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FIGHTING LEISHMANIASIS WITH NUTRITION: MALNUTRITION IMPAIRS TREATMENT AND ALTERS DISEASE PROGRESSION

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Abstract

Malnutrition and visceral leishmaniasis (VL) are major public health challenges, contributing to significant morbidity and mortality worldwide. The progression of leishmaniasis is closely linked to the host immune status, and malnutrition can severely compromise immune function, altering disease susceptibility and organ tropism. This study aimed to validate a dietary model that closely mimics marasmic malnutrition, assessing its impact on nutritional, biochemical, and hematological parameters and investigating how malnutrition influences the establishment, progression, and treatment response of *Leishmania infantum* BALB/c mice infection. Animals were fed either a restricted diet (36.26% carbohydrate, 8.79% protein, 4.95% fat, 7.62 kJ/100 g) or a control diet (65.93% carbohydrate, 24.18% protein, 9.89% fat, 15.24 kJ/100 g). Some malnourished mice underwent a refeeding process with the control diet. Nutritional status was evaluated through phenotypic, hematological, and biochemical markers. The restricted diet, induced mild malnutrition, resulting in 12% weight loss, reduced growth rates, lower BMI, a 47.5% decrease in leukocyte counts, and a two-fold increase in cholesterol levels. Following *L. infantum* infection and meglumine antimoniate treatment revealed that malnutrition significantly impaired splenic infection but enhanced hepatic parasite burden. Refeeding restored hepatic infection levels but did not fully reverse splenic impairment. While meglumine antimoniate effectively reduced liver parasite loads in control mice (10^5-fold reduction), its efficacy was significantly affected in malnourished mice (10^3-fold reduction). However, refeeding successfully restored treatment effectiveness in the liver, reaching a 10^5-fold decrease in liver parasite load. These findings suggest that marasmic malnutrition alters VL pathogenesis and reduces treatment efficacy, emphasizing the importance of nutritional interventions in managing VL in malnourished populations.

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