

# First Demonstration of the Effects of Remote Per- and Postconditioning on Ischemia and Reperfusion Induced Hepatic Injury

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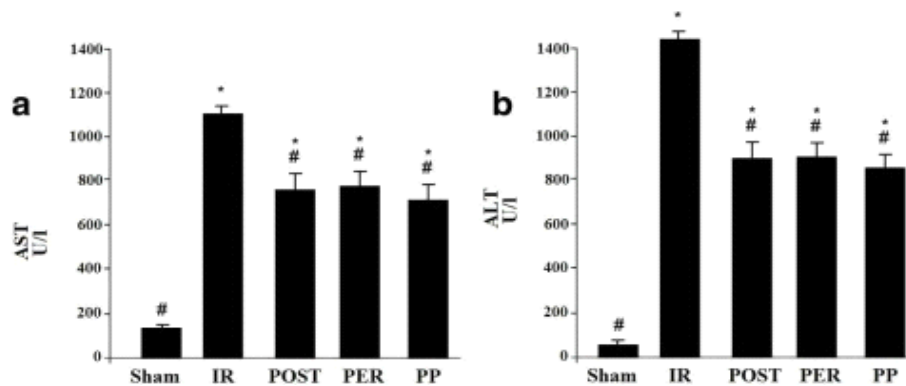
**Abstract:** Ischemia and reperfusion is a very frequently phenomenon that is presented in many clinical situations like in liver transplantation as well as in traumatic situation of these organs. One way of minimizing this injury is the remote ischemic preconditioning, described in myocardial ischemia, in which brief nonlethal cycles of ischemia and reperfusion of the arm or leg are applied remotely during index ischemia. Therefore, this current study aims to compare the effects of preconditioning and postconditioning on injury of ischemia and reperfusion in the liver.

**Keywords:** Transplantation, Liver failure, Reperfusion injury.

## INTRODUCTION

One of the most promising treatments for injuries from ischemia and reperfusion is ischemic conditioning that was described first as preconditioning, in 1986 [1], then as postconditioning, in 2003, and recently, as remote ischemic preconditioning, in 2007 [2]. The latter was described only in myocardial, cerebral and kidney ischemia. Studies on its effects on liver ischemia have not been reported so far. Therefore, the goal of this research is to evaluate the effects of this technique in protecting liver ischemia and reperfusion injury induced in rats [3].

Experiments were carried out on 25 Wistar rats, weighing from 270 to 300 g. These were randomly assigned into 5 groups (n=5). After anesthesia, the rats of sham group were subjected only to laparotomy and suture of abdominal wall. The rats of Ischemia and Reperfusion (IR) group were subjected to 1 hour of ischemia, by placing a microsurgical clamp in the hepatic triad that serves the left and median liver lobes, followed by 2 hours of free reperfusion. The rats from postconditioning ischemic group (POST) were subjected to the procedures of the IR group; however, after the period of index ischemia, 6 interspersed cycles of 10 seconds of ischemia and reperfusion were performed (total = 2 minutes), by application and withdrawal of the clamp. The



**Fig. (1).** Liver function indexes in the different groups of the experiment: (a) AST and (b) ALT. \*p<0.01 vs. sham group. \*\*p<0.01 vs. IR group. AST: Aspartate transaminase. ALT: Alanine transaminase. IR: Ischemia and reperfusion. POST: Post-conditioning. PER: Preconditioning. PP: Post and Preconditioning.

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rats from the remote ischemic preconditioning group (PER) were subjected to the procedures of the IR group. After the first 20 minutes of liver ischemia, 4 cycles of 5 minutes of remote ischemic preconditioning were performed (total = 40 minutes), by application and withdrawal (ischemia and

reperfusion) of a tourniquet on the animal's left posterior limb. The rats from the ischemic post and preconditioning groups (PP) were subjected, cumulatively, to procedures of PER and POST groups. At the end of reperfusion, a sample of blood was collected and aspartate transaminase (AST) and alanine transaminase (ALT) were measured.

Groups PER (AST:  $777.6 \pm 3.25\%$  / ALT:  $875.4 \pm 2.08\%$ ) and POS (AST:  $771.2 \pm 3.56\%$  / ALT:  $873 \pm 2.95\%$ ) were effective in the treatment of injuries from ischemia and reperfusion, showing an improvement in liver function. When the two techniques were simultaneously applied, in the PP group (AST:  $753.4 \pm 3.16\%$  / ALT:  $843 \pm 4.75\%$ ) the results were even better in absolute numbers. When groups PER, POST and PP were analyzed statistically among themselves by ANOVA test followed by Tukey test, there was no statistical relevance ( $p > 0.05$ ). However, when sham groups were compared (AST:  $144 \pm 2.46\%$  / ALT:  $63.4 \pm 6.93\%$ ) and IR (AST:  $1104.4 \pm 1.54\%$  / ALT:  $1414.6 \pm 1.25\%$ ) with all other groups, there was statistical significance ( $p < 0.01$ ), showing the success of the groups treated in this study Fig. (1).

Through the analysis of the data, it is possible to note that the remote ischemic preconditioning is an important and promising technique for the prevention of injury of liver ischemia and reperfusion. Its use is even more interesting

when taking into account the fact that this is a non-intrusive technique, unlike other ischemic conditionings. Preconditioning may be, within a short time, an important tool for attenuation of reperfusion injury in liver transplantation in humans.

#### CONFLICTS OF INTEREST

The authors confirm that this article content has no conflicts of interest.

#### ACKNOWLEDGEMENTS

None declared.

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