PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

L-arginine in the control of lung chemokine production

ArticleInfo		
ArticleID	:	1606
ArticleDOI	:	10.1186/rr-2001-68507
ArticleCitationID	:	68507
ArticleSequenceNumber	:	17
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001–9–14 Received : 2001–4–24 OnlineDate : 2001–9–14
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	129312211

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Keywords

Acute lung injury, chemokines, nitric oxide

Context

In experimental animals, acute lung injury (ALI) can be induced by lipopolysaccharide (LPS) administration. Accumulation of polymorphonuclear neutrophils (PMNs) during ALI involves chemoattractant cytokines such as cytokine-induced neutrophil chemoattractant (CINC) and macrophage inflammatory protein (MIP). LPS-induced PMN accumulation can be prevented by antibodies to these cytokines. Nitric oxide (NO) also prevents PMN accumulation in ALI. Nuclear factor ?B (NF?B) is a transcriptional regulator of CINC-1 and MIP-2; when bound to inhibitory factor ?B (I?B), NF?B is prevented from translocating to the nucleus and exerting its transcriptional effects. In this study the authors studied the effect of L-arginine, the precursor of NO, on modulation of NF?B expression.

Significant findings

L-arginine attenuated LPS-induced CINC-1 and MIP-2 production. Prior administration of L-arginine inhibited LPS-induced increases in NF?B binding of DNA, and maintained levels of free I?B after stimulation with LPS. These actions of L-arginine were abolished by an NO synthase inhibitor, this suggests that L-arginine and NO, the products of NO synthase action on L-arginine, are involved in regulation of NF?B. These results indicate that L-arginine would be useful in the prevention of ALI induced by LPS, and may prevent ALI induced by other agents.

Comments

During ALI, accumulation of PMNs occurs as a result of increased generation of various cytokines. As the beneficial effects of L-arginine were completely blocked by an NO synthase inhibitor, it is reasonable to presume that NO may mediate the downregulation of these cytokines. No studies were

performed using NO donors, so it would be interesting to see whether inhalation of NO could reduce ALI induced by LPS in experimental animals. It will also be important to determine whether there is a dose-dependent relationship between NO and chemokine production, and whether there is a time-dependent response. Results with NO in acute respiratory distress syndrome (ARDS) have been inconclusive; therefore, more studies are needed to ascertain the role of NO in both ALI and ARDS.

Methods

Animal study, northern blotting, ELISA

Additional information

References

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