Abstracts

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11.010 **Are Age and Sex Relevant Factors for the Pharmacokinetics of Benznidazole in Patients with Chronic Chagas Disease in the Indeterminate Form?**

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Introduction: Chagas disease (CD) is caused by the protozoan *Trypanosoma cruzi*. It is estimated that 70 million people are at risk of infection in 21 countries in the Americas. Benznidazole (BDZ) is the main drug used in CD chemotherapy and its toxicity can lead to discontinuation of treatment with a frequency close to 30%. The incidence of adverse events is higher among women. Very few and incomplete studies have focused on the pharmacokinetics of BDZ in patients. The aim of this study was to characterize the pharmacokinetic profile of BDZ in patients with chronic indeterminate CD, identifying possible factors of population variability. **Methods:** The research protocol was approved by research ethics committee (CAAE 47219021.5.0000.5262; opinion number 4.777.595) and conducted in Rio de Janeiro – Brazil. This is a single-center, non-blinding study. Adult patients of both sexes aged 18 to 70 years old with chronic indeterminate CD form were included in this study. The patients received 300 mg/day of BDZ for 60 days. BDZ plasma concentrations were monitored in blood plasma in the first, seventh, fourteenth, thirtieth and sixtieth days of treatment. HPLC-MS/MS was used to determine BDZ concentrations. Pharmacokinetic parameters of absorption, distribution and elimination were determined for each age group and sex. **Results:** BDZ exposure was higher in women compared to men after receiving a single dose (1st day). Cmax was 33% higher ($P = 0.00013$) and AUClast was 37% higher ($P = 0.000901$) among women. These differences, however, were no significant after normalizing the pharmacokinetic parameter for the administered dose by weight (mg/kg) (Cmax/D and AUClast/D). After multiple doses (14th day) no sex difference was observed ($P < 0.05$), although T1/2 was higher in men. The T1/2 calculated after chronic use of BDZ was higher for patients older than 50 years. Greater Cmax and AUC were observed at steady state for these patients compared to younger patients ($P < 0.05$). Patients with a body mass index (BMI) greater than 30 kg/m2 had lower Cmax and AUC compared to those with a lower BMI ($p < 0.05$), after a single dose. T1/2 was 70% higher in patients with BMI greater than 30 kg/m2 after multiple doses. **Conclusion:** Differences in BDZ pharmacokinetics observed between sexes appear to be related to the greater body mass of men compared to women. **Financial Support:** CNPq; FAPERJ