EVALUATION OF ANTI-LEISHMANIAL ACTIVITY BY INDUCTION OF NITRIC OXIDE AND INHIBITION OF PROSTAGLANDIN IN BALB/C MICE INFECTED WITH *LEISHMANIA MAJOR*

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Abstract. Cutaneous leishmaniasis is still one of the health problems in Iran and in the region. Nitric oxide (NO) has a key mechanism in the elimination of parasite from the body by its anti-leishmanial activity. Prostaglandin (PG) is a critical inhibitory factor of infected macrophage to decrease their anti-leishmanial activity. This study was designed to induce NO by L-arginine (L-Arg) precursor and inhibit PG production by anti-inflammatory Indomethacin (INDO) in *Leishmania major* infected Balb/c mice, in order to evaluate the effects of NO and PG on delay of lesion formation, size of lesion and proliferation of amastigotes inside macrophages. Liver, spleen and lymph nodes were also studied as target organs to detect amastigotes. Serum, liver and spleen suspensions were investigated for NO induction by using Griess microassay and serum PG was determined by ELISA. The results indicated that NO production was inhibited by *Leishmania* in infected Balb/c mice as compared with naive animals. Serum NO was inhibited by a combination therapy of L-Arg and INDO. Although NO was decreased in the liver by L-Arg, however it increased in the spleen after L-Arg and INDO application. A significant decline was observed in lesion size from Week 6 after infection by INDO. Both L-Arg and INDO had significant inhibitory effects on visceralization of leishmania in target organs. Only L-Arg decreased proliferation of promastigotes in macrophages. Pathophysiological signs including hepatomegaly, splenomegaly, survival rate and body weight all were affected in this experiment. Statistical analysis of data revealed an association between NO induction and PG inhibition in leishmaniasis. These data may indicate a possible candidatory for L-Arg and INDO as novel drugs for the treatment of leishmaniasis in mouse model.

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