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Clinical efficacy of a domperidone-based treatment program for the prevention of canine leishmaniosis

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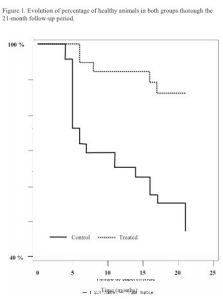
Objetives of the Study:

Domperidone, a dopamine D2 receptor antagonist, has recently been included in the list of anti-Leishmania drugs in the current consensus guidelines for treatment of canine leishmaniosis (Oliva G et al. 2010). Domperidone is effective in controlling and reducing clinical signs and antibody titers when orally administered to dogs naturally infected by Leishmania infantum through the activation of the cell-mediated immune response (Gómez-Ochoa P et al. 2009).



In healthy animals, repeated administration of domperidone progressively increases the phagocytic activity of neutrophil and monocyte peripheral blood populations leading to an increased resistance of these cells against in vitro experimental infection with Leishmania amastigotes (unpublished data). These results confer domperidone a potential use for prevention of canine leishmaniosis.

The aim of the present controlled, randomized clinical trial was to assess the efficacy of a Domperidone-based treatment program for the prevention of canine leishmaniosis in endemic areas.

Materials and Methods:

A total of 90 clinically healthy dogs, sero-negative to Leishmania, of different age, breed and sex, were included in the trial with the consent of their owners. All animals were living in the same geographic area in Valencia (Spain), with a previously known seroprevalence up to 30%. The study was performed with the authorization of the Spanish Medicines Agency (AEMPS).

Forty-four animals received domperidone orally at a dose of 0.5mg/kg/day for 30 consecutive days, on a 4-monthly basis during 21 months. The first treatment was scheduled to start at the beginning of the insect vector activity period. The remaining 46 animals did not receive any treatment. No insect repellents were applied at all to any animal throughout the study. All animals underwent periodic clinical examinations and blood samplings for serological determination of anti-leishmania antibody titers. Treatment failure was considered when, at a given examination, an animal was showing any clinical sign compatible with the disease and anti-leishmania antibody titers (IFAT) ≥ 1/80, indicative of active infection and disease progression. Animals with treatment failure were immediately withdrawn from the study and treated according to the practitioner's clinical decision. Two statistical analyses were performed with the results obtained up to 12 months and up to 21 months after study initiation, respectively.

Results:

The percentage of dogs having evidenced clinical signs of leishmaniosis and anti-leishmania antibody titers (IFAT) ≥ 1/80 was significantly lower in the domperidone treated group both at month 12 (7% vs. 35%; p=0.003) and at month 21 (11% vs. 48%; p<0.001). Statistically significant differences between groups (p<0.001) were also detected in favor of domperidone treated group, in time elapsed until animal withdrawal from the study (Figure 1).

Finally, the odds-ratios calculated for each period were 7.3 (p=0.001) at month 12 and 7.2 (p<0.001) at month 21, thus indicating that the overall risk (odds) for domperidone-treated dogs to clinically develop canine leishmaniosis is quite 7 times lower than for not treated animals.

Conclusions:

The results of this study demonstrate that the implementation of a strategic domperidone-based treatment program is highly efficacious in the prevention of canine leishmaniosis in endemic areas.

Bibliography:

Oliva G, Roura X, Crotti A et al.; Guidelines for the treatment of Leishmaniosis in dogs. J Am Vet Med Assoc. 2010, Jun 1;236(11):1192-1198.

Gómez-Ochoa P, Castillo JA, Gascón FM et al.; Use of Domperidone in the treatment of canine visceral leishmaniasis: A clinical trial. Vet J. 2009, Feb;179(2):259-263.

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CLINICAL EFFICACY OF A DOMPERIDONE-BASED TREATMENT PROGRAM FOR THE PREVENTION OF CANINE LEISHMANIOSIS

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INTRODUCTION

Repeated administration of a dopamine D2 receptor antagonist, domperidone, to healthy animals progressively increases the phagocytic activity of neutrophil and monocyte peripheral blood populations leading to an increased resistance of these cells against *in vitro* experimental infection with *Leishmania* amastigotes (unpublished data). **This confers domperidone a potential use for prevention of canine leishmaniosis**, in addition to its already reported clinical efficacy in the treatment of naturally diseased animals (Gómez-Ochoa P *et al*. 2009, Oliva G *et al*. 2010).

OBJECTIVE

The aim of the study was to assess the efficacy of a treatment program based on domperidone for the prevention of canine leishmaniosis under real field conditions.

MATERIAL AND METHODS

- Ninety clinically healthy dogs, serologically negative to Leishmania (IFAT<1/40), living in a highly endemic geographic area in Valencia (Spain) were included, with the consent of their owners, in a clinical trial performed under the authorization of the Spanish Medicines Agency (AEMPS).
- Dogs were randomly distributed in two homogenous groups (Table 1):

  Treated group (n=44)

  Oral suspension of domperidone at 0.5 mg/kg/day during 30 consecutive days, on a 4-monthly basis, with the first treatment being started at the beginning of the *Phlebotomus* season.

  Control group (n=46)

  Non-treated.
- No other treatment nor insect repellents were used.
- 21-month follow-up period with periodic clinical examinations and serological determination of anti-*Leishmania* antibody titers.
- Active infection / disease progression was considered when, at a given examination, a dog showed any clinical sign compatible with the disease + positive anti-*Leishmania* antibody titers (IFAT ≥ 1/80).
- Main parameter = cumulate percentage of dogs with active infection / disease progression up to 12 and 21 months of follow-up.

		Treated Group	Control Group	*p value*
Sex (n and %)	Males	25 (56.8%)	25 (54.3%)	0.981 (1)
	Females	19 (43.2%)	21 (45.7%)	
Age (years)	mean (SD)	5 (2.2)	5 (2.3)	0.595 (2)
	range	1-10	1-10	
Weight (kg)	mean (SD)	20.3 (10.83)	20.4 (8.46)	0.683 (2)
	range	6.5 - 54	7 - 43	
Breed (n and %)	Mongrel	13 (29.5%)	23 (50.0%)	0.606 (3)
	Other*	31 (70,5%)	23 (50.0%)	

* up to 24 different breeds
(1) Pearson chi-square test
(2) Student's T-test
(3) Mann-Whitney Rank Sum test

Table 1. *Distribution of animal baseline characteristics and analysis of homogeneity between the two groups.*

RESULTS

- The cumulate percentage of dogs showing active infection / disease progression was significantly lower in the domperidone-treated group both at month 12 and at month 21 of follow up period (Fig. 1).

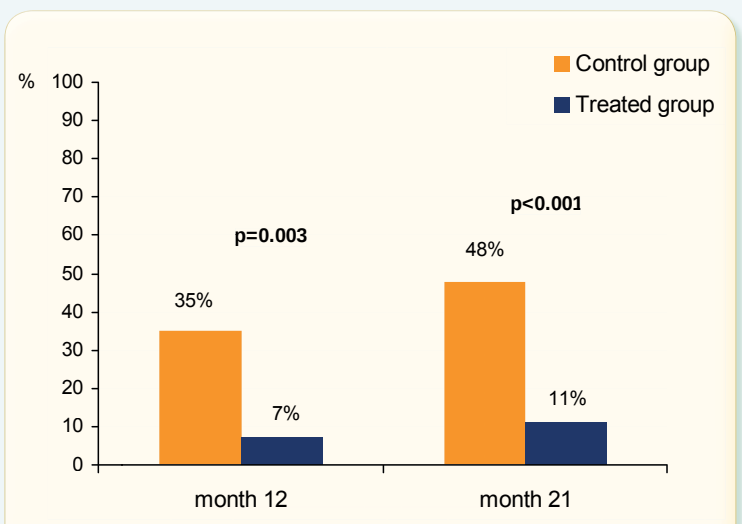

Figure 1. *Cumulate percentage of diseased dogs and statistical comparisons between groups (Pearson chi-square test).*

- Dogs treated with domperidone offered a consistent and significantly higher degree of resistance to active infection / disease progression over time (Fig. 2).

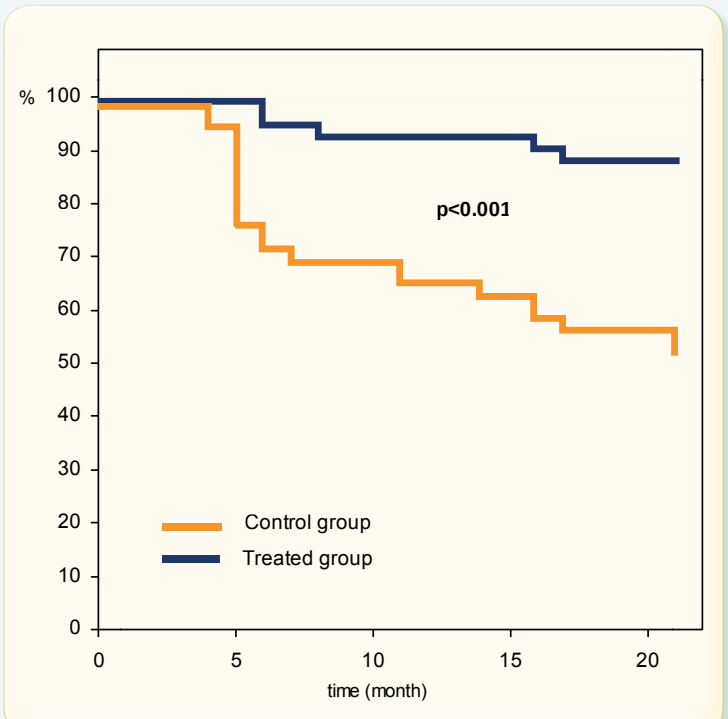

Figure 2. *Evolution (Kaplan Meyer estimates) of percentage of healthy animals in both groups thorough the whole 21-month follow-up period and statistical comparisons (Logrank test).*

- The odds-ratios calculated for each period were 7.3 (p=0.001) at month 12 and 7.2 (p<0.001) at month 21, thus indicating that **the overall risk (odds) for Domperidone-treated dogs to clinically develop canine leishmaniosis is quite 7 times lower than for not treated animals.**
- Repeated treatment with Domperidone was well tolerated and accepted, with only two dogs showing a transient mild galactorrhea and two other dogs showing soft faeces.

CONCLUSIONS

The results of this study demonstrate that the implementation of a strategic domperidone-based treatment program is highly efficacious in the prevention of canine leishmaniosis in endemic areas.

REFERENCES

Gómez-Ochoa P, Castillo JA, Gascón FM *et al*.; Use of Domperidone in the treatment of canine visceral leishmaniasis: A clinical trial. Vet J. 2009; 179: 259-63.

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