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TOXICITY OF FERRIC OXIDE AND BENZO[A]PYRENE ALONE OR IN COMBINATION IN RESPIRATORY TRACT OF SPRAGUE DAWLEY RATS

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SUMMARY

The association of small quantities of ferric oxide with Benzo[a]Pyrene (BaP) appears to increase in vivo the toxic effect of BaP. The effect of Fe_2O_3 may be mediated by the recruitement of alveolar macrophages. These cells would contribute to the production of toxic and carcinogenic BaP metabolites and would stimulate development of tumors by producing cellular mediators of inflammation. In order to understand the mechanism of the synergic effect, we have instillated male Sprague Dawley rats 3 weeks of age with a single dose: Fe_2O_3 (3 mg) or BaP (3 mg) /combination Fe_2O_3-BaP (3 mg-3 mg) in 200 µl of physiological saline solution. Control group of identical size (treated with physiological saline solutions and untreated) were used for this study. Animals were sacrified 48 hours after instillation and a bronchoalveolar lavage (BAL) was performed. With each BAL we have obtained protein measurement, cells were stained with May-Grünwald-Giemsa method and slides were studied with polarised light. The malonaldehyde (MDA) was measured by High Performance Liquid Chromatography. The PMN elastase determination was performed by IMAC (immuno-activation) technology. An automated kinetic method for measuring cathepsins B and L was carried out using a fluorogenic substrate: Z-Phe-Arg-AMC, a specific inhibitor E64 and AMC as an internal standard. After a quantitative Dot-Blot of the samples of BAL, an immunodetection of α_1- antitrypsin (α_1AT) was performed. The inhibitory capacity of α_1AT was determined by an enzymatic reaction with porcine pancreatic elastase. We have observed an increased MDA level for rats intoxicated with Fe_2O_3 (123 %), BaP (31 %) and Fe_2O_3 + BaP (56 %). The levels of PMN elastase and cathepsin B and L were increased: Fe_2O_3 (51–58 %), BaP (52–27 %). This effect was not seen for rats intoxicated by Fe_2O_3 + BaP. The free α_1AT was decreased with the three toxics (Fe_2O_3: 44 % – BaP: 42 % – Fe_2O_3: 41 %). The inhibitory capacity of α_1AT was lower in groups of rats instilled with toxics.

Key words: ferric oxide, benzo[a]pyrene, combined exposure, rat

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