Renal transcription of high affinity type-2 cationic amino acid transporter is upregulated in LPS-stimulated rodents

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摘要

Abstract

OBJECTIVE: Sepsis stimulates renal nitric oxide (NO) biosynthesis through up-regulation of inducible NO synthase (iNOS) expression. Type-2 cationic amino acid transporter (CAT-2) mediation of trans-membrane L-arginine (L-Arg) transportation has been identified as one of the crucial regulatory mechanisms involved in the formation of NO by iNOS. We had previously shown that CAT-2B, a high-affinity alternative-spliced transcript of the CAT-2, is involved in induced NO biosynthesis by iNOS (Nitric Oxide, 2002). In this present study, we sought to assess the effects of sepsis on the expression of CAT-2B in lipopolysaccharide (LPS)-stimulated rat kidney. METHODS: Forty rats were randomized to either a normal saline (N/S)-treated group or a LPS-treated group. Renal NO production was determined using chemiluminescence. Semi-quantitative RT-PCR was used to determine the mRNA concentrations of iNOS and L-Arg transporters (CAT-1, CAT-2 and CAT-2B) in kidney. RESULTS: Lipopolysaccharide-coinduced iNOS, CAT-2 and CAT-2B mRNA expression in kidney and caused renal NO overproduction. A significant linear regression relationship was defined between renal NO concentrations and iNOS, CAT-2 and CAT-2B, respectively. On the contrary, CAT-1 expression was not affected by LPS-stimulation. CONCLUSIONS: We provide the first evidence to illustrate that sepsis/septic shock induces the transcription of high-affinity CAT-2B in renal tissues. Transcription of iNOS, CAT-2 and CAT-2B correlates well with renal NO biosynthesis. Regulation of L-Arg uptake by modulating the expression regulation of induced CAT-2 and CAT-2B might be a potential target for therapies against renal pathologic conditions related to NO overproduction.