Propofol suppresses tumor necrosis factor-alpha biosynthesis in lipopolysaccharide-stimulated macrophages possibly through downregulation of nuclear factor-kappa B-mediated toll-like receptor 4 gene expression.

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Abstract

Lipopolysaccharide (LPS), a gram-negative bacterial outer membrane component, can activate macrophages via a toll-like receptor 4-dependent pathway. Our previous study has shown that propofol, an intravenous anesthetic reagent, has anti-inflammatory effects. This study was further aimed to evaluate the roles of toll-like receptor 4 in propofol-caused suppression of tumor necrosis factor-alpha (TNF-alpha) biosynthesis in LPS-stimulated macrophages and its possible molecular mechanisms. Exposure of macrophages to propofol and LPS did not affect cell viability. Meanwhile, the LPS-caused augmentations in the productions of TNF-alpha protein and mRNA were significantly decreased following incubation with a therapeutic concentration of propofol (50 microM). Analysis of toll-like receptor 4 small interference (si)RNA revealed that this membrane receptor might participate in the propofol-caused suppression of TNF-alpha biosynthesis. Treatment of macrophages with LPS-induced toll-like receptor 4 protein and mRNA productions. Propofol at a clinically relevant concentration could inhibit such induction. In parallel, the LPS-induced translocation and transactivation of transcription factor nuclear factor-kappa B (NFkappaB) were significantly alleviated following propofol incubation. There are several NFkappaB DNA-binding motifs found in the promoter region of toll-like receptor 4. Therefore, this study shows that propofol at a therapeutic concentration can downregulate TNF-alpha biosynthesis possibly via inhibition of NFkappaB-mediated toll-like receptor 4 gene expression.