

EFFICACY OF A COMBINED THERAPY WITH MEGGLUMINE ANTIMONIATE AND DOMPERIDONE FOR TREATMENT OF CANINE LEISHMANIOSIS

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Introduction. Meglumine antimoniate is a leishmanicidal compound that has been largely used for treating canine leishmaniosis (Oliva et al., 2010, Solano-Gallego et al., 2011). Domperidone is a dopamine D2 receptor antagonist that has been demonstrated to be effective for the control and reduction of clinical signs and antibody titers in dogs naturally infected by *Leishmania infantum* (Gómez-Ochoa et al., 2009). Meglumine antimoniate and domperidone have different mechanisms of action potentially leading to a complementary therapeutic effect against canine leishmaniosis, particularly in moderate or severe cases. However, combined therapy with both drugs as a therapeutic approach to this disease has not been described until now.

Cases description. The combination of meglumine antimoniate and domperidone for the treatment of dogs with canine leishmaniosis has been implemented in our hospital during the last four years with very good results. For this work we have selected fifty-three cases belonging to stages C (n=33), D (n=12) and E (n=8) according to the G.S.L.C. guidelines (Oliva et al. 2008). Dogs from stages C (moderately sick) and D (severely sick) had not been previously treated. Among animals from stage E (refractory/relapse), some dogs had not responded to an initial therapy with meglumine antimoniate (75-100 mg/kg sid, 90 days) or miltefosine (2 mg/kg sid, 28 days) + allopurinol (10mg/kg bid, 6 month) and others had showed early relapse after treatment within the following 30 days (stages Ea and Eb, respectively). All dogs were seropositive with high anti-*Leishmania* antibody titers and showed abnormal serum protein electrophoresis (SPE) patterns, with hyperbeta- hypergammaglobulinemia and hypoalbuminemia. In addition, they presented generalized lymphadenomegaly (53 cases), poor body condition and muscular hypotrophy (41 cases), pale mucous membranes (14 cases), hepatosplenomegaly (53 cases), epistaxis (3 cases), generalized exfoliative dermatitis (44 cases), ulcerative dermatitis (30 cases), nasal lesions (15 cases), ocular lesions (7 cases), and other clinicopathological alterations as anemia, thrombocytopenia, biochemical alterations of hepatorenal parameters, proteinuria and changes of PU/CU ratio. All animals were treated with meglumine antimoniate at a lower dose (50 mg/kg sid, 30 days) and domperidone (1 mg/kg bid, 90 days). During/after treatment animals underwent periodic clinical examinations for more than one year. At each examination, clinical evolution as well as biochemical/hematological and SPE parameters were evaluated. All dogs showed a significant improvement of both the clinical status and biochemical/hematological and SPE parameters. This was observed even in the more severe cases. In addition, all these parameters improved much faster than would have been expected after a conventional treatment. Some relapses were reported after one year among the most severe cases and in some dogs not responding to the initial conventional treatment. To control these recurrences, cyclic treatments with domperidone alone were administered with very good results (fast improvement of clinical status and biochemical/hematological and SPE values).

Conclusions. During treatment with meglumine antimoniate + allopurinol, clinical amelioration together with an improvement in hematologic and serum biochemical values is usually observed after a period of 1 or more weeks. However, restoration of SPE abnormalities back to reference limits is usually slower (Oliva et al., 2010). Our cumulative experience on combined use of meglumine antimoniate and domperidone has led us to the conclusion that this therapeutic approach significantly accelerates the improvement of both the clinical status and the biochemical/hematological and SPE values, compared to other treatments. In addition, when meglumine antimoniate is administered in association with domperidone its dose can be lower (50 mg/kg sid) and be administered for a shorter period (30 days) than normally used (75 - 100 mg/kg sid, 90 days).

On the other hand, the results described in this work show that, after a first treatment with meglumine antimoniate at low dose in combination with domperidone, cyclic treatments with domperidone alone can control the disease progression.

According to all the above mentioned, in our opinion this is an efficacious therapeutic approach for treatment of dogs with moderate to severe canine leishmaniosis, even in cases not responding to conventional treatments or showing early relapse.

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