Evolving spectrum of dexmedetomidine preconditioning for Ischemia–reperfusion injury amelioration

Madam,

Ischemia–reperfusion injury (IRI) is inexorably linked to a wide gamut of clinical settings such as myocardial revascularization, organ transplantation, vascular procedures, gastrointestinal surgeries, and intraoperative tourniquet application. The restoration of perfusion to ischemic tissues is characterized by microvascular dysfunction, endothelial cell activation, generation of oxygen free radicals, and leukocyte adhesion. This complex inflammatory milieu predisposes to organ dysfunction which accounts for an elevated morbidity and mortality. Therefore, diverse techniques such as ischemic preconditioning, remote ischemia preconditioning, ischemic postconditioning, and pharmacological preconditioning have been evaluated for the attenuation of IRI.

In this context, many anesthetic medications (inhalational agents, propofol, ketamine, etc.) have been evaluated for pharmacological preconditioning.[1] Interestingly, a considerable degree of evidence regarding the role of dexmedetomidine in IRI amelioration has emanated from the animal studies over the last decade.[1] These laboratory studies have demonstrated a promising potential of dexmedetomidine in reducing the inflammatory and oxidative stress in major organs.

The aforementioned fact has motivated the recent emphasis on a formal evaluation of the impact of dexmedetomidine on IRI across diverse predisposed clinical settings. Initial few studies have revealed that dexmedetomidine infusion markedly reduces the ischemia–reperfusion markers (hypoxanthine and malondialdehyde, respectively) associated with tourniquet application.[2] Another study by Kundra *et al.* in patients undergoing aortobifemoral bypass procedure demonstrated an attenuated skeletal muscle IRI as suggested by lower postprocedural creatine phosphokinase levels.[3] Chi *et al.* outlined reduced postoperative cardiac troponin I and creatine kinase MB following the administration of dexmedetomidine in off-pump coronary artery bypass grafting.[4] Recent clinical studies characterized a hepatic protective effect attributable to dexmedetomidine in living donors and in subjects undergoing hepatectomy.[1,5]

A number of caveats surface on a meticulous evaluation of the literature regarding the role of dexmedetomidine in IRI amelioration. First and foremost, the timing of drug administration is closely related to the subsequent impact on IRI, with most of the researchers depicting a beneficial impact only with an initiation prior to ischemia.[1] The literature elucidates that dexmedetomidine induces subtle alterations in signaling pathways, membrane receptors, mediators, and transmitters which formulate the putative mechanisms of protection. Second, albeit the demonstration of a dose-dependent attenuation of IRI, the optimal dosage regimen continues to be investigated in order to closely balance the efficacy and safety profile. Third, there is a definitive lack of human trials over a range of many other predisposed perioperative scenarios evaluating reperfusion lung injury. Similarly, renal IRI, particularly in diabetic and hypertensive cohort, merits further evaluation.

To conclude, the era of translational research continues to unveil a number of novel discoveries. However, it is certainly the right time to move to more human trials evaluating the role

of dexmedetomidine in ameliorating IRI aimed at ensuring favorable perioperative outcomes, particularly pertinent in the clinical setting of organ transplantation and revascularization.

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Conflicts of interest
There are no conflicts of interest.

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