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JA SYMPOSIUM

Effects of oxidative stress on vascular function, and the role of anesthetics

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The roles of reactive oxygen species and oxidative stress continue to be an area of interest in vascular biology and pathology [1]. Oxidative stress can be defined as imbalance between reactive oxygen species and antioxidants (Fig. 1). Oxygen-derived free radicals, including superoxide and hydroxyl radicals, are a subgroup of reactive oxygen species containing one or more unpaired electrons [2]. Superoxide, which is generated from molecular oxygen, is a precursor of several reactive oxygen species and, therefore, it seems necessary to reveal its role in oxidative stress of the vasculature. Previous studies demonstrated multiple sources of superoxide within vascular endothelial and smooth muscle cells, including mitochondria, cyclooxygenase, NADPH oxidase, xanthine oxidase, lipoxygenase, and dysfunctional nitric oxide synthase [2, 3]. Among these, NADPH oxidase is known to be a crucial system for superoxide production in vascular pathology [3, 4]. The vascular NADPH oxidases include the NOX1, NOX2, NOX4, and NOX5 subtypes [5]. NOX1 and NOX2 subtypes are particularly important sources of superoxide production within the vascular wall in many diseased states, including hypertension, diabetes mellitus, inflammation, metabolic syndrome, and heart failure [6–9].

It is unclear whether clinically used anesthetics modify the enzymatic activity of NADPH oxidase in blood vessels. We have recently shown that propofol at clinically relevant concentrations impairs the activity of NADPH oxidase by reducing translocation of cytosolic NOX2 subunit p47phox toward cellular membrane, resulting in reduced levels of superoxide within arterial walls [10–12]. In contrast with these beneficial effects of anesthetics, one group reported that high concentrations of morphine augment superoxide production related to potential activation of NOX2 [13]. In addition, a clinical study examining forearm endothelial function revealed endothelial dysfunction related to hyperhomocysteinemia after inhalation of 70% nitrous oxide for 5 h [14]. It is likely that the high concentration of nitrous oxide augments superoxide production, resulting in impaired endothelial function, because hyperhomocysteinemia has been shown to activate the NOX1 subtype in an animal model [15]. Research leading to insight into molecular mechanisms of regulation of NADPH oxidase activity induced by anesthetics has just begun. Further studies are clearly needed to reveal the effects of anesthetics on vascular pathology related to oxidative stress.

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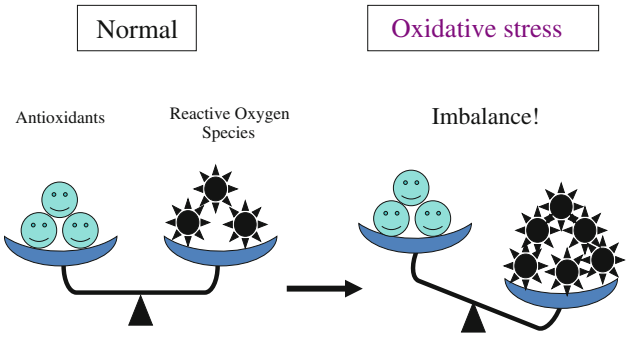

Fig. 1 Schematic description of oxidative stress

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