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Pseudomonas aeruginosa as a Cause of Nosocomial Infections

Silvia Labovská

Abstract

Pseudomonas aeruginosa, as a gram-negative aerobic rod, is still one of the most resistant agents of nosocomial infections. It is used for the development of respiratory, urinary and wound infections. It causes bacteremia, especially in patients who are hospitalized for anesthesiology and resuscitation department or ICU, who often have respiratory insufficiency and hemodynamic instability and require artificial lung ventilation. Mechanical ventilation itself is a significant risk factor for the development of pseudomonad pneumonia. *Pseudomonas aeruginosa* has enzymes that are encoded on both chromosomes and plasmids, often in combination with other mechanisms of resistance, such as reducing the permeability of the outer or cytoplasmic membrane. Due to carbapenemases, *Pseudomonas aeruginosa* loses sensitivity to carbapenem and becomes resistant to this antibiotic. It also becomes resistant to aminoglycosides, cephalosporins and ureidopenicillins. It is also resistant to Quaternary disinfectants. The reservoir of pseudomonas nosocomial infection is hospital water, taps, shower roses, swimming pools, healing waters and others. The intervention of anti-epidemic measures in the case of infections caused by pseudomonad strains has not yet reached such sophistication as in the case of MRSA for time, personnel and economic reasons. In the absence of an epidemic, intervention in sporadic cases consists of informing nursing staff of the occurrence of a multidrug-resistant agent, including providing all patient demographics and relieving careful adherence to the barrier treatment, cleansing, disinfection and isolation regimen.

Keywords: nosocomial infections, respiratory insufficiency, pneumonia, lung ventilation, resistance

1. Introduction

Nosocomial infections (NI) are a global problem in hospital care. This is a significant complication that worsens the prognosis of the underlying disease, increases mortality, prolongs hospitalization, worsens the quality of life of patients and increases the cost of treatment, so NI pays special attention. In the United States, the Center for Disease Control and Prevention (CDC) is the leading authority in this area. CDC procedures and guidelines are the most widely used standard worldwide. In the USA, a nationwide NI surveillance system has been organized since the 1970s. The United Kingdom also has a long tradition in the control of NI, which is organized in the system of laboratory service of the British public health service (Public Health Laboratory Service). The main guarantor, which organizes congresses dedicated to NI, is the Hospital Infection Society (HIS), which publishes a globally

important and recognized journal - the Journal of Hospital Infection [1]. The aim of the journal is to publish high-quality research and information related to the prevention and control of NI [2]. NIs need to be diagnosed and treated in time, but the most important thing is their prevention in various hospital wards, especially in intensive care units. Infections acquired in connection with hospitalization can lead to significant morbidity and mortality, but preventive anti-infective measures can significantly affect these results. Equally important is prevention in hospital staff in order to reduce the risk of infections spreading to other patients and staff. In this way, it is possible to prevent the absence of staff from work, which can have a positive effect on the skills of the staff of the intensive care unit. Nosocomial infections are also associated with financial expenses, which include hospital expenses, reduced productivity of sick staff as well as their income due to absence from work.

Pseudomonas aeruginosa, as a gram-negative aerobic rod, is still one of the most resistant agents of nosocomial infections. *P. aeruginosa* causes 10-11% of all NI. This result is due to the resistance of this microorganism to disinfectants and many antimicrobials. It is involved in the development of respiratory, urinary and wound infections. It causes bacteremia, especially in patients who are hospitalized at anesthesiology and resuscitation department or ICU, who often have respiratory insufficiency and hemodynamic instability and require artificial lung ventilation. Mechanical ventilation itself is a significant risk factor for the development of pseudomonad pneumonia. *P. aeruginosa* has enzymes that are encoded on both chromosomes and plasmids, often in combination with other mechanisms of resistance, such as reducing the permeability of the outer or cytoplasmic membrane. Due to carbapenemases, *P. aeruginosa* loses sensitivity to carbapenem and becomes resistant to this antibiotic. It also becomes resistant to aminoglycosides, cephalosporins and ureidopenicillins. It is also resistant to Quaternary disinfectants. The reservoir of pseudomonad nosocomial infection is hospital water, taps, shower roses, swimming pools, healing waters and others. It occurs in sinks, humidifiers, anesthesia machines, inhalers, hand brushes and other places that meet suitable conditions, which means ambient humidity. Pseudomonads contaminate lubricating gels and disinfectants [3].

The intervention of anti-epidemic measures in the case of infections caused by pseudomonad strains has not yet reached such sophistication as in the case of MRSA for time, personnel and economic reasons. In the absence of an epidemic, intervention in sporadic cases consists of informing nursing staff of the occurrence of a multidrug-resistant agent, including providing all patient demographics and relieving careful adherence to the barrier treatment, cleansing, disinfection and isolation regimen [3].

If we add eye, ear, nose, and throat infections to pneumonia, then respiratory tract infections are the most common site of nosocomial infections for almost all age groups in pediatric JIS [4]. Much attention has been paid to ventilator-associated pneumonia (VAP) as the most common and potentially preventable nosocomial infection. Other nosocomial respiratory infections include sinusitis, otitis media and tracheitis. Contamination of the patient's respiratory tract may come from a device with which the patient has been in direct contact, namely an endotracheal tube, nasogastric tube, aspiration catheters, bronchoscopes, but also from a device with which he has not been in direct contact, such as a mechanical ventilator, ventilator hose, nebulizers and devices that supply oxygen. The human vector that most likely transmits infection to a patient is hospital staff. The most common risk factors are poor hand hygiene, insufficient isolation of patients and contaminated objects such as stethoscopes. Family members and other patients may also transmit the infection to patients hospitalized in a pediatric ICU. All of these factors must be considered and controlled to minimize the occurrence of nosocomial respiratory tract infections [2].

2. Ventilator-associated pneumonia

Nosocomial pneumonia is the second most common nosocomial infection in pediatric ICUs after catheter infections of the bloodstream. Nosocomial infection can occur in any patient, but is most common in infants, young children, and patients over 65 years of age. Patients in pediatric ICUs who are most at risk for pneumonia are patients who have been intubated and mechanically ventilated. The risk increases due to the circumvention and alteration of the host's defenses, as the vocal cords remain open and the risk of aspiration of gastrointestinal contents increases. The risk of nosocomial pneumonia is 6-20 times higher in ventilated patients compared to non-ventilated patients. Ventilator-associated pneumonia (VAP) is defined as the development of new pneumonia for at least 48 hours after the start of mechanical ventilation. Independent risk factors for the development of VAP in children are immunodeficiency, immunosuppression and neuromuscular blockade. Other risk factors are genetic syndromes with neuromuscular weakness, burns, steroid administration and total parenteral nutrition [2]. Children have a higher risk of VAP with antibiotics, with a longer stay in the ICU, with catheters in place with a risk of haematogenous spread, treatment with H₂-receptor blockers, reintubation and transport outside the ICU during intubation. The presence of a nasogastric tube increases the risk as it provides a direct pathway from the upper gastrointestinal tract to the oropharynx. In-line nebulizers and manipulation of the ventilator circuit can affect the risk of nosocomial pneumonia. VAP in children accounts for 10-26% of nosocomial infections. The incidence of pediatric nosocomial pneumonia within the hospital is highest at the neonatal JIS, followed by the pediatric JIS, and the pediatric ward. Nosocomial pneumonia has the highest mortality of all pediatric nosocomial infections and ranges from 20–70%. Although the duration of endotracheal intubation increases the risk of nosocomial pneumonia, the highest risk is during the first 2 weeks of intubation. Almost all intubated children have a colonized endotracheal tube with nosocomial microorganisms within 5 days [2]. The most frequently identified bacteria in pediatric JIS are gram-negative bacilli, especially *P. aeruginosa*. Mortality is higher with gram-negative microorganisms. *P. aeruginosa* is one of the leading causes of ventilator-associated pneumonia (VAP) in the US and Europe [5–7]. VAP due to *P. aeruginosa* is increasing in incidence and poses unique challenges for its clinical management.

2.1 Symptoms and diagnosis of VAP

The diagnosis of VAP in children can be made on a clinical basis without the use of bronchoscopy. A set of clinical diagnostic criteria and alternative criteria that vary with age are given in the table (**Table 1**). The presence of pneumatoceles on chest X-rays in children under 12 months of age meets the radiographic criteria for pneumonia, which are listed in the table. The diagnosis of VAP can be made based on clinical and radiographic criteria. Identification of the causative microorganism is essential for targeted antibiotic therapy. Identification of the microorganism is difficult because endotracheal tube culture is inaccurate due to colonization of the endotracheal tube and upper airways by gram-negative bacilli and staphylococci, which occurs within a few days after intubation. In adult and older children, bronchoalveolar lavage and protected swab specimens have been used successfully. In young children, it is not possible to obtain a protective sample for the size of the required bronchoscope, and the bronchoalveolar lavage performed has a high incidence of contamination. Methods for determining the causative microorganism are positive blood culture that cannot be explained by other sources, positive pleural fluid cultures, and a positive bronchoalveolar lavage sample despite its limitations, >5% of bronchoalveolar lavage cells containing intracellular bacteria and positive

	All patients	1-12 year of age	<12 months of age
Chest film	At least 2 serial CXR with new or progressive and persistent infiltrate or consolidate or cavitation that developes later than 48 hrs post initiation of mechanical ventilation		
Additional Criteria	At least one of shaded criteria AND At least two of the non-shaded criteria	At least 3 of the criteria below	Worsening gas exchange AND at least 3 of the criteria below
Temperature	>38°C without other recognized cause	>38,4°C or <37°C without other recognized cause	Temperature instability without other recognized cause
WBC count	<4000/mm3 OR >12,000/mm3	<4000/mm3 OR >15,000/mm3	<4000/mm3 OR >15,000/mm3 and band forms >10%
Altered mental status	If >70 years of age without other recognized cause	Not applicable	Not applicable
Sputum/ Secretions	New onset purulent sputum OR change in character of sputum OR increased respiratory symptoms		
Respiratory Symptoms	New onset or worsening of cough, dyspnea, or tachypnea		Apnea, tachypnea, increased work of breathing, or grunting
Auscultation findings	Rales or bronchial breath sounds		Wheezing, rales, or ronchi
Cough	Not applicable as separate criteria		+
Worsening oxygenation or ventilation	Present	Present	Required criteria
Heart rate	Not applicable		<100 beats/min OR > 170 beats/min

Table 1.
Clinical criteria for diagnosing VAP by age [2].

pulmonary parenchyma culture. When nosocomial pneumonia is suspected, empirical treatment should be initiated to cover the most likely microorganisms, taking into account hospital resistance. Once the agent is identified, the antibiotic coverage needs to be adjusted [2].

2.2 Prevention of VAP

In 2004, The Institute for Healthcare Improvement developed a set of evidence-based recommendations for practitioners to reduce mortality. The evidence was based on research in adults.

The package of recommendations for VAP in adults includes the following interventions [8]:

- a. raising the patient’s head above the bed between 30 and 45°,
- b.a break in sedation and daily reassessment of extubation,
- c. prophylaxis of stress ulcers,
- d.prophylaxis of deep vein thrombosis.

The application of these measures can reduce the incidence of VAP to 45%, although the last 2 points do not directly lead to nosocomial pneumonia, but are designed to treat complications in monitored, sedentary adult patients with ICU. In children, many centers use only low-risk interventions such as raising the head above the bed, considering extubation, and using stress ulcer prophylaxis. Intervention such as omission of sedation is unpredictable and risky in young children due to the high risk of unwanted extubation [9].

Measures often used in pediatric centers focus on specific risk factors [2]:

- measures to prevent iatrogenic spread of infection compliance with good hand hygiene use of general preventive measures use of appropriate isolation techniques according to infectious microorganisms
- measures to prevent aspiration of gastric contents elevated head above bed between 30 and 45 degrees monitor/drainage of gastric contents
- measures to improve oral hygiene mouthwashes/cleaning with chlorhexidine 0.12% use of toothbrush and oral swab in daily oral hygiene
- measures to reduce risk factors of the endotracheal tube use of in-line suction device, where is suitable and available preferential suction of the hypopharynx over endotracheal suction and relocation of the ET tube
- measures to prevent contamination of respiratory equipment single-purpose oropharyngeal suction device prevention of condensate accumulation in the respiratory circuit prevention of contamination of respiratory device
- measures to reduce the length of mechanical ventilation daily consideration of extubation attempts interruption of neuromuscular blockade.

Hygiene of hands with alcoholic solutions or soap and water, together with adherence to general precautions and appropriate isolation, are the most effective methods. The raised position of the head prevents aspiration of the stomach contents. The risk of aspiration can be further minimized by decompression of the stomach with a gastric tube and continuous monitoring of the residue. Mouth hygiene is important. The American Dental Association recommends starting continuous oral hygiene in infants before the appearance of dentition. The recommendation for the use of oral swabs and brushing teeth in critically ill patients is based on the fact that the dental plaque consists predominantly of gram-negative bacteria and forms within 48 hours of admission to the ICU [2].

In children, secretion of secretions from the hypopharynx is recommended to prevent VAP. It is recommended that this aspiration be performed prior to aspiration from the endotracheal tube, to prevent aspiration of secretions from the hypopharynx, and prior to manipulation of the endotracheal tube. In some centers, they also aspirate secretions before positioning the patient on the bed. The use of a closed in-line extraction system may not have a direct effect on reducing the incidence of VAP, but may be effective in preventing contamination of the extraction device. Condensed steam in the respiratory circuit can potentially contaminate and theoretically cause infection, so condensate must be removed from the circuit. Staff should be conscientious and avoid contaminating the respirator and its accessories [9].

In the prevention of nosocomial pneumonia, it is important to minimize the length of the patient's mechanical ventilation. The presence of an endotracheal tube poses a risk of VAP and not the positive pressure ventilation associated with it.

Daily consideration is recommended as to whether the patient can be extubated. Discontinuation of sedation is impractical for most children in pediatric ICUs, as it can potentially lead to unwanted extubation, especially in children who are small enough to cooperate or understand the need for intensive care interventions. Studies in adults and children show that the use of non-invasive ventilation in ICU contributes to reducing the incidence of VAP [2].

3. Treatment

One of the most important challenges for physicians is the adequate treatment of infections due to Gram-negative pathogens because of the increasing antimicrobial resistance in the healthcare setting [10].

Among infections caused by Gram-negative rods, *P. aeruginosa* has a leading role [11], especially in critically ill and immunocompromised patients. Antimicrobial resistance has led to a serious restriction in treatment options for *P. aeruginosa* infections.

An anti-pseudomonal cephalosporin, or a carbapenem, or an anti-pseudomonal β -lactam/BLI represents potential options for definitive therapy. Aminoglycosides should not be used as monotherapy because success rates for aminoglycosides are low [8]. This may be due to the poor penetration of aminoglycosides into the lung, which require high peak serum concentrations to obtain adequate lung concentrations, thus increasing the risk of nephrotoxicity or ototoxicity [12, 13]. However, because in Europe fluoroquinolone resistance rate in *P. aeruginosa* exceeds 30% [14], it is appropriate to use combination therapy including aminoglycosides for empirical therapy of serious VAP. A based approach is recommended of the prescription of an anti-pseudomonal β -lactam (piperacillin/tazobactam, ceftolozane/tazobactam, ceftazidime, cefepime, or a carbapenem) plus a second anti-pseudomonal agent (aminoglycoside or a fluoroquinolones). As for aerosol therapy, there is not routinely recommended the use of inhaled antibiotics for the treatment of *P. aeruginosa* VAP. However, they may be considered as an adjunctive to intravenous therapy in cases of infections due to MDR (Multi-drug resistance) strains [15].

4. Factors of nosocomial infections

Factors that affect the complex process of origin and spread of nosocomial infections are divided into internal and external:

- internal factors are closely related to the biological balance of the patient: age (over 60 years, up to 3 years), alcoholism, drug addiction, hormonal disorders (diabetes), malignant tumors, immunodeficiency, obesity, malnutrition, circulatory disorders, polytraumas, burns, pressure ulcers, ulcer cruris, other serious diseases (liver disease, AV shunt, cardiomyopathy),
- external factors are related to therapeutic, prophylactic and diagnostic interventions and are used exclusively in treatment of patients in hospital facilities: length of hospital stay, surgery, transplantation, tracheostomy, endotracheal cannula, gastric tube, urinary catheterization, iv catheterization, infusion, transfusion, foreign bodies, drainage, instrumental procedure, repeated anesthesia, endoscopy, hemodialysis, radiation therapy, cytostatic therapy, immunosuppressive therapy, broad spectrum ATB therapy, hormonal therapy [3].

Hospital placement: plays an important role, with the highest incidence being typical of ICU. The incidence of nosocomial infection also depends on the type of ICU, while the different incidence will be on surgical, traumatological, burn, neurological, neurosurgical or cardiological ICU. Pediatric ICU is unique in that it provides care in all of these areas for all children except newborns [2].

The patient's age may affect the risk of nosocomial infection. In the pediatric population, young children are most at risk, especially newborns. The highest incidence of nosocomial infections among pediatric patients is in children less than 1 year of age. The relative immaturity of the newborn's immune system, associated with routine ICU procedures that bypass the physical barriers of infection such as skin and mucous membranes, is responsible for the increased risk. Parenteral nutrition with high concentrations of glucose and lipids is another risk factor for infection. The fact that premature infants are most affected by these risk factors explains why neonatal ICUs have a higher incidence of nosocomial infections than pediatric ICUs [2, 4, 16]. Pediatric ICU is also unique in that each childhood has a different incidence depending on the type of nosocomial infection. In children under 5 years of age, the 3 most common nosocomial infections are in the following order: bloodstream infections, so-called bloodstream infections, pneumonia and urinary tract infections. In children aged 5 to 12 years, the 3 most common are nosocomial infections: pneumonia, bloodstream infections and urinary tract infections. In adolescents, the order of the most common nosocomial infections is: bloodstream infections, urinary tract infections, and then pneumonia [2, 4, 16]. Immunosuppressed patients after chemotherapy, human immunodeficiency virus infection, or steroid use are equally at risk for developing nosocomial infection.

Nosocomial infections do not have an apparent sex predilection.

Particular risk factors for the development of nosocomial infection are length of hospital stay and initial antibiotic therapy [17].

Staff shortages are a particular risk factor for the increased incidence of nosocomial infections, due to increased staff workload and poor hand hygiene [18].

Erythrocyte transfusion is a risk factor for the development of nosocomial infections in critically ill patients on ICU. In a prospective study, the incidence of nosocomial infection was 14.3% in patients with blood transfusions and 5.8% in patients without blood transfusions. In the group of patients with blood transfusions, there was a higher incidence of nosocomial infections, which was significant in seriously ill patients with a probability of survival of less than 25%. Patients with more than a 25% chance of survival had higher mortality, longer stays on the ICU, and longer hospitalizations compared with patients who did not receive a blood transfusion [19].

5. Prevention

It is not possible to eliminate all nosocomial infections, but one third of cases could be prevented if organized infection control programs were put in place.

Preventive measures can be divided into 2 categories, namely standard measures and transmission-based measures. Standard measures can always be used and are designed to prevent personnel from coming into contact with potentially infectious body fluids. The most important standard measure is hand hygiene. Washing hands with soap and water is considered the gold standard. The use of anhydrous antiseptic agents is accepted, but not in cases where visible dirt is present, proteinaceous body fluids such as blood, or spores contamination is suspected. In these cases, it is necessary to use soap and water. Hand hygiene must be observed before and after

the patient's examination, but also when gloves are worn. In case of contact with body fluids or secretions, it is advisable to use barriers such as gloves, masks, eye protectors and coats [2, 3].

Transmission-based measures aim to protect against the transmission of infectious micro-organisms from patients with a proven or suspected infection, as well as from patients colonized by specific micro-organisms. These additional measures are more than standard measures and are based on the path of transmission: contact, droplets, or airborne transmission.

Contact transfer measures apply to a wide range of micro-organisms that spread by direct contact with the patient or by indirect contact through contaminated objects such as toys, a stethoscope and unwashed hands. Preventive measures include, in addition to standard measures, isolation rooms for the patient or group, coats and gloves.

Droplet transfer measures are directed against microorganisms that spread a short distance from the patient by coughing and sneezing. These measures include isolation rooms for one patient or for a group of patients with the same microorganism. Healthcare professionals should wear masks with eye protection in addition to standard measures.

Measures to prevent airborne transmission include additional precautions against microorganisms which spread through the air stream. Patients should be isolated in rooms with ionized air. For other airborne microorganisms, a respirator is required when entering the patient's room. Isolation of a patient may be based on clinical symptoms or circumstances present on admission to the hospital and should always be initiated before isolating the microorganism [2, 3].

6. Conclusions and further directions

Nosocomial infections are a major cause of morbidity and mortality in the intensive care unit, which can usually be prevented. Although not all nosocomial infections can be eliminated due to the specific nature of JIS patients, the incidence can be significantly reduced by control measures. Simple measures such as strict hand hygiene, isolation, sterility, elevated head position, judicious use, and prompt removal of central catheters, urinary catheters, and endotracheal tubes can dramatically affect the frequency of nosocomial infections. Although not all nosocomial infections can be prevented, intensive care targets should be zero. Consistent application and monitoring of the effectiveness of infection control measures must go a long way towards achieving the goal. The medical community must take steps to reduce and prevent nosocomial infections. Future efforts should be made to distinguish community-acquired infection from nosocomial infection, to reduce the development of resistant organisms through prudent use of antibiotics, to design JIS to isolate patients and ensure hand hygiene, and to develop barrier design [2, 3].

6.1 Further directions

- Adherence to infection control procedures, including hand hygiene, is one of the most useful and well-established methods for preventing nosocomial infections.
- Isolation measures are crucial in preventing the transmission of infections among hospitalized patients.
- Following cultures at the time of patient admission may reduce the spread of nosocomial resistant organisms.

- Prevention of catheter blood infections begins at the time of insertion with sterility. Catheter care and the use of catheters that are impregnated with antiseptics or antibiotics may further reduce the risk of infection.
- Routine removal of central venous catheters does not reduce the risk of catheter blood infections.
- VAP prevention is facilitated by the use of a protocol that includes raising the head above bed level and considering extubation daily.

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