A Novel Microneedle-Based Transdermal Infection Model for Leishmania Research: Enhancing Safety and Mimicking Natural Transmission

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Abstract

Leishmaniasis is a disease caused by *Leishmania* protozoa, has various clinical forms and is endemic in Brazil. Traditional infection methods with intradermal and subcutaneous needles do not mimic natural sandfly transmission and carry laboratory accident risks owing to the use of low-gauge needles. This study investigated the application of microneedles for transdermal infections to better replicate the natural infection environment while ensuring safe handling. Experiments involved transdermal infections with cartridges containing 12, 7, and 1 microneedle, compared with conventional intradermal infections in BALB/c mouse ears. Further tests used a 12-microneedle cartridge at different depths (0.25 mm, 0.5 mm, 0.75 mm, 1.0 mm, and 1.5 mm) followed by challenge with different doses of *Leishmania amazonensis*. The results showed that transdermal infections produced similar lesion development and parasite loads as

intradermal infections. Higher doses led to increased tissue damage, whereas lower doses resulted in significant parasite loads in the ear, lymph node, and spleen. Regardless of the differences between the infection methods, parasite loads in the ear and lymph nodes were similar between the two approaches at the early stages, specifically at 30 minutes and 12 hours post-infection. Thirty minutes post-infection, cytometry analysis indicated recruitment of neutrophils to the lesion site, regardless of the infection model used. The transdermal model specifically attracts neutrophils, independent of the presence of parasites. This novel microneedle infection model enables smaller parasite doses, better mimics natural infection conditions, and reduces risks during animal experimentation. This technique holds promise for future studies of leishmaniasis therapy.

Keywords: leishmaniasis; microneedle, infection, transdermal, model, BALB/c, ear