



Efficacy of Arteether Against Theileriosis in Cattle

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ABSTRACT

The present study was done with the objective of comparative efficacy of arteether and buparvaquone against theileriosis in cattle. Total 67 cattle suspected for theileriosis were screened on the basis of clinical and blood smear examination. Group I (n=6) was treated with Inj. buparvaquone @ 2.5 mg/kg body weight once and Group II (n=6) was treated with Inj. arteether @ 5 mg/kg body weight intramuscularly for three consecutive days. Rectal temperature, heart rate and respiration rate were significantly increased before treatment and in both the groups after treatment showed significant improvement. Haematological parameters showed significant decreased in Hb, PCV, TEC, TLC and neutrophil and significant increase in lymphocytes, monocytes and eosinophil. Non significant difference in basophil count was observed. After treatment, significant improvement was observed in mean hemoglobin, PCV, TEC, TLC, neutrophil, lymphocyte and eosinophil. Non significant improvement was observed in monocyte and basophil count. Present study revealed percent efficacy of arteether was 66.66% and buparvaquone 100%.

Keywords: Arteether, Theileriosis, Buparvaquone, Cattle, *Theileria annulata*

Theileriosis is a tick borne disease caused by *Theileria annulata* and transmitted by genus *Hyalomma* spp.. Bovine tropical theileriosis is most prevalent and economically important disease of dairy herd which cause production loss. *Theileria annulata* is an intracellular parasite that infects both wild and domestic bovidae all over the world and some species also infect small ruminants. They are transmitted with *Ixodid* ticks and have complex life cycle in vertebrate as well as invertebrate hosts, (OIE, 2014). The disease occurs when there is more tick activity, mainly in summer and rainy seasons. The overall occurrence of theileriosis in cattle is 22.38 % (Khawale *et al.*, 2019). A single tick can cause deadly infection as it generally contains countless sporozoites in its salivary glands. The incubation period of theileriosis is 4 to 14 days after attachment of the tick on the host body.

Buparvaquone is the only drug which is used for all type of theileriosis as treatment and prophylaxis. It is a second-generation parvaquone-related hydroxyl-

naphthoquinone derivative acts by binding to cytochrome b (cyt-b) inhibiting the electron transport chain in the parasite (Mhadhbi *et al.*, 2015). Recent reports regarding development of resistance against buparvaquone and lack of cost effective treatment in theileriosis and the published utility of Arteether in different haemoprotozoan infection, the present research work was designed.

Arteether is a semi-synthetic artemisinin derivative, a natural product of the Chinese plant *Artemisia annua*. It is a well-known medicinal plant that has been utilized for a number of purposes, including malaria, for centuries. It is a fast acting blood schizonticidal drug specifically meant for the treatment of chloroquine-resistant *Plasmodium falciparum* malaria and cases of cerebral malaria (Okunlola *et al.*, 2013). Several semisynthetic derivatives of artemisinin have been used increasingly over the past

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two decades as antimalarials. Artemisinin is the active ingredient of the Chinese herb 'qinghaosu' (*Artemisia annua*) that was traditionally used for treating fevers.

MATERIALS AND METHODS

The animals were selected from areas like Teaching Veterinary Clinical Complex, Instructional Livestock Farm Complex, COVAS, Parbhani and nearby villages from Parbhani District, Maharashtra, India. The study was carried out for six months from January – June 2019. Total 67 suspected cattle were examined in different age, sex and breed randomly belonging to different localities in Parbhani district. The screening was done based on the clinical signs like high body temperature, enlargement of lymph nodes, conjunctiva petechiae, tick infestation and haemoglobin level more than 6 g/dl. Total 12 positive cases of theileriosis were examined of clinical, haematological and biochemical studies.

Clinical examination includes recording of rectal temperature by clinical thermometer, heart rate by auscultating heart for 1 minute and respiration rate by holding back hand in front of nostrils and the air current was counted for period of 1 minute. The animals were examined for high temperature, enlargement of lymph nodes, conjunctiva petichie and presence of ticks on animal's body.

Blood samples from theileriosis affected cattle for hematological analysis from jugular vein in a clean, sterile tube containing Ethylene Diamine Tetra Acetic Acid (EDTA) at the rate of 2 mg/ml of blood. For diagnosis of theileriosis, blood smear was prepared from the blood taken from ear tip at the height of temperature. Blood samples from jugular vein were collected at day 0th, day 7th and day 21st for haematological investigation. Twelve clinically positive cases of theileriosis were distributed in two equal groups (n=6). Group I was treated with inj. buparvaquone @ 2.5 mg/kg body weight once and Group II was treated with inj. arteether @ 5 mg/kg body weight intramuscularly for three consecutive days.

RESULTS AND DISCUSSION

The clinical parameters in treatment group I treated with Inj Buparvaquone and group II treated with Inj Arteether showed significant improvement in rectal temperature

(°F) and heart rate on day 7th and day 21st post treatment as compared to day '0' before treatment. Mean respiration rate in group I was non significantly decreased on day 7 but significant decreased on day 21st after treatment as compared to day '0' before treatment and in group II, mean respiration rate was significantly decreased on day 7th and 21st post treatment as compared to 0th day before treatment. The clinical parameters showings various alterations in buparvaquone and arteether treated groups before treatment and after different intervals is depicted in table 1.

The analysis of variance revealed significant variation in pooled mean of rectal temperature (°F) between both groups (I and II) and pooled mean between periods showed significant decrease on 7th and 21st day post treatment as compared to '0' day before treatment. However, the analysis of variance revealed non significant variation in pooled mean of heart rate and respiration rate between both groups (I and II). The pooled mean of heart rate between periods showed significant decrease in day 7th and 21st post treatment as compared to 0th day before treatment.

Haematological observations revealed the treatment group I and group II showed non significant but apparent improvement in haemoglobin concentration at 7th day and significant improvement at 21st day post treatment. The packed cell volume in treatment group I showed non significant but apparent improvement at 7th day and significant improvement at 21st day post treatment. However, in group II the mean PCV values were increased non significantly but apparent improvement observed on 7th day and 21st day post treatment as compared to '0' day before treatment. Similar findings were reported by Nayak *et al.* (2018) and Siddiqui *et al.* (2017).

The analysis of variance revealed non-significant variation in pooled mean of haemoglobin and PCV between both groups (I and II). The pooled mean of haemoglobin concentration of periods showed non--significant but apparent increase in haemoglobin concentration on 7th day post treatment and showed significant increase on 21st day post treatment as compared to '0' day before treatment.

The treatment group I showed non-significant but apparent increase in TEC values on 7th day and significant increase on 21st day post treatment as compared to '0' day before treatment. The analysis of variance revealed non significant variation in pooled mean of total erythrocyte

Table 1: Clinical parameters in Buparvaquone and Arteether treated groups before treatment and at different intervals after treatment

Clinical parameters		0 th day	7 th day	21 st day	Pooled mean
Rectal temperature	Group-I	105.47 ^b ± 0.37	102.05 ^a ± 0.22	102.05 ^a ± 0.12	103.19 ± 1.14
	Group-II	106.37 ^b ± 0.29	103.03 ^a ± 0.25	102.55 ^a ± 0.12	103.98 ± 1.20
	Pooled mean	105.92^B ± 0.45	102.54^A ± 0.49	102.30^A ± 0.25	
Heart rate	Group-I	80.83 ^b ± 5.12	67.83 ^a ± 3.32	69.50 ^a ± 1.02	72.72 ± 4.08
	Group-II	77.83 ^b ± 3.30	71.33 ^a ± 0.80	69.83 ^a ± 1.01	73.00 ± 2.45
	Pooled mean	79.33^B ± 1.50	69.58^A ± 1.75	69.66^A ± 0.17	
Respiration rate	Group-I	48.33 ^{bc} ± 6.27	29.33 ^{ab} ± 3.25	25.17 ^a ± 0.94	34.28 ± 7.13
	Group-II	61.17 ^{bc} ± 8.29	31.50 ^{ab} ± 4.38	27.00 ^a ± 1.59	39.89 ± 10.72
	Pooled mean	54.75^B ± 6.42	30.42^A ± 1.08	26.08^A ± 0.92	

Table 2: Haematological parameters in Buparvaquone and Arteether treated groups before treatment and at different intervals after treatment

Haematological parameters		0 th day	7 th day	21 st day	Pooled mean
Hb	Group-I	6.68 ^a ± 0.17	6.70 ^a ± 0.16	7.25 ^b ± 0.15	6.88 ± 0.18
	Group-II	6.63 ^a ± 0.16	6.73 ^a ± 0.16	7.23 ^b ± 0.11	6.87 ± 0.18
	Pooled mean	6.66^A ± 0.02	6.72^A ± 0.02	7.24^B ± 0.01	
PCV	Group-I	19.13 ^a ± 0.77	20.07 ^a ± 0.72	22.58 ^b ± 0.19	20.59 ± 1.03
	Group-II	19.12 ^a ± 0.89	20.43 ^a ± 1.01	21.87 ^a ± 0.81	20.47 ± 0.79
	Pooled mean	19.12^A ± 0.01	20.25^A ± 0.18	22.22^B ± 0.38	
TEC	Group-I	3.98 ^{ab} ± 0.39	4.10 ^{ab} ± 0.41	4.56 ^b ± 0.33	4.22 ± 0.18
	Group-II	3.55 ^a ± 0.19	3.72 ^{ab} ± 0.19	4.14 ^{ab} ± 0.23	3.80 ± 0.17
	Pooled mean	3.76 ± 0.21	3.91 ± 0.19	4.36 ± 0.22	
TLC	Group-I	7.42 ^a ± 0.25	9.30 ^a ± 0.28	10.33 ^b ± 0.76	9.02 ± 0.85
	Group-II	7.95 ^a ± 0.84	9.21 ^{a c} 1.16	10.35 ^b ± 1.81	9.17 ± 0.69
	Pooled mean	7.68^A ± 0.27	9.26^A ± 0.04	10.34^B ± 0.01	

count between both groups (I and II) and between periods showed apparent but non significant increase on 7th day and 21st day post treatment as compared to 0th day before treatment. The treatment group I and group II showed non significant but apparent improvement in total leucocyte count after 7th day and significant improvement 21st day post treatment as compared to day '0' day before treatment. The analysis of variance revealed non significant variation in pooled mean of total leucocyte count between both groups (I and II). The pooled mean of TLC in periods showed non significant but apparent increase on 7th day and significant increase on 21st day post treatment as compared to '0' day before treatment. The haematological parameters showings various alterations in buparvaquone

and arteether treated groups before treatment and after different intervals is depicted in table 2.

Differential leucocyte count showed various alterations in treatment group I treated with Inj. buparvaquone and group II treated with Inj. arteether. The neutrophil count showed significant improvement in treatment group I on 7th day and 21st day post treatment as compared to day '0' before treatment. In group II, significant improvement was observed on day 7th and day 21st after treatment as compared to '0' day before treatment. Pooled mean of neutrophil between periods showed significant increase in values on 7th and 21st day post treatment as compared to 0th day before treatment.

The treatment group I and group II showed significant improvement in lymphocyte count on 7th day and 21st day post treatment as compared to '0' day before treatment. Pooled mean of lymphocyte between periods showed significant improvement after 7th and 21st day post treatment as compared to 0th day before treatment. The treatment group I showed non significant but apparent improvement in monocyte and eosinophil count after 7th day and 21st day post treatment as compared to '0' day before treatment. In group II, significant improvement observed on day 7th and day 21st after treatment as compared to '0' day before treatment. Pooled mean of monocytes between periods showed non significant variation on 7th and 21st day post treatment as compared to '0' day before treatment and pooled mean of eosinophil count between periods showed significant improvement after 7th day and 21st day post treatment as compared to '0' day before treatment. The analysis of variance revealed non significant variation in pooled mean of basophil count in both the treatment groups and pooled mean of basophil between periods on 7th and 21st day post treatment as compared '0' day before treatment. The differential leucocyte count showings various alterations in buparvaquone and arteether treated groups before treatment and after different intervals is depicted in table 3.

Analysis of variance revealed non significant variation in pooled mean of neutrophil, lymphocyte, monocyte, eosinophil and basophil between groups indicating the arteether has at par efficacy as compared to buparvaquone.

Clinical and haematological studies revealed that Arteether has at par efficacy as compared to Buparvaquone in theileriosis affected cattle.

In present research work, out of 6 animals treated with Inj. arteether @ 5 mg/kg B.W. intramuscularly, four animals recovered clinically after 21st day post treatment contributing percent efficacy of 66.66%. However, Inj. buparvaquone @ 2.5 mg/kg B.W. deep intramuscularly given to one of the treatment group which showed 100.00 % efficacy in theileriosis affected cattle.

The rise in rectal temperature might be due to liberation of endogenous progeny because of cellular lysis and high level of parasitemia which leads to the stimulation of thermoregulatory centre in hypothalamus (Al-Emarah *et al.*, 2012). However, the rise in heart rate and respiration rate might be due to the cytokines like, tumor necrosis factor- α and interleukins (TNF- α , IL-1 and IL-6) produced by infected mononuclear cells which are responsible for the diverse clinical symptoms of tropical theileriosis (Kacchawa *et al.*, 2016).

Table 3: Differential leucocyte count in Buparvaquone and Arteether treated groups before treatment and at different intervals after treatment

DLC		0 th day	7 th day	21 st day	Pooled mean
Neutrophil	Group-I	22.00 ^a ± 1.73	31.50 ^b ± 3.08	37.33 ^b ± 3.10	30.28 ± 0.18
	Group-II	22.17 ^a ± 2.98	34.00 ^b ± 2.12	43.00 ^c ± 1.59	33.06 ± 0.17
	Pooled mean	22.08^A ± 0.21	32.75^B ± 0.19	40.17^C ± 0.22	
Lymphocyte	Group-I	71.00 ^c ± 1.63	59.17 ^b ± 1.62	55.33 ^a ± 2.23	61.83 ± 4.75
	Group-II	68.83 ^c ± 2.98	59.67 ^b ± 2.01	52.00 ^a ± 1.65	60.17 ± 4.86
	Pooled mean	69.92^C ± 1.08	59.42^B ± 0.25	53.67^A ± 1.66	
Monocyte	Group-I	4.83 ^a ± 0.30	4.00 ^a ± 0.25	4.67 ^a ± 0.33	4.50 ± 0.25
	Group-II	5.67 ^b ± 1.33	4.33 ^a ± 0.33	3.83 ^a ± 0.16	4.61 ± 0.55
	Pooled mean	5.25 ± 0.42	4.17 ± 0.17	4.25 ± 0.42	
Eosinophil	Group-I	2.17 ^a ± 0.16	1.83 ^a ± 0.16	2.00 ^a ± 0.44	2.00 ± 0.83
	Group-II	2.83 ^b ± 0.30	2.17 ^a ± 0.30	1.17 ^a ± 0.16	2.06 ± 0.50
	Pooled mean	2.50^B ± 0.33	2.00^A ± 0.17	1.58^A ± 0.41	
Basophil	Group-I	0.00 ± 0.00	0.00 ± 0.00	0.17 ± 0.17	0.06 ± 0.06
	Group-II	0.17 ± 0.17	0.17 ± 0.17	0.00 ± 0.00	0.11 ± 0.06
	Pooled mean	0.08 ± 0.09	0.08 ± 0.09	0.08 ± 0.09	

The decline in haemoglobin concentration has been attributed to the toxic metabolites of *Theileria* spp. which is having harmful effect on bone marrow as they hamper erythropoiesis. Persistent loss of blood caused by continuous blood sucking ticks which play an important role in haemoglobin loss, Somu *et al.*, (2017) and Al-Emarah *et al.*, (2012). The decrease in packed cell volume (%) might be due to presence of reticulocytes in the blood smear of the infected animals revealing increase in activity of the bone marrow by natural infection of *T. annulata* (Tuli *et al.*, 2015). The decrease in total erythrocyte count might be due to intraerythrocytic piroplasms or an autoimmune reaction although it may also be attributed to erythro-phagocytosis rather than a parasite induced lysis. TNF- α released by infected cells are required for causing suppression of haemopoietic progenitors and reduction in RBC production. It reduces life span of RBCs resulting into anaemia (Tuli *et al.*, 2015) and decrease in total leucocyte count might be due to persistence harmful effect of toxic metabolites of *Theileria* on the haemopoietic organ especially bone marrow and their interference with the process of leucogenesis (Hussein *et al.*, 2007).

The decrease in neutrophil percentage might be attributed to persistent harmful effect of toxic metabolites of *Theileria* spp. on hemopoietic organs specially bone marrow and there interference with the process of leucogenesis and due to proliferation of lymphocytes in the lymphoid organ as defensive response to invading parasite (Al-Emarah *et al.*, 2012). The increase in lymphocyte percentage might be due to persistent harmful effect of toxic metabolites of *Theileria* on hemopoietic organs specially bone marrow and there interference with the process of leucogenesis and proliferation of lymphocytes in the lymphoid organ as defensive response to invading parasite. The lymphocytosis might be due to intralymphocytic *Theileria* parasites transforming the host cell, leading to clonal growth of lymphocytes (Ganguly *et al.*, 2015). The change in monocyte percentage might be attributed to persistent harmful effect of *Theileria* spp. on hemopoietic organs specially bone marrow and there interference with the process of leucogenesis and due to proliferation of lymphocytes in the lymphoid organ as defensive response to invading parasite (Hussein *et al.*, 2007). The increase in eosinophil count might be due to most of the animals in both the groups were tick infested, relating to hypersensitivity exhibiting eosinophilia (Tuli *et al.*, 2015).

CONCLUSION

Inj Arteether has showed at par efficacy as compared to Inj Buparvaquone in respect to clinical parameters and hematological parameters. In respect to treatment Inj arteether revealed percent efficacy of 66.66 % and Inj buparvaquone showed 100 %. However, buparvaquone was found to have higher efficacy as compared to arteether.

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