# THE USE OF RECOMBINANT GAMMA INTERFERON ASSOCIATED WITH PENTAVALENT ANTIMONY IN THERAPY FOR VISCERAL LEISHMANIASIS.

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Immunologic dysfunction is an important aspect of the visceral leishmaniasis. Several defects have been described including the absence of gamma interferon (IFN) and interleukin 2 production during the active disease. The failure of the current therapy ($Sb^v$) for visceral leishmaniasis is about 15%. The alternative drug, amphotericin B, has high toxicity and it is not easily administered to some patients. Leishmania is an intracellular parasite of monocytes/macrophages. Interferon gamma has been demonstrated to augment monocyte/macrophage capacity to eliminate intracellular leishmania and other intracellular microrganisms. IFN-gamma has been given to patients with leprosy, AIDS and cancer with minimal toxic effects. Monocytes from IFN-gamma treated patients have increased capacity to generate oxygen-metabolites, an important mecnanism for intracellular killing of microbes. Based on these observations, we evaluated the combination of recombinant human interferon gamma (rhuIFN-gamma) and pentavelnt antimony ($Sb^v$) in patients with refractory visceral leishmaniasis or patients with severe form of the disease. Daily administration of rhuIFN-gamma at a dose of 100ug/m² IM daily in combination with $Sb^v$ in a dose of 20mg/kg was given for 10-20 days. The trials were carried out into two groups: group A: six patients who failed to respond to several courses of pentavalent antimonial alone. group B: nine patients with severe manifestation of the disease. The criteria for the diagnosis and the control of the therapeutic response in both groups was made by the demonstration of viable leishmania in splenic aspirate. In the group A 2 of 6 patients did not respond to the first 10 days course of combined therapy and required an extra 20 days therapy. From the 9 patients of the group B, one

required an extra 10 day course of combined therapy. The clinical course showed that the signs and symptoms dramatic disappeared during therapy, and the immune response to L.donovani antigen was restored earlier than in retrospective controls. The combination therapy was well tolerated. Fever was the only side effect noted during the gamma interferon therapy. We conclude that the use of rHuIFN-gamma plus SbV is a potential therapy for Visceral Leishmaniasis.