Prophylactic antibiotics for burns patients: systematic review and meta-analysis
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CRD summary
This generally well-conducted review concluded that prophylaxis with systemic antibiotics had a beneficial effect in burns patients. The authors rightly acknowledged that the reliability of the results may be compromised given the paucity of good quality evidence.

Authors' objectives
To evaluate the use of systemic prophylactic antibiotics in burns patients in perioperative and general settings.

Searching
PubMed, EMBASE, the Cochrane Library and LILACS were searched without language restrictions. Search terms were reported. Search dates spanned 1966 to October 2009. Reference lists of included studies and conference proceedings of five societies were also searched.

Study selection
Randomised controlled trials (RCTs) in patients with any degree or location of burn, with or without inhalation injury, that compared the use of prophylactic antibiotics (administered via any route at any time after admission) with placebo or no treatment, were eligible for inclusion. Trials using non-antibiotic antimicrobials or antifungals were only included if these were administered in all arms of the trial. Comparisons of different antibiotic regimens were excluded. The primary outcome assessed was all-cause, in-hospital, mortality.

The included trials evaluated a wide range of prophylactic regimens. The duration of antibiotic prophylaxis was between one and 14 days, or based upon wound/graft healing or graft application. Where reported, the mean age of participants ranged from 1.5 to 48.2 years, the mean proportion of body surface burnt ranged from 8 to 67%, the proportion with third degree burns from 19 to 100%, and inhalation injury from 0 to 100%.

Two independent reviewers performed the study selection.

Assessment of study quality
Study quality was assessed in terms of randomisation, allocation concealment, blinding, outcomes assessed and their definitions, the use of an intention-to-treat analysis, and the surveillance of cultures for resistance. The two independent reviewers graded each criterion as adequate, unclear, not described, or inadequate.

Data extraction
Data were extracted on a per protocol basis, in order to calculate relative risk (RR) for all-cause, in-hospital, mortality, and rate ratios (ratio of events per patient day), along with corresponding 95% confidence intervals (CI), for bacteraemia, pneumonia, wound infection, duration of hospital stay, fungal and specific bacterial infections, resistance, and adverse events. Authors were contacted for missing data.

Two independent reviewers performed the data extraction; disagreements were resolved by a third reviewer.

Methods of synthesis
Pooled risk and rate ratios, with 95% confidence intervals, were calculated using a fixed-effect (Mantel-Haenszel method) meta-analysis, stratified by antibiotic regimen. Number needed-to-treat (NTT) was calculated. Heterogeneity was assessed using the $X^2$ ($p<0.1$) and $I^2$ (>50%) statistics. Where statistically significant heterogeneity was observed, a narrative synthesis was presented. Sensitivity analyses were conducted to assess the impact of adequate allocation concealment.

Results of the review
Seventeen trials met the inclusion criteria (37 comparison arms; n=1,113 patients; range 15 to 149 patients). Of the 17 trials, five reported adequate randomisation, six adequate allocation concealment, seven reported being double blind, 14 used an intention-to-treat analysis for all outcomes on a patient basis, and 14 reported some form of surveillance.

Systemic general antibiotic prophylaxis significantly reduced all-cause, in-hospital, mortality (RR 0.54, 95% CI 0.34 to 0.87; NNT 8, 95% CI 5 to 33; five RCTs), and pneumonia (RR 0.52, 95% CI 0.33 to 0.83; two RCTs), but not wound infection (five RCTs) or bacteraemia (four RCTs). The benefit in terms of mortality was increased when only trials with adequate allocation concealment were considered (RR 0.42, 95% CI 0.22 to 0.79; three RCTs). Perioperative prophylaxis did not significantly reduce the incidence of these outcomes. Significant heterogeneity was not observed for any analysis.

Results for topical, local and non-absorbable prophylactic regimens, adverse events, resistance rates, individual bacterial infections, and fungal infections were also reported.

**Authors' conclusions**
Prophylaxis with systemic antibiotics had a beneficial effect in burns patients, but the methodological quality of the available evidence was weak.

**CRD commentary**
The review addressed a clear research question, supported by appropriate inclusion criteria. Several relevant sources were searched without language restrictions, and attempts to identify unpublished data were made. Publication bias was not assessed. Each stage of the review was conducted in duplicate, reducing the risk of error and bias. Appropriate criteria were used to assess trial quality. Most of the included trials were small and had methodological weaknesses that could impact on the reliability of their results. Appropriate methods of synthesis were employed. This was a generally well-conducted review, but the authors rightly acknowledged that the reliability of the pooled results may be compromised by the paucity of good quality data.

**Implications of the review for practice and research**
**Practice:** The authors stated that the results of the review contrast with current guidelines, which recommend only perioperative prophylactic antibiotics.

**Research:** The authors stated that future trials should: assess a full selective decontamination regimen; limit systemic administration to the first 4 days; investigate perioperative prophylaxis targeting Gram positive bacteria; ensure consistent, optimal, care across treatment arms; use effective infection control practices to avoid cross-contamination; be methodologically sound; use surveillance cultures; record adverse events; be powered to assess all-cause mortality; and use a fixed time point for assessing mortality relevant to the assessment of benefits and harms.

**Funding**
None.

**Bibliographic details**

**PubMedID**
20156911

**DOI**
10.1136/bmj.c241

**Original Paper URL**
http://www.bmj.com/cgi/content/abstract/340/feb15_1/c241
Other URL
http://ukpmc.ac.uk/articlerender.cgi?artid=1971982&rendertype=abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Antibiotic Prophylaxis; Burns /drug therapy /mortality; Humans; Randomized Controlled Trials as Topic; Treatment Outcome; Wound Infection /drug therapy /mortality

AccessionNumber
12010001208

Date abstract record published
03/03/2010

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.