGEMENT OF NOSOCOMIAL INFECTION

Many antimicrobial agents are available today and antibiotic therapy should theoretically be chosen when the infecting organism and its susceptibility has been established in a given infection. More frequently and particularly in the ICU, antibiotic therapy is empirical because of emergency situations, severity of infections in immunodepressed, neutropenic and elderly patients, so optimal therapy in those difficult to treat situations should take into account the local microbiological backgrounds and their current resistance pattern. The most appropriate empiric

treatment is best achieved on the basis of resistance surveillance.

The choice of empiric antibiotic therapy for the treatment of any NI before microbiology requires:

- Surveillance data on a regular basis of predominant organisms in the hospital/ICU
- Surveillance of the current resistance patterns of these organisms
- identification^{8,12}

Principles of Empiric Therapy

The conventional empiric therapy has to be broad enough to ensure

coverage of most of the suspected pathogens. Combination therapy with an antipseudomonal penicillin (piperacillin) plus an aminoglycoside or an antipseudomonal cephalosporin (Ceftazidime) plus an aminoglycoside have been for long the initial regimen recommended officially. However, in situations suggestive of gram positive organisms such as MRSA (in institutions where this organism is endemic) the addition of a glycopeptide forms part of empiric therapy. Rifampicin, fusidic acid Streptogramins (Quinupristin-Daltopristin) also cover most gram positive organisms. During outbreaks of NI with high probability of cross contamination of a previously identified endemic multiresistant organism such as *Pseudomonas aeruginosa*, carbapenems (e.g., imipenem or meropenem) in combination with either an aminoglycoside (amikacin) or a fluoroquinolone (Ciprofloxacin) should be recommended. Any empirical therapy should be reassessed 2 or 3 days after its initiation. Treatment should be readjusted on the basis of report of antibiotic sensitivity tests available on day 2 or 3, and clinical response of the patient. Potential choice of more suitable combination therapy or switch to less expensive/toxic antibiotics when the clinical status of patient suggests to do so is recommended.^{8,10}

Antibiotic use

Appropriate use of antibiotics is important. Up to 30% of ventilator associated pneumonias are treated inadequately. There is increasing evidence to suggest that the use of appropriate and early antibiotics improves morbidity and mortality. Appropriate antibiotic use requires a thorough knowledge of their mode of action, previous antibiotic history, local bacterial resistance profile and local pathogen prevalence. Antibiotics should be administered at the right dose and for the appropriate duration. The local antibiotic

formulary and consultant microbiologist are valuable resources. Daily ICU ward rounds with the microbiologist can lead to rational use of antibiotics tailored to benefit individual patients. Antibiotic-resistant bacteria prolong hospitalization, increase the risk of death, and require treatment with toxic and expensive antibiotics. Empirical use of antibiotic is often necessary as laboratory results are often not available for 48 h after the samples are sent to the laboratory for culture. Appropriate specimens include blood, urine, sputum, bronchoalveolar lavage, pus and wound swabs. Blood cultures are only positive for pathogens in a third of cases. Once the antibiotic profile is available, a narrow-spectrum antibiotic can be commenced. Indicators of response to treatment include temperature, leucocyte count and C-reactive protein (CRP) levels. Procalcitonin is secreted by macrophages in response to septic shock and is an early and a more specific marker of bacterial infection than CRP. These parameters must be interpreted in the clinical context. Improvements in the ventilatory and inotrope requirements can provide additional and indirect evidence for response to treatment. Any antibiotic policy or guideline should aim to limit the use of antibiotics and reduce the selective pressure for resistant microorganisms. Policies designed to encourage rational antibiotic use

in ICU are an important element in quality of care, infection control and cost containment. De-escalation therapy, selective digestive decontamination (SDD), antibiotic rotation (cycling) therapy and restrictive guidelines can address these concerns. Optimizing any antimicrobial therapy includes both shortening the duration of antimicrobial use and appropriate use of combination therapy to reduce the emergence of resistance. Research into these antibiotic management programs is limited and results are controversial.

Therapeutic strategies for management of nosocomial infections ⁹			
Microorganism	Monotherapy	Combination therapy	Alternative therapy
Gram-positive organisms			
Methicillin-resistant <i>Staphylococcus aureus</i>	Vancomycin, imipenem-cilastatin, meropenem fusidic acid	Rifampicin + vancomycin, fusidic acid + glycopeptide, fosfomycin + aminoglycoside, vancomycin + fluoroquinolone	Imipenem + vancomycin, fusidic acid + fosfomycin, fusidic acid + glycopeptide, fusidic acid + rifampicin
Methicillin-susceptible <i>S. aureus</i>	Penicillins, cloxacillin, cefazolin cephalothin: Second-generation cephalosporin: cefotaxime, aminoglycosides	Penicillin + aminoglycoside (oxacillin + gentamicin), tetracycline + aminoglycoside, amoxicillin + clavulanic acid, ampicillin + sulbactam	Fluoroquinolone + fusidic acid, fosfomycin + L-lactam, + fusidic acid + cloxacillin

Coagulase-negative Staphylococci	Same indications as for MRSA, with higher resistance rates to quinolones, aminoglycosides, clindamycin, co-trimoxazole		Imipenem + fosfomycin, aminoglycoside
<i>Enterococcus spp.</i>	Ampicillin, imipenem, piperacillin, glycopeptide (in nosocomial UTI only)	Ampicillin + gentamicin, vancomycin + aminoglycoside	Teicoplanin + penicillin, imipenem + glycopeptides, piperacillin + teicoplanin
Gram-negative organisms			
<i>Escherichia coli</i>	Ceftazidime/aztreonam/cefpirome/cefepime, amoxicillin-clavulanic acid, fluoroquinolone (in UTI)	Cefotaxime + amikacin, piperacillin + tazobactam, cefoxitin/aztreonam + aminoglycoside	Imipenem alone imipenem + aminoglycoside imipenem + fluoroquinolone
ESBL +	Imipenem/cefepime, fluoroquinolone (in UTI)	Imipenem + aminoglycoside: piperacillin + tazobactam + amikacin	Imipenem + ciprofloxacin
<i>Klebsiella spp.</i> ESBL -	Ceftazidime/cefoperazone/cefepime/cefpirome, amoxicillin-clavulanic acid	Piperacillin + tazobactam, ticarcillin + clavulanic acid, cefotaxime + aminoglycoside	Imipenem alone imipenem + aminoglycoside, imipenem + fluoroquinolone
<i>Acinetobacter spp.</i>	Colistin/polymyxin B/subactam (high dose)	Meropenem/cefoperazone-sulbactam/ticarcillin-clavulanic acid/tigecycline, cefepime + tazobactam	Imipenem + cefoperazone sulbactam / piperacillin + tazobactam/ticarcillin-clavulanic acid
<i>Pseudomonas aeruginosa</i>	Penicillins (ticarcillin, piperacillin azlocillin) Cephalosporins (ceftazidime, cefpirome/cefepime) imipenem, meropenem	Ticarcillin aztreonam or ceftazidime + sulbactam + tobramycin or amikacin, ceftazidime + fluoroquinolone	Antipseudomonal penicillin + fluoroquinolone, aztreonam + amikacin, aminoglycoside + ciprofloxacin, fosfomycin + ciprofloxacin
<i>Enterobacter spp.</i>	Imipenem or meropenem cefpirome/cefepime, piperacillin + tazobactam	Third-generation cephalosporin + aminoglycoside, aztreonam + amikacin	Imipenem + fluoroquinolone, aminoglycoside + ciprofloxacin
Fungal sprains			
<i>Candida spp.</i> <i>Aspergillus spp.</i>	Amphotericin/caspofungin Caspofungin/amphotericin		

De-escalation

De-escalation involves early initiation of broad-spectrum antibiotic therapy in patients with suspected sepsis without the availability of microbiology results. The increase in antibiotic resistant pathogens such as MRSA has led some investigators to suggest broader antibiotic coverage by adding a glycopeptides to carbapenem as the initial empirical therapy. This aggressive empirical regimen is continued for 24–48 h by which time laboratory tests have confirmed the causative organisms and sensitivities. This allows for de-escalation of antibiotic therapy. This regimen should be reserved for selected patients on ICU who are seriously ill, with an extended antibiotic history and evidence of colonization by multi-resistant organisms. Unnecessary continuation of this regime will increase the risk of colonization with resistant bacteria.⁶

Rotational antibiotic therapy

Rotational antibiotic therapy is a strategy to reduce antibiotic resistance by withdrawing an antibiotic, or class of antibiotics, from ICU for a short period, to allow resistance rates to decrease

or remain stable. The persistent use of one class of antibiotics leads to the emergence of resistant strains of bacteria; this is known as selective pressure. Rotational regimens are thought to reduce this selective pressure. There is growing support for this regimen. Kollef and colleagues demonstrated a statistical decrease in nosocomial pneumonia in a large ICU after the introduction of an antibiotic rotation policy. Restrictive antibiotic policies are less flexible and, to a certain extent binding, with respect to prescribing. They require the prescriber to give written justification for any deviation from the policy. Automatic stop orders restrict prolonged antibiotic administration. In the general hospital setting, these measures have had some success with significant reductions in antibiotic resistance. However, the overall survival in ICU was unchanged. The concept that commensals within the bowel may provide a protective role against more virulent organisms is called colonization resistance. Translocation of Gram-negative bacteria across the intestinal wall is thought to be a major cause of nosocomial infections. SDD aims to eliminate Gram-negative aerobic bacteria by decontamination of the oral cavity and intestinal tract. There are several

variations of the SDD regimen. One such regimen is non-absorbable polymyxin E, tobramycin, and amphotericin B for gastrointestinal decontamination and cefotaxime for systemic prophylaxis. Cephalosporins are usually given as prophylaxis as they act on commensal respiratory flora such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *S. aureus*. Meta-analysis has demonstrated that SDD regimens decrease the incidence of nosocomial pneumonia but overall survival or duration of intensive care treatment is unchanged. The cost effectiveness of SDD has not been evaluated.⁶

CONCLUSION

Medical advances have brought lifesaving care to patients in need, yet many of these come with the risk of NI which can be devastating and fatal. As our ability to prevent NIs grows, these infections are extremely unacceptable. Recent successes in NI elimination have been very encouraging but much more remains to be done. Improvement in hospital epidemiology surveillance, strict adherence to infection control practices, formulation of empiric antibiotic policy and implementation of guidelines for prevention of NI should result in decreasing the incidence of patient morbidity and mortality and preventing an epidemic of NI.

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