

# Highly diluted medication reduces parasitemia and improves experimental infection evolution by *Trypanosoma cruzi*

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**Background:** In *Trypanosoma cruzi* infection, the pathogenesis is the result of a break in the host-parasite relationship. There is no research in the literature about the parasitological and clinical evolution of mice experimentally infected with *T. cruzi*.

**Aim:** Evaluate animals infected with *T. cruzi* and treated in different ways using biotherapeutic, a highly diluted medicine prepared with blood trypomastigotes.

**Methodology:** To evaluate the effect of different ways of treatment using biotherapeutic *T. cruzi* 17x(BIOTTc17x) on clinical and parasitological evolution of mice experimentally infected with *T. cruzi* Y strain, a blind randomized by draw controlled trial was performed, using 72 male swiss mice, aged 28 days, divided in six groups according to treatment: *CI-* treated with 7% alcohol-water solution, diluted in water (10 $\mu$ L/mL) given *ad libitum*; *BIOTPI:* treated with BIOTTc17x in water (10 $\mu$ L/mL) given *ad libitum* during a period that started on the day of infection and finished when animals died; *BIOT4DI:* treated with BIOTTc17x in water (10 $\mu$ L/mL) given *ad libitum* from the 4th day of infection to the death of animals; *BIOT4-5-6:* treated with BIOTTc17x by gavage (0.2mL/animal/day) on 4th, 5th and 6th days after infection; *BIOT7-8-9:* treated with BIOTTc17x by gavage (0.2mL/ animal/day) on 7th, 8th and 9th days after infection. The parameters evaluated were: parasitemia, pre patent period (PPP), patent period (PP), total parasitemia (Ptotal), parasitemiapeak, clinical aspects and mortality.

**Results:** Our results showed that the constant use of highly diluted medication in water has resulted in better benefits, with a lower AUC (p<sub>value</sub>=0.00001), lower Ptotal average (p<sub>value</sub>=0.0137), lower Pmax of parasitemia (p<sub>value</sub>=0.0003), higher PPP (p<sub>value</sub>=0.0006), and lower PP (p<sub>value</sub>=0.0006), besides a tendency towards higher survival rates in these animals (p<sub>value</sub>=0.1360) (table1). The results for the correlation between parasitological parameters and the survival period of the animals pointed PPP as the best parameter in showing the difference in the performance of different schemes of treatment.

**Conclusions:** The BIOT4DI group showed better performance with reduced parasitemia and a trend towards lower mortality with longer periods of survival. The clinical use of these results in humans, should consider the allometric system dosing of drugs that takes into account the metabolic rate of each organism.

**Table 1:** Mean and standard deviation of parasitological parameters of animals undergone to different treatment schemes using BIOT<sub>7c17dH</sub>.

GROUP	AUC (x10 <sup>5</sup> )	P <sub>total</sub> (x10 <sup>5</sup> )	DAY OF P <sub>max</sub>	PPP	PP	SURVIVAL	DEATH (%)
CI	10.9±8.23	12.5±8.98	5.02±7.07	6.02±1.85	9.63±2.74	15.33±3.39	100%
BIOT <sub>4-5-6</sub>	9.23±3.26*	9.33±3.25*	5.82±2.14 *	3.86±1.36*	7.43±1.99*	12.14±1.25 *	100%
BIOT <sub>7-8-9</sub>	8.78±2.34*	9.32 ±2.48*	4.05±2.42	4.38±1.32*	8.88±1.62	14±1.5	100%
BIOT <sub>PI</sub>	5.95±4.55	6.63 ±5.02	2.25±1.65 *	13.67±33.11	6.61±2.69 *	29±42.79	88%
BIOT <sub>4PI</sub>	4.28±2.89	4.63 ±3.19	1.45±1.00 *	21.5±42.87*	5.78±1.03 *	27.1±40.98 *	90%

\*statistical significance (p<0.05). CI: control group – infected animals treated with 7% water-alcohol solution diluted in water (10µL/mL) offered ad libitum; BIOT<sub>PI</sub>: infected animals treated with BIOT<sub>7c17dH</sub> diluted in water (10µL/mL) from the day of infection until the death of the animals; BIOT<sub>4-5-6</sub>: infected animals treated with BIOT<sub>7c17dH</sub> diluted in water (10µL/mL) from the 4<sup>th</sup> day of infection until the death of the animals; BIOT<sub>7-8-9</sub>: infected animals treated with BIOT<sub>7c17dH</sub> by gavage on the 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> day of infection; BIOT<sub>7-8-9</sub>: infected animals treated with BIOT<sub>7c17dH</sub> by gavage on the 7<sup>th</sup>, 8<sup>th</sup> and 9<sup>th</sup> day of infection. (AUC=area under the curve; P<sub>total</sub>= Total parasitemia; P<sub>max</sub>= maximum peak of parasites; PPP=pre patent period; PP=patent period; SURVIVAL= days of survival per animal per group; DEATH n/N= percentage of death per group).

**Keywords:** Biotherapy; Mice infection; Parasitological evaluation, Clinical evaluation, Pre Patent Period.

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