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 E2 (PGE2) 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-α (TNF-α), interleukin-1β (IL-1β), 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 PGE2 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 μM). 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 PGE2 production in macrophages. LPS also significantly increased the production of TNF-α, IL-1β, IL-6 and IL-10 in macrophages. Bupivacaine significantly inhibited the effects of LPS on COX-2 transcription and PGE2 production in a dose-dependent manner. In a dose-dependent manner, bupivacaine also significantly inhibited the effects of LPS on the production of TNF-α, IL-1β, and IL-6. However, bupivacaine exerted no significant effects on LPS-induced IL-10 production.

Conclusion: Bupivacaine significantly inhibited COX-2 expression, PGE2 and cytokine production in endotoxin-activated macrophages.