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[Intervention Review]

Pharmacological interventions for ischaemia reperfusion injury in liver resection surgery performed under vascular control

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ABSTRACT

Background

Vascular occlusion used during elective liver resection to reduce blood loss results in significant ischaemia reperfusion (IR) injury. This in turn leads to significant postoperative liver dysfunction and morbidity. Various pharmacological drugs have been used in experimental settings to ameliorate the ischaemia reperfusion injury in liver resections.

Objectives

To assess the relative benefits and harms of using one pharmacological intervention versus another pharmacological intervention to decrease ischaemia reperfusion injury during liver resections where vascular occlusion was performed during the surgery.

Search methods

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register*, the *Cochrane Central Register of Controlled Trials (CENTRAL)* in The Cochrane Library, *MEDLINE*, *EMBASE*, and *Science Citation Index Expanded* until January 2009.

Selection criteria

We included randomised clinical trials, irrespective of language or publication status, comparing one pharmacological agent versus another pharmacological agent during elective liver resections with vascular occlusion.

Data collection and analysis

Two authors independently identified trials for inclusion and independently extracted data. We analysed the data with both the fixed-effect and the random-effects models using RevMan Analysis. We planned to calculate the risk ratio (RR) or mean difference (MD) with 95% confidence intervals (CI) based on intention-to-treat analysis or available case analysis. However, all outcomes were only reported on by single trials, and meta-analysis could not be performed. Therefore, we performed Fisher's exact test on dichotomous outcomes.

Main results

We identified a total of five randomised trials evaluating nine different pharmacological interventions (amrinone, prostaglandin E1, pentoxifylline, dopexamine, dopamine, ulinastatin, gantaile, sevoflurane, and propofol). All trials had high risk of bias. There was no significant difference between the groups in mortality, liver failure, or perioperative morbidity. The ulinastatin group had significantly lower postoperative enzyme markers of liver injury compared with the gantaile group. None of the other comparisons showed any difference in

any of the other outcomes. However, there is a high risk of type I and type II errors because of the few trials included, the small sample size in each trial, and the risk of bias.

Authors' conclusions

Ulinastatin may have a protective effect against ischaemia reperfusion injury relative to gantaile in elective liver resections performed under vascular occlusion. The absolute benefit of this drug agent remains unknown. None of the drugs can be recommended for routine clinical practice. Considering that none of the drugs have proven to be useful to decrease ischaemia reperfusion injury, such trials should include a group of patients who do not receive any active intervention whenever possible to determine the pharmacological drug's absolute effects on ischaemia reperfusion injury in liver resections.

PLAIN LANGUAGE SUMMARY

No clear evidence that any pharmacological intervention is better than another in decreasing ischaemia reperfusion injury in liver resections

Elective liver surgery undertaken for a variety of reasons may require occlusion of the blood supply to the liver in order to reduce bleeding from the cut liver surface. This temporary interruption of blood supply causes liver damage for a variety of reasons. In experimental studies many drugs have shown some promise in decreasing liver damage caused by the occluded blood supply. The relative benefits of pharmacological agents compared with one another is unknown in the setting of liver damage caused by occlusion of the blood supply to the liver during surgery. We identified a total of five randomised trials evaluating nine different pharmacological interventions (amrinone, prostaglandin E1, pentoxifylline, dopexamine, dopamine, ulinastatin, gantaile, sevoflurane, and propofol). All trials had risk of bias ('systematic error') and risk of play of chance ('random errors'). There was no significant difference between the groups in mortality, liver failure, or postoperative complications. The ulinastatin group had significantly lower postoperative enzyme markers of liver injury compared with the gantaile group. None of the remaining pharmacological agents showed any significant difference in any of the remaining outcomes. However, there is a high risk of type I (erroneously concluding that an intervention is beneficial when it is actually not beneficial) and type II errors (erroneously concluding that an intervention is not beneficial when it is actually beneficial) because of the few trials included, the small sample size in each trial, and the risk of bias. Ulinastatin may have a protective effect relative to gantaile against liver injury sustained during elective liver surgery involving blood supply occlusion. The absolute benefit of ulinastatin in this setting remains unknown. None of the pharmacological agents can be recommended for routine clinical practice. Considering that none of the agents have been proven to be useful to decrease ischaemia reperfusion injury, such trials should include a group of patients who do not receive any active intervention whenever possible to determine their absolute effect on ischaemia reperfusion injury in liver resections.