HAEMATO-BIOCHEMICAL AND THERAPEUTIC EVALUATION OF DOXORUBICIN AND VINCRISTINE IN CANINE TRANSMISSIBLE VENEREAL TUMOUR

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ABSTRACT

Twenty-four dogs affected with Transmissible Venereal Tumour (TVT) were treated with either vincristine at 7d interval (n=8), doxorubicin at 14d interval (n=8) or doxorubicin with similar dose rate at 21d interval (n=8). Vincristine and doxorubicin therapy had no impact ($p>0.05$) on haematological (Haemoglobin, Total Leukocyte Count) and biochemical parameters (Alkaline Phosphatase, Alanine Amino Transferase, Total Proteins, Creatinine and Blood Urea Nitrogen). Out of treated dogs, the response to vincristine and doxorubicin was respectively observed in 87.5% and 75% patients. In conclusion, vincristine is a safe drug to treat the dogs suffering with transmissible venereal tumour.

Keywords: Dog, Doxorubicin, Haemato-biochemical, Transmissible venereal tumour, Vincristine

INTRODUCTION

For canine transmissible venereal tumour (TVT), chemotherapy is known effective therapy with vincristine sulphate being the most frequently used drug (Sudjaidee *et al.,* 2012). Other chemotherapeutic agents like cyclophosphamide, vinblastine and methotrexate were also used alone or in combination in treatment regimen. No apparent advantage in the combination of chemotherapy was observed over vincristine alone (Yang *et al*., 1991). The resistant cases of cyclophosphamide, and vincristine can be treated with doxorubicin. The present investigation was carried out to record alterations in haemato-biochemical parameters during pre- and post-treatment and to evaluate the therapeutic efficacy of Doxorubicin and Vincristine in dogs suffering with transmissible venereal tumour.

MATERIALS AND METHODS

Total 24 dogs (male and female) with the clinical history of bleeding from penis, prepuce and cauliflower like growth on base of penis in males and vaginal bleeding and cauliflower like growth in vagina in females following mating were divided equally into three groups; each comprising of eight dogs irrespective of sex. In first group, dogs were treated with vincristine sulphate @ 0.025 mg/kg b.wt., IV at weekly interval (d0, 7 and 14). In second group, dogs were treated with doxorubicin hydrochloride @ 30 mg/m² [Surface area= gm b. $wt^{0.67}$ X $K/10^4$; Sandhu and Rampal, 2006; where K=10] IV in 100ml NSS on d0, 14 and 28. In third group, the treatment was same as in second group, however, Doxorubicin was administered on d0, 21 and 42. The therapeutic efficacy of all treatment regimens was evaluated and compared on the basis of regression of tumour as observed by post-treatment clinical examinations.

On each day before administration of drug, blood samples in EDTA vacutainer (2 ml) and serum vacutainer (5 ml) were collected for haematological and biochemical analysis, respectively. Serum was stored at -20ºC until analysed for biochemical parameters. Haematological parameters viz. Total erythrocytes count (TEC) and Total luecocyte count (TLC) were

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analysed by standard methods. Haemoglobin was estimated by using Sahli's haemoglobinometer. Serum biochemical profile viz. Alanine Amino Transferase (UV kinetic, IFCC method), Alkaline Phosphatase (P nitrophenyl phosphate, PNPP method), Creatinine (Picrate method), Blood Urea Nitrogen (UV method) and Total proteins (Biuret Method) concentrations were determined by auto analyser. The experimental data was subjected to ANOVA to compare values between days within particular group. Differences at 5% ($p<0.05$) was considered statistically significant.

RESULTS AND DISCUSSION

In present study, the most common clinical signs observed in all the dogs with TVT were similar to previous observations (Panchbhai *et al.,* 1989). A lower incidence of clinical symptoms viz. anorexia, vulvuar edema (female), prepucial edema (male) and dehydration was due to delayed presentation of affected dogs as these clinical signs are much common during the early phase of disease (Gandotra *et al*., 1993).

The dogs treated with vincristine and doxorubicin had decreasing ($p>0.05$) trend of haemoglobin from d0 to d14, but ranged within normal values. The declining pattern was consequential to bone marrow suppressive effect of these cytotoxic drugs (Sandhu and Rampal, 2006). Furthermore, the dogs registered continuous decreasing ($p>0.05$) pattern in Total Leucocyte Count during post-treatment vincristine and doxorubicin period which concurs with the earlier observations (Padile *et al.,* 1998). These cytotoxic drugs suppress the replicating precursor cells of bone marrow, thus, resulting in reduced production of leucocytes (Dobson and Gorman, 1993). Furthermore, Total Erythrocyte Count in TVT affected dogs also had consistent decreasing ($p<0.05$) trend during post-treatment period due to suppression of erythropoiesis in bone marrow (Jumean *et al*., 2006).

With regard to results of biochemical parameters, a rise ($p>0.05$) in alkaline phosphatase (ALP) and alanine aminotransferase (ALT) was observed after vincristine and doxorubicin therapy from d0 to last day of treatment in TVT affected dogs. An increase in ALP and ALT activity in TVT affected dogs evidenced cytotoxic effect of chemotherapy on liver metabolism (Behera *et al*., 2012 and Cizmeci *et al*., 2012). Serum total proteins showed marginal drop on d7 followed by rise ($p>0.05$) on d14 and elevated profiles continued during post-treatment period. Similar pattern was observed by Padile *et al*. (1998). In contrast, Dinesh *et al*. (1993) reported reduction in total proteins following vincristine therapy. The marginal irregular pattern of serum total proteins after chemotherapy could be consequential to gastro-intestinal disorder of cytotoxic drugs (Sandhu and Rampal, 2006). Serum creatinine evidenced decreasing ($p>0.05$) pattern during post-treatment in vincristine group. Further, serum creatinine was slightly elevated ($p>0.05$) on d7 and d14 after doxorubicin therapy and then declined ($p>0.05$) till d28. However, creatinine values remained within the normal physiological range in all the groups. The recorded variations could be ascribed cytotoxic effect of chemotherapy. Blood Urea Nitrogen (BUN) registered non-significant ($p<0.05$) undulating trend during whole study period in all three treatment groups. The observed undulating pattern of BUN after vincristine and doxorubicin therapy could be ascribed to transient renal dysfunction after chemotherapy (Eleanor and David, 1982).

Out of eight TVT affected dogs, seven dogs responded to vincristine treatment regimen. Moreover, four out of eight dogs responded to only two doses of vincristine. Complete regression of canine TVT with vincristine was recorded in dogs by several scientists (Nak *et al*., 2005 and Gandhimathi *et al*., 2011). In each doxorubicin group, six out of eight TVT affected dogs responded with three doses of doxorubicin. Moreover, eight out of sixteen dogs responded to two doses of doxorubicin. Others also reported complete regression of canine TVT following treatment with doxorubicin (Gandhimathi *et al.,* 2011).

In brief, Vincristine Sulphate therapy recorded higher therapeutic efficacy (87.5%) as compared to Doxorubicin (75%) in canine TVT. The present findings are suggestive that still vincristine is the treatment of choice for TVT in dogs.

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