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THERAPEUTIC POTENTIAL OF EXTRACELLULAR VESICLES FROM MESENCHYMAL STEM CELLS IN CUTANEOUS LEISHMANIASIS

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Cutaneous leishmaniasis (CL), caused by *Leishmania braziliensis*, is characterized by chronic ulcers and intense inflammation. Current treatments have limitations, including severe side effects and increasing parasite resistance. Extracellular vesicles derived from human umbilical cord mesenchymal stem cells (HuMSCs-EVs) offer immunomodulatory and regenerative potential, raising the possibility of using them in a combination treatment with Meglumine Antominate, the standard chemotherapy. We propose that HuMSC-EVs can regulate the overt immune response associated with CL pathogenesis and facilitate wound healing. To this end, we investigated the effects of exposure of L. braziliensis-infected macrophages to HuMSCs-EVs and their wound healing potential. BMDM infected with *L. braziliensis* and exposed to HuMSCs-EVs showed reduced infection rates, decreased parasite load (39% *vs* 23%), and a shift toward the anti-inflammatory M2 phenotype. *In vitro* cytokine analysis revealed increased levels of TNF-α, IL-10 and IL-1β, highlighting the immunomodulatory role of EVs. In keratinocyte wound-healing assays, HuMSCs-EV accelerated closure rates and promoted cell migration at different time points. Employing a pre-clinical model of CL, BALB/c mice infected with *L. braziliensis* and treated with HuMSCs-EV (applied intravenously) displayed smaller lesions without significant changes in parasite burden. These results indicate that HuMSC-EV promotes immune regulation and tissue repair, presenting a novel therapeutic approach for CL.

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