Suppression of allergen-induced respiratory dysfunction and airway inflammation in sensitized guinea pigs by Mn(II)(Me(2)DO2A), a novel superoxide scavenger compound.

Cinci L, Masini F, Bencini A, Valtancoli B, Mastroianni R, Calosi L, Bani D.
Department of Anatomy, Histology and Forensic Medicine, Section of Histology Italy.

Abstract
Reactive oxygen species produced during allergen inhalation are key players of the pathophysiology of asthma, leading to oxidative tissue injury and inactivation of endogenous manganese superoxide dismutase (MnSOD). On this ground, removal of excess superoxide anion by scavenger molecules would be beneficial and protective. Here we show that a novel manganese(II)-containing polyamino-polycarboxylic compound, termed Mn(II)(Me(2)DO2A), with potent superoxide dismutating properties decreases the respiratory and histopathological lung abnormalities due to allergen inhalation in a model of ovalbumin (OA)-induced allergic asthma-like reaction in sensitized guinea pigs. Severe respiratory dysfunction in response to OA aerosol exposure arose rapidly in the sensitized animals and was accompanied by bronchoconstriction, alveolar hyperinflation, mast cell activation, increased leukocyte infiltration (evaluated by myeloperoxidase assay), oxidative lung tissue injury (evaluated by the thioribarbituric-reactive substances and nitrotyrosine immunostaining), decay of endogenous MnSOD activity, production of pro-inflammatory prostaglandins, and lung cell apoptosis. Treatment with Mn(II)(Me(2)DO2A) (15mg/kg, given 1h before allergen challenge), but not the inactive congener Zn(II)(Me(2)DO2A) lacking redox-active metal site, significantly attenuated all the above functional, histopathological and biochemical parameters of allergic inflammation and restored the levels of MnSOD activity. In conclusion, our findings support the potential therapeutic use of Mn(II)(Me(2)DO2A) as a novel superoxide scavenger drug in asthma and anaphylactic reactions.

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