Heparin versus citrate for anticoagulation in critically ill patients treated with continuous renal replacement therapy

Tillman J

CRD summary
The author concluded that regional citrate anticoagulation was associated with increased haemofilter circuit survival time and lower risk of bleeding, compared with systemic heparin anticoagulation in continuous renal replacement therapy for patients with acute renal failure. The reliability of this conclusion is unclear, given restrictions in the search strategy, and failure to minimise errors and bias in the review process.

Authors' objectives
To compare systemic heparin and regional citrate anticoagulation in continuous renal replacement therapy for patients with acute renal failure.

Searching
The Cochrane Library, MEDLINE from 1950, and EMBASE from 1999 were searched; search terms were reported. The journals Critical Care Medicine and Intensive Care Medicine were handsearched, reference lists of included articles were scanned, and experts were contacted to locate further studies. The included studies were limited to those published in English, and available at (or via) the library at King's College, London.

Study selection
Randomised controlled trials (RCTs) of patients, who were aged at least 18 years, had acute renal failure, and were in intensive care units, that used similar protocols for anticoagulation with regional citrate or systemic heparin, were eligible for inclusion. The primary outcome of interest was haemofilter circuit survival time. The secondary outcome of interest was the risk of bleeding. The included trials aimed to achieve an ionised calcium level below 0.3 mmol per litre following regional citrate, and activated partial thromboplastin time between 45 to 80 seconds following systemic heparin.

Trials were selected by one reviewer (the author).

Assessment of study quality
An established critical appraisal checklist was used and, where data were available, aspects of randomisation, blinding, study power, and follow-up were assessed.

This was carried out by one reviewer (the author).

Data extraction
For the primary outcome, data were extracted on median circuit survival time and analysed using Kaplan-Meier survival curves. For risk of bleeding, data were extracted on the units of packed red cells transfused per day of continuous venovenous haemofiltration. Ninety-five percent confidence intervals, the interquartile range, and p values were presented.

Authors were contacted for further information, where necessary. The data extraction was carried out by one reviewer (the author).

Methods of synthesis
Trials were synthesised narratively and differences were presented in tables and in the text.

Results of the review
Three crossover RCTs were included in the review (98 patients; 270 haemofilter circuits). The method of randomisation was described, and single blinding was applied in all three RCTs. One RCT reported a power calculation and follow-up to hospital discharge or death was reported in one RCT.
Two RCTs (50 patients; 128 haemofilter circuits) reported statistically significant differences in circuit survival time (p≤0.01 and p=0.0007) in favour of regional citrate anticoagulation. The third RCT showed similar survival times between groups. All three RCTs reported an increased risk of bleeding in the systemic heparin group, which resulted in a higher transfusion rate; two of these were statistically significant (p=0.01 and p=0.0008).

**Authors’ conclusions**
Regional citrate anticoagulation was associated with an increased haemofilter circuit survival time and lower risk of bleeding when compared with systemic heparin anticoagulation in continuous renal replacement therapy for patients with acute renal failure.

**CRD commentary**
The review question was clear and this was supported by detailed inclusion criteria, which appear to be reproducible. The search strategy included some relevant sources, but the restriction to published English-language articles means that important trials may have been missed and language and publication biases could not be ruled out. The review process was conducted by the author, and (as acknowledged in the paper) the absence of attempts to minimise errors and bias was a potential threat to the reliability of the findings.

Appropriate items were used to assess the quality of the included trials, but the full results were not presented. The chosen method of synthesis was appropriate for the few trials. Few characteristics of the included patients were reported, which limited the generalisability of the review findings. One of the included trials received industry sponsorship.

These potential methodological limitations, together with those acknowledged by the author, mean that the reliability of the conclusion is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that regional citrate should be used with caution, in clinical practice, and it should be assessed on an individual patient basis.

**Research:** The authors stated that more rigorous research was required.

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**AccessionNumber**
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.