

Antimicrobial prescribing for hospital-acquired pneumonia

The impact of hospital-acquired pneumonia and the pressure to reduce unnecessary antibiotic prescribing has led to the publication of prescribing guidelines from the National Institute for Health and Care Excellence. This editorial gives an overview of the guidelines and emphasises the need for more high-quality evidence to inform decision making in this group of patients.

Hospital-acquired pneumonia is a severe respiratory infection that occurs in all hospitals, wards and specialities. Europe-wide point prevalence surveys have shown that hospital-acquired pneumonia is responsible for more deaths and morbidity than other healthcare-associated infections (Cassini et al, 2016). In-hospital mortality attributable to hospital-acquired pneumonia has been estimated to be between 18% and 29% (Sopena et al, 2005; Burton et al, 2016).

Hospital-acquired pneumonia is associated with potentially resistant Gram-negative bacteria such as Enterobacteriaceae (eg *Escherichia coli*, *Klebsiella* spp.) and *Pseudomonas aeruginosa* which require treatment with extended-spectrum antibiotics. However, hospital-acquired pneumonia that occurs early in an admission is often caused by bacteria such as *Streptococcus pneumoniae*, which require antibiotics with a narrower spectrum (Sopena et al, 2005). Currently, it is exceedingly rare to know the causal pathogen before starting treatment for pneumonia. Empirical antibiotic choices must therefore balance the desire to cover all possible causal pathogens with the substantially increased risk of *Clostridium difficile* infection, death and antimicrobial resistance attributed to extended spectrum antibiotics (Kumar and Wootton, 2019).

Prescribing guidelines

In the context of these difficult antibiotic choices, the National Institute for Health and Care Excellence (2019) has published prescribing guidelines for patients with hospital-acquired pneumonia. The recognition this document gives to hospital-acquired pneumonia is welcome since the syndrome represents a substantial unmet need and has been over-shadowed by a focus on community-acquired and ventilator-associated pneumonia (Ewan et al, 2017).

The National Institute for Health and Care Excellence prescribing guidelines for hospital-acquired pneumonia, in line with other international guidelines, triage patients into two groups based on clinical severity and the risk of resistant pathogens (Kalil et al, 2016; Torres et al, 2017). The National Institute for Health and Care Excellence guidelines recommend that oral co-amoxiclav is given to patients with low clinical severity and low risk of resistant bacteria. For sicker patients, or those with risk factors for resistant bacteria, there are seven options for first-line empirical treatment with the choice being based on microbiological advice taking into account local resistance patterns. Options suggested are piperacillin-tazobactam, ceftazidime, ceftriaxone, cefuroxime, meropenem, ceftazidime-avibactam or levofloxacin. The National Institute for Health and Care Excellence does not recommend routine use of antibiotics to cover meticillin-resistant *Staphylococcus aureus*, which should only be considered where proven or in the presence of specific risk factors.

A separate treatment table is provided for children over 1 month old where a triage system similar to that used for adults is recommended. Children with low severity hospital-acquired pneumonia who have a low risk of harbouring resistant bacteria should be treated with co-amoxiclav or, if penicillin allergic, clarithromycin. Suggestions for children with severe hospital-acquired pneumonia or those with risk factors for resistant bacteria are piperacillin-tazobactam, ceftazidime or ceftriaxone, each dosed by age and weight. The recommendations regarding meticillin-resistant *S. aureus* for children are identical to those

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for adults. No specific recommendations are made for babies under 1 month of age where the advice is to seek local specialist microbiological guidance.

A striking feature of the National Institute for Health and Care Excellence prescribing guideline, in common with the 2014 National Institute for Health and Care Excellence pneumonia management guidelines, was the lack of evidence available to support the committee's recommendations. No systematic reviews were available and only nine randomised controlled trials met evidence criteria. The UK contributes only 10 patients to the evidence used by the National Institute for Health and Care Excellence, drawn from one multicentre trial (Torres et al, 2018). This is important since the regions contributing most patients to the research on which these guidelines draw (China, USA and Eastern Europe) may have a very different spectrum of pathogens than those encountered in NHS practice.

As a consequence of this sparse evidence base, many of the National Institute for Health and Care Excellence recommendations represent a pragmatic attempt to improve antibiotic stewardship by reducing the unnecessary use of extended spectrum antibiotics. For example, the guidelines reinforce the importance of sending microbiological samples (eg sputum or nasopharyngeal swabs) to guide treatment rationalisation. National Institute for Health and Care Excellence recommends that antibiotics are administered within 4 hours of X-ray confirmation of a diagnosis of hospital-acquired pneumonia or within 1 hour where sepsis criteria are met. This 4-hour target comes from the 2014 pneumonia guideline where 'no suitable studies examining the timing of antibiotic administration in hospital-acquired pneumonia were available' (National Institute for Health and Care Excellence, 2014). Similarly National Institute for Health and Care Excellence suggests a standard treatment duration of 5 days for all age groups and levels of severity with extension of this based on clinical review.

Possible areas of confusion

However, by attempting to reduce extended spectrum prescribing in the absence of robust evidence, some of the recommendations in this guideline are likely to worsen the already confusing system of pneumonia classification. The National Institute for Health and Care Excellence, in common with the European Respiratory Society and American Thoracic Society, defines hospital-acquired pneumonia as pneumonia that begins 48 hours after hospital admission (Kalil et al, 2016; Torres et al, 2017). However, they then recommend that patients who develop hospital-acquired pneumonia between day three and five of their admission should be empirically treated as per community-acquired pneumonia guidelines. This ambiguous situation – hospital-acquired pneumonia being treated as community-acquired pneumonia – adds to the current confusion stemming from the 2009 British Thoracic Society guidelines for the management of community-acquired pneumonia (Lim et al, 2009). Those guidelines, which are deeply embedded into UK pneumonia practice, specifically excluded patients who had a hospital admission within 10 days of developing pneumonia – regarding those patients as having hospital-acquired pneumonia. So we have some cases of community-acquired pneumonia being treated as hospital-acquired pneumonia and some cases of hospital-acquired pneumonia treated as community-acquired pneumonia.

This potential for confusion, resulting in practice variation, is further exemplified by the suggestion that empirical antibiotic choice should be determined by clinical severity and risk of resistant pathogens. This seems sensible but the lack of evidence results in vague definitions of severity and resistance risk. The National Institute for Health and Care Excellence (2019) says 'no validated severity assessment tools are available for hospital-acquired pneumonia, and severity of symptoms or signs should be based on clinical judgement'. Resistance risk includes as '...recent use of broad-spectrum antibiotics... and recent contact with health and social care settings before current admission' but no attempt is made to define 'recent' nor what counts as a 'contact with health or social care'.

Conclusions

The National Institute for Health and Care Excellence antimicrobial prescribing guidelines for hospital-acquired pneumonia highlight the importance of the condition and attempt to improve antibiotic stewardship but are hampered by the paucity of high quality, particularly

Key points

- Hospital-acquired pneumonia is associated with significant morbidity and mortality.
- The National Institute for Health and Care Excellence 2019 guidelines emphasise the importance of microbiological cultures to guide treatment rationalisation.
- Broad-spectrum empirical antibiotics are required to treat potential pathogens which include Gram-positive as well as susceptible and resistant Gram-negative bacteria.
- Further research is urgently required to address the paucity of evidence identifying the optimal management of patients with hospital-acquired pneumonia.

UK focused, research in this area. They highlight the root problem in pneumonia, which is the inadequacy of empirical prescribing. Clinicians urgently need evidence to support the use of rapid diagnostic strategies to allow personalised treatment in the form of antibiotics targeted at the causative bacteria.

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