

WHAT'S NEW IN INTENSIVE CARE



Antibiotic prophylaxis in the ICU: to be or not to be administered for patients undergoing procedures?

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Critically ill patients receive antimicrobials for multiple reasons. Antimicrobials may be prescribed as perioperative “prophylaxis” when an intensive care unit (ICU) patient is transferred to the operation room. Such practice is intended to ensure bactericidal serum antibiotic concentrations at the time of surgical incision, as accepted in non-ICU patients. At other times, “prophylactic” antibiotic administration is driven by concerns regarding the tolerance of fragile patients to bacteraemia, even when transient [1, 2], and the high likelihood of patient exposure to multiple environmental contaminants [3].

However, administration of unnecessary prophylactic antimicrobial therapy comes at a price; clinicians are often reluctant to stop antimicrobial therapy once it has been initiated, regardless of the appropriateness of treatment [4]. A study conducted in 281 Australian hospitals found that 40% of >20,000 antibiotics prescribed in hospital wards were inappropriate, mainly due to carryover of treatment that should have been terminated [5]. Redundant use of antibiotics increases consumption unnecessarily [6] and may ultimately be associated with more adverse reactions and *Clostridium difficile* infections [7]. Most importantly, antimicrobial pressure is considered the main driver for development of MDR pathogens. While the relation between antibiotic prophylaxis and development of bacterial resistance is not always clear [8], timely cessation of antimicrobial

treatment should go hand-in-hand with any prophylactic antimicrobial treatment.

We used predefined criteria and key words to search the literature systematically for publications describing patient outcomes related to and recommendations for “prophylactic” intravenous antimicrobial administration for invasive procedures performed on ICU patients in the OR and the ICU (Supplement A).

Definitions and prevalence of “prophylactic” antimicrobial therapy in the ICU

Definition: The expression “prophylactic” antimicrobial therapy has multiple uses in the context of intensive care (Supplement B) [9]. There is also significant overlap in the use of “prophylactic” and “pre-emptive” antibiotic administration in the literature [10]. Prophylactic therapy usually entails administration of a single dose or, at most, a day of antibiotic treatment for prevention of infection when there is no evidence or suspicion of infection already being present [4]. There is also little-to-no literature on the ideal time for antimicrobial prophylaxis; this time frame may eventually vary depending on patient and environmental conditions and the type of procedure to be performed. Such time frames should ideally be determined in multicentre studies randomising critically ill patients to different timing of antimicrobial administration. In the interim, extrapolation from populations that are not critically ill and from database analyses suggests that prophylactic antimicrobial therapy is generally best timed to around 1 h before performance of invasive procedures [11, 12].

Prevalence: Several studies suggest that prophylactic administration of antimicrobials is commonly practiced in the ICU. A single-centre prospective study conducted

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in Belgium showed that among 10,731 antibiotic treatment courses recorded for 3 years, 42% ($n=4525$) were prescribed for prophylaxis [13]. A nationwide, single-day survey conducted among 52 ICUs in Japan found that 34% ($n=331/1028$) of the prescriptions for intravenous antibiotics written that day were for prophylaxis [14].

Indications for antimicrobial prophylaxis in ICU patients

Antimicrobial prophylaxis may be administered to patients undergoing a surgical procedure during their ICU stay and as a non-surgical prophylaxis to ICU patients who undergo insertion of an external–internal foreign body that remains in situ for a prolonged period of time. These two clinical scenarios differ and are, therefore, discussed separately.

Surgical procedures: Surgical antimicrobial prophylaxis (SAP) for prevention of surgical site infections is the most frequent hospital-wide indication for antimicrobial use. However, SAP is also commonly practiced in many ICUs. A single-centre study conducted recently in a Belgian ICU showed that SAP and prophylaxis for immunocompromised patients constituted two-thirds of prophylactic antibiotic treatments prescribed [13]. In non-ICU patients, it is recommended that SAP be administered 30–60 min before surgical incision to enable achievement of a high serum concentration of antibiotics prior to incision [11, 12]. Re-injection is recommended during the procedure every two half-lives of the antibiotic [12].

If surgery is conducted prior to ICU admission and/or within the first 48 h of ICU admission, the recommendations for SAP remain unchanged; they are similar to the recommendations of any department of emergency medicine or ward [15]. However, in ICU, patients undergoing unplanned surgery after staying > 2 days in the ICU other considerations come into play. Colonization with MDR pathogens increases during the hospital stay [16]. Prior antibiotic treatment and prior environmental exposure also affect the prevalence of colonization by MDR pathogens [17]. In such cases, the spectrum of antibiotics required constitutes a major challenge because of the potential need to cover and manage MDRs in the operative setting and because in fragile patients, there is an unproven concern not only for surgical site, but also for systemic infection [18]. A single-centre, observational study which reported on a small number of patients ($n=44$) has shown great variability of practices in these patients [19]. To date, there is no evidence to support the universal use of prophylaxis targeted against MDR. This approach should be investigated in future studies, as it can constitute a vicious circle for the development of MDR. Some of the multiple factors that should be taken into account when determining the choice of antibiotic

in such cases are presented in Table 1. There are no randomised controlled trials on the effects of timing or choice of antibiotic prophylaxis on the outcomes of ICU patients requiring unplanned surgical procedures. Nor are there recommendations for antibiotic prophylaxis in critically ill patients.

Non-surgical prophylaxis: Many ICU patients require insertion of an external–internal foreign body. Questions arise regarding prophylaxis before insertion and for tubing remaining in situ for a prolonged period of time. We discuss three of these many dilemmas; endotracheal intubation due to an altered level of consciousness, chest drain insertion and insertion/maintenance of an intracranial ventricular drain.

Endotracheal intubation: Prophylactic antimicrobial treatment following endotracheal intubation of patients with an altered level of consciousness is not recommended in most guidelines for prevention of health-care-associated pneumonia [20, 21]. However, French guidelines for the prevention, diagnosis and treatment of hospital-acquired pneumonia in ICU suggest consideration of selective digestive decontamination with both topical and systemic antibiotics (for a maximum of 96 h) to decrease the rate of pneumonia immediately after urgent intubation based on indirect evidence from several studies [22]. Sirvent et al. randomised 100 comatose patients undergoing intubation to 2 doses of cefuroxime versus no treatment. Patients receiving cefuroxime had a lower rate of ventilator-associated pneumonia (VAP) briefer hospital and ICU length of stay [23]. Aquarolo et al. randomised 38 comatose mechanically ventilated patients with brain injury to ampicillin-sulbactam prophylaxis plus standard treatment or standard treatment alone and showed that antibiotic prophylaxis reduced the occurrence of early-onset pneumonia (21% vs 58%, $P=0.022$). [24]. Similar findings have been reported in other ICU settings [25]. More recently, a systematic

Table 1 Factors that should be taken into account when determining the choice of an antibiotic

Factors	Reasons to consider
Recent antimicrobial use	Possibility of resistant pathogens
Colonization resistant organism	Possibility of resistant pathogens
Hospital LOS	Possibility of resistant pathogens
Prostheses	Drug distribution
Weight	Underdosing
Renal function	Overdosing
Allergy status	Alternative to standard prophylaxis
Comorbidities	Interactions with previous drugs
Immunosuppression	Possibility of resistant pathogens

review and meta-analysis reported that systemic administration of antibiotics for no more than 24 h following intubation did not affect mortality [relative risk (RR) 1.03; 95% confidence interval (CI) 0.7–1.53], but was associated with a reduction in the incidence of early-onset VAP and briefer ICU lengths of stay [26]. The literature does seem to suggest that a short course of prophylactic antibiotic following intubation may confer some benefit. However, this finding is inconsistent and if it does exist, the strength of this effect remains to be determined. At this time, the results of a trial planned to include 320 patients with brain injury randomised to either one dose of ceftriaxone within 12 h of intubation or placebo are expected [27]. Additional multicentre prospective studies are required.

Chest drains: Placement of a chest drain may theoretically be accompanied by bacteraemia, particularly if placed in a source of infection or nearby already infected lung. Alternatively, the chest drain is a foreign body which could theoretically become a source of ascending infection (i.e. pneumonia, empyema). There are no recommendations regarding antibiotic prophylaxis in ICU patients requiring chest drain insertion. A meta-analysis of studies focused on antibiotic prophylaxis for chest drain insertion in non-ICU patients (i.e. thoracic injury), concluded that treatment after chest drain insertion was significantly associated with a reduced risk of empyema (RR 0.25; 95% CI 0.13–0.49) and pneumonia (RR 0.41; 95% CI 0.24–0.71) when compared with placebo alone [28]. This study is often quoted as a reason to provide prophylactic antibiotic treatment to patients who undergo chest drain insertion or who have a chest drain in situ. However, a trauma setting may differ in both urgency and hygiene conditions, and young trauma patients are very different from most surgical patients who are older and comorbid, thus extrapolation may be inappropriate.

Furthermore, the length of required prophylactic treatment (if any) also remains unclear. This question is particularly pertinent in patients that undergo drain insertion in sterile conditions (e.g. during elective thoracic surgery). Most of these patients receive antibiotic prophylaxis before surgery in accordance with perioperative guidelines [12]. Meta-analysis of the data on this topic in the literature suggests that prolonged postoperative antibiotic prophylaxis does not reduce the number of infectious complications related to chest drains compared with preoperative prophylaxis only [29].

Cerebral intra-ventricular drains—Current Neurocritical Care Society recommendations suggest that one dose of antimicrobials be administered prior to insertion of an external ventricular drain. This recommendation is based on a weak level of evidence [30].

In conclusion, antimicrobial prophylaxis constitutes a large part of antibiotic prescriptions in the ICU.

Antimicrobial prophylaxis could theoretically prevent appearance of infectious complications in critically ill ICU patients that must undergo an invasive procedure in the ICU or the OR. On the other hand, redundant antimicrobial prophylaxis could drive emergence of MDR pathogens and increase the rate of adverse drug reactions. There is an urgent need to conduct methodologically sound multicentre randomised clinical trials in the ICU environment on this topic; the literature is particularly poor with regards to both surgical and non-surgical procedures in critically ill patients.

Electronic supplementary material

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Compliance with ethical standards

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