Bupivacaine inhibits COX-2 expression, PGE2, and cytokine production in endotoxin-activated macrophages

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摘要

Abstract

BACKGROUND: Upregulation of cyclooxygenase-2 (COX-2) and resultant prostaglandin E(2) (PGE(2)) overproduction has been shown to play a crucial role in initiating a systemic inflammatory response during sepsis. Sepsis also induces robust production of pro-inflammatory cytokines tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and IL-6 as well as anti-inflammatory cytokine IL-10. We sought to elucidate the effects of bupivacaine on COX-2 expression and production of PGE(2) and cytokines using an endotoxin-activated murine macrophages model. METHODS: Confluent murine macrophages (RAW264.7 cells) were treated with lipopolysaccharide (LPS, 100 ng/ml) or LPS plus bupivacaine (1, 10, or 100 microM). Bupivacaine was added immediately after LPS. After reacting for 18 h, cell cultures were harvested for subsequent analysis. RESULTS: LPS significantly upregulated COX-2 transcription and PGE(2) production in macrophages. LPS also significantly increased the production of TNF-alpha, IL-1beta, IL-6 and IL-10 in macrophages. Bupivacaine significantly inhibited the effects of LPS on COX-2 transcription and PGE(2) production in a dose-dependent manner. In a dose-dependent manner, bupivacaine also significantly inhibited the effects of LPS on the production of TNF-alpha, IL-1beta, and IL-6. However, bupivacaine exerted no significant effects on LPS-induced IL-10 production. CONCLUSION: Bupivacaine significantly inhibited COX-2 expression, PGE(2) and cytokine production in endotoxin-activated macrophages.