EFFECT OF IN VIVO N-ACETYL CYSTEINE TREATMENT ON OXIDATIVE STRESS, RAGE CONTENT AND BRAIN TAU PHOSPHORYLATION INDUCED BY LEISHMANIA AMAZONENSIS INFECTION

Senger, M.R.1,2; Gasparotto, J.1; Kunzler, A.1; Freitas de Souza, C.S.2; de Simone, S.G.2; Bortolin, R.C.1; Dantas, R.F.2; Somensi, N.1; Dal-Pizzol, F.3; Moreira, J.C.F.1; Calabrese, K.2, Silva-Jr, F.P.2, Gelain, D.P.1

1Departamento de Bioquímica, Universidade Federal do Rio Grande do Sul, Rio Grande do Sul, Brazil; 2Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil; 3Programa de Pós-Graduação em Ciências da Saúde, Universidade do Extremo Sul Catarinense, Santa Catarina, Brazil.

INTRODUCTION: Leishmaniasis is a parasitic disease caused by several species of the Leishmania genus. This obligate intra-macrophagic parasite affects around 12 million people around the world. Characteristics of the redox metabolism of L. amazonensis indicate that these parasites present high resistance against oxidative stress (OS) generated by host inflammatory cells. On the other hand, however, oxidative stress may result in a backfire to biomolecules and can trigger the development of a pathological process at host cellular level. OBJECTIVES: The present work investigate if peripheral infection of mice with L. amazonensis affects oxidative stress, tau-phosphorylation (tau-p) and receptor of advanced glycation endproducts (RAGE) protein content in mice organs and the in vivo effect of N-acetyl cysteine (NAC) treatment in these parameters. MATERIALS AND METHODS: Four months after a single right hind footpad subcutaneous injected with 10^5 amastigotes, brain, liver, kidneys, spleen, heart and lungs from BALB/c mice were isolated. RESULTS AND DISCUSSION: In liver, L. amazonensis infection led to increased thiol oxidation and nitrotyrosine formation; besides, SOD activity and SOD2 and RAGE protein content were up-regulated. In spleen and heart, the status of non-enzymatic antioxidant defense was also altered, but no changes in parameters of OS to biomolecules or antioxidant enzyme activation were detected. Western blot analysis indicated an increase in tau-p (Ser396) and RAGE in brain of infected animals. Brain tissue TNF-a, IL-1b, and IL-6 levels were not affected; however, increased protein carbonylation, decreased IFN-c levels and impairment in antioxidant defenses were detected. Systemic antioxidant treatment (NAC 20 mg/kg, i.p.) inhibited brain tau phosphorylation and recovered IFN-c levels. CONCLUSIONS: This is the first demonstration of alterations in biochemical parameters of neurodegeneration in an experimental model of Leishmania infection and open perspectives for the development of new therapeutic approaches.

Keywords: Leishmania amazonensis, Neurodegeneration, tau Phosphorylation

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