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Influence of MnTE-2-PyP on Inflammation and Lipid Peroxidation in Mouse Asthma Model

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ABSTRACT

Our aim was to investigate the effects of MnTE-2-PyP on some markers of inflammation and lipid peroxidation in mouse asthma model. 24 female mice were divided into four groups: group 1, controls; group 2, injected with ovalbumin (OVA); group 3, treated with MnTE-2-PyP; and group 4, treated with ovalbumin and MnTE-2-PyP. The mice from groups 2 and 4 were injected with 10 µg OVA and 1 mg Imject Alum[®] in 100 µL phosphate buffered saline (PBS) on days 0 and 14. The animals from groups 1 and 3 were injected with 100 µL PBS + Imject Alum[®] (1:1). The animals from groups 2 and 4 were subjected to a 30 min aerosol challenge of 1% ovalbumin on days 24, 25 and 26 and those from groups 1 and 3 were subjected to aerosol challenge of PBS at the same time and duration. One hour before inhalation, and 12 hours later the animals from groups 3 and 4 were injected with 100 µL MnTE-2-PyP solution in PBS containing 5 mg/kg. The total cell number, total protein content and 8-isoprostane, IL-4 and IL-5 levels in the bronchoalveolar lavage fluid increased in group 2 as compared to the control group. Malonaldehyde content in the lung homogenate and IgE levels in the serum also increased in this group. The total cell number, total protein content, and levels of 8-isoprostane, IL-4, IL-5 and IgE decreased significantly in group 4 as compared to the OVA group. The parameters set out above in group 3 did not differ significantly from those of the control group. MnTE-2-PyP administered intraperitoneally, 48 hours after the last nebulization, reduced the inflammation and lipid peroxidation in mouse asthma model.

Keywords: Asthma; Inflammation; Interleukins; 8-Isoprostane; Lipid Peroxidation; MnTE-2-PyP

1. Introduction

Asthma is a lung disease characterized by airspace inflammation and oxidative stress [1-4]. Elevated levels of reactive oxygen species (ROS), released by inflammatory cells, either directly or through the formation of products of lipid peroxidation, play a role in enhancing the inflammatory response in these diseases. The presence of oxidative stress is important in the pathogenesis, severity and treatment of asthma [5]. Increasing evidence suggests that abnormalities in mitochondria are involved in several mitochondrial diseases, but also in the development of asthma [6,7]. Recently, antioxidants to prevent and to treat mitochondria in patients with mitochondrial diseases, including asthma, has received much attention, especially because antioxidant approaches seem to have few or no adverse effects [8]. Different classes of antioxidants are known. Among them, the group of catalytic

manganese metalloporphyrins takes center stage with their accumulation into mitochondria. They have at least four antioxidant properties, such as removal of superoxide (O_2^-), hydrogen peroxide (H_2O_2), peroxynitrite ($ONOO^-$), and lipoperoxides [9,10]. Based on this information, we set the goal to investigate the effects of MnTE-2-PyP (Manganese(III) 5, 10, 15, 20-tetrakis (*N*-ethylpyridinium-2-yl)porphyrin), a manganese-mesoporphyrin also known as AEOL-10113, on markers of inflammation and lipid peroxidation in a mouse ovalbumin (OVA) sensitization model of asthma [11].

2. Materials and Methods

2.1. Chemicals

Ovalbumin, grade V, and phosphate buffered saline (PBS), were purchased from Sigma-Aldrich Company, Nitrocellulose filters with 5 µm pores were from Milli-