Propofol抑制酯多醣於巨噬細胞所誘發之iNOS、CAT-2及CAT-2B的表現

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

黃俊仁

Liu MC;Tsai PS;Yang CH;Liu CH;Chen CC;Huang CJ

摘要

背景：Propofol會抑制酯多醣(LPS)於巨噬細胞所誘發一氣化氮合成酶(iNOS)的表現及一氣化氮(NO)之合成。第二型正電荷胺基酸運輸酶（包括CAT-2及CAT-2B）可經由控制左旋精胺(L-arginine)之運輸來調控iNOS之活性。此研究之目的乃在於探討propofol對CAT-2及CAT-2B表現及L-arginine運輸之影響。方法：吾人採用LPS刺激老鼠巨噬細胞(RAW264.7)之模式來誘發NO之產生、L-arginine之運輸及iNOS、CAT-2與CAT-2B的表現，而propofol(25, 50, and 75 μM)則分別於LPS刺激前四小時、LPS刺激後或LPS刺激後四小時加入細胞培養中；待與LPS反應十八小時後，吾人收集巨噬細胞並加以分析。結果：於LPS刺激前四小時加入之propofol對LPS所誘發NO之產生、L-arginine之運輸及iNOS與CAT-2的表現並無明顯作用；令人意外的是，於LPS刺激後立即加入之25 μM propofol加強了iNOS之表現及NO之產生，而於LPS刺激後立即加入之50 μM propofol 對iNOS之表現及NO之產生並無明顯作用，於LPS刺激後立即加入之75 μM propofol則明顯抑制iNOS之表現及NO之產生。於LPS刺激後立即加入之50及75 μM propofol則明顯抑制CAT-2之表現及L-arginine之運輸，而25 μM propofol則無此作用。另外，於LPS刺激後四小時加入之75 μM propofol明顯抑制NO之產生、L-arginine之運輸及iNOS與CAT-2之表現，而25及50 μM propofol則無此作用。CAT-2B之表現則明顯受到於LPS刺激前四小時、LPS刺激後或LPS刺激後四小時加入之propofol的抑制。結論：Propofol對LPS於巨噬細胞所誘發之NO之產生、L-arginine之運輸及iNOS、CAT-2與CAT-2B的表現具明顯的抑制作用。而propofol之劑量及施與之時間點均會影響此一作用。

Abstract

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 μM) 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 μM propofol administered immediately after LPS. NO production and iNOS transcription were not affected by 50 μM propofol but significantly inhibited by 75 μM propofol administered immediately after LPS. CAT-2 transcription and L-arginine transport were significantly inhibited by 50 and 75 μM but not 25 μM propofol administered immediately after LPS. When administered 4 hours after LPS, 75 but not 25 and 50 μM 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.