

주요 논문초록

Increased Nitric Oxide Synthase in the Lung after Ozone Inhalation is Associated with Activation of NF- κ B

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출처 : Environ Health Perspect 106(suppl 5): 1175-1178(1998).

오존의 급성 흡입은 조직의 여러 장소에서 대식세포의 집합으로 특징지어지는 염증성 반응과 관련되어 있다. 이러한 세포들은 국소의 폐포 상피세포와 함께 활성화되어 세포독성을 갖는 산화질소(nitric oxide, \cdot NO) 등과 같은 전염증성 매개물질(proinflammatory cytokine, IL- 1β , TNF- α)들을 분비한다. 따라서 오존은 폐포상피세포에 독성을 주는 흔한 도시성 대기오염물질로 알려져 있다. 인간에게 있어서 0.1-0.2 ppm의 오존을 흡입하였을 경우 부종, 기도과민성, 폐포상피세포손상 및 숙주의 방어기전을 약화시키는 충분한 요건이 된다. 저자들은 과거 오존에 의한 폐포대식세포 및 폐포상피세포에 대한 손상기전에 대해 연구하였던 결과, 동물실험 모형에서 실험동물이 오존에 노출되었을 경우 호중구 및 폐포대식세포가 급속도로 폐장내로 침윤되었으며, 그후 폐포대식세포와 제2형 상피세포(type II epithelial cell)가 활성화되는 것을 관찰할 수 있었다. 이후 활성화된 세포들에서 전염증성 매개물질들을 분비하여 염증성 반응을 일으키는 것을 보고한 바 있다. 알려진 바와 같이 전염증성 매개물질은 일련의 신호전달과정을 거쳐 전사요소(transcription factor)인 Nuclear factor kappa B(NF- κ B)의 활성화에 관여한다. 본 연구에서는 폐포대식세포와 제2형 상피세포에 오존을 폭로시켰을 경우 발생하는 전염증성 물질이 NF- κ B의 결합활성화에 변이를 일으키는 지 여부를 규명하고자 하였다.

실험모형은 동물(rats, Taconic Farms, Germantown, NY)을 사용하였으며, 관찰군에게는 2 ppm의 오존을 대조군에게는 ultrapure air(5.5-ft³ air-tight plexiglass chambers)를 3시간동안 폭로시켰다. 오존처리후 3시간에서 48시간에 걸쳐 폐포세척 및 조직채취(elastase를 이용하여 tissue digestion)방식으로 실험에 필요한 세포들을 분리하였다. NF- κ B의 분석을 위해 Nuclear Extraction and Electrophoretic Mobility Shift Assay를 이용하였다.

오존을 처리한 군에서 대조군에 비해 NF- κ B를 길항하는 물질인 pyrrolidine dithiocarbamate(PDTC)의 작용이 덜 민감한 것으로 나타났다. Electrophoretic Mobility Shift Assay를 이용하여 NF- κ B의 결합능력을 분석한 결과 오존처리군에서 폐포대식세포 및 폐포상피세포 모두에서 시간별 결합능력이 상승하였으며, 이러한 현상은 12~24시간에서 최고조에 달하였다.

이상의 결과를 종합할 때 NF- κ B 신호의 활성도 변화는 오존에 노출된 폐포대식세포 및 폐포상피세포의 cytokine 분비반응에 중요한 구실을 한다고 저자들은 밝히고 있다.

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