Comparative anthelmintic efficacy of ivermectin delivered through different routes in gastrointestinal nematode infected dogs

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Abstract Ivermectin is one of the most effective and widely used antiparasitic agents ever discovered because of its broad spectrum activity against nematodes and arthropods. Therefore, the study was conducted to determine the comparative anthelmintic efficacy of ivermectin by giving through oral and subcutaneous routes in clinically infected dogs and also to check the prevalence of gastrointestinal nematode in dogs in Bhubaneswar, Odisha. Total 154 dogs with clinical signs of gastroenteritis were examined for the presence of nematodal ova in their faecal sample and 64 were found positive (41.56 %). The screened dogs were divided in to two groups ($n = 10$ each), first group of animals were treated with ivermectin @ 0.5 mg/kg body weight by subcutaneous route and the second group with same dose of ivermectin through oral route. Efficacy of ivermectin was evaluated based on egg per gram (EPG), haematological and biochemical parameters. It is concluded that, Prevalence of gastrointestinal nematodes are

high in dogs in the climatic condition of Bhubaneswar, Odisha. Ivermectin was found effective when administered through either of the routes. Haemato-biochemical parameters were restored after administration of ivermectin and also significant reduction in EPG was found in dogs treated with ivermectin by both the routes, but no significant difference was observed in EPG between oral and subcutaneous treated dogs in various intervals of study.

Keywords Ivermectin · Dog · Nematode · Egg per gram · Hemato-biochemistry

Introduction

Gastrointestinal helminthiasis is the most commonly encountered disease in dogs rearing across the globe including India (Traub et al. 2007). Among the gastrointestinal helminths, both *Ancylostoma* spp. and *Toxocara* spp. are the important nematode affecting dogs especially in newly whelped or neonates and causing tremendous health hazard. Prevalence of gastrointestinal helminthiasis is influenced by many factors. The distribution and intensity of the disease are mainly influenced by geographical, climatic, cultural and economic factors (Robertson et al. 2000). Furthermore, the level of hygienic conditions, lack of veterinary supervision and less awareness concerning zoonotic diseases exacerbate the transmission of these diseases. Epidemiological pattern of the parasitic diseases in the different agro-climatic zones of the country usually provides a basis for developing strategic and tactical control systems against them (Traub et al. 2002).

Ivermectin is one of the most effective and widely used antiparasitic agents ever discovered because of its broad-spectrum activity against numerous endoparasites and

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ectoparasites, especially nematodes and arthropods (Geary 2005; Omura 2008). It can be given by various routes i.e. orally or subcutaneously as an anthelmintic drug. Ivermectin acts by selectively binds to glutamate-gated and gamma-aminobutyric acid (GABA)-gated chloride channels in the nervous system of insects, resulting in hyperpolarization of cell, paralysis and finally death. Safety in mammals is due to the lack of glutamate gated chloride channels in the peripheral nervous system and restriction of GABA to a central nervous system (Macdonald and Gledhill 2007). Trematodes and cestodes are having the natural resistance against ivermectin because they do not use GABA as a PNS neurotransmitter.

Huge numbers of researches had been conducted on ivermectin-as an ectoparasiticide agent around the globe including India. But, a few literatures are available on ivermectin as an endoparasitic agent especially in dogs and there was no literature on comparative efficacy of ivermectin as an anthelmintic given by different routes in dogs. Therefore, the study was conducted to check the comparative anthelmintic efficacy of ivermectin by giving through oral and subcutaneous routes in gastrointestinal nematode infected dogs on the basis of hemato-biochemical parameters and eggs per gram of faeces, before and after treatment.

Materials and methods

Animal

The present study was undertaken in the Department of Medicine and Teaching Veterinary Clinical Complex, College of Veterinary Science and Animal Husbandry, Orissa University of Agriculture and Technology, Bhubaneswar, Odisha from December 2012 to June, 2013. Dogs ($n = 154$), of any breed, either male or female, of any age groups, with clinical signs of gastroenteritis were examined for the presence of parasitic ova in their faecal sample through direct smear and floatation technique. The screened dogs were randomly divided into two groups of 20 animals each. The first group of animals were treated with ivermectin @ 0.5 mg/kg body weight by subcutaneous (S/C) route and the second group of animals were treated with same dose of ivermectin through oral route. Along with ivermectin the dogs were also treated with hematemics (iron dextran), antiemetic (metoclopramide), fluid and electrolyte therapy (colloidal followed by crystalloid solutions) and supportive therapy according to their clinical signs.

Collection of samples

Faecal sample was collected from the screened animal ($n = 40$) directly from the rectum in pre-labelled plastic

specimen bottle in morning time, before the commencement of the experiment (day 0) and thereafter on day 7 and 15 post-treatment. Pre-labelled specimen bottles were given to the dog owners with the strict instructions to collect the faeces of dogs into the bottle in the morning hours of above schedule days.

Blood samples were collected from the recurrent tarsal vein of the dogs ($n = 40$) before the commencement of the experiment (day 0) and thereafter on day 7 and day 15. The blood sample was collected from all the dogs in two separate vials i.e. one with disodium EDTA as anticoagulant for conducting the haematological parameters and other vial without anticoagulant for harvesting serum to perform biochemical assay. Both haematological and biochemical parameters were carried out within 24 h of collection of the blood sample.

Haematological parameters

Blood sample (5 ml) from each dog was collected in a screw capped sterile collecting vial containing disodium EDTA. Haemoglobin (gm/dl) was estimated by Sahli's method as recommended by Benjamin (1978). Packed cell volume (PCV) was determined using Wintrobe's method as described by Coles (1986). Total erythrocyte count (TEC) and total leukocyte count (TLC) was done according to the method described by Benjamin (1978). Differential leukocyte count (DLC) was made on blood films stained by Giemsa staining method (Schalm et al. 1986), MCV, MCH and MCHC were estimated as per the standard methods (Jain 1986).

Serum biochemistry

Liver and kidney function tests i.e. activity of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatinine, glucose, total protein, albumin, globuline and albumin:globuline ratio were estimated by semi auto analyser (Merck) using commercial reagent kits as per manufacturer's instruction.

Examination of faeces

The collected faecal samples of dogs were examined for presence of nematodal ova by direct smear method and/or floatation method by using saturated NaCl solution of specific gravity 1.18–1.19. Identification of the parasitic ova was made according to the morphological characteristics and keys as outlined by Soulsby (1982). After finding positive for nematodal ova in the above methods, the faecal sample was examined for egg per gram (EPG) by McMaster's method (Soulsby 1982).

Egg per gram (EPG) of faeces was calculated by following formula

EPG = Average number eggs on each chamber $\times$ 100

Calculation of efficacy of ivermectin

Efficacy of ivermectin was calculated by following formula

% of drug efficacy = $A - B/A \times 100$

where A is the average number of parasitic eggs in gram of faeces before treatment, B is the average number of parasitic eggs in gram of faeces after treatment.

Statistical analysis

Data were subjected to statistical analysis as per Snedecor and Cochran (1994).

Results

A total of hundred and fifty four dogs with clinical sign of gastroenteritis were examined for presence of ova of gastrointestinal nematode (*Ancylostoma* and *Toxocara*) by faecal sample examination. Out of 154 dogs, 64 dogs were found positive for either *Ancylostoma* spp. or *Toxocara* spp. or both of them. Hence, the overall prevalence of gastrointestinal nematode was 41.56 %.

Clinical observation

The dogs were dull, depressed, inappetent to anorectic and having moderate to severe dehydration before treatment. Most of the dogs had intermittent bloody diarrhoea, vomiting, pallor of mucous membrane, and normal to sub-normal body temperature. After giving ivermectin, along with fluid and electrolyte therapy, antiemetics, hematenics and other supportive therapy, physical condition of animals were improved gradually in both the groups leading to remission of the clinical signs and symptoms.

Hematology

The haematological findings revealed significant ($P < 0.05$) changes in Hb, TEC, TLC, PCV, MCV, MCH, eosinophil and lymphocyte count before and after the treatment, but, non-significant changes among the two groups (group I and group II) at different intervals of study (Table 1).

There was significant ($P < 0.05$) increase in mean values of Hb, TEC and PCV on 15 days post treatment within both the groups, in comparisons to the respective values before treatment (Table 1). Significant ($P < 0.05$) decrease in mean value of MCV and MCH was observed after administration of ivermectin by subcutaneous route as compared to day 0 value. But, a non-significant decreasing

trend was observed in oral treated group. The mean value of TLC decreased significantly ($P < 0.05$) after treatment on day 7 and then non-significantly on day 15 in both the groups.

The differential leucocytes count revealed a significant decrease in eosinophil concentration post treatment in comparison to respective values before treatment in both the groups but, no significant differences were recorded in mean concentration of neutrophil, monocyte and basophil either between the groups or within groups at different observation periods of the study.

Serum biochemistry

Significant ($P < 0.05$) decrease in ALT and AST activity was recorded on day 7 and day 15 in both the groups as compared to day 0 values (Table 2). The above trend was also followed in mean BUN concentration but not any significant changes were recorded in creatinine concentration within or between groups and the value were statistically similar.

On the other hand, the mean total protein, albumin, globulin and serum glucose concentration increased significantly ($P < 0.05$) after administration of ivermectin by both subcutaneous and oral routes in comparison to respective values before treatment.

Egg per gram (EPG)

There was significant ($P < 0.05$) decrease in mean EPG value in both the groups after administration of ivermectin with respect to day 0 values, but there was no significant difference between the groups at different interval of study (Table 3). The percentage reduction in eggs per gram was 92.10 and 98.02 %, respectively on 7 and 15th day post treatment in group I and 91.12 and 96.05 %, respectively on 7 and 15th day post treatment in group II animals (Table 4).

Discussion

Gastrointestinal helminthiasis accounts for important health hazard in human being and animals around the globe. India, as a tropical country, has a wide range of climatic zones, from montane (cold, wet alpine) and semi-arid regions to the wet tropics, which make it suitable for a diverse range of parasites and pathogens of medical and veterinary importance. Their transmission and distribution are mostly influenced by geographical, climatic, cultural and socio-economic factors.

In the present investigation, the overall prevalence of gastrointestinal nematode in dogs was 41.56 %. Similar

Table 1 Haematological parameters in dogs before and after treatment

Parameters	Group (<i>n</i> = 20)	Day 0	Day 7	Day 15
Hb (g/L)	I	88.8 ± 3.93 ^a	108.8 ± 3.99 ^b	113.0 ± 4.50 ^b
	II	91.6 ± 3.86 ^a	102.4 ± 4.32 ^{ab}	112.2 ± 4.42 ^b
TLC (10 ⁹ /L)	I	19.36 ± 3.17 ^b	11.60 ± 1.33 ^a	10.94 ± 1.20 ^a
	II	19.21 ± 3.05 ^b	12.60 ± 1.44 ^a	11.67 ± 0.93 ^a
TEC (10 ¹² /L)	I	3.65 ± 0.22 ^a	4.89 ± 0.24 ^b	5.33 ± 0.20 ^b
	II	4.10 ± 0.19 ^a	4.61 ± 0.20 ^{ab}	5.09 ± 0.19 ^b
PCV (L/L)	I	0.26 ± 0.09 ^a	0.32 ± 0.07 ^b	0.33 ± 0.07 ^b
	II	0.27 ± 0.08 ^a	0.30 ± 0.06 ^{ab}	0.33 ± 0.08 ^b
MCV (fl)	I	72.92 ± 1.13 ^b	66.44 ± 1.93 ^a	62.61 ± 1.30 ^a
	II	66.93 ± 1.16	66.55 ± 1.24	66.02 ± 1.31
MCH (pg)	I	24.49 ± 0.36 ^b	22.28 ± 0.69 ^a	21.15 ± 0.39 ^a
	II	22.48 ± 0.40	22.34 ± 0.42	22.07 ± 0.43
MCHC (g/L)	I	336.0 ± 5.13	335.3 ± 5.54	337.9 ± 5.92
	II	335.9 ± 5.16	335.8 ± 6.02	334.4 ± 5.88
N (%)	I	72.70 ± 2.66	71.70 ± 1.62	71.20 ± 1.69
	II	73.00 ± 3.32	72.70 ± 1.41	72.00 ± 0.95
E (%)	I	10.80 ± 0.89 ^c	7.60 ± 0.37 ^b	4.70 ± 0.37 ^a
	II	10.60 ± 0.83 ^c	7.80 ± 0.47 ^b	4.90 ± 0.55 ^a
L (%)	I	16.10 ± 2.28 ^a	20.90 ± 1.77 ^{ab}	22.80 ± 1.60 ^b
	II	15.50 ± 2.62	18.20 ± 1.04	21.00 ± 0.77
M (%)	I	0.80 ± 0.20	0.80 ± 0.13	1.30 ± 0.26
	II	0.90 ± 0.23	1.30 ± 0.21	1.50 ± 0.22
B (%)	I	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	II	0.00 ± 0.00	0.00 ± 0.00	0.10 ± 0.10

Group I ivermectin given through subcutaneous route, Group II ivermectin given through oral route

Values (Mean ± SE) bearing no common superscripts differ significantly at $P < 0.05$

findings were also obtained in various surveys in different countries across the world (Ahmad et al. 2011; Basu et al. 2010; Komatangi 2005; Ramirez-Barrios et al. 2004) but no such recent study was done in Bhubaneswar, Odisha. Minor variation in the results in these surveys is attributable to geographical variation, environmental factors, species composition and other stress factors involved in parasite transmission.

Significantly lower concentration of Hb, TEC and PCV was observed in dogs before treatment as compared to respective values after treatment in both the groups. This might be due to loss of blood in dogs affected with hookworm leads to depletion of the body's iron by both the blood sucking habits of the worms, as well as to bleeding of intestinal bite wounds (Hotez and Cerami 1983; Kelly et al. 1977). *Ancylostoma spp.*, the most common pathogenic hookworm of dog, can cause a daily loss of 0.01 to 0.2 ml of blood for each adult worm, which can result in the daily loss of 25 % or more of the host animal's total blood volume (Miller 1966, 1971). These findings are also in accordance with the earlier reports i.e., Chattha et al. (2009); Cury et al. (2002); Okewole et al. (2003); Miller

(1966, 1971); Kelly et al. (1977); Hotez and Cerami (1983).

There was mild eosinophilia in dogs before treatment and the values were significantly decreased after administration of ivermectin by oral and subcutaneous routes. This may be due to constant irritation caused by the migration of the larvae through intestinal mucosa causing damage and inflammation along the way. Similar observation was also reported by Leder and Weller (2000).

Serum biochemistry revealed significant higher values of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and urea in affected animals, and the values were restored after treatment with ivermectin in both the groups. These findings may be a result of damage of liver and kidney due to migrating larvae of *ancylostoma* and *toxocara* causing liver and kidney dysfunction. Decreased concentration of glucose, total protein, albumin and globulin were returned to normal after administration of ivermectin through subcutaneous or oral routes. Lower concentration of above mentioned parameters are due to poor absorption of the dietary constituents from intestinal tract, which might have been due to gastrointestinal

Table 2 Serum biochemical parameters before and after treatment

Parameters	Group (<i>n</i> = 20)	Day 0	Day 7	Day 15
ALT (U/L)	I	45.23 ± 4.04 ^b	30.57 ± 2.66 ^a	25.51 ± 2.75 ^a
	II	41.32 ± 2.66 ^b	30.53 ± 1.80 ^a	26.51 ± 2.07 ^a
AST (U/L)	I	31.80 ± 2.68 ^b	25.03 ± 1.77 ^a	21.16 ± 2.37 ^a
	II	35.71 ± 2.25 ^b	25.06 ± 1.56 ^a	21.71 ± 1.65 ^a
Urea (mmol/L)	I	4.01 ± 0.26 ^b	2.82 ± 0.25 ^a	2.19 ± 0.31 ^a
	II	4.03 ± 0.24 ^b	2.89 ± 0.24 ^a	2.23 ± 0.22 ^a
Creatinine (μmol/L)	I	51.27 ± 4.11	45.08 ± 3.68	44.2 ± 3.54
	II	48.62 ± 3.98	48.17 ± 4.02	46.85 ± 3.86
TP (g/L)	I	44.9 ± 2.14 ^a	50.8 ± 2.16 ^b	53.4 ± 2.12 ^b
	II	45.1 ± 2.12 ^a	50.4 ± 2.13 ^b	53.5 ± 2.12 ^b
Albumin (g/L)	I	25.4 ± 1.08 ^a	28.8 ± 1.11 ^b	30.5 ± 1.08 ^b
	II	26.2 ± 1.07 ^a	29.9 ± 1.06 ^b	30.5 ± 1.07 ^b
Globulin (g/L)	I	19.5 ± 1.10 ^a	22.0 ± 1.09 ^b	22.9 ± 0.94 ^b
	II	19.0 ± 0.92 ^a	20.6 ± 1.07 ^{ab}	23.0 ± 0.96 ^b
A/G ratio	I	1.33 ± 0.06	1.32 ± 0.06	1.33 ± 0.02
	II	1.43 ± 0.12	1.46 ± 0.02	1.33 ± 0.03
Glucose (mmol/L)	I	4.43 ± 0.32 ^a	5.25 ± 0.44 ^{ab}	5.68 ± 0.18 ^b
	II	4.56 ± 0.22 ^a	5.26 ± 0.16 ^{ab}	5.72 ± 0.61 ^b

Group I ivermectin given through subcutaneous route, Group II ivermectin given through oral route

Values (Mean ± SE) bearing no common superscripts differ significantly at *P* < 0.05

Table 3 Mean value of EPG in dog before and after treatment

Group (<i>n</i> = 20)	Day 0	Day 7	Day 15
I	2,210 ± 333.37 ^b	190 ± 45.0 ^a	55 ± 17.40 ^a
II	2,260 ± 321.60 ^b	220 ± 62.45 ^a	110 ± 33.7 ^a

Group I ivermectin given through subcutaneous route, Group II ivermectin given through oral route

Values (Mean ± SE) bearing no common superscripts differ significantly at *P* < 0.05

Table 4 Percentage reduction in EPG values after treatment

Period of observation	Group I (<i>n</i> = 20)	Group II (<i>n</i> = 20)
Day 7	92.10 %	91.12 %
Day 15	98.02 %	96.05 %

disturbances caused by parasitic infection (Hayat et al. 1999). Roundworms are known to cause necrosis and desquamations of epithelial layer and villi of intestine leading to reduction of absorption area for degraded protein. Low absorption of proteins coupled with less dietary intake as a result of anorexia during infection period could also attribute to reduction in glucose, total protein, albumin and globulin (Benjamin 1986). These observations corroborate with the report of Padmaja et al. (2006) and Nwoha et al. (2013) in different animals due to helminth infection, but no such earlier findings reported in dogs in India.

In the present study, there was significant decrease in mean EPG value in post treatment animals, in comparison to respective values of pre treatment animals in both the groups. However, there was no significant difference between the groups at different interval of study. The percentage reduction in egg per gram was 92.10 and 98.02 %, respectively on 7 and 15th day post treatment in S/C treated group and 91.12 and 96.05 %, respectively on 7 and 15th day post treatment in oral ivermectin treated animals. The dose of the ivermectin was selected based on the published literatures (Khayatnouri and Garedaghi 2012a, b). Various workers also reported similar results about efficacy of ivermectin delivered through different routes in dogs in different country e.g., efficacy of 96–100 % orally (Heejeong et al. 2012; Yazwinski et al. 1982), 90–100 % effective through subcutaneously (Ahmad et al. 2011; Seward 1983) and 98 % on 28th days of administration @ 0.5 mg/kg through pour-on technique (Khayatnouri and Garedaghi 2012a, b).

It is concluded that, Prevalence of gastrointestinal nematodes especially *Ancylostoma* and *Toxocara* are high in dogs in the climatic condition of Bhubaneswar, Odisha. Ivermectin was found effective when administered through either of the routes i.e., oral and subcutaneous. Haemato-biochemical parameters were restored after administration of ivermectin and also significant reduction in EPG was found in dogs treated with ivermectin by oral or subcutaneous routes.

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