COMBINED DRUG THERAPY FOR SUCCESSFUL MANAGEMENT OF *BABESIA GIBSONI* INFECTION IN DOGS

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ABSTRACT

The present study was undertaken to assess the therapeutic efficiency of a trio-combination in treatment of *Babesia gibsoni* infection in dogs. Eight dogs tested positive for *B. gibsoni* infection, at Small Animal Medicine Unit, Teaching Veterinary Clinical Campus, Rajiv Gandhi Institute of Veterinary Education and Research, were selected for the current study. All the affected dogs were treated with imidocarb diproprionate(6.0 mg/kg s/c, single dose), diminazene aceturate (3.5 mg/kg, deep i/m, single dose) and clindamycin phosphate (30 mg/kg, po bid for 14 days). Efficacy of the therapy was assessed by evaluation of haemato-biochemical parameters before and after therapy. Blood smear examination and/or polymerase chain reaction was implemented to evaluate the presence/ absence of parasitaemia in the host. All the eight dogs were negative for parasitaemia on 21st day of initiation of therapy. Significant difference in haemoglobin, haematocrit, red blood cell count and platelet count along with increase in glucose, total protein and reduction in creatine kinase (CK) post-treatment was noticed. Present study reveals that the trio-combination of imidocarb diproprionate, diminazene aceturate and clindamycin phosphate was effective in therapeutic management of *Babesia gibsoni* infection in dogs.

***Key words*:** Dogs, trio-combination, *Babesia gibsoni,* imidocarb diproprionate, diminazene aceturate and clindamycin phosphate

Introduction

Canine babesiosis caused by *Babesia gibsoni* is often difficult to treat. Most anti-babesial drugs can not eliminate the *Babesia gibsoni* parasites from the infected dogs (Ruff *et al.,* 1973 and Adachi *et al.,* 1993). High inter-individual pharmacokinetic variations were observed in *B. gibsoni* affected dogs hence he opined that treatment becomes difficult due to conventional drug resistance (Miller *et al.*, 2005). Several concepts were proposed for elimination of *Babesia gibsoni* infection in canines. Birkenheuer *et al.* (2004) observed that *B. gibsoni* infection was resistant to conventional therapy with anti-babesial drugs like imidocarb dipropionate and diminazene aceturate, thus an alternative therapy with atovaquone and azithromycin combination has been recommended whereas, Lin *et al.* (2012) reported that instead of individual drug therapy, a combination of diminazene aceturate, imidocarb diproprionate along with clindamycin was an effective strategy for treating *Babesia gibsoni* when compared to atovaquone and azithromycin combination. Based on the available literature, combination of imidocarb, diminazene and clindamycin was found to be effective in treatment of the infection without any relapse of the disease.

Materials and Methods

Dogs presented to Small Animal Medicine Unit, Teaching Veterinary Clinical Campus, Rajiv Gandhi Institute of Veterinary Education and Research, were selected for the current study. After being diagnosed for babesiosis, treatment with trio-combination was initiated for eight dogs. Six milli-litres of whole blood was collected from each dogs and was dispensed into EDTA vials and clot activator vials equally and were subjected for haemato-biochemical analysis. Haemoglobin, packed cell volume, red blood cell count, white blood cell count, platelet count and absolute differential leucocyte count using the standard methods (Jain, 1986) were analyzed. The erythrocytic indices such as mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration values were calculated according to Schalm *et al.* (1975). From the serum samples, glucose, BUN, creatinine, ALT, AST, bilirubin, total proteins, albumin, globulin and creatine kinase were analyzed both in control and disease group as well and were interpreted. All the parameters were analyzed both at the initiation and post-therapy on 21st day.

Diminazene aceturate @ 3.5 mg/kg, deep i/m, single dose, imidocarb dipropionate @ 6.0 mg/kg s/c, single dose and clindamycin phosphate @ 30 mg/kg, PO b.i.d for 14 days, starting from the first day of treatment. Atropine sulphate @ 0.04 mg/kg, s/c, was given 30 min prior to the administration of imidocarb dipropoionate to avoid cholinergic reactions. Dogs with anaemia and thrombocytopoenia were given oral haematinics (Hemobest®) and syrup to improve platelet count (Thrombofit®) for one-month period. The dogs with tick infestation were treated with ivermectin @ 0.2 mg/kg s/c and those with severe tick infestation were treated with fipronil spot on (Protector) according to the body weight. Efficacy of the treatment was evaluated through anamnesis, clinical signs, haemato-biochemistry, blood smear examination and/or PCR. The dogs were observed for a period of 21 days from the day of initiation of treatment and were reexamined.

Statistical analysis

Data obtained was statistically analyzed and interpreted as described by Snedecor and Cochran (1994) and discussed. Graph pad prism software was used for analysis. $P \leq 0.05$ was statistically significant.

Results and Discussion

The data pertaining to the haematologicaland serum biochemistry values before and after the treatment of the

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diseased group were depicted in Table 1 and Table 2, respectively.

Haemogram in dogs showed a significant difference in haemoglobin, PCV, RBC and platelet count post treatment when compared to the respective means prior to the initiation of treatment. The mean values of MCV, MCH, MCHC, WBC, neutrophils, lymphocytes, monocytes and eosinophils had no significant difference.

Serum biochemistry in diseased group showed significant increase in glucose, total protein and significant reduction in mean of creatine kinase, whereas the values of BUN, creatinine, ALT, AST, total bilirubin, direct bilirubin, indirect bilirubin, albumin, globulin and albumin:globulin ratio had not differed significantly when compared to the mean values of the respective parameters, prior to the treatment.

In the present study, all the dogs had clinically recovered and there was a significant increase in levels of Hb, PCV, RBC and platelet counts on 21st day, when compared to the first day. Serum glucose and total protein levels were also significantly increased post treatment with reduction in creatine kinase levels indicating the clinical improvement of the animal. All the eight dogs were found to be negative for *B. gibsoni* both by blood smear and PCR, post treatment. Parasitemia was found to be nullified by the day of 21.

The proposed combination of drugs, diminazene aceturate, imidocarb diproprionate and clindamycin phosphate was found to be an effective strategy to eliminate *B. gibsoni* from the dogs without any relapse. The efficacy of the trio combination noticed in the present study was in concordance with Lin *et al.* (2012) who proposed that the combination of diminazene aceturate, imidocarb diproprionate and clindamycin phosphate was a promising alternative to conventional therapies to treat *B. gibsoni* infected dogs without any relapse.

Table 1: Comparison of haemogram of dogs with babesiosis before and after treatment

Parameter	Disease Group		P value
	Pre-treatment (n=8)	Post treatment (n=8)	
Hb (g/dl)	10.99±13.05	13.05±0.842	0.003**
PCV (%)	32±3.4	36±1.8	0.0274*
RBC ($\times 10^6$/mm^3)	4.79±0.32	5.79±0.22	0.0026*
MCV (fl)	67.6±6.26	62.6±2.93	0.1429 NS
MCH (pg)	23.1±2.04	22.6±1.28	0.3667 NS
MCHC (%)	34.6±1.12	36.1±1.15	0.1491 NS
WBC ($\times 10^3$/mm^3)	12900±5450	9310±1660	0.1912 NS
Neutrophils ($\times 10^3$/mm^3)	8362±2553	6517±1103	0.1538 NS
Lymphocytes ($\times 10^3$/mm^3)	3370±1920	2380±559	0.2727 NS
Monocytes ($\times 10^3$/mm^3)	313.4±173.6	158.5±47.42	0.1996 NS
Eosinophils ($\times 10^3$/mm^3)	191±99.4	253±85.2	0.0982 NS
Platelet ($\times 10^5$/mm^3)	1.68±0.351	2.84±0.304	0.0079**

**: Significant (P≤0.01): *: Significant (P≤0.05); NS: Not Significant (≥0.05)

Table 2: Comparison of serum biochemistry of dogs with babesiosis before and after treatment

Parameter	Disease Group		P value
	Pre treatment (n=8)	Post treatment (n=8)	
Glucose (mg/dL)	76.6±4.88	94±3.77	0.0136*
BUN (mg/dL)	21.44±2.07	21.25±1.38	0.4469 NS
Creatinine (mg/dL)	0.793±0.08	0.763±0.07	0.276 NS
ALT (IU/L)	52.38±6.414	50.38±6.126	0.2599 NS
AST (IU/L)	57.88±8.17	53±5.79	0.091 NS
Bilirubin (total) mg%	0.6750±0.19	0.6375±0.166	0.098 NS
Bilirubin (direct) mg%	0.225±0.11	0.2±0.1	0.0852 NS
Bilirubin (indirect) mg%	0.45±0.08	0.43±0.06	0.1753 NS
Total protein (g/dL)	5.77±0.22	6.13±0.12	0.0074**
Albumin (g/dL)	2.28±0.12	2.55±0.12	0.052 NS
Globulin (g/dL)	3.48±0.189	3.588±0.14	0.268 NS
Albumin:Globulin	0.67±0.05	0.723±0.05	0.2310 NS
Creatine Kinase (U/L)	213±45.35	150.7±22.09	0.0204*

**: Significant (P≤0.01): *: Significant (P≤0.05); NS: Not Significant (≥0.05)

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