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Hematological Alteration Induced After Intramuscular Administration of Long Acting Moxifloxacin in Sheep

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Abstract

Aim: The present study was carried out to investigate hematological alterations induced after single intramuscular administration of long acting moxifloxacin at the dose rate of 7.5 mg/kg body weight in six healthy male sheep.

Materials and methods: Blood samples were collected from treated animals from jugular vein into K_2EDTA tubes at 0, 6, 12 hour and 2th, 3rd, 4th, 5th, 6th, 7th day after treatment were analyzed for hematological parameters (total leukocyte count, differential leukocyte count, total erythrocyte count, Hemoglobin, HCT, MCV, MCH, MCHC, RDW and MPV) analysis.

Results: The results of the study clearly demonstrated that single intramuscular administration of long acting moxifloxacin in therapeutic dose produced non-significant difference ($p<0.05$) in values of hematological parameters in sheep when compared with control values (0 day).

Conclusion: Lack of clinical signs of adverse reactions and absence of significant difference hematological alteration following intramuscular administration may be open a new avenue for insight into the strategy for clinical treatment of various bacterial diseases in sheep.

Keywords: Long acting moxifloxacin; Sheep; Fluoroquinolone, Antibacterial

Introduction

The fluoroquinolones are the fastest growing antibacterial class in terms of global revenue, increasingly being used in dairy animals to treat a wide range of infectious diseases [1]. Moxifloxacin a fourth generation fluoroquinolone having broad spectrum of antibacterial activity against organisms Gram-positive and Gram-negative bacteria, has great future potential for clinical use in the treatment of bacterial infections in domestic animal including sheep. Moxifloxacin is not only effective against Gram-positive and Gram-negative bacteria but also effective against anaerobes and atypical organism such as *Mycoplasma* and *Chlamydia spp* [2]. It has the highest potency in its class against *Staphylococcus aureus* and *Staphylococcus epidermidis* which are the common pathogens causes mastitis and other bacterial infections in domestic animals including in sheep [3]. It's spectrum of activity and pharmacokinetic properties favour its use in veterinary practice. However, the data on safety of single intramuscular administration of long acting moxifloxacin in sheep are scarce. The hematological parameters as a part of assessment of safety profile are impact indication of toxicity or adverse drugs reaction associated with clinical use of antimicrobial drugs. At clinically use dosage. The safety profile of any drug must be investigated before it is recommended for clinical use in any species of domestic animal. So in the context, the present study was planned with objective of hematological alteration induced after intramuscular administration of long acting moxifloxacin in sheep.

Material and Methods

Experimental animals

An animal of Patanwadi breed of sheep from Sheep and Goat Research Station, SDAU, Sardarkrushinagar, was included in the present study. Six healthy sheep (*Ovis aries)*, having body weight between 25-35 kg and age of 2-4 years, were randomly selected for the study. Animals were housed in loose housing shed system with sandy floor in Sheep and Goat Research Station, Sardarkrushinagar Dantiwada Agricultural University, Sardarkrushinagar. Animals were maintained as per Sheep and Goat Research Station maintenance schedule. Water was made available *ad libitum* and free from any contaminants. Animals were kept under constant observation for two weeks prior to beginning of experiment. All necessary managemental practices were followed so that the sheep remained free from stress and diseases. In this period they were subjected to clinical examinations in order to exclude the possibility of any disease.

Drugs and chemicals

Long acting moxifloxacin (10% moxifloxacin in solution with L-arginine, N-butyl alcohol and benzyl alcohol) injectable solution and moxifloxacin base powder were obtained from INTAS Animal health, Gujarat, India. Reagents kits for hematological analysis were purchased from Merck specialties private limited, Mumbai.

Experimental design

Six sheep were utilized for single dose intramuscular administration safety assessment study of long acting moxifloxacin (7.5 mg.kg^{-1}). Blood samples were collected from treated animals from jugular vein into K_2EDTA tubes at 0 day and 6 and 12 hours and on 2, 3, 4, 5, 6 and 7 day for hematological analyses. Plasma was separated after centrifugation of blood samples at 1600 revolutions per minute (rpm) for 10 minutes. The plasma samples were transferred to cryo-vials (3 ml capacity)

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Parameters	Days (Mean ± S.E)								
	0	6 h	12 h	2	3	4	5	6	7
Total leukocyte (×10³/cm)	11.26 ± 0.13	11.71 ± 0.50	12.00 ± 0.42	11.88 ± 0.27	11.88 ± 0.57	11.64 ± 0.44	11.43 ± 0.23	11.74 ± 0.40	11.58 ± 0.28
Neutrophil (%)	36.31 ± 0.98	37.50 ± 0.43	38.40 ± 0.43	33.86 ± 2.55	33.71 ± 0.61	36.56 ± 1.41	35.66 ± 1.59	34.96 ± 0.39	35.53 ± 1.18
Lymphocyte (%)	74.50 ± 0.69	67.82 ± 0.75	70.21 ± 0.66	66.18 ± 0.46	72.20 ± 1.77	72.58 ± 1.74	71.81 ± 0.85	72.10 ± 0.50	71.95 ± 0.45
Monocyte (%)	2.64 ± 0.33	2.21 ± 0.37	2.66 ± 0.39	2.97 ± 0.31	3.09 ± 0.26	3.32 ± 0.25	3.38 ± 0.29	2.42 ± 0.12	2.70 ± 0.34
Eosinophil (%)	2.48 ± 0.06	2.14 ± 0.20	2.06 ± 0.28	2.43 ± 0.18	2.37 ± 0.23	2.76 ± 0.15	2.61 ± 0.19	2.52 ± 0.29	2.36 ± 0.23
Hemoglobin level (g/dl)	10.60 ± 0.28	10.86 ± 0.27	10.26 ± 0.36	10.46 ± 0.40	10.85 ± 0.33	10.56 ± 0.27	10.38 ± 0.34	10.40 ± 0.28	10.39 ± 0.30
PCV (%)	22.56 ± 0.27	22.35 ± 0.41	22.35 ± 0.27	21.35 ± 0.50	22.10 ± 0.30	22.05 ± 0.38	21.58 ± 0.50	20.58 ± 0.88	21.08 ± 0.60
MCV (fl)	27.01 ± 0.33	25.52 ± 0.26	25.97 ± 0.38	26.31 ± 0.39	26.51 ± 0.24	26.34 ± 0.30	25.85 ± 0.44	26.50 ± 0.19	26.17 ± 0.27
MCH(pg/dl)	12.61 ± 0.27	12.10 ± 0.36	12.18 ± 0.29	12.70 ± 0.61	13.08 ± 0.60	12.63 ± 0.39	12.06 ± 0.34	12.47 ± 0.27	12.27 ± 0.27
MCHC (g/dl)	48.78 ± 0.55	46.64 ± 0.42	47.30 ± 0.35	47.85 ± 0.32	48.63 ± 2.25	49.03 ± 1.31	49.58 ± 0.62	49.30 ± 0.43	49.44 ± 0.48
Total erythrocytes (×10⁶/µl)	7.68 ± 0.10	7.77 ± 0.13	7.65 ± 0.06	7.49 ± 0.12	7.75 ± 0.13	7.42 ± 0.06	7.36 ± 0.96	7.55 ± 0.16	7.45 ± 0.10

All values in treatment groups are not significantly different ($p<0.05$) when compared to control (0 h).

Table 1: Hematological parameters (Mean ± S.E) after single intramuscular administration of long acting moxifloxacin (7.5 mg/kg of body weight) in male sheep.

and then stored at 2-8°C until assayed for enzyme estimation. Blood smear for determination of Differential Leukocyte Count (DLC) were prepared from fresh blood at the time of blood collection [4]. Values of the hematological parameters before and after long acting moxifloxacin treatment (7.5 mg.kg^{-1} body weight) in sheep, including White Blood Cell (WBC) count, differential leucocyte counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), Red Blood Cell (RBC) count, hemoglobin (HGB) concentration, hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW) and Mean Platelet Values (MPV) analysis. The samples were analyzed by using automatic hematology analyzer (Medonic CA 620/530 VET, Boule Medical AB, Sweden).

Statistical analysis

Data generated on various parameters were subjected to statistical analysis by paired t- test, using SPSS version 16.0 for window.

Results

Values of the hematological parameters before and after long acting moxifloxacin treatment (7.5 mg.kg^{-1} body weight) in sheep, including white blood cell (WBC) count, differential leucocyte counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), red blood cell (RBC) count, hemoglobin (HGB) concentration, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW) and mean platelet values (MPV) are presented in Table 1. Mean value of all hematological parameters observed in the study when compared with control values (0 day), have been found non significant ($p<0.05$). All animals were not exhibited any local or systemic adverse reactions after daily intravenous and intramuscular administration of long acting moxifloxacin in sheep. Animals did not show change in behavior and pain on palpation of joints during study period.

Discussion

Safety of long acting moxifloxacin following single dose intramuscular administration given at the rate of 7.5 mg.kg^{-1} of body weight in sheep consequently for seven days was monitored by studying various hematological parameters. The hematological indices included the determination of Haemoglobin (Hb), Packed Cell Volume (PCV), Total Erythrocyte Count (TEC), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Total Leukocyte Count (TLC) and Differential Leukocyte Count (DLC). The results of the present study indicate non-significant differences (no alteration) in the values of these parameters estimated when compare with 0 day sample collection. Close similarity was seen between the present finding and these obtained by Kumari [5], who found that hematological values unaffected by long acting moxifloxacin (7.5mg/kg, b.wt.) treatment in goats. This result supported by Modi [6], who mentioned that, moxifloxacin (5mg/kg, b.wt.) evoked non-significant differences in hematological parameters between pre and post drug treatment period in sheep. Patel [7], stated that, Fluoroquinolones antibacterial moxifloxacin in therapeutic dose evoked non significant differences in WBC, neutrophil, lymphocyte, eosinophil, nomocyte, HGB, HCT, MCH, MCHC, RDW and MPV parameters when compared with pre-moxifloxacin treatment values in goats. Also our results were in agreement with Chaudhari [8], who reported that lactating goats showed non significant alterations in total erythrocytic count, haemoglobin content, packed call volume and total leucocytes count. The results of the present study on effect of long acting moxifloxacin (given consequently once a day for seven days) on hematological parameters are in consistent with the same type of study performed in rats by Sadariya et al. [9], where in the effect of repeated intramuscular administration of moxifloxacin (5.0 mg.kg^{-1} body weight repeated at 24 h interval for 14 days) in wistar rats did not alter (non significantly) any hematological parameters studied (Hb, RBC, WBC, MCV, MCH, MCHC, HCT and DLC). Likewise Khargharia [10] have found no alterations in hematological parameters after repeated intravenous administrations of one of the most widely used fluoroquinolone, enrofloxacin (5 mg.kg^{-1}, repeated at 24 h for 5 days) in yak.

Results of present study were in support of Kubin and Reiter [11] that moxifloxacin is safe and well tolerated in comparison with other commonly prescribed antibacterial drugs in humans. Fluoroquinolones as a class of antibacterial agents causes less common effects on blood physiology (about 5% only) [12]. Results of our study were supported by report of non significant change in hematological parameters following repeated administration of ciprofloxacin in calves, enrofloxacin in yak, levofloxacin in layer birds, levofloxacin in sheep and moxifloxacin in human [10,13-16]. Fluoroquinolones as a class are generally well tolerated; most adverse effects are mild in severity, self-limiting and rarely result in treatment discontinuation [12,17]. Similarly ciprofloxacin was also found safe in cow calves following repeated administration at dose rate 5 mg/kg body weight as no alterations were found in joint cartilage [13]. In contrast, significant change in hematological and biochemical parameters following repeated administration moxifloxacin in rats was reported by von Keutz and Schluter [18].

Conclusion

The present study was carried out to investigate the lack of clinical signs of adverse reactions and absence of significant hematological alteration following intramuscular administration may be open a new avenue for insight into the strategy for clinical treatment of

various bacterial diseases in sheep. In future the drug may be potential candidates to be used in the treatment of infectious diseases in sheep.

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