Reviewer's report

Title: Mobilization of xanthine oxidase from the gastrointestinal tract in acute pancreatitis

Version: Date: 11 December 2003

Reviewer: Ashok Saluja

Reviewer's report:

General

Discretionary Revisions (which the author can choose to ignore)

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

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Xanthine oxidoreductase has been proposed to play role in development of local and systemic effects of acute pancreatitis. In experimental models of acute pancreatitis the conversion of Xanthine dehydrogenase to xanthine oxidase by the action of proteolytic enzymes has been reported. Circulating xanthine oxidase seems to be the source of systemic oxidative stress. In the present study, using taurocholate induced pancreatitis model in rats, authors have shown that there is increase in the plasma xanthine oxidase activity during pancreatitis. Increase in circulating amylase can cause increase in circulating XDH/XOD. Peritoneal lavaging prevented the increase in ?-amylase and XDH/XOD in plasma after induction of pancreatitis. It was observed that ?-amylase is absorbed from peritoneal fluid by the blood vessels associated with the intestine.

Based upon these findings authors have concluded that during early pancreatitis ?-amylase is absorbed from ascites fluid through gastrointestinal tract vessels, which interfere with binding of XDH/XOD attached to glycoprotein of the endothelial cells. Pancreatic proteolytic enzymes convert XDH into its oxidase form, promoting an increase in circulating XOD that is involved in systemic inflammatory process. The study presents some interesting findings but some of the assumptions made by the authors for explaining their results are not correct.

There is no evidence in literature to suggest that capability of ?-amylase to hydrolyze internal ?1-4 linkages of polysaccharide can be used for hydrolysis of similar linkages in glycoprotein. The binding of amylase to glycoprotein is as a result of certain sites (which are different from catalytic site) of the enzyme interacting with glycoprotein on endothelial cells. However, there remains a possibility that using these non-catalytic sites, amylase and xanthine dehydrogenase are competing for the same binding site on glycoproteins. It does not seem likely that catalytic activity of amylase has any role in release of xanthine oxidase. These possibilities should be discussed.

There is no experimental evidence in the current study to support the conclusion that pancreatic proteolytic enzymes are involved in conversion of XDH to XOD during pancreatitis. In view of the authors’ other recent study in which they have shown that heparin also mobilizes xanthine oxidase, it would be interesting to find out if heparin and amylase target same binding sites for the purpose of
releasing xanthine oxidase/XDH. Authors should carry out such an experiment.

Figure 3 a, b the difference in amylase and XOD levels between EAP and EAP+PL groups are not very high but MPO levels are highly significant which indicates the participation of additional factors in lung injury. This should be discussed.

Figure 5-the captions ‘gastrointestinal endothelium’ and ‘lung endothelium’ used are some what confusing. Is the mobilization of XDH/XOD from the gastrointestinal tract or from the endothelium of blood vessel associated with gastrointestinal tract? This point need to be elaborated and suitable modification made in text and caption. Also it is not clear how XDH is being converted to XOD by pancreatic proteases. Are the authors proposing that this reaction is taking place in the plasma? There are strong protease inhibitory activities in plasma. Uric acid, one of the products of XOD reaction is known to have antioxidant properties and is considered main antioxidant in plasma. The role of uric acid should be included in the discussion.

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

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

none