

Propofol significantly attenuates iNOS, CAT-2, and CAT-2B transcription in lipopolysaccharide-stimulated murine macrophages.

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BACKGROUND: Propofol significantly inhibits inducible nitric oxide synthase (iNOS) expression and nitric oxide (NO) biosynthesis in stimulated macrophages. L-arginine transport mediated by the isozymes of type-2 cationic amino acid transporter (including CAT-2 and CAT-2B) has been reported to play a crucial role in regulating iNOS activity. We sought to evaluate the effects of propofol on L-arginine transport and transcription of CAT-2 and CAT-2B. **METHODS:** Confluent murine macrophages (RAW264.7 cells) were stimulated with lipopolysaccharide (LPS) to induce NO production, L-arginine transport and the transcriptions of iNOS, CAT-2, and CAT-2B. Propofol (25, 50, and 75 microM) was added to the cells 4 hours before, immediately after, or 4 hours after LPS administration. After reacting with LPS for 18 hours, cell cultures were harvested and assayed. **RESULTS:** Propofol administered 4 hours before LPS had no significant effects on NO production, L-arginine transport, and the transcriptions of iNOS and CAT-2. To our surprise, NO production and iNOS transcription were significantly enhanced by 25 microM propofol administered immediately after LPS. NO production and iNOS transcription were not affected by 50 microM propofol but significantly inhibited by 75 microM propofol administered immediately after LPS. CAT-2 transcription and L-arginine transport were significantly inhibited by 50 and 75 microM but not 25 microM propofol administered immediately after LPS. When administered 4 hours after LPS, 75 but not 25 and 50 microM propofol significantly inhibited NO production, L-arginine transport, and the transcription of iNOS and CAT-2. In addition, CAT-2B transcription was significantly inhibited by propofol that was administered 4 hours before, immediately after, or 4 hours after LPS. **CONCLUSIONS:** Propofol had significantly inhibitory effects on LPS-induced NO production, L-arginine transport, and the expressions of iNOS, CAT-2 and CAT-2B in stimulated murine macrophages in a dose-dependent manner. In addition, timing of administration also affected this regulatory effect of propofol.