Diesel exhaust induces systemic lipid peroxidation and development of dysfunctional pro-oxidant and pro-inflammatory high-density lipoprotein.

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Source

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Abstract

OBJECTIVE:

To evaluate whether exposure to air pollutants induces oxidative modifications of plasma lipoproteins, resulting in alteration of the protective capacities of high-density lipoproteins (HDLs).

APPROACH AND RESULTS:

We exposed apolipoprotein E-deficient mice to diesel exhaust (DE) at ≈ 250 μg/m(3) for 2 weeks, filtered air (FA) for 2 weeks, or DE for 2 weeks, followed by FA for 1 week (DE+FA). DE led to enhanced lipid peroxidation in the brochoalveolar lavage fluid that was accompanied by effects on HDL functionality. HDL antioxidant capacity was assessed by an assay that evaluated the ability of HDL to inhibit low-density lipoprotein oxidation estimated by 2',7'-dichlorofluorescein fluorescence. HDL from DE-exposed mice exhibited 23,053 ± 2844 relative fluorescence units, higher than FA-exposed mice (10,282 ± 1135 relative fluorescence units, $P<0.001$) but similar to the HDL from DE+FA-exposed mice (22,448 ± 3115 relative fluorescence units). DE effects on HDL antioxidant capacity were negatively correlated with paraoxonase enzymatic activity, but positively correlated with levels of plasma 8-isoprostanes, 12-hydroxyeicosatetraenoic acid, 13-hydroxyoctadecadienoic acid, liver malondialdehyde, and accompanied by perturbed HDL anti-inflammatory capacity and activation of the 5-lipoxygenase pathway in the liver.

CONCLUSIONS:

DE emissions induced systemic pro-oxidant effects that led to the development of dysfunctional HDL. This may be one of the mechanisms by which air pollution contributes to enhanced atherosclerosis.

KEYWORDS:

air pollution, diesel exhaust, dysfunctional high-density lipoproteins, oxidative stress

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