Abstract:

SUMMARY

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We have shown previously that lignocaine inhibits the upregulation of inducible nitric oxide synthase (iNOS), a crucial factor that initiates the systemic inflammatory response during sepsis, possibly through voltage-sensitive sodium channels (VSSC). Toll-like receptor-4 (TLR-4), nuclear factor (NF)- κ B and mitogen activated protein kinases (MAPKs) participate in the upstream regulation of iNOS expression induced by endotoxin. In the present study, we investigated the effects of lignocaine in the regulation of the expression of these enzymes. The role of VSSC in the effects of lignocaine was also investigated.

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Confluent murine macrophages (RAW264.7 cells) were randomized to receive lipopolysaccharide (LPS; 100 ng/mL), LPS + lignocaine (50 μmol/L), LPS + tetrodotoxin (TTX; 1 μmol/L; a VSSC inhibitor), LPS + lignocaine + veratridine (Ver; 50 μmol/L; a VSSC activator) or LPS + TTX + Ver. After reacting with LPS for 0, 15, 30, 45 and 60 min, cell cultures were harvested and enzyme expression was evaluated.

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We found that LPS significantly increased the concentrations of TLR-4, NF- κ B and MAPKs, including extracellular regulated kinase (ERK), c-jun N-terminal kinase (JNK) and p38 MAPK, in activated macrophages. Lignocaine and TTX significantly attenuated the effects of LPS on TLR-4, NF- κ B, ERK and p38 MAPK expression, but not on JNK. Veratridine mitigated the effects of lignocaine and TTX.

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These data demonstrate that lignocaine has significant inhibitory effects on the activation of TLR-4, NF- κ B and MAPKs in activated macrophages. Moreover, these effects involve VSSC.