

Pharmacological Preconditioning With Desflurane in Liver Surgery

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Study protocol

Objective

Ischemia-reperfusion injury is a major concern for hepatectomies. During hepatic resection the surgeon implements ischemia through inflow occlusion (Pringle maneuver) to prevent excessive and life threatening hemorrhage. Though, the pathophysiologic events occurring during ischemia are further promoted upon reperfusion. This entity may lead to liver failure and even Multiple Organ Disease Syndrome. Preconditioning has been identifying as a measure tackle ischemia – reperfusion injury in many organs. It refers to the exposure of a tissue at ischemic conditions to mitigate the subsequent reaction at re-exposure. Pharmacological preconditioning with the volatile anesthetic sevoflurane has been studied and proved beneficial for liver surgery. Our objective is to investigate the potential hepatoprotective role of another volatile anesthetic, desflurane. As sevoflurane has some properties that have been characterized as hepatotoxic, we have posed the hypotheses that desflurane may provide a beneficial advantage over ischemia – reperfusion injury.

Design

This is a randomized, double blind, clinical trial. Participants were allocated 1:1 using electronic software to receive either pharmacological preconditioning with desflurane (Group Desflurane, D) or no intervention (Group Control, C). 46 adult patients presented for elective hepatic excision of two or more liver segments, were recruited in the study. Informed consent was obtained by all patients. Exclusion criteria were presence of Hepatitis B, Hepatitis C or Human immunodeficiency virus infection, pregnancy, autoimmune disease, inflammatory bowel disease, liver cirrhosis, liver ablation therapy.

Methods

All patients were managed by the same surgical team and the same anesthesiologist. Only the anesthesiologist was aware of the group assigned to each patient. The surgeon was blinded as to the intervention and was asked to inform the anesthesiologist 30 minutes before the initiation of ischemia. At that point, the propofol infusion used to maintain anesthesia was substituted by desflurane to achieve pharmacological preconditioning for 30 minutes. After that interval, propofol infusion was reinitiated and desflurane ceased. Upon preoperative visit and at 30 minutes post reperfusion blood samples were taken for MMP 2, 9 and TIMP 1, 2 measurement. Specimens for histological test were taken before inflow occlusion and 30 minutes post reperfusion.

Statistical Analysis Plan

The SPSS v.22.0 software (SPSS, Inc., Chicago, Ill, USA) was utilized for all statistical analyses. . The significance level was set at $p \leq 0.05$ for the tested hypotheses. All data distributed normally according to Kolmogorov - Smirnov test. Independent samples T-test and independent samples Mann-Whitney test were performed for group (investigation and control) comparisons. The Fisher's Exact test and X^2 test were used for comparisons of groups relative to qualitative variables. Data for biological markers were explored within the frame of General Linear Models with the ANOVA method according to the model which involves one factor between patients (factor "Group" with two levels) and one factor within patients (factor "Time" with five levels, with repeated measures). Means' comparisons were done with the Least Significant Difference (LSD) criterion.