THE ROLE OF NOCICEPTIN/ORPHANIN FQ (N/OFQ) IN INFLAMMATION AND REMODELLING OF THE SMALL AIRWAYS IN A MURINE MODEL OF AIRWAY HYPERRESPONSIVNESS

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Asthma is a lung disease characterized by inflammation and remodelling of the airways. It is now widely recognized that airway inflammation and remodelling take place not only in the central airways but also in the small airways and also in the lung parenchyma, representing important therapeutic target in the treatment of asthma. Furthermore, the peripheral parts of the bronchial tree have been also accepted as a predominant site of airflow obstruction in many asthmatic subjects (Hamid 2012). Human small airways consist of membranous, terminal and respiratory bronchi with a diameter less than 2mm diameter. In mice, however, we defined small airways as those with a diameter including 0–200 μm (Toshiro et al. 2006).

Our previous studies showed that the neuropeptide Nociceptin/Orphanin FQ (N/OFQ), an endogenous peptide (Meunier et al. 1995) and its receptor N/OFQ peptide (NOP) are involved in airway hyperresponsiveness (AHR) (Sullo et al. 2013), suggesting its potential role in the regulation of the inflammatory process of the airways. Therefore, to understand the involvement of N/OFQ in the inflammation and remodelling of the small airways, we used a conventional murine model of AHR. Balb/c mice were sensitized to ovalbumin (OVA) and treated with saline solution or N/OFQ, at days 0 and 7. From day 21 to 23, all OVA-sensitized mice were aerosol-challenged with 1% OVA in PBS. 24 h after the last challenge, animals were sacrificed, and bronchopulmonary function, pulmonary tissue and bronchoalveolar lavage (BAL) fluid collection were perfomed. In the animals that received N/OFQ, was observed an important reduction of pulmonary resistences and an increase of airway compliance (Caw). These data, indicate that N/OFQ improves bronchial reactivity, as well as small airways compliance. The analysis of BAL showed an important increase of the total number of cells in OVA mice, with typical changes in differential cell count. N/OFQ reduced in total cell number. When compared with OVA group, N/OFQ significantly reduced the proportion of eosinophils and lymphocytes and increased the fraction of macrophages, indicating the potential involvement of the peptide in the inflammatory process.

Bronchial wall thickness and hypertrophy and hyperplasia of smooth muscle represent the structural changes of asthmatic airways and predominant factors to define mechanical properties of the small airways. For these reasons, we have conducted such assessments. We observed that OVA sensitization caused significant increase of bronchial wall thickness and airway smooth muscle mass (due to hypertrophy and hyperplasia) of the small airways.

In the same way, we observed, that N/OFQ treatment caused an important reduction of the thickness of the bronchial wall and it has attenuated hyperplastic phase of ASM.

These data confirmed the capability of N/OFQ to modulate the inflammation in the lung, suggesting a possible role of N/OFQ as well as the inflammatory process also on remodelling of the small airways.

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