The uses of heparin to treat burn injury
Oremus M, Hanson M, Whitlock R, Young E, Gupta A, Dal Cin A, Archer C, Raina P

CRD summary
This review assessed the efficacy and safety of heparin in the treatment of burns. The authors concluded that there was insufficient evidence to support the use of heparin, but that further specific randomised trials should be conducted. This is a generally well-conducted review and the conclusions are likely to be reliable.

Authors' objectives
To assess the evidence for the benefits and harms of heparin in thermal injury care in relation to different methods of application, the effect of different types or degrees of burn, and comparison with current treatment which does not include heparin; and to identify contraindications for the use of heparin.

Searching
MEDLINE (from 1966), EMBASE (from 1980), CINAHL (from 1982), the Cochrane CENTRAL Register (from 1995), Web of Science (from 1976) and BIOSIS Previews (from 1976) were searched. Literature in the European and U.S. patent offices was also searched, members of the technical expert panel and partner organisation were contacted to identify additional studies (including unpublished studies), and the references of included articles were checked.

Study selection
Study designs of evaluations included in the review
Studies with a comparison group were eligible for inclusion. The included studies were randomised controlled trials (RCTs), non-randomised comparison studies and cohort studies.

Specific interventions included in the review
Studies of any formulation of heparin, administered by any route, were eligible for inclusion. The included studies administered heparin topically, subcutaneously, as an infusion, intravenously and as an aerosol.

Participants included in the review
Studies of patients with any type, grade or size of burn were eligible for inclusion. In most studies which reported data the majority of the patients were men. The included studies had adult, paediatric and mixed populations, and assessed patients with first-, second- and third-degree burns, the aetiology of which included flame, inhalation injury and ‘thermal’ injury.

Outcomes assessed in the review
Studies reporting any of the following outcomes were eligible for inclusion: requirement for surgical procedure; pain; mortality; length of hospital stay; scarring; decrease in range of motion, function or activities of daily living; respiratory measures; thrombosis and embolism; complications such as infection or bleeding; rehabilitation; quality of life; and psychiatric adjustment.

How were decisions on the relevance of primary studies made?
Two reviewers assessed the studies for inclusion in the review, and any disagreements were resolved through consensus.

Assessment of study quality
Two reviewers assessed the studies for validity and any disagreements were resolved through consensus. The assessment used the criteria of the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies, which includes an assessment of selection bias, study design, confounding, blinding, data collection methods, withdrawals and drop-outs, and analysis.
Data extraction
The authors stated that the data were abstracted into standardised forms, but did not state how many reviewers performed the abstraction. Data were abstracted on participant characteristics, aspects of study design and primary outcomes.

Methods of synthesis
How were the studies combined?
The studies were presented in a detailed narrative synthesis. A meta-analysis of some included studies is presented elsewhere (Oremus et al 2007, see Other Publications of Related Interest field below for bibliographic details).

How were differences between studies investigated?
Differences between the studies were discussed in the narrative synthesis in terms of study design and validity, method of application of heparin and outcomes reported. Differences were also evident from the data tables.

Results of the review
Eighteen studies (n at least 1,061) were included in the review. Five studies were RCTs, 2 were non-randomised comparison studies and 11 were cohort studies. Some studies did not report numbers of patients.

The overall quality of the included studies was poor.

Effectiveness and safety.
One poor-quality RCT (n=50) found improvements in mortality, infection rate, graft healing and eschar separation in the heparin group compared with the standard therapy group. A second RCT (n=64) found a significant reduction in primary scarring in the topical heparin group compared with the standard therapy group; there were concerns about the validity of this trial. A third RCT (n=100) found that the heparin group had significantly shorter hospital stays than the control group; there were concerns about the validity of this trial also.

Authors' conclusions
There is no strong evidence that heparin improves clinical outcomes in the treatment of burn injury, nevertheless the poor-quality evidence available suggests some benefit, indicating a requirement for further research.

CRD commentary
The review question and the inclusion criteria were clear. The authors searched a number of relevant databases and made substantive efforts to identify unpublished studies, thereby reducing the risk of publication bias. The review methods, with the possible exception of the data extraction process, also aimed to reduce the risk of reviewer error and bias. The validity of the included studies was assessed using appropriate criteria and the reliability of the data was considered in the data synthesis. The decision to employ a narrative synthesis appeared appropriate, and the authors' cautious conclusions reflect the results of the review and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any recommendations for practice.

Research: The authors recommended that two RCTs be conducted. The first would assess the application of topical heparin following skin graft in adult and adolescent patients, with outcomes including wound healing and scarring; the second would assess aerosolised heparin for the treatment of burn-related inhalation injury in adult and paediatric patients, with outcomes including reintubation rates and the duration of intensive care stay.

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