

Original Research Article

<https://doi.org/10.20546/ijcmas.2018.712.091>

Study of Kidney Function Tests in Pre and Post-treated Dogs on Chemotherapy with Doxorubicin and Vincristine in Venereal Granuloma

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ABSTRACT

Keywords

Creatinine, BUN, Canine transmissible venereal tumor, Vincristine and Doxorubicin

Article Info

Accepted:
07 November 2018
Available Online:
10 December 2018

The present study was carried out in TVCC, Hisar on twenty-four dogs affected with venereal granuloma. Affected dogs were divided equally into three groups viz. vincristine therapy (Group I) with 7 day cycle and doxorubicin therapy consisting two groups i.e. Group II with 14 day cycle and group III with 21 day cycle. Blood sample collection was done at weekly interval and before administration of drug i.e. Day 0,7,14 in Group I, Day 0,7,14,21,28 in Group II and Day 0,7,14,21,28,35,42 in Group III. Kidney Function Tests viz. Creatinine, Blood Urea Nitrogen, Total protein was undertaken for study. Non-significant effect of vincristine and doxorubicin recorded on serum total protein. Serum creatinine evidenced decreasing pattern in Group I. Serum creatinine values were slightly elevated till Day 14 and then declined till day 28 in Group II. Non-significant but continuous decreasing pattern was observed in Group III. BUN registered non-significant undulating trend in Group I, non-significant but continuous decreasing pattern in Group II and gradual increasing pattern from Day 7 to Day 28 and distinct drop till Day 42 in Group III.

Introduction

In enzootic areas, where there are high numbers of free-roaming sexually active dogs, TVT is the most common canine tumor (Das and Das, 2000; Ganguly *et al.*, 2016). Venereal Granuloma also known as Canine transmissible venereal tumor (TVT) is a

contagious, naturally occurring, horizontally transmitted venereal round cell tumor (Murgia *et al.*, 2006). Transmission of TVT occurs normally by direct contact through coitus by viable tumor cells through injured mucosa and tumour cells are seeded onto mucous membrane but may be transmitted through licking, biting, and sniffing tumor affected

areas (Bloom, 1954; Dass, 1986; Das and Das, 2000). The lesions of TVT are usually confined to the mucous membranes of the external genitalia of dogs of both sexes of any breeds (Amaral *et al.*, 2004). TVT lesion usually remain localized, but metastasis to the adjacent oral, ocular, nasal, skin and conjunctiva mucosae and inguinal lymph nodes was reported in many cases. Chemotherapy with vincristine sulfate is the most frequently used drug and venereal granuloma responds well (Calvet *et al.*, 1982; Cohen, 1985; Johnson, 1994). Other chemotherapeutic agents like cyclophosphamide, vinblastine and methotrexate have also been used alone or in combination (Richardson, 1981; Johnston, 1991; Brown *et al.*, 1981; Yang *et al.*, 1991). Resistant cases can be treated with doxorubicin (Richardson, 1981; Souza *et al.*, 1998). Serum total proteins show irregular pattern (due to gastro-intestinal disorder caused by cytotoxic drugs), serum creatinine and BUN levels are elevated (due to renal dysfunction) recorded due to adverse effects of chemotherapy (Medway *et al.*, 1969; Camacho and Laus, 1989; Behera *et al.*, 2012; Dobson and Gorman, 1993; Sandhu and Rampal, 2006).

Materials and Methods

Twenty four dogs (male and female) with history of bleeding from genital organs were selected. Blood samples were collected from the distal *cephalic vein or saphenous vein* of male and female dogs from all three groups. Blood samples were collected at weekly interval till 3rd cycle of chemotherapeutic treatment in each group and before administration of drug on the day of treatment. Site of blood collection was shaved and cleaned with antiseptic and 5 ml blood was collected by using 20 and 22 or 24 gauge scalp vein by using 20 and 22 or 24 gauge scalp vein set in plastic centrifugal tube, for serum

separation. Centrifugal tube was kept in slanting position at 4°C for 3 hrs and thereafter it was centrifuged at 3000 rpm for ten minutes for serum separation. Thereafter, serum was stored at -20 °C until analysed for biochemical parameter analysis. Kidney function tests viz. Creatinine (Picrate method), Blood Urea Nitrogen (UV method), Total protein (Biuret Method) concentrations were determined by auto analyser using Erba Mannheim kit supplied by transasia bio-medicals Ltd.

Results and Discussion

Serum total proteins

Serum total proteins showed marginal drop on Day 7 followed by distinct rise on Day 14 and elevated profiles continued during post-treatment period in vincristine therapy dogs. Similar pattern of serum total protein was recorded by Padile *et al.*, (1998). However, significant reduction in the serum total proteins was reported following vincristine therapy in dogs (Dinesh *et al.*, 1993) (Fig. 1).

Serum total proteins registered gradual increasing pattern following doxorubicin chemotherapy (Group II and III) except for slight drop on Day 7 in in Group II. Present observations agree well with reported increasing pattern of serum total proteins after doxorubicin therapy in canine TVT (Todorova *et al.*, 2005).

Recorded non-significant effect of vincristine and doxorubicin on serum total protein in canine TVT indicates negligible cytotoxic effect of antineoplastic drugs.

Marginal irregular pattern of serum total proteins after chemotherapy could be consequential to gastro-intestinal disorder of cytotoxic drugs (Dobson and Gorman, 1993; Sandhu and Rampal, 2006).

Serum creatinine

Serum creatinine evidenced decreasing pattern during post-treatment period in vincristine group (Group I) (Fig. 2).

Serum creatinine values were slightly elevated on Day 7 and Day 14 after doxorubicin therapy and then declined till day 28 (Group II). Non-significant but continuous decreasing pattern was observed following doxorubicin therapy (Group III). However, creatinine values remained within the normal range in both vincristine (Group I) and doxorubicin therapy (Group II and III). Similarly, non-significant variations in serum creatinine were recorded in canine TVT following doxorubicin therapy (Todorova *et al.*, 2005).

Serum creatinine levels are elevated in renal dysfunction (Medway *et al.*, 1969). Recorded variations in serum creatinine profiles in

canine TVT could be due to cytotoxic effect of chemotherapy (Gadmade, 2006).

Blood Urea Nitrogen (BUN)

BUN registered non-significant undulating trend in canine TVT following vincristine therapy (Group I). Similarly, non-significant variations in BUN were recorded in canine TVT following vincristine (Padile *et al.*, 1998).

Non-significant but continuous decreasing pattern in BUN was recorded from Day 14 to Day 28 after doxorubicin therapy (Group II) and BUN values followed gradual increasing pattern from Day 7 to Day 28 and thereafter showed distinct drop till Day 42 after doxorubicin therapy (Group III). Todorova *et al.*, (2005) also recorded non-significant variations in BUN in canine TVT after doxorubicin therapy (Fig. 3; Table 1–3).

Table.1 Kidney function tests parameters (Mean±SE) in TVT affected dogs during pre and post treatment of vincristine (Group I (n=8))

Parameter	DAY0 (1 st dose)	DAY7 (2 nd dose)	DAY14 ((3 rd dose)
Total serum protein (gm/dl)	4.45±0.06	4.59±0.09	4.67±0.10
Creatinine (mg/dl)	0.95±0.02	0.94±0.01	0.91±0.02
Blood urea nitrogen (mg/dl)	19.34±0.32	19.21±0.42	19.42±0.45

Day 0-pre-treatment; Days 7 and 14-post treatment
Means with different superscripts (a, b) within a row differ significantly (p<0.05)

Table.2 Kidney function tests parameters (Mean±SE) of TVT affected dogs during pre and post treatment of doxorubicin (Group II (n=8))

Parameters	DAY0 (1 st dose)	DAY7	DAY14 (2 nd dose)	DAY21	DAY28 (3 rd dose)
Total serum protein (gm/dl)	5.73±0.08	5.61±0.18	5.78±0.07	5.85±0.11	5.86±0.11
Creatinine (mg/dl)	0.63±0.01	0.66±0.4	0.64±0.02	0.63±0.02	0.61±0.01
Blood urea nitrogen (mg/dl)	18.52±0.13 ^{ab}	19.02±0.36 ^b	18.45±0.15 ^{ab}	18.35±0.13 ^a	18.27±0.10 ^a

Day 0 – Pre-treatment; Days 7, 14, 21, 28- Post -treatment
Means with different superscripts (a, b) in a row differ significantly (p<0.05)

Table.3 Kidney function tests parameters (Mean±SE) of TVT affected dogs during pre and post treatment of doxorubicin (Group III (n=8))

Parameters	DAY0 (1 st dose)	DAY7	DAY14	DAY21 (2 nd dose)	DAY28	DAY35	DAY42 (3 rd dose)
Total serum protein (gm/dl)	5.74±0.17	5.78±0.17	5.81±0.18	5.88±0.15	5.97±0.14	6.05±0.15	6.10±0.14
Creatinine (mg/dl)	0.62±0.01 ^c	0.61 ^{bc} ±0.01	0.60±0.01 ^{abc}	0.59±0.01 ^{abc}	0.58±0.02 ^{ab}	0.57±0.01 ^a	0.56±0.02 ^a
Blood urea nitrogen(mg/dl)	18.54±0.08 ^{abc}	18.66±0.07 ^{abc}	18.67±0.08 ^{abc}	18.78±0.13 ^{abc}	18.93±0.23 ^c	18.30±0.18 ^{ab}	18.27±0.19 ^a

Figure.1 Histogram showing Kidney function tests (Mean±S.E.) of different parameters in TVT affected dogs (Group I)

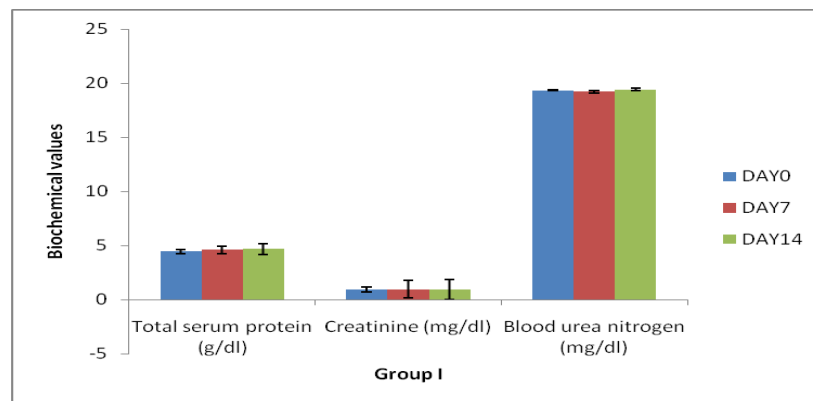


Figure.2 Histogram showing Kidney function tests (Mean±S.E.) of different parameters of TVT affected dogs during pre- and post-treatment of Doxorubicin

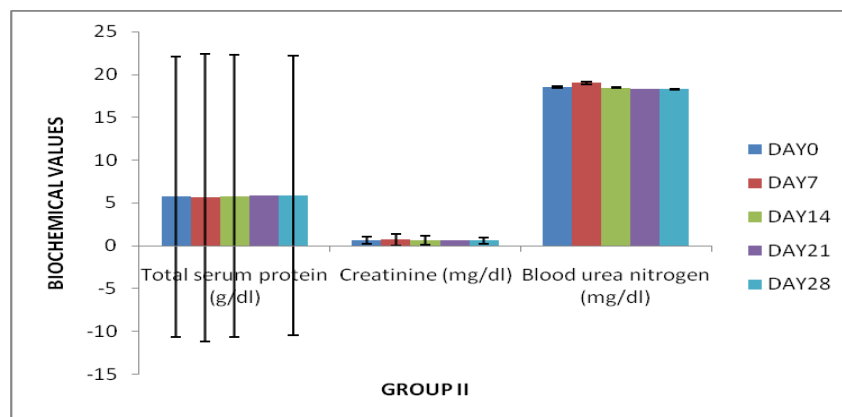
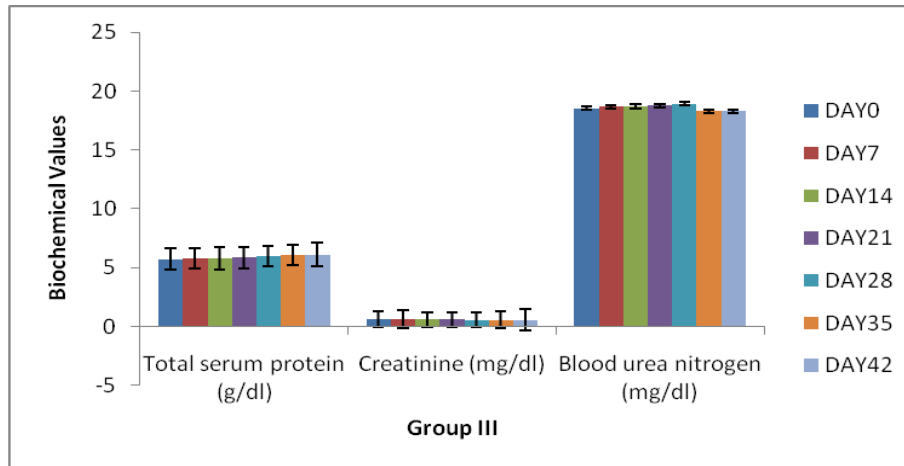


Figure.3 Histogram showing kidney function tests values (Mean±S.E.) of different parameters of TVT affected dogs during pre- and post-treatment of Doxorubicin (Group III)



Chemotherapy causes renal damage (Eleanor and David, 1982). The observed undulating pattern of BUN after vincristine therapy and periodic gradual increasing trend in BUN after doxorubicin therapy could be ascribed to transient renal dysfunction after chemotherapy (Benjamin, 1979; Eleanor and David, 1982).

In conclusion, venereal granuloma is a tumour of canines that invariably affects susceptible dogs of both sexes. It is mainly transmitted from infected dog to a susceptible one through coitus. Exact cause of tumour is obscure. There is no specific breed or age relationship with the disease. Although clinical signs and symptoms of disease are indicative of its diagnosis but general elevation of Kidney function tests values viz. serum total proteins, serum creatinine and BUN is observed following chemotherapy due to cytotoxic effect of drugs affecting renal dysfunction and causing gastrointestinal disorders. So in future reference early diagnosis of disease, timely and cost effective treatment strategy with chemotherapeutic drugs should be devised along with immunobooster syrups must be adopted to control this disease.

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How to cite this article:

Anup Yadav, Praveen Kumar, Lokesh, Ashwani Kumar, Pankaj Kumar, Rajendra Yadav, N.S. Bugalia and Diwakar, R.P. 2018. Study of Kidney Function Tests in Pre and Post-treated Dogs on Chemotherapy with Doxorubicin and Vincristine in Venereal Granuloma. *Int.J.Curr.Microbiol.App.Sci.* 7(12): 740-745. doi: <https://doi.org/10.20546/ijcmas.2018.712.091>