Centro: Saúde

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Titulo: **Oxidative and nitrosative stress markers in liver parenchyma of acute liver failure patients**

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RESUMO

Acute liver failure (ALF) is a severe acute inflammatory liver disease that has liver transplant as single therapeutic option. The extensive liver damage in ALF can be induced by several etiologies, whose classical symptoms are jaundice, encephalopathy and bleeding tendency developing abruptly. Reactive oxygen and nitrogen species, such as superoxide and nitric oxide (NO) generated by NADPH and inducible nitric oxide synthase are present in liver parenchyma and probably are involved in liver failure by recruitment of inflammatory cells. In the liver parenchyma, the major sources of reactive oxygen are mitochondria, neutrophils and Kupffer cells. NO affects the transcription of many different genes in hepatic microenvironment, including that related to hepatocyte proliferation and apoptosis. Also, excessive amounts of NO produced by nitric oxide synthase (iNOS) up-regulation can react with superoxide anions forming peroxynitrite, that promote nitrosative stress by nitration of tyrosine residues in proteins. Thereby, nitrotyrosine may be used as a marker for the nitrosative stress. Oxidative and nitrosative stress are well known to be related to several inflammatory pathologies, but their roles in liver damage during ALF remains to be clarified. This study aimed to investigate the presence of iNOS and nitrotyrosine, besides the Kupffer cells by CD68 detection in liver parenchyma from human patients that developed acute liver failure. The study protocol was approved by the Ethical Committee for Human Research of the Oswaldo Cruz Foundation (Fiocruz) and informed consent was obtained from all subjects (CEP Fiocruz.no. 22/03). Liver samples from patients who developed ALF were obtained during liver transplantation procedures. Tissue samples of liver donors were used as controls. Immunofluorescence methods were used to identify surface cell markers, nitrotyrosine and iNOS. Preliminary findings showed a strong presence of iNOs and high number of CD68 positive cells in periportal space, not detected in liver samples of healthy controls. It was also possible the detection of nitrotyrosine in liver of ALF patients, not observed in hepatic parenchyma of healthy liver donors. These finding suggests a role of the oxidative and nitrosative stress leading to imbalance of regenerative process of hepatic parenchyma during inflammation liver and probably associated to ALF.