Abstract

In many in vivo systems exposure to endotoxins (LPS) leads to the co-induction of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), which is important to the regulation of the function of different systems during infection. In submandibular glands (SMG) neural (n)NOS is localized in neural terminals and in striated, granular convoluted and excretory ducts, endothelial (e)NOS in vascular endothelium and ducts, and iNOS in macrophages and in tubules and ducts. In normal adult male rats, injection of an inhibitor of NOS decreased the stimulated salivary secretion and a donor of NO potentiated it, indicating that NO exerts a stimulatory role. A single high dose of LPS (5 mg/kg, i.p.) induced an increase in NOS activity measured by the 14C-citrulline method, increased PGE content almost 100% as measured by RIA, and blocked stimulated salivary secretion. The administration of a specific iNOS inhibitor, aminoguanidine (AG), with LPS not only decreased NOS activity but significantly decreased PGE content, indicating that NO triggered the activation of COX-2. LPS increased conversion of labeled arachidonate to prostaglandins (PGs) showing that COX was induced. Since a PGE1 analogue blocked stimulated salivation, the LPS-induced inhibition of salivation is probably due to release of PGs. Therefore, the use of inhibitors of iNOS and COX-2 could be very useful to increase salivation during infection since saliva has antimicrobial actions.