CLINICAL EFFICACY OF A LEISGUARD®-BASED PROGRAM STRATEGICALLY ESTABLISHED FOR THE PREVENTION OF CANINE LEISHMANIOSIS IN ENDEMIC AREAS WITH LOW PREVALENCE

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Work type: ***Original Research***
Topic: ***Leishmaniasis***

Purpose of the work. *In leishmaniosis, the innate immune response has been claimed not only to be the first barrier against the parasite but also to play a pivotal role in the establishment of a cell-mediated (Th1) adaptive immune response protective against the disease (Bonilla-Escobar, 2005). In this respect, the adequate activation of the phagocytic cell populations involved in antigen processing and presentation to T-lymphocytes is of paramount importance.*
Leisguard® is a domperidone based oral suspension recently marketed in several European countries for both the treatment and prevention of canine leishmaniosis. Its repeated administration to dogs induces activation of phagocytic cells leading to an increase in their anti-Leishmania potential (Gomez-Ochoa et al. 2012), being this the rationale of its clinical indications.
In accordance to the manufacturer instructions, when administered for preventive use, repeated treatments with Leisguard® have to be strategically scheduled during the year according to both the parasite's transmission season and prevalence of the disease in a given geographical area.
The aim of the present controlled, randomized clinical trial was to evaluate the clinical efficacy of a Leisguard®-based program specifically established for the prevention of canine leishmaniosis in endemic areas with low prevalence.
Materials and used methods. *A total of 240 clinically healthy dogs, sero-negative to Leishmania (Direct Agglutination Test, DAT<1/400), of different age, breed and sex, were included in the study. All dogs were housed in open-air premises in a dog kennel located in Valladolid (Spain), with a previously known seroprevalence around 7%. The study was performed with the authorization of the Spanish Medicines Agency.*
All animals were included simultaneously in the study and randomly assigned either to a Treated or to a Non-Treated group with 120 dogs each. The Leisguard®-based program implemented in the Treated group consisted in two treatments with Leisguard® (1ml/10kg/day, during 30 consecutive days), one at the beginning of the estimated vector's activity period (May-June) and another one at the end of this period (September-October). The 120 animals in the Non-Treated group did not receive any product. No insect repellents were applied at all to any animal in both groups.
During the study, all animals underwent periodic blinded clinical examinations and two blood samplings determination of anti-Leishmania antibody titters: before the initiation of the first treatment and 3 months after the end of the second treatment (December-January). When, at a given examination, an animal was showing any clinical sign compatible with the disease, it underwent complementary serological analyses for anti-Leishmania antibody titters' determination. In case of positive results (DAT = 1/400) the animal was withdrawn from the study and treated according to the decision of the kennel's veterinary staff.
Outcomes. *All animals under the Leisguard®-based program remained healthy and seronegative to Leishmania right up to the end of the 9-month follow-up period. In contrast, seven dogs out of 120 in the Non-Treated group developed clinical signs compatible with canine leishmaniosis (peripheral lymphadenomegaly and alopecia) and anti-Leishmania antibody titters (DAT>1/400) during the last month of the study, thus indicating active infection and disease progression. In all seropositive dogs the presence of the parasite was confirmed by means of direct visualization in lymph node or bone marrow aspirate. Differences between groups in terms of incidence of the disease were statistically significant (0% vs 5.83% in the Treated and Non-Treated groups, respectively; p<0.001). Finally, no side effects were observed during the administration of the drug in the treated group.*
Conclusions. *The results of this study confirm that the implementation of a Leisguard®-based program consisting in two treatments with Leisguard® (1ml/10kg/24h, during 30 consecutive days), at the beginning and at the end of the estimated vector's activity period is highly efficacious in the prevention of canine leishmaniosis in dogs living in an endemic region with low prevalence.*

Bibliography

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CLINICAL EFFICACY OF LEISGUARD® FOR THE PREVENTION OF CANINE LEISHMANIOSIS IN AN ENDEMIC AREA WITH LOW RISK OF INFECTION

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OBJECTIVE

The aim of the present study was to evaluate the efficacy of a Leisguard®-based program strategically established for the prevention of canine leishmaniosis in an endemic area with low prevalence.

INTRODUCTION

Leisguard® is a domperidone-based oral solution recently marketed in several European countries for the treatment and prevention of canine leishmaniosis. Its repeated administration to dogs induces activation of phagocytic cells leading to an increase in their anti-*Leishmania* potential (Gomez-Ochoa et al. 2012) being this the rationale of its clinical indications. When administered for preventive use, repeated treatments with Leisguard® have to be strategically scheduled during the year according to the parasite's transmission season and the prevalence of the disease in a given geographical area (Llinás et al, 2011).

MATERIAL AND METHODS

- Two hundred and forty clinically healthy dogs of different sex, age, weight and breed, serologically negative to Leishmania (Direct Agglutination Test, DAT<1/400), were included in a controlled, randomized clinical trial performed under the authorization of the Spanish Medicines Agency (AEMPS).
- Dogs were housed in open-air premises in a dog kennel located in Valladolid (Spain) with a seroprevalence reported to be around 7%.
- Dogs were randomly distributed in two homogenous groups:

  Treated group (n=120):

  Prevention program consisting of two 30-day treatments with Leisguard® at 1ml/10kg/24h, at the beginning and at the end of the Phlebotomus season (May/June – September/October).

  Control group (n=120):

  Non-treated.

- No other preventive treatment or insect repellents were used during the study.
- 9-month follow-up period with periodic clinical examinations and serological determinations of anti-*Leishmania* antibody titers performed at the end of the study (January-February) or when compatible clinical signs were found.
- Active infection / disease progression was considered when, at a given examination, a dog showed any clinical sign compatible with the disease and positive anti-*Leishmania* antibody titers (DAT≥1/400).
- Main parameter = cumulate percentage of dogs with active infection / disease progression at the end of the study.

RESULTS

- All animals under the Leisguard®-based program remained healthy and seronegative to Leishmania up to the end of the 9-month follow-up period (Figure 1).
- In contrast, seven dogs out of 120 in the Control group were seropositive to *Leishmania* (DAT>1/400) at the end of the study and had developed clinical signs compatible with canine leishmaniosis (peripheral lymphadenomegaly and alopecia) during the last month of the study, thus indicating active infection and disease progression.

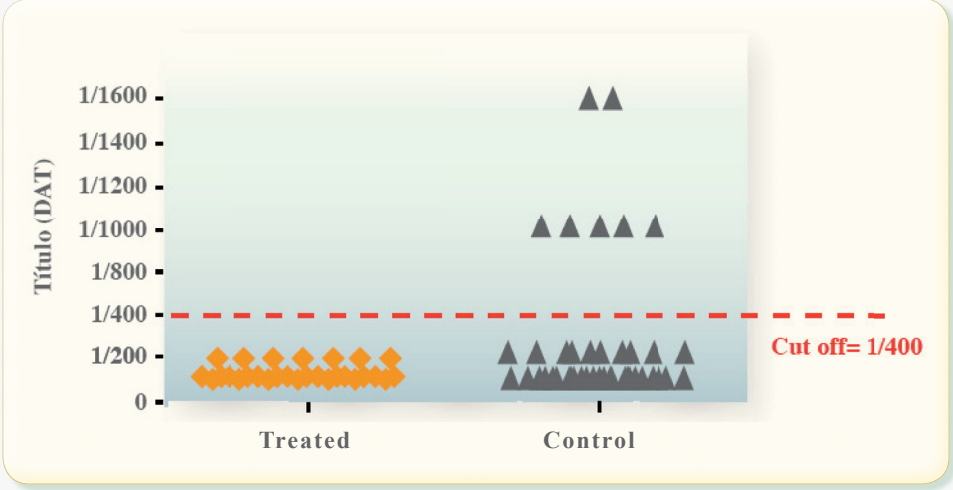

Figure 1. *Anti-Leishmania antibody titters' distribution in both groups, up to the end of the study (Direct Agglutination Test, cut-off titter <1/400).*

- The presence of the parasite was confirmed in all seropositive animals by means of direct visualization in lymph node or bone marrow aspirates.
- Differences between groups in terms of incidence of the disease were statistically significant (0% vs 5.83% in the Treated and Control groups, respectively; p<0.001) (Figure 2).

	Diseased	Healthy	p-value*
Control group (n=120)	7 (5,8%)	113 (94,2%)	< 0,001
Treated group (n=120)	0 (0%)	120 (100%)	

** Pearson's Chi-squared test.*

Figure 2. *Distribution of Diseased/Heathy dogs at the end of the study.*

- Leisguard® was well accepted by all dogs and no adverse reactions were reported during the study.

REFERENCES

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CONCLUSIONS

The results of this study confirm the excellent efficacy and safety of Leisguard® when administered for the prevention of canine leishmaniosis according to an strategically established program for endemic areas with low risk of infection.