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Methylprednisolone alone or combined with cyclosporine or mycophenolate mofetil for the treatment of immune-mediated hemolytic anemia in 43 dogs. A prospective randomized study

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Objective

To evaluate hematological response (HR) and clinicopathological outcomes in dogs affected by non-associative immune-mediated hemolytic anemia (naIMHA) treated with three different immunosuppressive protocols

Materials and Methods

Open label, unblind, randomized controlled prospective study. Diagnosis of IMHA was based on the presence of hemolytic anemia (PCV<37%), associated with at least one of the following criteria: positive Coombs' test, saline erythrocyte agglutination and spherocytosis. Immunosuppressive doses of methylprednisolone (M) were administered to all patients; then dogs were randomized to receive one of the following: only M (M group), M plus Cyclosporine (MC group), M plus Mycophenolate Mofetil (MM group). Clinical, clinicopathological data and HR were evaluated at different times. HR was defined as »Complete» (CR) when the following criteria were met: increase of PCV at >37%, negative saline agglutination test (SAT), absence of spherocytosis, serum total bilirubin concentration within the reference interval and absence of pathologic bilirubinuria (pathologic bilirubinuria defined as >1+ urine dipstick test for bilirubin). HR was defined «Partial» (PR) in patients with a modest increase of PCV not exceeding 37%, negative SAT, absence of spherocytosis, hyperbilirubinemia and pathologic bilirubinuria. Dogs not qualifying for CR or PR were classified as non-responders (NR).

Results

HR, number of transfusion treatments, time to hospitalization, frequency of relapse and complications were not significantly different among treatment groups. At T14 evaluation, no dogs showed CR and only 3/41 (7%) dogs showed PR; at T30, 10/39 (26%) dogs achieved the hematological endpoint (7% CR, 19% PR). Finally, at T60, 17/39 (44%) dogs reached CR or PR (25% and 19%, respectively). Treatment response was not significantly different among groups at T14 (P= .42), T30 (P= .64) and T60 (P= .10). Ten dogs (24%) developed infectious complications and 17% of dogs (7/41) had thrombotic complications; three dogs (7%) had a relapse. One-year survival rate was significantly higher for dogs belonging to the MC group compared with M and MM groups (P= .03 and P=.01, respectively). [1]

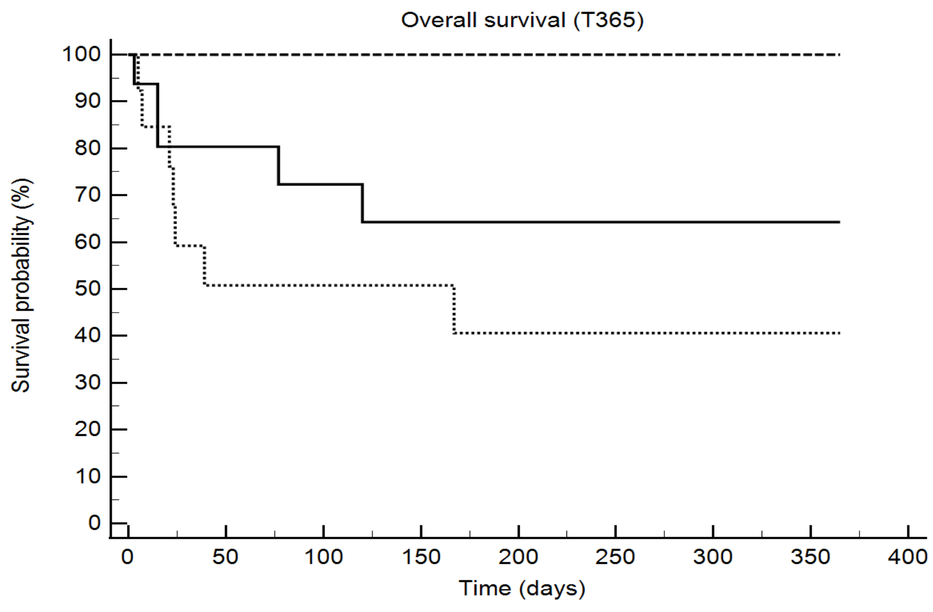

Figure 1. Kaplain Meyer curve depicting survival between therapeutic groups. Solid black line represents methylprednisolone sodium succinate group, dashed black line represents methylprednisolone and cyclosporine treatment group and grey dashed line stands for methylprednisolone and mycophenolate mofetil treatment group. Survival rate at T365 was significantly higher for dogs belonging to methylprednisolone and cyclosporine group compared with methylprednisolone and methylprednisolone and mycophenolate groups (P= .03 and P= .01, respectively).

Conclusions

Two different combined immunosuppressive regimens (MC and MM) have no additional beneficial effect over methylprednisolone therapy alone in the HR of naIMHA. Nevertheless, the combination of cyclosporine and methylprednisolone is associated with a higher survival rate at 365 days.

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Evaluation of in vitro agglutination with Point-of-care feline leukaemia virus test

Background: Point-of-care (POC) feline leukaemia virus (FeLV) screening tests are routinely performed in veterinary practice because of their wide availability, high sensitivity and specificity, and rapid results. FeLV testing is often performed in cats with immune-mediated hemolytic anemia (IMHA) as part of the investigation into comorbidities or triggering factors. Due to the conflicting results using point of care (POC) feline leukaemia virus (FeLV) tests and polymerase chain reaction (PCR) results observed in cats with immune-mediated haemolytic anaemia (IMHA), a one-year retrospective observational study was performed in Ars Veterinaria Hospital of Barcelona (Spain) and Veterinary Hospital of University of Bologna. Surprisingly 75% of patients had a positive POC test with a negative PCR and these patients responded to immunosuppressive treatment supporting IMHA diagnosis making the diagnosis of feline leukaemia infection unlikely.

Research Question: Our main hypothesis is that agglutination could have some effect in POC test causing a false positive result. This fact could be due to a cross-reaction between an antibody against red blood cells or platelets (targeting an unknown epitope) present in feline serum with either anti-p27 antibodies, reactants of the matrix or the conjugate of the in-house test.

Study Design: To evaluate the interference of agglutination with the POC test we would like to repeat this situation in vitro. Type A concentrated of red blood cells (cRBC) will be mixed with type B plasma, generating a fast agglutination. This process is consequence of the physiological presence of alloantibodies against type A RBC in type B patients. Control and agglutinating samples will be tested for POC FeLV and the presence of false positive results will be interpreted as an interference of agglutination with the test. The study will have two phases. The first (1) one will be the tester to define and improve the procedure and the second (2) one will be the serial testing on a healthy population.

Period Abroad: From July 2022, laboratory tests will be carried out at the Ars Veterinary Hospital of Barcelona.