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Therapeutic efficacy of homeopathy (*Crotalus horridus*) and allopathy (Doxycycline) drugs in Canine ehrlichiosis

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Abstract

Canine ehrlichiosis also known tropical "canine pancytopenia and Nairobi bleeding disorder is an earmarked rickettsial disease caused by an intracytoplasmic parasite *Ehrlichia canis*, seen in circulating monocytes and lymphocytes. It is characterised by fever, neurological, ocular signs and bleeding through natural orifices in the form of epistaxis, hematemesis and dermal petechiae, lymphadenomegaly, splenomegaly. Different treatment regimens have been tried with various success rate. Alternative therapy such as homeopathy have been tried and found to be effective, less toxic and cost effective. The present study was carried out in the Department of Veterinary Medicine, COVS & AH, Rewa. Therapeutic trial included four groups, Healthy group as control (Group I), Allopathy (Doxycycline) group (Group II), Homeopathy (*Crotalus horridus*-200C) group (Group III) and Allopathy + Homeopathy group (Group IV). The resolution of symptoms in dogs along with time duration for hemato-biochemical parameters to return to normal values, were used as criteria for deciding therapeutic efficacy of different drugs. Present study revealed that combination therapy, group III (Allopathy + Homeopathy) is better as compared to group I (Allopathy) or group II (Homeopathy) as the values of haemogram and thrombocyte count increased and the monocyte count, liver and values returned to normal at a faster rate in comparison to other groups.

Keywords: *Ehrlichia canis*, *Crotalus horridus*, doxycycline, homeopathy, rickettsial diseases

Introduction

Canine ehrlichiosis also known as canine rickettsiosis, canine hemorrhagic fever, canine typhus, tracker dog disease, tropical "canine pancytopenia and Nairobi bleeding disorder (Price and Sayer, 1983) has been observed as an emerging and earmarked rickettsial diseases. In recent years, there is growing recognition of the importance of rickettsial pathogens in dogs and humans worldwide because of their severe pathogenicity leading to significant morbidity and mortality (Nilcholson *et al.*, 2010). It is currently reported throughout the world but at higher frequencies in tropical and subtropical regions (Suksawat *et al.*, 2001) ^[13] due to presence of their vectors. The disease also affects dogs, other domestic and wild animal species as well as humans (Dumler *et al.*, 2001) ^[4].

Rhipicephalus sanguineus, the brown dog tick, is the most widespread tick in the world and is a well-recognized vector of *Ehrlichia canis* (Smith *et al.*, 1975) ^[11] and occasionally humans. A variety of clinical symptoms like fever, leukopenia, thrombocytopenia, depression, anorexia, diarrhoea, depression, lethargy, neurological, ocular signs, and bleeding through natural orifices in the form of epistaxis, hematemesis, hematuria and melena have been reported (Kumar and Varshney, 2006) which vary considerably in severity and frequency of occurrence in the initial and terminal phases of infection. It is a multisystemic disease with three distinct infection phases: acute, sub-clinical and chronic. The outcome of the latter form is death (Mylonakis *et al.*, 2004) ^[9].

Doxycycline has been identified as the drug of choice for treating canine ehrlichiosis. But it has some side effects in dogs which include nausea, indigestion, vomiting, photosensitivity, and loss of appetite (Tripathi *et al.*, 2008) ^[14]. Doxycycline also causes hepatotoxicity and nephrotoxicity in long term use. Alternative therapies with homeopathy medicines which more effective, less toxic and cost effective have been tried by some workers with satisfactory results (Chaudhuri and Varshney, 2007) ^[2]. Reports on comprehensive study on these homeopathy medicines for the treatment of *Ehrlichia canis* are pertinently lacking.

Studies on the prevalence of canine ehrlichiosis in Rewa (M.P.) are also lacking. Therefore, the present study was undertaken with an objective to study the comparative efficacy of allopathic and homeopathic (*Crotalus horridus*) anti-ehrlichiosis drugs in affected dogs.

Material and Methods

The cases of ehrlichiosis for the study were screened from those presented to Medicine outdoor patient department (OPD) at Veterinary Clinical Complex (V.C.C.) of the College of Veterinary Science & Animal Husbandry and from private clinics in and around Rewa, Madhya Pradesh. A total of eighteen *ehrlichia* positive dogs based on blood smear and PCR were selected and randomly divided into three groups (n=6) for the therapeutic trial. In addition, six apparently healthy animals were taken in control group for comparative studies of therapeutic trial.

Treatment was carried out for 14 days by forming four groups, Healthy group as control (Group I), Allopathy (Doxycycline, Doxypet 300- @Savavet Pharm. Ltd. @10 mg/kg/Bwt.) group (Group II), Homeopathy (*Crotalus horridus*-200C-Dr Reckeweg & Co. GmbH, Berliner Ring 22, 64625 Bensheim, Germany @4 pills qid) group (Group III) and Allopathy + Homeopathy group (Group IV). All the dogs will be given ancillary treatment with NSAIDS (Meloxicam, Melonex-@Intas Pharma Ltd.) @ 0.2mg/kg Bwt, and antacid (Pantoprazole, Pantop-40-@ Aristo Pharma. Ltd @ 1mg/kg bwt). Supportive treatment with Haematinics (aRBC Rakkt-@Vetoquinol Pharma. Ltd.), liver tonics, multivitamins, fluid therapy, antiemetic Metochlorpramide @ 0.2-0.5mg/kg b. wt.) were given as per requirement and according to symptoms produced.

Blood samples were collected aseptically from all the eighteen animals in the study group including the animals in healthy group. The samples were taken from cephalic/saphenous vein on day 0 (pre-treatment) and 3rd, 7th and 14th day (post-treatment). About 5 ml of venous blood sample was collected from each animal, using dry disposable syringe. Immediately after collection, about one ml blood was transferred to EDTA (@1.5 mg/ml) vials for complete blood count (CBC).

The remaining four ml of blood was transferred into a clean and dry test tube without any anticoagulant and allowed to clot in slanting position for about one hour and then serum was harvested gently after centrifugation for 10 minutes at 2,000 to 3,000 rpm. The supernatant serum was collected carefully in a dry eppendorf with the help of micropipette and finally well labelled sera samples were preserved at -20°C in a deep freeze for further biochemical estimation.

Monitoring of treatment response in ehrlichiosis in dogs was done on the basis of Blood smear examination, Haematological and Biochemical studies. Thin blood smear were prepared and stained with standard stains and examined under microscope again on 3rd, 7th and 14th day (post-treatment) for presence *ehrlichia* organisms. Reduction in the number of infected monocytes and positive changes in DLC and thrombocyte count were used as criteria to monitor the efficacy of treatment.

For haemato-biochemical studies, 3 ml blood was collected aseptically from all the animals in the study group including the animals in healthy group. The samples were taken on 0, 3rd, 7th and 14th day. Haematological parameters like Hb, TEC, TLC, DLC, PCV and thrombocytes were studied as per standard laboratory procedures described by Jain (1986).

Biochemical parameters like ALT, AST, Total Protein, Serum albumin, serum Globulin, Blood Urea Nitrogen and Serum creatinine were determined using the serum obtained from the blood samples. The data is analyzed as per standard method as described by Snedecor and Cochran (1994) [12].

Results and Discussion

Efficacy of the therapy was evaluated on the basis of time duration of recovery period, percentage of reduction in the clinical symptoms (pyrexia, dermal petechiae, anorexia, etc.) and improvement in the haemogram values. Based on these parameters a rough score card for evaluation was prepared as follows: Negative (-) = No change, Positive (+) = Fair Improvement, Positive (++) = Mild Improvement, Positive (+++) = Moderate Improvement, Positive (+++++) = Good Improvement.

Group I (Doxycycline)

In this group all the affected dogs were treated with Doxycycline @ 10 mg/Kg Bwt. PO OD for 14 days. Clinical improvement was noticed on 7 day post treatment and on 14 day post treatment all dogs showed complete clinical recovery. Hematological parameter showed gradual increase in Haemoglobin, TEC, PCV, and platelets count post treatment and on day 14 post treatment, all the parameters returned to the normal range but towards the lower limit in the reference range as compared with healthy control (Table 1).

Table 1: Degree of improvement in clinical parameters in animals at different intervals in group I

Animals	Days			
	0	3	7	14
1	----	+++	++++	++++
2	----	+++	++++	++++
3	----	+++	++++	++++
4	----	+++	++++	++++
5	----	+++	++++	++++
6	----	+++	++++	++++

Findings in the present study of doxycycline therapy for 14 days corroborate with the reports of Breitschwerdt *et al.* (1998) [1] who reported therapeutic efficacy of doxycycline in eliminating *ehrlichia* from dogs at the dose rate of 10 mg/kg bwt OD daily for 14 days. Harrus *et al.* (2004) [5] who reported clinical recovery of infected dogs by 72 hrs post treatment with doxycycline and complete clinical and hematological recovery from acute phase of infection along with elimination of ehrlichial DNA from blood and splenic aspirates at 16 days post treatment onwards. They further suggested that the duration of doxycycline treatment should be reduced to 16 days which would reduce the cost, probable side effects and risk of antibiotic resistance.

CME is usually successfully treated with antibiotics that belong to the tetracycline family. Doxycycline is an effective drug against ehrlichiosis in dogs and when dogs are treated in the acute phase of ehrlichiosis, they improve quickly, within 24-48 h, with good prognosis (Harrus *et al.*, 1997) [6].

Several researchers have reported complete response in the majority of cases with doxycycline therapy at 5 mg/kg twice daily or 10 mg/kg once daily for 4 weeks (McClure, 2010) [10].

Group II- Homeopathy (*Crotalus horridus* 200C)

In this group, dogs were treated with 4 pills QID for 14 days with homeopathic drug *Crotalus horridus* in the dilution of

200C. Clinical improvement was noticed on 9 day post treatment and on 14 day post treatment all dogs showed complete clinical recovery. Hematological parameter showed gradual increase in Haemoglobin, TEC, PCV, and platelets count post treatment and on day 14 post treatment, all the parameters returned to the normal range but towards the lower limit in the reference range as compared with healthy control (Table 2).

Table 2: Degree of improvement in clinical parameters in animals at different intervals in group II

Animals	Days			
	0	3	7	14
1	----	+---	+++	++++
2	----	----	+++	++++
3	----	+---	+++	++++
4	----	+++	+++	++++
5	----	+++	+++	++++
6	----	----	+++	+++

Tungnunga *et al.* (2016) [15] studied the therapeutic effect of homeopathic medicine *Crotalus horridus* 200C on ehrlichiosis in dogs in an endemic area of Aizawl district of Mizoram state of India and reported that the drug showed satisfactory results in treating *E. canis* infection. They reported that reduction in parasitaemia in case of *Crotalus horridus* was slower as compared to that seen in case of doxycycline treatment group but overall clinical efficacy of the homeopathic drug was comparable with modern allopathic drug doxycycline.

Homeopathic drug have been used in the treatment of various animal diseases (Macleod, 1981) [7]. Many allopathic drugs against ehrlichiosis show various side effects including toxicity to different organs and so they are not been approved for clinical use. When the dog has liver problems, the use of doxycycline should be reconsidered. In any case, liver function tests should be performed before and during treatment; when liver parameters increase, the treatment regime should be stopped.

Homeopathic drugs however have not been reported with adverse side effects, they are economical and have long term beneficial effects. *Crotalus horridus* is indicated for fluid haemorrhages, yellow skin and black vomit. It affects blood, heart, and liver and producing profound nervous shock with trembling and prostration. There is a similarity between the symptoms of *Crotalus horridus* and ehrlichiosis caused by *E. canis* in dogs. Therefore, the drug was used in the study trial. Murphy (2002) [8] reported *Crotalus horridus* as a drug of choice for haemorrhagic diathesis. These properties of *Crotalus horridus* matched well with the clinical manifestations of ehrlichiosis in the present study.

Group III- Combination Group (Allopathy and Homeopathy)

In this group, dogs were treated for 14 day with a combination of allopathic drug (Doxycycline@ 10mg/kg bwt) and Homeopathy (*Crotalus horridus*200C@ 4 pills QID). Clinical improvement was noticed on 3rd day post treatment and on 14th day post treatment all dogs showed complete clinical recovery. Hematological parameter showed gradual increase in Hb, TEC, PCV, and platelets count post treatment and on day 14 post treatment, all the parameters returned to the normal range but towards the lower limit in the reference range as compared with healthy control (Table 3).

Table 3: Degree of improvement in clinical parameters in animals at different intervals in Group III

Animals	Days			
	0	3	7	14
1	----	+++	+++	++++
2	----	+++	+++	++++
3	----	+++	++++	++++
4	----	+++	+++	++++
5	----	+++	++++	++++
6	----	+++	+++	++++

Combination of allopathy and homeopathy is likely to synergize the effect due to interaction of several drugs acting on parasite at different targets and thus is beneficial in suppressing parasite growth and activity. Also, homeopathic drugs work at nano levels and they might also play an active role in improving the immunity of the animal thereby mitigating the infection at a faster rate when given in combination with allopathic medicines.

Comparative therapeutic evaluation of all the treatment groups

In the present study, based on the earlier clinical improvement, lowered degree of parasitemia, improvement in the values of haemogram and thrombocyte count increased, decrease in monocyte count and faster rate of return of liver to normal in comparison to group I (Allopathy) or group II (Homeopathy), group III (Allopathy + Homeopathy) was considered as the most efficient drug combination against ehrlichiosis followed by group I and group II.

The therapeutic study revealed that group III (Combination Therapy) was considered as the most efficient drug against ehrlichiosis followed by group I and group II. The order of drug efficacy against ehrlichiosis in dogs on the basis to recovery from parasitemia and clinical improvement is Combination>Allopathy> Homeopathy. (Fig.1)

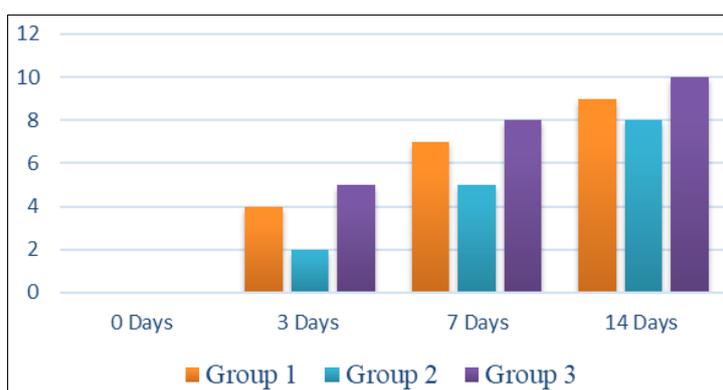


Fig 1: Comparative therapeutic evaluation of all the treatment groups

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