Reviewer's report

Title: Protection of Early Phase Hepatic Ischemia-Reperfusion Injury by Cholinergic Agonists

Version: 1 Date: 14 November 2005

Reviewer: Juan L Contreras

Reviewer’s report:

General
This is a well-written, interesting and well-controlled study aimed to evaluate the pharmacological modulation of the cholinergic pathway in warm I/R-injury to the liver. However, the manuscript could be strengthen if the authors addresses the following points:

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
It was surprising the results regarding the clear beneficial effects of DMPP on “early” I/R-injury demonstrated by significant reduction in ALT at 3 and 6 hours post-reperfusion, significant reduction in TNF-a but without histopathological correlation. In this regard, previous studies conducted to down-regulate TNF-a demonstrated direct correlation with lower plasma ALT and improvement of the liver histology. It is well discussed the discrepancies between chemokine expression and PMN infiltration but is unclear on the explanation of the authors regarding the failure to correlate ALT/TNF results with histopathology.

Although it was described in methods that the livers histopathology was evaluated based on sinusoidal congestion, cytoplasmic vacuolization, hepatocellular necrosis, and neutrophil infiltration, it is unclear many samples were analyzed and how each of these alterations was used to provide an histopathological report. I think the paper could be strength if the authors conduct a morphometric assessment of the I/R-injury to the liver, as previously published (Hepatology 1997;26:1513-20). Authors may find a significant difference between experimental groups.

Having demonstrated significant reduction in ALT and TNF-a in animals given DMPP vs controls without histopathological and PMN infiltration between treated and control groups, will be informative to know if pharmacological modulation of the cholinergic pathway have any in vivo implications. To this end, will be informative to evaluate the effect of DMPP and nicotine in a lethal model of warm I/R-injury (Transplantation 1998 Jun 15 65 (11):1433).

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.