Propofol reduces nitric oxide biosynthesis in lipopolysaccharide-activated macrophages by downregulating the expression of inducible nitric oxide synthase.

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Abstract

Nitric oxide is an active oxidant that contributes to the physiology and pathophysiology of macrophages. Propofol has been widely used in intravenous anesthesia. It possess antioxidant and immunomodulating effects. This study aimed to evaluate the effects of propofol on nitric oxide production in lipopolysaccharide-activated macrophages. Exposure of macrophages to propofol (25, 50 and 75 micro M), to lipopolysaccharide (0.5, 1, 1.5 and 2 ng/ml) or to a combination of propofol and lipopolysaccharide did not affect cell viability. However, propofol at 100 micro M led to significant cell death (P<0.05). The levels of nitrite, an oxidative product of nitric oxide, were increased in lipopolysaccharide-treated macrophages in a concentration-dependent manner (P<0.01), while propofol could concentration-dependently decrease the lipopolysaccharide-enhanced nitrite levels (P<0.01). Immunoblotting analysis revealed that lipopolysaccharide increased the protein level of inducible nitric oxide synthase (iNOS). The co-treatment of propofol and lipopolysaccharide significantly reduced this lipopolysaccharide-induced iNOS protein (357+/-49 x 10(3) versus 92+/-6 x 10(3) arbitrary units, P<0.01). Analysis by reverse transcriptase-polymerase chain reaction showed that lipopolysaccharide induced mRNA of iNOS, but that the inductive effect was inhibited by propofol (95+/-7 x 10(2) versus 30+/-4 x 10(2) arbitrary units, P<0.01). This study has demonstrated that propofol, at therapeutic concentrations, could suppress nitric oxide biosynthesis by inhibiting iNOS expression in lipopolysaccharide-activated macrophages. The mechanism of suppression was at a pretranslational level.