Tratamiento para niños y, siempre que sea posible, para adultos en las estructuras de atención primaria

Treatment of children, and where posible, for adults at the primary healthcare level

Villar JC, Villar LA, Marin-Neto JA, Ebrahim S, Yusuf S. Trypanocidal drugs for chronic asymptomatic Trypanosoma cruzi infection. Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD003463. DOI: 10.1002/14651858.CD003463.

Summary:
Studies testing anti-parasitic drugs for people infected, but still free of Chagas' disease, are scarce and fail to provide evidence about them as preventive medications.

Trypanosoma cruzi, a parasite causing Chagas' disease, infects about 18 million people living across Latin America. About 30% of them develop a major heart disease in their 30s or 40s, after decades of silent infection. No treatment is considered useful for preventing the disease among those infected, but still healthy. Drugs aimed to destroy the parasites may have this potential. Reviewers found only five published trials including 756 participants testing such agents. Although the anti-parasitic activity of most of these compounds was documented, no study addressed the efficacy of the drugs in terms of signs or symptoms of the disease.

de Andrade AL, Zicker F, de Oliveira RM, Almeida Silva S, Luquetti A, Travassos LR, Almeida IC, de Andrade SS, de Andrade JG, Martelli CM , Randomised trial of efficacy of benznidazole in treatment of early Trypanosoma, Lancet. 1996 Nov 23;348(9039):1407-13. cruzi infection.

BACKGROUND: Benznidazole, a nitroimidazole derivative, has been recommended for the treatment of acute and congenital Trypanosoma cruzi infection (Chagas' disease). We have examined the safety and efficacy of this drug in the treatment of the early chronic phase of T cruzi infection.
METHODS: Between 1991 and 1995, we carried out a randomised, double-blind, placebo-controlled trial in a rural area of Brazil with endemic Chagas' disease. 82% of 2434 schoolchildren (aged 7-12 years) identified in a census were screened for antibodies to T cruzi by indirect immunofluorescence, indirect haemagglutination, and ELISA. 130 were positive in all tests and were randomly assigned benznidazole (7.5 mg/kg daily for 60 days by mouth) or placebo. The primary endpoint for efficacy was the disappearance of specific antibodies (negative seroconversion) by the end of 3-year follow-up. The secondary endpoint was the reduction of antibody titres on repeated serological tests. One child moved away from the area just after randomisation and was excluded from the analyses. Insecticidal measures were taken throughout the trial to reduce the risk of reinfection.
FINDINGS: Minor side-effects requiring no specific medication were recorded in a small proportion of individuals. On a chemiluminescent ELISA with purified trypomastigote glycoconjugate, serum from all participants was positive at the beginning of the trial. At the end of follow-up, 37 (58%) of the 64 benznidazole-treated participants and 3 (5%) of those who received placebo were negative for T cruzi antibodies. The efficacy of benznidazole treatment estimated by intention to treat was 55.8% (95% CI 40.8-67.0). At the end of follow-up, children who received benznidazole had five-fold lower geometric mean titres by indirect immunofluorescence than placebo-treated children (196[147-256] vs 1068[809-1408], $p < 0.00001$).
INTERPRETATION: The trial showed that a 60-day course of benznidazole treatment of early chronic T cruzi infection was safe and 55.8% effective in producing negative seroconversion

of specific antibodies. The results are very encouraging and justify the recommendation of treatment for seropositive children as public health policy.

Estani, Sergio Sosa and Segura, Elsa Leonor Treatment of Trypanosoma cruzi infection in the undetermined phase. Experience and current guidelines of treatment in Argentina . Mem. Inst. Oswaldo Cruz, Sept 1999, vol.94, suppl.1, p.363-365

First paragraph:
The goals of specific treatment against *Trypanosoma cruzi* infection, at an individual level, are to eliminate the parasite, to diminish the probability of developing illness (Chagas disease), and to hinder the chain of *T. cruzi* transmission as actions for the control of vectorial and non vectorial transmission (Sosa Estani 1993). Around 1930, investigations began in Argentina to obtain an effective drug against *T. cruzi*. Of all the substances evaluated, only nifurtimox (1972) and benznidazol (1974) have been accepted by the Ministry of Health as anti-*T. cruzi* drugs. Both drugs began to be assessed on the acute phase, and later, on the chronic phase of the disease.

Viotti R, Vigliano C, Lococo B, Bertocchi G, Petti M, Alvarez MG, Postan M, Armenti A., Long-term cardiac outcomes of treating chronic Chagas disease with benznidazole versus no treatment: a nonrandomized trial. Ann Intern Med. 2006 May 16;144(10):724-34.

BACKGROUND: Benznidazole is effective for treating acute-stage Chagas disease, but its effectiveness for treating indeterminate and chronic stages remains uncertain.
OBJECTIVE: To compare long-term outcomes of patients with nonacute Chagas disease treated with benznidazole versus outcomes of those who did not receive treatment.
DESIGN: Clinical trial with unblinded, nonrandom assignment of patients to intervention or control groups.
SETTING: Chagas disease center in Buenos Aires, Argentina.
PATIENTS: 566 patients 30 to 50 years of age with 3 positive results on serologic tests and without heart failure.
MEASUREMENTS: The primary outcome was disease progression, defined as a change to a more advanced Kuschnir group or death. Secondary outcomes included new abnormalities on electrocardiography and serologic reactivity.
INTERVENTION: Oral benznidazole, 5 mg/kg of body weight per day for 30 days (283 patients), or no treatment (283 patients).
RESULTS: Fewer treated patients had progression of disease (12 of 283 [4%] vs. 40 of 283 [14%]; adjusted hazard ratio, 0.24 [95% CI, 0.10 to 0.59]; P = 0.002) or developed abnormalities on electrocardiography (15 of 283 [5%] vs. 45 of 283 [16%]; adjusted hazard ratio, 0.27 [CI, 0.13 to 0.57]; P = 0.001) compared with untreated patients. Left ventricular ejection fraction (hazard ratio, 0.97 [CI, 0.94 to 0.99]; P < 0.002) and left ventricular diastolic diameter (hazard ratio, 2.45 [CI, 1.53 to 3.95]; P < 0.001) were also associated with disease progression. Conversion to negative results on serologic testing was more frequent in treated patients than in untreated patients (32 of 218 [15%] vs. 12 of 212 [6%]; adjusted hazard ratio, 2.1 [CI, 1.06 to 4.06]; P = 0.034).
LIMITATIONS: Nonrandom, unblinded treatment assignment was used, and follow-up data were missing for 20% of patients. Loss to follow-up was more common among patients who were less sick. Two uncontrolled interim analyses were conducted.
CONCLUSIONS: Compared with no treatment, benznidazole treatment was associated with reduced progression of Chagas disease and increased negative seroconversion for patients presenting with nonacute disease and no heart failure. These observations indicate that a randomized, controlled trial should now be conducted.

Sosa Estani S, Segura EL, Treatment of Trypanosoma cruzi infection in the undetermined phase. Experience and current guidelines of treatment in Argentina. Mem Inst Oswaldo Cruz. 1999;94 Suppl 1:363-5.

Viotti R, Vigliano C, Armenti H, Segura E. Treatment of chronic Chagas' disease with benznidazole: clinical and serologic evolution of patients with long-term follow-up. Am Heart J. 1994 Jan;127(1):151-62.

Viotti R, Vigliano C, Etiological treatment of chronic Chagas disease: neglected 'evidence' by evidence-based medicine. Expert Rev Anti Infect Ther. 2007 Aug;5(4):717-26.