Evaluation of the anti-inflammatory response of angiotensin 1-7 associated with liposomes administered via inhalation in mice with experimental autoimmune encephalomyelitis

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Multiple sclerosis (MS) is a chronic, progressive and autoimmune disease characterized by inflammatory infiltrates, gliosis, demyelination and neuroaxonal degeneration in the central nervous system. Several forms of treatment have been used to minimize the clinical effects of MS. However, many of these drugs used for MS treatment are expensive and have serious side effects, decreasing patients' adherence to treatment and in some cases being lethal. Therefore, it is relevant and necessary to evaluate new pathways and treatment therapeutic options strategies for treatment of MS. The objective of this study was to evaluate the neuroinflammatory response in mice with experimental autoimmune encephalomyelitis (EAE) nebulized with liposomes containing Angiotensin 1-7 [Ang-(1–7)] .The EAE model was induced in C57Bl/6 wild-type mice, aged 8-12 weeks, by subcutaneous administration of emulsion containing MOG_{35-55}, Mycobacterium tuberculosis and complete Freund's adjuvant. Animals of the Control (healthy) group, and EAE animals, were nebulized every 72 hours, either with saline, Ang-(1-7), or with empty liposomes, or with Ang-(1-7) encapsulated into liposomes, over 20 days. Body weight and clinical manifestations were evaluated. On the 20th day after induction the brain, spinal cord, lung and spleen vascular permeability was evaluated, as well as the concentration of interleukins IL-10, TNF-α, IL-1β and IL-6 in brain and spinal cord homogenyates tissue. In addition, the leukocyte-endothelium interaction in the spinal cord microvasculature was quantified by intravital microscopy, and inflammatory infiltrate in the spinal cord was evaluated by histological analysis. The group treated with liposomes containing Ang-(1-7) presented lower clinical score and weight loss, reduced cerebral vascular, pulmonary permeability and cerebral IL-6 concentration and an increase of the medullar leukocyte bearing rolling in the microvasculature. In conclusion, for the first time showed that, animals with EAE showed an improvement of clinical signs and inflammatory improvement response after the nebulization of liposomes containing Ang-(1-7).

Keywords: experimental autoimmune encephalomyelitis; Angiotensin 1-7, inhalation leukocyte infiltration; liposomes; neuroinflammation.