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Review

Systemic antimicrobial prophylaxis in burn patients: systematic review

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SUMMARY

Objective: To review studies of systemic antibiotic prophylaxis in burn patients.
Methods: Electronic databases were searched for human clinical trials performed between 1966 and 2016 that compared prophylactic systemic antibiotics with placebo or no intervention.
Results: Nineteen trials met the selection criteria. Early postburn prophylaxis was assessed in non-severe burn patients (six trials) and severe burn patients (seven trials). Antimicrobial prophylaxis showed no effectiveness for the prevention of toxic shock syndrome or burn wound infection (Grade 1C), but could be useful in patients with severe burns and requirement for mechanical ventilation (Grade 2B). Perioperative prophylaxis was assessed in six trials. Antimicrobial prophylaxis during resection of devitalized tissue is of no benefit in most burn patients (Grade 2B); however, there is insufficient evidence to make a recommendation for patients with extensive burns. Antibiotic prophylaxis may also be effective in preventing split-thickness skin graft infections in selected procedures (Grade 2B).
Conclusions: The available evidence does not support the role of systemic antibiotic prophylaxis in the management of the majority of burn patients. Nevertheless, it may be useful in patients with severe burns who require mechanical ventilation, and in selected split-thickness skin grafting procedures.

Introduction

Nosocomial infections are among the most important and potentially serious complications in severe burn patients [1–3]. Burn wounds provide an ideal medium for bacterial proliferation and a portal of entry into the bloodstream. Epithelial barrier loss, hypermetabolic/hypercatabolic states and immunosuppression predispose burn patients to infections [4]. Moreover, the support of vital organs requires the use of invasive procedures that undermine natural defence mechanisms. Nosocomial infection rates, including intravascular-catheter-related infections and ventilator-associated pneumonia, are higher in burn units than other medical or surgical units [5].

As nosocomial infections in burn patients are prevalent and dangerous, systemic antibiotic prophylaxis is often considered, alongside other infection prevention and control interventions. However, the use of prophylaxis has been questioned because there is controversy about the effectiveness of the intervention, and whether any benefits of prophylaxis outweigh the risk

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of harm, such as drug toxicity and development of multi-drug resistance [1,6]. For this reason, many recommendations for management do not include systemic antimicrobial prophylaxis [7—10], limit its use to the perioperative period [1,11,12] or advise explicitly against its use [13—18].

A recent meta-analysis showed clearly that the use of systemic antibiotic prophylaxis after burn injury was beneficial, lessening pneumonia mortality and burn wound infections [19]. However, great heterogeneity among burn patient populations, types of antibiotics used as prophylaxis, and stages of burns obfuscate the issue regarding when antibiotic prophylaxis may be effective in clinical practice. A Cochrane review concluded that the benefits of prophylaxis in preventing burn wound infections was unclear [15]. However, highly restrictive inclusion and exclusion criteria left very few studies for analysis in the Cochrane review.

The aim of this review was to seek evidence for the effectiveness of systemic antibiotic prophylaxis in burn patients, taking account of the type of antibiotic, different patient populations and different surgical procedures.

Materials and methods

Search strategy

Electronic databases (PUBMED, EMBASE) were searched with no restriction on language, sex or age; publications between 1966 and 2016 were included. The search terms were 'burns' or 'thermal injury' and the keywords were 'antibiotic prophylaxis', 'bacteremia', 'infection', 'sepsis' and 'toxic shock syndrome'. Additional publications were identified by evaluating the reference lists of studies identified in the original search. Two reviewers searched and screened titles and abstracts from relevant studies. Appropriate trials were analysed based on the full text using a standardized data extraction form.

Selection

Inclusion and exclusion criteria were established before reviewing abstracts and articles. Randomized controlled trials and non-randomized human clinical trials that recruited inpatients with burn injuries [any total body surface area (TBSA) or burn degree, with or without inhalation injury] were included. The intervention assessed was antibiotic systemic prophylaxis vs placebo or no treatment. Prophylaxis was defined as the administration of systemic antibiotics to patients without clinical or documented infection, administered by intravenous, intramuscular or gastrointestinal routes. Trials were excluded if at least one antibiotic was not administered systemically (non-absorbable antibiotics administered enterally or topical antibiotics applied to wounds). Antibiotics could be administered at any time after hospital admission.

Data extraction

Data from the studies were extracted using standardized and summarized forms using a data extraction sheet.

The following data were sought from each study and reported in a data extraction form: authors; year of study; country where the study was performed; study design; type of population included; number of patients in each arm; specific antimicrobials used and routes; burned surface (% of TBSA), full-thickness burns, inhalation injury, and time postburn.

Any discrepancies were resolved by consensus among the reviewers.

Quality assessment

The quality of evidence and strength of recommendation of these guidelines were based on the GRADE system [20]. The GRADE system classifies the evidence as high (Grade A), moderate (Grade B), low (Grade C) or very low (Grade D). The grade may be decreased due to limitations in implementation, inconsistency or imprecision of the results, evidence obtained by an indirect method, and possible errors reported.

Analysis

Where possible, study results were stratified to allow subgroups as follows:

- Prophylaxis period: 'early postburn' was considered as the period from admission to five days postburn. 'Perioperative' was stratified into wound cleaning or resection and skin grafting.
- Severity of burns: burns involving less than 20% of TBSA and burns involving more than 20% TBSA.
- Age of participants: children (age 0—18 years) and adults (age >18 years)

The end points were mortality, wound infection, toxic shock syndrome, pneumonia and bacteraemia.

Results

The search yielded 53 publications related to the subject, but only 19 met the inclusion criteria [i.e. systemic antibiotics were compared with control group (no intervention or placebo)]. The trials were published between 1982 and 2016. There were 12 randomized prospective trials, three before and after studies comparing consecutive periods with and without the intervention, and four retrospective studies. Systemic antibiotics were used in all trials, but one trial added immunoglobulins and two trials also employed selective digestive decontamination (SDD). Twelve trials assessed early postburn prophylaxis, six trials assessed perioperative prophylaxis, and one trial assessed both. Eight trials were conducted in children and 10 trials were in adults; one trial included children and adults (Table I).

Early postburn prophylaxis

Six of the 13 studies were performed on non-severe burn patients and seven studies were performed on severe burn patients [21—33]. Of the six studies on non-severe cases, three compared antibiotic prophylaxis with no intervention in consecutive periods; all of the studies were in paediatric burn cases [21—23]. Penicillin, erythromycin or flucloxacillin was used as prophylaxis for three to five days after burn injury. The largest trial included 917 patients accrued over a six-year period; the average TBSA was 10% [21]. Another study included 269 patients accrued over a three-year period [22].