IMMUNOMODULATION OF *TRYPANOSOMA CRUZI*-INFECTED ADIPOSE TISSUE TREATED WITH BENZNIDAZOLE: IMPACT ON INFLAMMATORY RESPONSE AND INTERACTION WITH IMMUNE CELLS

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Adipose tissue (AT) plays a crucial role in energy homeostasis and also exhibits refined immunological mechanisms, making it a promising target for parasites such as *Trypanosoma cruzi*. As an effective barrier to parasite evasion, the effectiveness of the recommended drug, Benznidazole (BZ), may be questionable. To address this, we evaluated the immunomodulation of *T. cruzi*-infected AT treated with BZ (1 µg/mL) in cell culture (n=4). Additionally, to assess the influence of immune response cells, we simulated a co-culture microenvironment (n=5) between infected and BZ-treated AT in indirect contact with peripheral blood mononuclear cells (PBMCs). In both culture models, after 72 hours, culture supernatants were collected to measure inflammatory mediators (cytokines, chemokines, and adipokines), AT was harvested to quantify parasite load, and PBMCs were collected to detect activation/inhibition markers. Our findings showed that in the model assessing only infected and treated AT, although BZ did not eliminate the parasite, it reduced the inflammatory state by lowering IL-6 compared to the untreated condition ($p=0.0352$). In contrast, in the model evaluating PBMC influence in this microenvironment, we observed that AT induces upregulation of IL-2, IL-6, and MCP-1 but downregulates TNF and IL-8 in the presence of PBMCs and *T. cruzi*. However, this phenomenon was not associated with BZ treatment, as observed in the previous model; this time, PBMCs were crucial for modulating the immune response. Additionally, we found that BZ decreases adipsin in *T. cruzi*-infected AT in the presence of PBMCs ($p=0.0207$), which may be beneficial, as this adipokine is linked to inflammatory conditions. Therefore, we propose that although BZ reduces inflammatory mechanisms, AT-associated cells can modulate the immune response in favor of the parasite, making AT a significant ally of *T. cruzi*.

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