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Editorial – Propofol as an intraoperative strategy for organ protection

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Liver ischemia could be a consequence of arterial occlusion, shock, and organ transplantation and is a common cause of hepatic cell death, delayed graft function, liver graft rejection and acute liver failure (ALF). The mortality rate of ALF remains elevated among patients in intensive care and ranges between 25 and 100% in postoperative patients suffering from ALF[1]. The prognosis is complicated by the fact that reperfusion is responsible for additional damage, contributing to liver dysfunction and injury. Organ damage is triggered by a complex series of biochemical events, which include among others oxidative stress and the release of pro-inflammatory mediators. Thus, the role of endogenous antioxidant and cytoprotective enzymes involved in cell survival and redox balance maintenance assumes great importance. In this context, Wei et al[2] in their recent work evaluated the potential effect and mechanism of propofol in protecting rat liver from I/R injury. In particular, the authors showed that propofol significantly reduced liver injury as measured by reduction of AST and ALT levels and apoptosis. The authors suggested that PI3K/AKT/mTOR signaling pathway may be involved in propofol-mediated protection. Authors' findings are of great clinical relevance and agree with previous works suggesting the protective effect of propofol in liver I/R injury[3,4]. Propofol is an intravenous sedative-hypnotic agent introduced in the United States in 1989 by Zeneca Pharmaceuticals and is widely used for total intravenous anesthesia. Furthermore, it is also indicated for induction and maintenance of general anesthesia as well as for sedation of intubated, mechanically ventilated adults in the Intensive Care Unit. Propofol is characterized by a phenolic structure similar to that of α-tocopherol and presents antioxidant properties that have been demonstrated both *in vitro* and *in vivo*. Therefore, propofol possesses both an intrinsic protective effect based on its phenolic structure as well as a protective effect related to its ability to trigger specific antioxidant and survival pathways. As far as concern the first protective mechanism, propofol has been reported to inhibit lipid peroxidation in various experimental models[5,6], to protect cells against oxidative stress, and to increase the antioxidant capacity of plasma in humans[7,8]. To this regard, Mathy-Hartert et al[9] demonstrated that propofol reacts with peroxynitrite, a key mediator of oxidative stress, leading to the formation of a propofol-derived phenoxyl radical, and has, therefore, been hypothesized to be a peroxynitrite scavenger. As far as concern the activation of specific antioxidant and survival pathways, propofol has been shown to activate the Nrf2 axis, which in turn leads to the early antioxidant gene response responsible for the maintenance of cellular redox balance. Consistently with these results, we previously showed that the antioxidant properties of propofol depend on its ability to induce heme oxygenase-1 (HO-1) expression via the NFkB pathway[10]. HO-1 catalyze the conversion of heme to carbon monoxide (CO) and biliverdin with a concurrent release of iron and several lines of evidence suggest that its pleiotropic functions play a major role in cellular protection[11-14]. Finally, recent findings[15,16] suggest that propofol may exploit its beneficial effect via an epigenetic effect regulating the expression of miR-133a-5p. Therefore, propofol may offer additional protective mechanisms besides those already established for other pharmacological and cellular strategies. Noteworthy, such beneficial effects seem to be specific for propofol since previous reports showed that inhaled sevoflurane failed to prevent liver mitochondrial dysfunction following I/R[17]. However, it should be noted that data from randomized clinical trials are not able to offer a unique interpretation on the possible advantages of using propofol *vs.* gaseous anesthesia[18]. To this regard, it should be noted that such heterogeneous results may be dependent of the differences between the

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different indications for patients' surgery as well as the timing of the measured endpoints. Taken all together, these data suggest that propofol may be considered a safe and effective pharmacological strategy for organ protection.

Conflict Interests

The Authors declare that they have no conflict of interests.

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