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RESEARCH NOTE

Antimicrobial prophylaxis to prevent surgical site infections in a rural sub-Saharan hospital

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ABSTRACT

A prospective cohort study was performed to collect baseline data concerning surgical site infections (SSIs) and antimicrobial prophylaxis (AMP) in a remote sub-Saharan district hospital. The SSI rate of 22% was high. Most (88%) of the patients received prophylaxis after incision, and only 5% within the 30-min period before incision. Of all pathogens isolated from SSIs, 60% were resistant to the agent administered. The antibiotics given most frequently were chloramphenicol (60%), aminopenicillins (23%) and benzylpenicillin (15%). *Staphylococcus aureus* (36%), *Escherichia coli* (5%) and enterococci (4%) were the pathogens isolated most commonly from SSIs.

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Surgical site infections (SSIs) are the second most common cause of nosocomial infection, resulting in considerable morbidity and mortality. Antimicrobial prophylaxis (AMP) reduces the rate of SSI in non-clean surgery. In accordance with guidelines, perioperative AMP is administered routinely in industrialised countries to all patients who qualify [1,2]. Data concerning comparative perioperative AMP in non-industrialised and industrialised nations are scarce [3–6]. The present study provides, for the first time, data concerning AMP in a rural sub-Saharan district hospital.

The study was conducted in the 82-bed department of general surgery, which includes gynaecology and obstetrics, of the St Francis Designated District Hospital in Ifakara, southern Tanzania. The St Francis Designated District Hospital is a 371-bed hospital that serves a region with a population of >550 000. A mean of 155 surgical procedures are performed every month in the two main operating rooms. Between November 2003 and March 2004, all consecutive adult patients admitted for surgery were enrolled in the study. Data concerning patient characteristics, laboratory results, type of surgical intervention and administration of AMP were recorded continuously by study nurses (24 h, 7 days a week). No written guidelines concerning the use of AMP were available in the hospital; antibiotics and dosages were chosen by the surgeon.

In cases of suspected SSI, the site of infection was documented with a digital camera and swab samples were taken. During the study, data were reviewed and checked prospectively by a senior infectious diseases specialist. Material from swabs was analysed by Gram's stain and plated on CHROMagar Orientation and CHROMagar *Staphylococcus aureus* (Becton Dickinson, Heidelberg, Germany) in the local laboratory. Colonies isolated were subcultured and transported to the Microbiology Laboratory, University Hospital Basel, Switzerland, for further analysis using stand-

ard microbiological methods [7,8]. SSIs were classified according to CDC recommendations, i.e., superficial, deep, organ or space [1]. Statistical analyses were carried out using SAS v.8 software (SAS Inc., Chicago, IL, USA).

In total, 613 patients underwent surgery during the 4-month period of study, of whom 527 (84% female; median age 28 years, range 16–84 years) qualified for routine AMP. Of these, 114 (21.6%) developed an SSI (Fig. 1); 49 (43%) infections were superficial, 51 infections (45%) were deep, and 14 (12%) infections were organ or space SSIs. Seven (1%) patients died; five deaths were possibly attributable and two deaths were clearly attributable to SSI. Twenty-two (19%) SSIs were identified only by post-discharge surveillance. Caesarian sections (n = 332, 63%) were the surgical interventions performed most frequently, followed by other gynaecological procedures (11%). Overall, 56% of all interventions were classified as emergencies. The median duration of the most frequent interventions was 30 min (range 10–150 min). In total, 222 (42.5%) patients failed to return for a follow-up visit (on day 30), presumably because of the need to travel >8 h to reach the hospital; however, none showed evidence of SSI at discharge.

AMP was administered to 524 (99%) patients; prophylaxis was not given to three patients for unknown reasons. The antibiotics used most frequently were chloramphenicol (n = 314, 60%) and aminopenicillins, such as ampicillin (n = 122, 23%) or benzylpenicillin (n = 77, 15%). In 118 (23%) of 524 cases, more than one agent was administered prophylactically. Ampicillin and cloxacillin (n = 69, 59%) was the combination used most often.

Overall, 88% (460/527) of patients received prophylaxis after incision, including 55% who received prophylaxis >30 min after incision (Fig. 2). Only 5% of cases received prophylaxis within the 60-min period before surgery, but

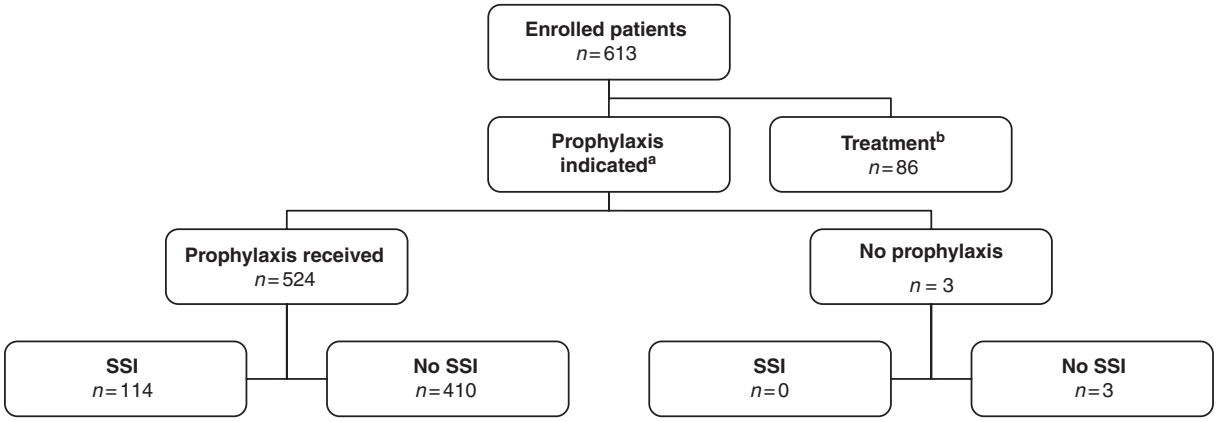

Fig. 1. Patient enrolment in the study. [a]Prophylaxis indicated, i.e., according to CDC definition of clean or clean-contaminated wounds (class I or class II). [b]Treatment situation, i.e., according to CDC definition of dirty or dirty-infected wounds (class III or class IV). SSI, surgical site infection.

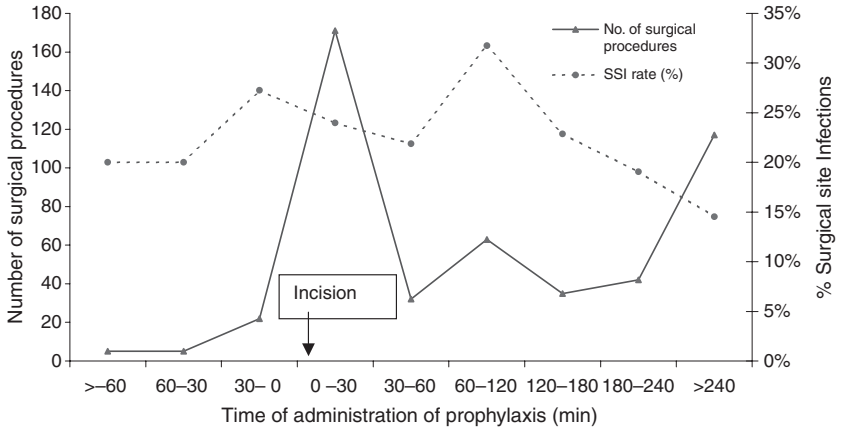

Fig. 2. Time of administration of antimicrobial prophylaxis in relation to the incidence of surgical site infections.

>90% of patients received prophylaxis for a duration of 5 days. AMP was not effective against 60% of the pathogens isolated. The pathogen found most frequently was *S. aureus* in 36% (n = 41) of the cases, followed by *Escherichia coli* in 5% (n = 6) and enterococci in 4% (n = 4). Other clinically relevant bacteria, e.g., *Klebsiella* spp., *Proteus* spp., other Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter* spp. were found in 7% of cases. Coagulase-negative staphylococci, *Corynebacterium* spp. and *Bacillus* spp. (n = 34) were considered to be contaminants and were grouped together with 'no growth' (n = 21; total, n = 55, 48%). Chloramphenicol resistance was detected in 33% (n = 13) of *S. aureus*, 35% (n = 2) of *E. coli* and 25% (n = 1) of enterococci. Resistance to penicillin was detected in 95% of *S. aureus* isolates, but methicillin-resistant *S. aureus* comprised only one of 114 isolates in this remote hospital. Surprisingly, 29% (4/14) of all Gram-negative pathogens expressed extended-spectrum β-lactamases. Two isolates of enterococci were insusceptible to vancomycin.

The SSI rate of 22% was high compared with incidence rates reported from other continents [9,10]. The principles of asepsis, disinfection and sterilisation, as well as surgical techniques, were not deviated from significantly. Sterilisation was performed with a hot-air steriliser; however shortage of disposable items was common. Nevertheless, an assessment of the infrastructure was unable to explain the high rate of SSI in this relatively young population [11], and inappropriate AMP may have contributed significantly to the rate of SSI. First, AMP was not directed against the spectrum and corresponding resistance patterns of the pathogens causing SSIs. It is of concern that healthcare providers working in this remote hospital were already confronted with highly resistant pathogens, including methicillin-resistant *S. aureus*, extended-spectrum β-lactamase-producing organisms and enterococci that were insusceptible to vancomycin. Second, AMP was generally not administered during the recommended time window, thereby severely reducing the effect of prophylaxis [12]. US guidelines recommend that the optimal time window for administration of AMP is <60 min before incision [13,14]. The goal of AMP is to achieve serum and tissue drug levels that exceed the MICs for the organisms likely to be encountered during surgery. Although multiple studies have demonstrated no benefit for delayed AMP, this practice was used in the current setting and is still common in many institutions [15]. Moreover, AMP extended for 5 days may favour the emergence of multiply resistant pathogens [16]. Even the administration of correctly timed antimicrobial agents did not lower the infection rate in this study effectively, probably because AMP was not active against the pathogens encountered (Fig. 2).

Currently *c.* 700 million individuals live in sub-Saharan Africa, with a high percentage having access to only primary healthcare facilities. The results of the present study underline the importance of conducting further studies in this area, and of establishing surveillance programmes to allow the formulation of international guidelines that take regions with limited resources into account.

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RESEARCH NOTE

Effectiveness and nephrotoxicity of colistin monotherapy vs. colistin–meropenem combination therapy for multidrug-resistant Gram-negative bacterial infections

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ABSTRACT

A retrospective cohort study evaluated the effectiveness and nephrotoxicity of intravenous colistin monotherapy vs. colistin–meropenem combination therapy for patients with multidrug-resistant Gram-negative bacterial infections. Fourteen patients received intravenous colistin monotherapy and 57 received colistin–meropenem. No significant differences were found concerning clinical response of the infection (12/14 (85.7%) vs. 39/57 (68.4%), p 0.32) and development of nephrotoxicity (0/14 (0%) vs. 4/57 (7%), p 0.58). A favourable association was revealed between survival and treatment with colistin monotherapy compared to colistin–meropenem (0/14 (0%) vs. 21/57 (36.8%) deaths, p 0.007), even after adjusting for the variables for which significant differences were found.

Keywords Colistin monotherapy, combination therapy effectiveness, Gram-negative infection, multidrug resistance, nephrotoxicity

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Most recent clinical studies with polymyxins have reported data concerning the clinical outcome for patients treated with combinations of polymyxins and various other antimicrobial agents [1–5]. However, data concerning the comparative effectiveness and toxicity of colistin monotherapy vs. colistin–β-lactam combination therapy in patients other than those with cystic fibrosis are lacking.

A retrospective cohort study was conducted at the tertiary-care Henry Dunant hospital in Athens, Greece. The study was approved by the Institutional Review Board of the hospital. Patients with infections caused by multidrug-resistant Gram-negative bacilli who were hospitalised during the period October 2000 to May 2005 and were managed with intravenous colistimethate sodium were identified from the pharmacy electronic databases and included in the study. Two physicians (PIR and SKK) reviewed the patients' records and classified the outcomes. Patients were excluded from further analysis if they had received intravenous colistin therapy for <72 h. This group of patients was compared with patients treated concomi-