LETTER TO THE EDITORS

A SYSTEMIC REVIEW OF THE USES OF HEPARIN TO TREAT BURN INJURY

Dear Sirs

Last year I had the opportunity to participate in a review study conducted by McMaster University Evidence-based Practice Center, Hamilton, Ontario, Canada, to assess the evidence for using heparin in the treatment of burn injury or the complications of burn injury in adults and children. Principal Investigators were Mark Oremus, PhD and Mark Hanson, MD, Med, in addition to Gurvaneet Randhawa, MD, MPH, AHRQ (Agency for Healthcare Research and Quality) Task Order Officer of the US Department of Health and Human Services. Other investigators included Richard Whitlock, MD, MSc, Ed Young, PhD, Alok Gupta, MS, Arianna Dal Cin, MD, BSc, FRCSC, Carolyn Archer, MSc, and Parminder Raina, PhD. A technical expert panel was consulted during the course of this study. In addition to myself, the panel included David Herndon, MD, Leo Klein, MD, PhD, Ján Koller, MD, CSc, Michael J. Saliba Jr., MD, Glenn Warden, MD, MBA, and Steven E. Wolf, MD.

Key questions

Two questions were addressed by the review study:

1. – What is the evidence for the benefits and harms of heparin use in thermal injury care?
   – Does the method of application make a difference?
   – Do the outcomes vary by the type or degree of burn?
   – How do the outcomes of burn treatment with heparin compare to current treatment without heparin?
2. What are the contraindications of heparin use in burns?

Data Sources

The following databases were searched: MEDLINE® (1966-current), EMBASE (1980-current), Cumulative Index to Nursing & Allied Health (CINAHL) (1982-current), The Cochrane Central Database of Controlled Trials (1995-current), Web of Science (1976-current), and BIOSIS (1976-current). Additional data sources included the U.S. and European Patent Offices, technical experts, the partner organization, and reference lists.

Review methods

Studies identified from the data sources went through two levels of title and abstract screening. Passing studies advanced to full text screening. Studies that met the full text screening criteria were abstracted. Criteria for abstraction included publication in any language, human patients of any age, and burns of any type, grade, or total body surface area. All formulations of heparin, and all application methods (e.g., topical, subcutaneous), were eligible for inclusion in the report. Abstracted studies required a comparison group. Outcomes of interest included mortality, pain, length of stay in hospital, thrombosis and emboli, psychiatric adjustment, and adverse effects (e.g., bleeding).

Results

Nineteen articles from 18 unique studies were abstracted and included in this report. In these articles, there were multiple uses of heparin to treat burns (e.g., wound healing, inhalation injury, sepsis, pain). However, the overall quality of the articles was weak. Examples of weakness included unclear or inappropriate treatment allocation, no blinding, no control of confounding, poorly defined burn characteristics (e.g., thickness), unclear duration of treatment, incomplete description of heparin treatment, and use of inadequately described or invalid outcome measures.

Overall, the evidence from these weak articles was insufficient to determine whether the effectiveness of heparin to treat burn injury was different from the effectiveness of other treatments, or whether treatment effectiveness varied according to (a) the method of applying heparin to (b) burn etiology.

1. Based on the small number of identified studies (only 19 studies met the eligibility criteria), and the poor quality of evidence, it cannot be determined if patients treated with heparin have better outcomes (e.g., decreased pain, improved wound healing) compared to patients receiving standard treatments.
2. The types of burns for which heparin could potentially provide benefit cannot be determined because the studies provided incomplete information on the cause, type, and extent of burns.
3. There is no evidence to determine the preferred route (intravenous, subcutaneous, or topical) for administering heparin for treatment of burns.

4. Four studies identified burn patients who should not receive heparin, including patients with bleeding disorders, active bleeding or a history of bleeding, liver disease, kidney disease, or allergy to heparin. Heparin use is contraindicated in these patients.

**Conclusion**

There is no strong evidence in the 19 abstracted articles to suggest that heparin should be used in the treatment of burn injury on account of its non-anticoagulant wound healing properties. There is no strong evidence that the use of heparin did lead to better clinical outcomes in burn care than other treatments. However, since the lack of evidence is largely a function of the poor design and quality of the available studies and the poor quality of published articles, further research is needed to investigate the potential uses of heparin in the treatment of burn injury. Additional well-designed research into heparin use in burn care is necessary.

The Evidence Report has been posted to the AHRQ Web site. It is available at http://www.ahrq.gov/clinic/tp/heparin.htm. Print copies can be obtained free of charge from the AHRQ Publications Clearinghouse at ahrqpubs@ahrq.hhs.gov or 1-800-358-9295.

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