Antagonizing reactive oxygen species during ex vivo lung perfusion

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TO THE EDITOR: The stop of flow (ischemia) would be interpreted as membrane depolarization, through the inhibition of KATP channels, leading to increased reactive oxygen species (ROS) production (1). The resultant ROS are claimed to be an effective mediator for ischemic preconditioning (IPC), as proved by the observation that the presence of antioxidants during the preconditioning phase can diminish the degree of protection (2). However, another important mediator would be KATP channels, whose activation was found to protect against subsequent ischemic events (3). In short, to follow the recommendations of Chatterjee et al. (1) in the IPC model, the method of choice to protect against increased ROS production would be the use of K+ channel agonists.

In lung transplantation, the graft is subjected to a period of cold static ischemia followed by reperfusion, in the recipient or during ex vivo lung perfusion (EVLP). After EVLP the lung would be subjected again to a period of no flow (ischemia). Considering this scenario, EVLP might be considered as IPC, with the same recommendation applied. In addition, of the different ischemic reperfusion lung injuries (e.g., pulmonary bypass during surgery), lung transplantation takes the big focus regarding initiation of immune reactions and graft rejection. In this regard, increased ROS production and diminished K+ channel activity would be involved in the activation of inflammasomes, which when activated result in activation of caspase 1, which in turn activates pro-IL-1β and IL-18, which are proinflammatory cytokines (e.g., IL-1β was found to induce IL-6) (4, 6).

In a previous study, the use of 2% hydrogen inhalation during EVLP resulted in improved mitochondrial function and improved ATP production. The improved ATP production would improve the activity of KATP channels. The outcome was significantly diminished cytokine production within the graft (5).

Accordingly, the inclusion of antioxidants and K+ channel agonists during lung graft preservation and EVLP would be of great value from the aspect of antagonizing the role of ROS in the expression of endothelial cell adhesion molecules, which is important for inflammatory cells migration and graft infiltration (1), as well as from the aspect of antagonizing inflammasomes activation and increased cytokine production.

REFERENCES


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