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## EFFECTS OF HIGH DOSED LONG ACTING OXYTETRACYCLINE ON SOME HAEMOTOLOGICAL INDICES IN GOATS

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### ABSTRACT

The present study assessed effects of high dosed long acting oxytetracycline (Oxy LA) on some haematological indices in six goats. Each goat was intramuscularly administered with a high dose (30 mg/kg BW) of Oxy LA for the period of 07 days with an interval of 48 hours. The blood samples were taken at different time-points from 0-148 h after final dose of Oxy LA for the assessment of haematological indices. The results showed that Oxy LA administration significantly decreased ( $p < 0.05$ ) leucocytes count at various time points from 6 to 120 h and the decrease in leucocyte count was highly significant ( $P < 0.01$ ) at 72 and 96 h post-administration. Oxy LA treatment caused significant decrease ( $P < 0.05$ ) in the lymphocytes count (1000/cu.mm) at all observed time-points from 6 to 148 h and the decrease in lymphocyte count was highly significant ( $P < 0.01$ ) at various time points from 12 to 120 h. Significant decrease in the RBC count (millions/cu.mm), haemoglobin concentration (g/dl) and packed cell volume (PCV, %) was recorded at 24, 120, 148 h ( $P < 0.05$ ) and at 48, 72, 96 h ( $P < 0.01$ ) after administration of high dosed Oxy LA. Maximum decrease in RBC count, haemoglobin level and PCV occurred at 72 h post-administration.

**Keywords:** Anaemia, goats, haematology, immunity, oxytetracycline.

### INTRODUCTION

Oxytetracycline (Oxy LA), member of tetracyclines group, is a bacteriostatic and broad spectrum antibiotic with a wide range of activity which includes Gram-positive and Gram-negative bacteria, as well as aerobic and anaerobic, and certain protozoa, rickettsia and mycoplasma organisms (Edward, 2005). The Oxy LA is exceptional among the tetracyclines for having a conventional as well as long-acting formulation. Recommended therapeutic dose of Oxy LA in small ruminants is 20 mg kg<sup>-1</sup> BW (Korchi *et al.*, 2001; Payne *et al.*, 2002). The differences in formulation being in the different vehicles and solvent systems used to suspend the oxytetracycline for injection. Use of a long-acting formulation, particularly in food animals, has the main advantage of obtaining

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clinically useful sustained serum and tissue concentrations for longer period of time (up to 3-5 days) without frequent dosing (Adams, 2001). Longer therapy of a Oxy LA with a high dose of 30 mg/kg body weight has also been used as it is expected that it prevents occurrence of relapse of infection by prolonging their persistence in the body. The Oxy LA in different animal species with high dosage regime (22 mg kg<sup>-1</sup> BW in buffalo calves, 25 mg kg<sup>-1</sup> BW in sheep, 30 mg kg<sup>-1</sup> BW in Holstein calf and 40 mg kg<sup>-1</sup> BW in Veal calves) has been used (Radwan *et al.*, 1998; Adams, 2001; Coetzee *et al.*, 2005). Some adverse effects such as anemia, leucopenia; immunosuppressive actions, etc. have been observed after administration of Oxy LA (Mikota and Plumb, 2006). By administration of frequent and large doses than recommended therapeutic dosages, some prominent effects on blood values (decrease in leukocytes, erythrocytes, lymphocytes, hemoglobin and packed cell volume) were also observed. To prevent adverse effects during long term therapy with high dosage regime, periodic laboratory evaluation of hematology should be performed to obtain clinically useful sustained serum and tissue concentration for long period of time. In our environment such studies have not been conducted in small ruminants especially in goats. Therefore, the present study was designed to assess the effects of administration of high dosage regime of Oxy LA on some haematological indices in goats.

## **MATERIALS AND METHODS**

Six goats weighing average 20 kg were used in this study. Goats were kept at livestock experimental station Department of Livestock Management, Faculty of Animal Husbandry and Veterinary Sciences, Sindh Agriculture University, Tandojam. Animals were given acclimatization period of 21 days prior the experiment. Each animal received a high dose (30 mg kg<sup>-1</sup>) of long acting oxytetracycline (Oxy LA, OXTRA<sup>®</sup> L.A., FATRO, Italy); intramuscularly (I/M) at the gluteal muscle region with an interval of 48 hours for the period of one week. Blood samples were collected in heparinized tubes from jugular vein under aseptic condition at 0, 6, 12, 24, 48, 72, 96, 120 and 148 hrs after completion of the dosage regime. Samples were brought to postgraduate laboratory, Department of Veterinary Physiology and Pharmacology for analysis of haematological indices. Leukocytes (White Blood Cells, WBC) and erythrocytes (Red Blood Cells, RBC) count was done through haemocytometer method, lymphocytes through differential leukocyte count (DLC) method, hemoglobin through acid-hematin method and packed cell volume (PCV) through microhematocrit method.

### **Statistical analysis**

Data (means  $\pm$  SEM) were analyzed by using statistical software SPSS12.0 (StatSoft, Tulsa, OK), and the differences were considered significant at  $P < 0.05$ . For the time course effect the data were subsequently analyzed by the GLM procedure with repeated measures (within-subject model) to determine significance and, if the F-value was significant, then the Student-Newman-Keul's

post hoc test was applied to determine the significance between baseline versus various time points.

## RESULTS AND DISCUSSION

The average value of leukocyte cells count (1000/cu.mm) before administration (0 h) of long acting oxytetracycline (Oxy LA) was  $8.82 \pm 0.5$ . After Oxy LA administration the leucocyte count significantly decreased ( $P < 0.05$ ) at various time points from 6 to 120 h and the decrease in leukocyte count was highly significant ( $P < 0.01$ ) at 72 and 96 h (Table 1). In agreement with our results, previous studies have shown similar findings on administration of high dose (25 mg/kg.BW) of OXY LA in various animal species (Deore *et al.*, 2004; Sovobodov *et al.*, 2006; Kasagala and Pathiratne, 2008). High dose of Oxy LA may cause decrease in leukocyte population in many ways. The Oxy LA has been shown to form chelating complex that decreases in migration and movement of polymorphonuclear leukocyte (Gabler and Creamer, 1991). Moreover, it has been reported that Oxy LA inhibits the enzyme activities in polymorphonuclear leukocyte required for leucocyte maturation and eventually leads to decrease in blood leucocyte count (Glette *et al.*, 1984). In addition to inhibit maturation and migration of leucocytes, Oxy LA suppresses the phagocytic and chemotactic activities of the leukocytes (Forsgren and Banck, 1978; Tafalla *et al.*, 2002).

Table 1. Effects of high dosed long acting oxytetracycline on some haematological indices of goats.

Time (Hr)	WBC (1000/cu.mm)	Lymphocytes (1000/cu.mm)	RBC (millions/cu.mm)	Haemoglobin (g/dl)	PCV (%)
0	$8.82 \pm 0.5$	$5.75 \pm 0.15$	$9.47 \pm 0.39$	$8.57 \pm 0.45$	$25.58 \pm 1.43$
6	$7.53 \pm 0.86^*$	$4.33 \pm 0.94^*$	$9.23 \pm 0.04$	$8.37 \pm 0.95$	$25 \pm 1.52$
12	$7.42 \pm 0.89^*$	$3.4 \pm 0.14^{**}$	$9.07 \pm 0.08$	$7.95 \pm 0.89^*$	$25.27 \pm 2.75$
24	$7.1 \pm 0.64^*$	$2.21 \pm 0.28^{**}$	$8.18 \pm 0.82^*$	$7.48 \pm 0.88^*$	$21.67 \pm 0.32^{**}$
48	$7.19 \pm 0.2^*$	$2.11 \pm 0.19^{**}$	$7.62 \pm 0.07^{**}$	$7.03 \pm 0.09^{**}$	$20.17 \pm 0.57^{**}$
72	$6.4 \pm 0.26^{**}$	$2.08 \pm 0.18^{**}$	$7.53 \pm 0.06^{**}$	$6.9 \pm 0.10^{**}$	$19.17 \pm 0.87^{**}$
96	$6.33 \pm 0.27^{**}$	$2.86 \pm 0.08^{**}$	$7.66 \pm 0.5^{**}$	$7.07 \pm 0.18^{**}$	$21.17 \pm 0.42^{**}$
120	$7.33 \pm 0.96^*$	$3.51 \pm 0.14^{**}$	$7.97 \pm 0.35^*$	$7.37 \pm 0.26^*$	$23.5 \pm 0.38^*$
148	$7.78 \pm 0.99$	$3.99 \pm 0.96^{**}$	$8.2 \pm 0.86^*$	$8.07 \pm 0.56$	$24.33 \pm 0.82$

Values are mean  $\pm$  SE. Significantly different from 0 (\*  $P < 0.05$  and \*\*  $P < 0.01$ ).

The lymphocyte cell count (1000/cumm) was  $5.75 \pm 0.15$  at 0 h. Oxy LA treatment caused significant decrease ( $P < 0.05$ ) in the lymphocytes count at all observed time-points from 6 to 148 h and the decrease in lymphocyte count was highly significant ( $P < 0.01$ ) at various time points from 12 to 120 h (Table 1). The results of present study are also in agreement with several researchers who reported that treatment with Oxy LA caused a significant decrease in lymphocytes count in rat, fish, ewe, human and goat (Goh and Ferrnate, 1984; Boon *et al.*, 1995; Deore *et al.*, 2004; Sovobodov *et al.*, 2006; Fairouz *et al.*, 2007). The effects of high dosed Oxy LA in the present study may be attributed to

adverse effect on the lymphoid tissues, causing lymphocyte depletion and finally suppression of major immune responses of humoral and cell mediated immunities (Bogert and Kroon, 1982; Walzer *et al.*, 1984; Sharma and Bansal, 1985; Tafalla *et al.*, 2002). The drug may directly or indirectly inhibit the T cell proliferation.

At 0 h, the mean values for RBC count (millions/cumm); hemoglobin concentration (g/dl) and PCV (%) were  $9.47 \pm 0.39$ ,  $8.57 \pm 0.45$  and  $25.58 \pm 1.43$ , respectively (Table 1). Significant decrease in the RBC count, HB concentration and PCV was recorded at 24, 120, 148 h ( $P < 0.05$ ) and at 48, 72, 96 h ( $P < 0.01$ ) after administration of high dosed Oxy LA (Table 1). Maximum decrease in RBC count, haemoglobin level and PCV occurred at 72 h post-administration. The results of our study are in agreement with previous researchers who reported the similar findings on RBC, HB and PCV in dog, fish, rat and ewes (Deore *et al.*, 2004; Serezli *et al.*, 2005; Prescott *et al.*, 2007). Previous studies have shown that Oxy LA in dose-dependent manner, produced differential pattern of anemic responses such as hemolytic, megaloblastic and iron deficiency anemia (due to chelating activity of the drug with iron) and the effects were resolved over time after discontinuation of drug from blood (Marcus *et al.*, 1985; Carroll, 2002). The high dosed Oxy, LA has been reported to decrease erythroid cells, haematopoietic tissue and interfere with erythropoiesis which leads to decrease in RBC count (Susan, 2007). Moreover, the drug also inhibits haemoglobin synthesis in immature erythrocytes in bone marrow (Erslev and Iossifides, 1962). In the present study, the adverse effects of Oxy LA on haematological indices were found at first observation (6 h post-administration) remained up to the last observation (148 h post-administration). The persistent effects of the drug suggest that the active drug ingredient persisted for longer period of time in the body fluids. Serezli *et al.* (2005) and Prescott *et al.* (2007) observed higher plasma oxytetracycline level post oxytetracycline administration, which remained higher for 9 days.

## CONCLUSION

It can be concluded from the present study that the administration of high dose (30 mg/kg BW) of oxytetracycline causes anemia and suppress immune function in goats as evidenced by decrease in RBC indices and number of lymphocyte count.

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