Histidine-tryptophan-ketoglutarate solution vs. University of Wisconsin solution for liver transplantation: a systematic review

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CRD summary
The authors concluded that there were no differences between histidine-tryptophan-ketoglutarate solution and University of Wisconsin solution for liver transplantation outcomes, with the exception of bile production. The authors also concluded that their review may have been influenced by bias. This was generally a well-conducted review, and the authors' cautious conclusions are likely to be reliable.

Authors' objectives
To compare the efficacy and safety of histidine-tryptophan-ketoglutarate solution versus University of Wisconsin solution for liver transplantation.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched from inception to June 2006 for English language publications. Search terms were provided. Reference lists of relevant publications were also checked for additional studies.

Study selection
Full-text papers of randomised controlled trials (RCTs) and cohort studies that compared histidine-tryptophan-ketoglutarate solution and University of Wisconsin solutions in deceased donor liver transplantation or living related liver transplantation were included in the review. Studies of registry data and in-vitro or animal studies were excluded from the review.

Primary outcome measures were: patient survival rates, graft survival rates and acute rejection; liver function after transplantation; and biliary complications. Secondary outcome measures included biochemical indicators after transplantation, bile production after transplantation, and other complications.

Most included studies used deceased donor liver transplantation, with one study using both living related liver transplantation and deceased donor liver transplantation. Where reported, the average age of donors ranged from 30.8 to 51.8 years, while the average age of recipients ranged from 3.3 to 59.9 years. Other characteristics of donors and recipients were also reported. Volumes of solutions evaluated were presented, as well as the method of perfusion. Where reported, duration of follow-up ranged from two months to five years.

Two reviewers independently selected the studies for inclusion.

Assessment of study quality
Quality was based on the following criteria: method of randomisation, allocation concealment, blinding, baseline comparability, loss to follow-up, intention-to-treat analysis, and analysis of bias. A maximum score that could be obtained was 18.

Two reviewers independently assessed quality.

Data extraction
For dichotomous data, relative risks (RR) and 95% confidence intervals (CI) were calculated. For continuous data, the evidence was expressed as weighted mean differences (WMD) with 95% confidence intervals. Missing data were obtained by contacting trial authors.

Two reviewers independently extracted the data, and any discrepancies were resolved by a third reviewer.

Methods of synthesis
Where possible, meta-analyses examining pooled relative risks or weighted mean difference were performed using a
random-effects model when there was heterogeneity between studies, or a fixed-effect model if there was no heterogeneity. Heterogeneity was assessed using Cochran's Q statistic and the I² test. Data were reported separately for deceased donor liver transplantation and living related liver transplantation for each outcome.

**Results of the review**
Ten trials (1,200 patients) were included in the review: two RCTs (81 patients), six prospective cohort studies (607 patients), and two retrospective cohort studies (512 patients). The sample sizes ranged from 21 to 378 patients. The quality scores of the included studies ranged from 0 to 7.

There were no significant differences between histidine-tryptophan-ketoglutarate solution and University of Wisconsin solution for patient survival rates (RR 1.01, 95% CI 0.92 to 1.10; two trials; non-significant data from individual studies that could not be included in the meta-analysis were also reported), graft survival rates (RR 1.01, 95% CI 0.92 to 1.11; two trials; non-significant data from individual studies that could not be included in the meta-analysis were also reported), acute rejection, primary non-function, primary dysfunction, delayed graft function, and alanine aminotransferase and aspartate aminotransferase after transplantation. Bile production after deceased donor liver transplantation was significantly higher in the histidine-tryptophan-ketoglutarate solution group compared to the University of Wisconsin solution group (WMD 38.06, 95% CI 18.65 to 57.47).

**Cost information**
Of four trials, three reported that the cost of histidine-tryptophan-ketoglutarate solution was lower than University of Wisconsin solution, and one trial reported costs were equal between the solutions.

**Authors' conclusions**
There was no statistical significant difference in the effects of histidine-tryptophan-ketoglutarate solution and University of Wisconsin solution, with the exception of bile production. However, the systematic review may have been influenced by bias.

**CRD commentary**
The review addressed a clear question and was supported by appropriate inclusion criteria. The search was restricted to English language publications, so some studies may have been missed, introducing the potential for language and publication biases. Validity was adequately assessed, and details regarding the number of reviewers involved were reported, limiting reviewer error and bias. Comprehensive details of the included studies were provided, and appropriate methods were used to pool the results (where possible) and to investigate statistical heterogeneity. This was generally a well-conducted review, and the authors' cautious conclusions are likely to be reliable.

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

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that adequately powered RCTs with longer follow-up periods that compare histidine-tryptophan-ketoglutarate and University of Wisconsin solutions are needed.

**Funding**
China Postdoctoral Science Foundation No. 20060390327; National Basic Research Program of China No. 2003CB515504; Natural Science Foundation of China No. 30500486; Program for Changjian Scholars and Innovative Research Team in University, Ministry of Education, PR China.

**Bibliographic details**

**PubMedID**
17665493

**DOI**
10.1002/lt.21208
Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Adenosine /chemistry /pharmacology; Allopurinol /chemistry /pharmacology; Animals; Clinical Trials as Topic; Cohort Studies; Glucose /chemistry /pharmacology; Glutathione /chemistry /pharmacology; Humans; Insulin /chemistry /pharmacology; Liver /pathology; Liver Transplantation /economics /instrumentation /methods; Mannitol /chemistry /pharmacology; Organ Preservation /adverse effects /methods; Organ Preservation Solutions /chemistry /pharmacology; Perfusion; Potassium Chloride /chemistry /pharmacology; Procaine /chemistry /pharmacology; Raffinose /chemistry /pharmacology; Treatment Outcome

AccessionNumber
12008103565

Date bibliographic record published
23/12/2008

Date abstract record published
21/10/2009

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.