

CLINICAL STUDIES OF EFFECTS OF NITROGEN OXIDES IN HEALTHY AND ASTHMATIC SUBJECTS

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SUMMARY

Traffic and cooking and heating using unventilated gas appliances are the major sources for environmental exposures to nitrogen oxides. The nitrogen oxides of importance for health effects are nitrogen dioxide (NO_2), and maybe the two derivatives nitric and nitrous acid (HNO_3 and HNO_2). Due to this, human exposure studies on NO_2 have been performed intensively during the last decades. Nitric oxide (NO) is quantitatively the major pollutant, but is not very toxic and may even be used in treatment of certain conditions of respiratory insufficiency. Major lung function effects shown in humans are a decrease in the forced expiratory volume in the first second (FEV_1), increased specific airway resistance (S_{Raw}), and increased responsiveness in bronchial provocation tests. Studies have been performed primarily on healthy and asthmatic subjects, but only asthmatic subjects show these reactions at levels relevant to exposures found in indoor and outdoor environments. Other effects found in animal studies and epidemiological studies like decreased mucociliary function, increased susceptibility to infections have not been proven in humans and are therefore still on debate. Human studies have furthermore shown that antioxidants like vitamin C and E may prevent effects of NO_2 , which is explained by that the mechanism of NO_2 -action is the oxidation of airway phospholipids. A large inconsistency in the results of the studies makes it very difficult to conclude about dose-response relationships and about no observed effect levels (NOEL). Single study observations and results of meta-analyses have indicated a biphasic dose-response relationship. However, such a relationship is hard to explain and need to be investigated further. Several other explanations, e.g. the limited statistical power of the studies, may exist and will be discussed.

Key words: NO_2 , clinical studies, causal interference, review, airway, asthma

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