Lidocaine inhibition of inducible nitric oxide synthase and cationic amino acid transporter-2 transcription in activated murine macrophages may involve voltage-sensitive Na+ channel.

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Lidocaine has been reported to inhibit nitric oxide (NO) production in activated murine macrophages, but the role of inducible NO synthase (iNOS) in lidocaine-induced inhibition of NO has not been explored. In addition, type-2 cationic amino acid transporter (CAT-2) and guanosine triphosphate cyclohydrolase I (GTPCH) also regulate iNOS activity. The effects of lidocaine on CAT-2 and GTPCH are unknown. To explore further these effects, confluent immortalized murine macrophages (RAW264.7 cells) were incubated with lipopolysaccharide (LPS) or in combination with lidocaine (5, 50, or 500 microM) for 18 h before harvesting. We also used tetrodotoxin (TTX) and veratridine to elucidate the possible role of voltage-sensitive Na+ channel. Our data demonstrated that LPS significantly upregulated transcription of iNOS and CAT-2 but not GTPCH in stimulated macrophages. In a dose-dependent manner, lidocaine significantly attenuated the LPS-induced upregulation of iNOS and CAT-2. Conversely, lidocaine significantly increased GTPCH transcription in LPS-stimulated macrophages. The effects of TTX on iNOS, CAT-2, and GTPCH expression were comparable to those of lidocaine. In addition, veratridine significantly attenuated the effects of lidocaine and TTX. We therefore concluded that lidocaine significantly inhibits iNOS and CAT-2 and, in turn, enhances GTPCH transcription in LPS-stimulated macrophages via a mechanism that possibly involves the voltage-sensitive Na+ channel.