Occasional review

Prevention of nosocomial bacterial pneumonia

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The term “nosocomial pneumonia” broadly covers all infections occurring 48 hours or more after hospital admission excluding any infection incubating at the time of admission, and has also been called hospital acquired pneumonia. Intensive care unit (ICU) acquired pneumonia (occurring within 48 hours of admission to the ICU) and ventilator associated pneumonia (occurring within 48 hours of starting mechanical ventilation) are also included in the broader term “nosocomial pneumonia”. The development of nosocomial pneumonia remains a major problem in the ICU with most studies reporting an incidence of between 9% and 45%, depending on the groups of patients being studied, the definition of nosocomial pneumonia, and the criteria used to diagnose it. It has been shown that nosocomial pneumonia acquired in the ICU markedly increases the length of hospital stay and the costs of hospital care. Mortality rates may also be increased, although it is not entirely clear whether all deaths from nosocomial pneumonia are directly related to the development of an infection. The so-called “attributable mortality”, defined as the mortality occurring as the direct result of the nosocomial pneumonia, may be especially high when Pseudomonas or Acinetobacter species are involved as pathogens.

The diagnosis of nosocomial pneumonia is not straightforward, particularly in patients who are critically ill, as routine parameters do not have a high specificity for pneumonia in these patients. For example, infiltrates on chest radiographs consistent with pneumonia may be due to many other processes including oedema, atelectasis, and infarction. Positive cultures from tracheal aspirates are also non-specific as the upper respiratory tract of most critically ill patients is colonised by potential pulmonary pathogens. Alternative diagnostic techniques such as protected specimen brush biopsies and bronchoalveolar lavage have therefore been used, although a recent pilot study suggested that complicated culture sampling using these techniques has no beneficial therapeutic influence over more simple endotracheal aspirate cultures. The various methods employed in the diagnosis of nosocomial pneumonia have been reviewed elsewhere. This review focuses on methods of preventing the development of bacterial nosocomial pulmonary infections.

Pathogenesis of nosocomial pneumonia

For a nosocomial pneumonia to occur, one or both of the following factors must be present: (1) the lower respiratory tract must be invaded by bacteria in sufficient numbers or of particular virulence and (2) pulmonary and systemic host defences must be downregulated.

With the high costs of nosocomial pulmonary pneumonia and the associated increased mortality, measures to prevent the development of such infections are important and can be considered in two groups—those aimed at preventing colonisation and those aimed at increasing host defences (table 1).

Prevention of colonisation

Colonisation of the upper respiratory tract is common in critically ill patients and may precede the development of nosocomial pneumonia. Measures to prevent colonisation are thus important in limiting nosocomial pneumonia. Infecting organisms may originate from exogenous (external) sources or from the patient’s own flora (endogenous sources). Bacterial entry into the lungs from exogenous sources may occur by various routes including the aspiration of bacteria from the environment (transmitted, for example, on the hands of staff) or direct penetration (for example, via the pleural space). Entry from the endogenous pool of organisms may occur by aspiration from the oesophageal/gastric contents or by haematogenous spread—for example, from the gut by translocation or from a distant site of infection such as an infected catheter. An important early pathogenetic event in colonisation is the adherence of bacteria to the epithelium of the respiratory tract. This bacterial adherence is influenced by alterations in the epithelial cells, bacterial surface characteristics, and exoproducts. The reduced mucociliary clearance and impaired local host immune responses commonly seen in critically ill patients facilitate increased colonisation.

Hygiene

The bacteria involved in nosocomial infections are frequently transmitted from the environment or from patient to patient on the hands of health care staff. Hand washing has long been recognised as an effective method of preventing this transfer of bacteria from the environment to the patient, yet such a simple technique is frequently under-performed. The use of an antimicrobial hand washing agent may be more
effectiveness than a non-medicated soap, and the use of disposable gowns and aprons during patient contact may also be an effective means of limiting the transfer of organisms from the environment.

VENTILATOR EQUIPMENT
Although transmission of bacteria via the respirator equipment was identified as a cause of pulmonary infections more than 15 years ago, recent studies have played down the importance of transmission of bacteria via the respiratory circuitry. Current systems are rarely a major source of bacteria. The use of sterile water in the humidifier reservoir, in particular, has significantly reduced the likelihood of bacterial colonisation of ventilator equipment. The frequency of ventilator circuit change has not been shown to influence the rate of infection and, similarly, the use of closed suction systems has not been shown to be beneficial. It has been suggested that the use of heat and moisture exchangers may reduce the rate of infection but this remains a controversial issue as these systems have other problems including an increase in airway resistance associated with the accumulation of tracheal secretions in the system.

SELECTIVE DIGESTIVE DECONTAMINATION (SDD)
The use of SDD has been based on the hypothesis of “colonisation resistance” in which anaerobic flora is considered to protect against the excessive growth of Gram negative bacteria. The systematic use of topical mixtures of antibiotics (usually polymyxin, tobramycin and amphotericin B) applied to the oropharynx and stomach, together with the intravenous administration of cefotaxime, has been shown to reduce the incidence of nosocomial pneumonia, although not all studies have confirmed this finding. A recent meta-analysis did conclude that SDD can reduce respiratory tract infections and overall mortality in critically ill patients but, in view of the risk of bacterial resistance, the systemic SDD approach has not gained widespread acceptance. Nevertheless, the use of SDD may be appropriate in particular clinical conditions including immunosuppressed patients and those undergoing liver transplantation and oesophagectomy. The topical use of antibiotics in the respiratory tract cannot be recommended.

INAPPROPRIATE ANTIBIOTIC THERAPY
It has been clearly shown that the prior administration of antibiotics contributes to the development of nosocomial pneumonia and increases mortality. However, inadequate early antibiotic coverage in nosocomial pneumonia is also associated with increased mortality. It is therefore important to be rational in our choice and use of antibiotics, restricting excessive and inappropriate use. Each patient should be assessed individually as to his/her need for antibiotics and, when treatment is necessary, the antibiotic regime should be carefully selected according to the likely pathogen(s) and local resistance patterns.

MAINTENANCE OF LOW GASTRIC pH
H₂-blockers and antacids are frequently used in patients in the ICU to prevent the development of stress ulcers and bleeding. However, these agents raise intragastric pH which may enhance the colonisation of the stomach by Gram negative bacteria and thereby contribute to the development of nosocomial pneumonia. The evidence on the effects of H₂-antagonists on the development of nosocomial pneumonia is conflicting with some studies reporting minimal differences in their incidence.

Table 1 Proposed strategies to prevent pulmonary nosocomial infections

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Relative importance</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Preventing colonisation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hygiene</td>
<td>+++</td>
<td>Anti-microbial soaps may be more effective than non-medicated (prospective multiple crossover trial)</td>
</tr>
<tr>
<td>Heat and moisture exchangers</td>
<td>++</td>
<td>Reduced incidence of nosocomial pneumonia (randomised trial, meta-analysis) but caution as increased endotracheal secretions (randomised trial)</td>
</tr>
<tr>
<td>Selective digestive decontamination</td>
<td>++ (especially in trauma patients)</td>
<td>Reduced respiratory tract infections (meta-analysis); risk of bacterial resistance remains a problem (prospective survey)</td>
</tr>
<tr>
<td>Subglottic drainage</td>
<td>++</td>
<td>Reduced incidence of nosocomial pneumonia (randomised trial, meta-analysis)</td>
</tr>
<tr>
<td>Semi-recumbent position</td>
<td>++</td>
<td>Reduces aspiration of gastric contents (randomised crossover trial)</td>
</tr>
<tr>
<td>Avoidance of H₂ blockers</td>
<td>+</td>
<td>May be of some benefit in reducing nosocomial pneumonia (meta-analysis) but increased risk of gastrointestinal bleeding</td>
</tr>
<tr>
<td>Kinetic beds</td>
<td>+</td>
<td>Reduces incidence of nosocomial pneumonia (randomised controlled trial) but not well tolerated by some patients</td>
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<tr>
<td>Influencing host response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early enteral nutrition</td>
<td>+++</td>
<td>Reduces risk of infection (meta-analysis); jejunal feeding may be preferable (randomised trial); immune supplemented feeds may provide more protection (randomised trial)</td>
</tr>
<tr>
<td>Cytokine administration</td>
<td>?</td>
<td>Remains experimental</td>
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potential increased risk of pneumonia related to the effects of H₂-blockers on gastric pH, sucralfate has sometimes been preferred and, indeed, several meta-analyses of the literature have concluded that there is a reduced incidence of pneumonia in patients treated with sucralfate compared with H₂-blockers or antacids. However, this has been a controversial issue. For instance, in the EPIC study the type of gastric protective strategy did not seem to influence the development of pulmonary infections, a finding supported by several other studies. These differences may be explained partly by the results of a study by Thomason et al. who found that the incidence of early onset pneumonia—during the first four days of stress ulcer prophylaxis—was the same with sucralfate, antacid or H₂-blocker but that there was a trend towards a reduced incidence of pneumonia in the sucralfate group after four days of treatment. Further fuelling this controversy, a recent study by Cook et al. has shown that sucralfate provides less efficient anti-ulcer prophylaxis than H₂-antagonists, with no difference in the rate of ventilator associated pneumonia between the two groups. We can conclude from the available evidence that the use of H₂-receptor antagonists may increase the risk of nosocomial pneumonia and their systematic use in all patients is not warranted. However, despite the potential increased risk of pneumonia, when an anti-ulcer prophylactic strategy is necessary H₂-blockers are preferable to sucralfate for their superior anti-ulcer efficacy.

INTUBATION

The use of intubation via the nasal route may predispose to nosocomial sinusitis which has been associated with the development of nosocomial pneumonia, so oral intubation is preferred whenever possible. Torres et al. have shown that endotracheal re-intubation may be an important risk factor in the development of ventilator associated pneumonia, and care should therefore be taken before deciding on endotracheal extubation to avoid the possible need for re-intubation.

SUBGLOTTIC DRAINAGE OF SECRETIONS

Aspiration of the secretions accumulating above the inflated endotracheal cuff may be helpful in preventing colonisation of the lung. Special endotracheal tubes have been developed which have a separate lumen open to the subglottic region to allow continuous aspiration of these secretions. Studies on the effects of these tubes have reported a reduced incidence of nosocomial pneumonia.

ROLE OF THE NASOGASTRIC TUBE

Duodenal reflux of gastric secretions may contribute to lung colonisation, and it has been suggested that placement of a nasogastric tube in the stomach may facilitate the passage of bacteria from the gut into the airways, and hence be a risk factor for the development of pneumonia. Some investigators have proposed using a small rather than a large nasogastric tube, and others have suggested bypassing the stomach by using a jejunal tube instead of a gastric tube. These issues are, however, still controversial and require further study before definite recommendations can be made regarding the use of the nasogastric tube.

AVOIDANCE OF EXCESSIVE SEDATION

Numerous studies have shown that coma and an altered level of consciousness can significantly contribute to the development of lung infections. Accordingly, sedative agents should be titrated to the individual patient using, for example, a sedation score. By this means the use of excessive sedation could be reduced.

SEMI-RECUMBENT POSITION

It may be helpful to place patients in the ICU at risk of developing nosocomial pneumonia in the semi-recumbent position rather than supine to limit the passage of bacteria into the airways. The supine position has been associated with an increased incidence of nosocomial pneumonia. The use of kinetic beds has also been proposed to limit the risks of lung colonisation and reduce the incidence of nosocomial pneumonia.

Modulating host defence

The host defence response is frequently impaired in critically ill patients, making them more prone to develop nosocomial infections. In the lungs the endotracheal tube bypasses host defences above the vocal cords and impairs lower respiratory tract defences such as cough and mucociliary clearance. Systemic host defence is reduced in the presence of chronic illness, malnutrition, prolonged surgery, and various co-morbid illnesses such as respiratory failure. Reducing factors which limit host response and administering agents to modulate host defence directly may prevent nosocomial pneumonia.

IMMUNOSUPPRESSIVE AGENTS

Immunosuppressive agents such as corticosteroids and cytotoxic agents impair various host defence mechanisms including gut barrier function, and immunosuppression has been identified as a risk factor for nosocomial pneumonia in children. Immunosuppressive agents should thus be avoided wherever possible and, when necessary, the minimal effective dose should be used and treatment should be regularly reviewed and stopped at the earliest opportunity.

NUTRITIONAL SUPPORT

By impairing host defence, malnutrition has been shown to be a major contributing factor to the development of pneumonia. Providing adequate nutritional support to intensive care patients is thus important in the prevention of nosocomial pneumonia, although the preferred route of administration and the nature of the feeds has been subject to debate. Enteral nutrition, particularly given early, is generally preferred to parenteral feeding and is associated with fewer septic complications. However, by raising the pH in the stomach, enteral feeds may encourage bacterial colonisa-
tion and hence increase the risk of pneumonia. Montecalvo et al\textsuperscript{76} therefore suggested the use of jejunal feeding tubes to bypass the stomach and, in a small group of ICU patients, this technique was found to reduce the incidence of nosocomial pneumonia and improve the nutritional status compared with gastric fed patients. Recently, the use of immune enhancing feeds enriched with a variety of nutrients including amino acids, arginine, glutamine, and nucleotides has been associated with fewer acquired infections.\textsuperscript{77} Further studies are needed to determine the precise combination of nutrients which will provide the most beneficial effects but early enteral nutrition to stimulate gut immunological function should be provided to patients in intensive care, initially supplemented by parenteral nutrition when enteral nutrition can only be tolerated in low volumes.\textsuperscript{74} 

ADMINISTRATION OF CYTOKINES TO ENHANCE HOST DEFENCE

As immunosuppression is a major factor in the development of nosocomial pneumonias,\textsuperscript{77} the restoration of an adequate immune response may represent an important strategy to prevent nosocomial lung infections. Docke et al\textsuperscript{77} have recently shown that the administration of interferon-\(\gamma\) (IFN-\(\gamma\)) may restore monocyte function, although clinical studies of the effects of prophylactic systemic IFN-\(\gamma\) on infection rates are inconclusive.\textsuperscript{77, 78} Local aerosol administration of IFN-\(\gamma\) may be an effective means of augmenting local host defences\textsuperscript{79} but this has not been assessed in clinical trials. Interleukin-12 (IL-12), a pro-inflammatory cytokine, can stimulate the Th-1 type immune responses and the administration of IL-12 has been shown to protect animals against lung infections.\textsuperscript{80} The administration of granulocyte colony stimulating factor (G-CSF) may also have a role in the prevention of nosocomial infections. Animals without G-CSF are less able to resist infection,\textsuperscript{81} and the administration of G-CSF to patients at risk of developing pneumonia may prove beneficial. However, a recent randomised, placebo controlled, clinical study\textsuperscript{82} using prophylactic G-CSF in patients with acute traumatic brain injury or cerebral haemorrhage reported no difference in the incidence of nosocomial pneumonia compared with placebo treated patients. Prophylactic immunomodulating agents represent an exciting area of ongoing research but many more studies are required before any recommendations can be made regarding their routine use in intensive care patients.

Conclusion

Nosocomial pneumonia poses a considerable load in terms of morbidity, mortality, and cost in the ICU. The prevention of such infections is therefore of considerable clinical and economic interest. A number of measures aimed at reducing the occurrence of nosocomial pneumonia have been suggested and investigated. Some methods, such as hand washing, have been unequivocally proved to be beneficial and should be a routine part of ICU patient care. The overzealous use of antibiotics and the administration of excessive sedative agents should certainly be discouraged. Oral intubation and, if possible, placing patients in the semirecumbent position rather than supine are also important factors in preventing nosocomial pneumonia. Other methods are more controversial and cannot be routinely recommended. H\(_2\)-blockers are of little value in reducing the incidence of nosocomial pneumonia and SDD is of benefit only in certain groups of patients. The administration of immunosuppressive agents should be kept to a minimum as these further reduce host defence. Early enteral nutrition should be administered, supported by parenteral nutrition in the early stages if enteral tolerance is poor. Immune supplemented feeds may prove to be of greater benefit but further studies are needed. The possibility of stimulating the immune response in its fight against infection is an exciting area of active research, but immuno-modulating agents remain at the experimental stage at the present time.

The appropriate use of some of the techniques discussed can certainly reduce the incidence of nosocomial pneumonia in some of the patients in the ICU. While simple methods such as hand washing should be part of routine practice, the use of predictive models to identify patients at high risk of nosocomial pneumonia can help us to focus other, more invasive, preventative measures on those most likely to benefit.\textsuperscript{83} The results of ongoing research, particularly into techniques to modulate immune defence, may strengthen our preventative capabilities and help to limit further the number of patients who currently develop nosocomial pneumonia.

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