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TITLE

BIOLOGICAL AND PROTEOMIC DIFFERENCES OF TWO SCHISTOSOMA MANSONI STRAINS

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ABSTRACT

Different strains of Schistosoma mansoni may exhibit variations in pathology and drug susceptibility. These differences can impact parasite distribution, control measures and the search for new therapeutic alternatives for schistosomiasis. In this study, we aimed to compare two strains of S. mansoni: BH (Belo Horizonte) and SE (Sergipe). To understand differences in pathology and praziquantel (PZQ) treatment response in the vertebrate host, BALB/c mice were infected with 80 cercariae of each strain and treated 45 days post infection (dpi) with either a subcurative dose of a 50 mg/kg, a curative dose of 150 mg/kg, or a higher dose of 300 mg/kg PZQ. Fecal egg count was performed weekly starting at 30 dpi, and euthanasia was performed at 60 dpi. BH strain presented higher infection rates, with a larger number of worms recovered from the mesenteric veins, a greater number of fecal eggs and intestine' retained eggs (oogram). Liver granuloma from SE strain infections were significantly smaller than those from the BH strain, which also had a higher number of granuloma, suggesting increased pathogenicity. No significant differences in parasite burden were found when mice were treated with a subcurative dose. However, in groups infected with BH strain and treated with 150 or 300 mg/kg PZQ we found a significant reduction in parasite burden and fecal egg count, a lower number of immature and mature eggs and a higher number of dead eggs in the oogram as well as a reduced number of hepatic and intestinal granuloma. SE strain showed significant differences only in the number of fecal eggs at 60 dpi following treatment with 300 mg/kg PZQ. To explore differences in pathology and susceptibility to praziquantel, we performed a comparative shotgun proteomic analysis of male and female worms from both strains using label-free quantification. Proteins were extracted from pools of parasites, followed by peptide digestion with trypsin and mass spectrometry analysis. We identified over 1000 proteins across groups. In untreated males, 16 proteins showed differential expression. PZQ treatment did not alter protein expression in BH strain males or females. In contrast, SE strain females showed upregulation of 3 proteins post-treatment, and SE strain males exhibited 74 differentially expressed proteins. Among treated females from both strains, subtle adaptations were observed, especially in SE strain, with structural proteins of the cytoskeleton and musculature suggesting potentially less PZQ-induced damage in this strain. Overall, results indicate that the BH strain produces and retains more eggs, which has implications for pathology, but is more susceptible to PZQ. In contrast, the SE strain appears to exhibit characteristics of PZQ resistance or tolerance in vivo. We also identified proteins upregulated in the SE strain related to adaptive mechanisms against oxidative stress induced by PZQ, potentially enhancing parasite survival and adaptation post-treatment

KEYWORDS

Schistosoma mansoni; Strains; Proteomics; Susceptibility to Praziquantel

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