MECHANISMS UNDERLYING CIGARETTE SMOKE INDUCED NF-κB ACTIVATION IN HUMAN LYMPHOCYTES: THE ROLE OF REACTIVE NITROGEN SPECIES

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Background: Cigarette smoke (CS) is an important source of reactive nitrogen species (RNS). It has been demonstrated that CS constitutes the highest source of exogenous nitric oxide and peroxynitrite to which humans are exposed. NF-κB is a key inflammatory, redox-sensitive transcription factor, whose role in CS-induced airway inflammation is unclear. Moreover, the role of RNS in the activation of NF-κB and in inflammation also remains vague.
Aim: This study investigated CS-induced NF-κB activation in human lymphocytes and assessed the involvement of CS-derived RNS in NF-κB activation and their possible biological effects.
Results: Mild exposure to CS induced NF-κB in lymphocytes through a reduction in the intracellular glutathione levels and an increase in oxidative stress. In addition, exposure to CS led to IKK activation and I-κB degradation. Peroxynitrite, but not NO, mimicked the effects of CS on NF-κB activation. A reduction in intracellular peroxynitrite formation by inhibition of the mitochondrial respiratory chain resulted in decreased activation of NF-κB by CS. NF-κB induced iNOS levels were increased in response to CS.
Conclusions: CS exposure induced the classical NF-κB activation pathway in lymphocytes *via* intracellular formation of peroxynitrite, through a reaction between smoke-derived NO and endogenously produced superoxide. This NF-κB activation resulted in inflammatory gene expression, which may contribute to CS-related airway inflammation.