EVALUATION OF HEMATOLOGICAL AND BIOCHEMICAL VALUES AFTER REPEATED CO-ADMINISTRATION OF MOXIFLOXACIN AND FLUNIXIN IN GOATS

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ABSTRACT

Moxifloxacin is a fourth generation fluroquinolone antimicrobial agent of popular choice among veterinarians due to advantage of concentration-dependent broad spectrum of bactericidal action and ease of ready to use injectable formulation for animals. Flunixin is a classic, well known veterinary specific non-steroidal anti-inflammatory drug (NSAID) used primarily for short-term treatment of moderate pain and inflammation in animals. The present experimental study was carried out to notice any chance of toxicity/ adverse drug reactions, visible by clinical inspection or alteration in haematological and blood biochemical parameters in goats when they were administered with moxifloxacin and meloxicam concomitantly daily for five days. Six healthy adult male *Sirohi* goats were used. Moxifloxacin was injected daily for five days at the dose rate of 10 mg/kg b.wt. intravenously. Flunixin was injected daily for five days at the dose rate of 1.1 mg/kg b.wt. intravenously at the same time. Blood samples were drawn daily from every experimental animal for haematology and biochemistry evaluations. Zero-day blood samples were drawn just before start of the experiment and considered as control. Haematological parameters namely, haemoglobin, PCV, TEC, TLC and DLC were estimated. Biochemical parameters namely, ALT, AST, ALP, GGT, total bilirubin, glucose, creatinine, urea nitrogen, total protein, albumin, cholesterol and TGL were estimated. The haematological and biochemical parameters did not show any significant difference from healthy control and remained within normal range during the course of treatment and post-treatment. The findings support that repeated co-administration of moxifloxacin and flunixin for therapeutic purpose is safe in goats.

Key words: Moxifloxacin, flunixin, haematological, biochemical, goat

Introduction

The goat population contributes to 27.8 per cent of total livestock population of India. Its population has increased by 10.14 per cent during the period between 20th and 19th livestock census of India, with major contribution from rural India and rearing of indigenous and local breeds of goat (Anonymous, 2019). A wide range of bacterial, viral, parasitic infections, causing heavy mortality and morbidity result in huge economic loss to different goat farming systems (Jindal, 2012). In small scale, household goat keeping in rural and urban India for religious, meat and milk purposes, often there is poor adherence to standards of biosecurity, balanced ration, regular deworming and mineral supplementation. These all add to the stressors that predispose the goats to various infectious and non-infectious diseases. Goats in India often suffer from digestive system, respiratory system, urogenital system, skin, foot, and mammary gland diseases which are characterised with ill diagnosed infections, inflammation, fever, pain leading to production and animal loss.

Fluoroquinolones, have been a popular choice for treatment of bacterial infections in veterinary medicine. They are used in practically all species and have a broad spectrum of concentration dependent bactericidal activity that includes most of the important veterinary bacterial pathogens. Moxifloxacin is fluoroquinolone antibacterial agent of the latest generation with broad spectrum bactericidal action and improved activity against Gram-positive bacteria due to methoxy substitution at position 8 of fluoroquinolone nucleus (Papich, 2018).

Due to ease of ready-to-use injection, once daily administration, and other beneficial pharmacodynamic and pharmacokinetic features, moxifloxacin use is increasing in veterinary medicine in India to eradicate the susceptible bacterial infection. In clinical treatment, there is co-administration of several drugs which may result in unpredictable therapeutic outcome. The non-steroidal anti-inflammatory drugs (NSAIDs) are frequently prescribed with antibacterial drugs for the treatment of various bacterial infections accompanied by fever and other inflammatory conditions in human and animal medicine. Flunixin is classic veterinary specific popular NSAID used primarily for short-term treatment of moderate pain and inflammation. It has been used to treat abdominal pain in horses, to decrease signs of sepsis in horses, to decrease clinical signs associated with coliform mastitis in cattle, as a single dose for treatment of diarrhoea in dairy calves, and as an adjunctive treatment with antimicrobial agents (Papich, 2016). It is understood that co-administration of two drugs may affect the absorption, distribution, biotransformation and/or excretion of both agents. It may result in either diminished therapeutic efficacy or increased toxicity of one or more of the administered drugs.

The presented experimental study was carried out to identify any possibility of toxicity/ adverse drug reactions, visible by alteration in haematological and blood biochemical parameters in group of goats (n=6) when the animals were administered moxifloxacin and flunixin concomitantly daily for five days.

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Materials and Methods

The present experiment was conducted on six, apparently healthy, one-year old male *Sirohi* goats, weighing between 25-30 kg, and maintained in standard management conditions at Livestock Research Station (LRS) Beechwal of Rajasthan University of Veterinary and Animals Sciences (RAJUVAS), Bikaner. The experimental protocol, general procedures and use of animals were clear from ethical angle and the same was communicated vide letter No CVAS/IAEC/2017-18/23-24 dated 04.10.2018. All animals were healthy and free from any other drug treatment at the commencement of experiment.

Moxifloxacin, as ready to use injection (Inj. Mofoi™; Bovian Healthcare Pvt. Ltd., Secunderabad, Telangana, India),was administered to experimental goats once daily at the dose rate of 10 mg/kg b.wt. intravenously for five days. The animals were co-administered flunixin, as ready to use injection (Inj. Megludyne®; Virbac Animal Health India Pvt. Ltd., Borivali East, Mumbai, Maharashtra, India), at the dose rate of 1.1 mg/kg b.wt. once daily intravenously for five days.

The experimental animals were carefully monitored for any clinical abnormality or disease during the period of experiment. Blood samples in EDTA tube (2 ml) were drawn from every animal before administration of drug/s which served as control (day 0) and at 1st, 2nd, 3rd,4th and 5th day post treatment. These samples were utilised same day for haematological estimations. Differential leucocyte counts (DLC) were done manually while other parameters *viz.* haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC) and total leucocyte count (TLC) were estimated with the help of an automatic veterinary haematology analyser (Mindray BC-2800 Vet).

For biochemical estimations, serum samples were harvested from blood samples (3 ml) collected in sterile plain centrifuge tubes, from every animal before administration of drug/s which served as control (day 0) and at 1st, 2nd, 3rd, 4th and 5th day post treatment. Serum biochemical parameters were analyzed with the help of a fully automatic biochemistry analyzer (TurboChem 100, Awareness Technologies, USA).

Table 1: Effect on various haematological parameters following repeated daily intravenous administration of moxifloxacin (10 mg/kg) and flunixin (1.1 mg/kg) for 5 days in goats

Parameter	Day					
	0 day	1st day	2nd day	3rd day	4th day	5th day
Hb (g/dl)	8.98 ± 0.10	8.85 ± 0.12	8.80 ± 0.05	8.82 ± 0.09	8.90 ± 0.09	8.97 ± 0.11
PCV (%)	26.55 ± 0.54	26.41 ± 0.49	25.75 ± 0.21	25.98 ± 0.34	26.67 ± 0.45	26.53 ± 0.51
TEC (10^6/µl)	8.86 ± 0.17	8.77 ± 0.16	8.78 ± 0.11	8.71 ± 0.12	8.76 ± 0.13	8.81 ± 0.16
TLC ($X10^3$/µl)	8.87 ± 0.34	9.12 ± 0.37	8.98 ± 0.32	9.17 ± 0.32	9.10 ± 0.27	9.15 ± 0.22
Neutrophils (%)	36.33 ± 2.26	36.50 ± 1.84	37.17 ± 2.02	35.67 ± 2.29	36.83 ± 2.39	39.00 ± 2.72
Basophils (%)	0.33 ± 0.21	0.67 ± 0.33	0.17 ± 0.17	0.50 ± 0.22	0.33 ± 0.33	0.50 ± 0.22
Monocytes (%)	2.83 ± 0.30	2.50 ± 0.56	1.67 ± 0.49	1.50 ± 0.43	1.83 ± 0.31	2.00 ± 0.37
Eosinophils (%)	1.00 ± 0.00	1.33 ± 0.33	1.00 ± 0.26	1.83 ± 0.17	1.33 ± 0.21	1.16 ± 0.40
Lymphocytes (%)	59.50 ± 2.23	59.00 ± 1.73	60.00 ± 1.86	60.50 ± 1.98	59.67 ± 2.62	57.33 ± 2.81

Results and Discussion

Values of haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leukocyte count (TLC) and differential leukocyte count (neutrophil, lymphocyte, basophil, eosinophil and monocyte) following daily intravenous administration of moxifloxacin (10 mg/kg) in combination with intravenous administration of flunixin (1.1 mg/kg) for five days in goats are presented in Table 1. Results of various biochemical parameters *viz.* serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), serum alkaline phosphatase (ALP), serum gamma- glutamyl transferase (GGT), serum bilirubin (total), glucose, serum creatinine, urea nitrogen, total protein, albumin, cholesterol and triglycerides (TGL) in goats are presented in Table 2. The values obtained from blood samples just before the beginning of the experiment or drug administration (at day zero) are taken as control data.

Following daily intravenous administration of moxifloxacin in combination with meloxicam for 5 days in goats, the values of haematological and biochemical parameters did not differ significantly ($P<0.05$) from the corresponding values of control (zero-day).

Results of our study are supported by report of no significant alterations in haematological and biochemical parameters in Wistar rats following daily intramuscular administration of moxifloxacin at 5 mg/kg for 14 days (Sadariya *et al*., 2010). In separate previous studies by others on sheep and goats with intramuscular administration of long-acting moxifloxacin at 7.5 mg/kg body weight, no significant alterations in haemato-biochemical values were observed (Modi *et al*., 2013; Kumari *et al*., 2014). Sharma *et al*. (2020) reported no significant alteration in haematological and biochemical parameters following coadministration of marbofloxacin (8 mg/kg) and meloxicam (1 mg/kg) for five days in sheep. Varia *et al*. (2012)

Table 2: Effect on various biochemical parameters following repeated daily intravenous administration of moxifloxacin (10 mg/kg) and flunixin (1.1 mg/kg) for 5 days in goats

Parameter	Day					
	0 day	1st day	2nd day	3rd day	4th day	5th day
ALT (IU/L)	17.13 ± 0.71	17.23 ± 0.64	17.32 ± 0.57	17.40 ± 0.58	16.92 ± 0.48	17.03 ± 0.50
AST (IU/L)	95.37 ± 4.45	98.28 ± 4.23	98.70 ± 3.50	99.20 ± 3.79	98.80 ± 4.60	97.83 ± 4.49
ALP (IU/L)	176.68 ± 5.41	179.60 ± 5.88	182.50 ± 6.39	180.00 ± 5.45	180.05 ± 4.84	181.42 ± 5.86
GGT (U/L)	36.57 ± 1.89	37.13 ± 1.68	37.57 ± 1.78	37.45 ± 1.75	37.13 ± 2.17	37.25 ± 1.94
Total bilirubin (mg/dl)	0.07 ± 0.02	0.09 ± 0.01	0.09 ± 0.01	0.10 ± 0.01	0.10 ± 0.01	0.09 ± 0.01
Glucose (mg/dl)	59.18 ± 1.68	60.62 ± 1.38	60.72 ± 1.89	60.07 ± 2.18	61.63 ± 1.96	60.60 ± 2.14
Creatinine (mg/dl)	1.31 ± 0.07	1.33 ± 0.07	1.35 ± 0.07	1.44 ± 0.08	1.37 ± 0.08	1.38 ± 0.08
Urea Nitrogen (mg/dl)	15.50 ± 0.77	15.75 ± 0.69	16.10 ± 0.68	16.15 ± 0.85	15.98 ± 0.79	15.90 ± 0.77
Total protein (g/dl)	6.66 ± 0.06	6.73 ± 0.06	6.69 ± 0.06	6.69 ± 0.05	6.69 ± 0.04	6.71 ± 0.05
Albumin (g/dL)	3.11 ± 0.10	3.11 ± 0.10	3.14 ± 0.11	3.11 ± 0.10	3.07 ± 0.09	3.12 ± 0.09
Cholesterol (mg/dl)	100.03 ± 4.35	100.88 ± 4.39	100.14 ± 4.29	100.38 ± 4.61	99.58 ± 4.22	99.60 ± 4.38
TGL (mg/dl)	53.89 ± 2.32	52.84 ± 2.64	53.73 ± 2.81	54.04 ± 2.76	54.45 ± 2.81	53.93 ± 2.71

also reported no significant alteration in haemato-biochemical parameters in broiler chickens following oral administration of levofloxacin (10 mg/kg) at 12 h interval for 14 days. Lei *et al*. (2018) studied the safety of marbofloxacin in beagle dogs after oral administration at graded doses (2 mg/kg, 6 mg/kg and 10 mg/kg) for 40 days and they reported decrease in platelets and increase in WBC at 6 mg/kg and 10 mg/kg dose rate. Total bilirubin, ALT, Na^+, and AST were significantly decreased whereas, ALP and BUN were significantly raised but these values did not fall outside the reference ranges. Non-significant change in haematological and biochemical parameters were reported following repeated administration of ciprofloxacin in calves (Bhavsar *et al*., 2004) and enrofloxacin in yak (Khargharia *et al*., 2007).

From the present study, it is concluded that repeated and concurrent administrations of moxifloxacin and flunixin do not alter the haematological and biochemical parameters in goats and can be safely and effectively used for combating infections with an inflammatory condition in sheep.

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