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Safety Assessment of Lincomycin following Repeated Intramuscular Administration in Goats

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Abstract

A safety evaluation of lincomycin was carried out to assess clinical impact of intramuscular administration of lincomycin on various haematological and biochemical parameters in goats to establish safety profile of lincomycin. Six healthy female goats were treated with single intramuscular dose of lincomycin @10.0 mg/kg body weight. The blood samples were collected at day 0 (before administration of drugs), and on 6th day of drug administration. The hematological and plasma biochemical analysis were done. No significant alterations ($p < 0.05$) were found in the mean value of haematological and biochemical parameters during treatment period except for significant elevation in values of Lactate dehydrogenase and Creatinine. Repeated intramuscular administration of lincomycin (10.0 mg/kg) for 5 days in goat was found safe. Thus, lincomycin may be useful to treat bacterial diseases accompanied by fever, pain and other inflammatory condition in goats.

Keywords: Goats, Lincomycin, Safety Assessment

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1. Introduction

Lincomycin belongs to a class of antibiotics known as lincosamides. It is produced by *Streptomyces linconensis*. It has been used for the last four decades both in human and veterinary medicine. Lincomycin is approved for veterinary use including food animals. It is also recommended for use in domestic animals as an alternative to other antibiotics of similar spectrum that are of greater importance for human medicine (Collignon *et al.,* 2008). It is active mainly against Gram-positive and many anaerobic bacteria. It has been shown to have efficacy against *Erysipelothrix insidiosa, Leptospira pomona, Mycoplasma* species, *Staphylococcus* species and *Streptococcus* species (Giguere, 2006). The drug exerts its antibacterial action by inhibiting RNA-dependent protein synthesis through action on the 50S subunit of the ribosome and preventing peptide bond formation (Barragry,1994). The lincosamides are usually considered as bacteriostatic in nature. It can be given orally in feed or drinking-water, by intramuscular injection, or as an intramammary infusion. The main indications are acute and chronic respiratory tract infection, sinusitis, skin, soft tissue, bone and joint infections, septicemia and endocarditis (Papich and Riviere, 2009). There are scanty reports on clinical impact of lincomycin on hematology and biochemistry in goats or in other veterinary species. Biochemical alteration and Hematological profile as a part of safety profile induced by Lincomycin needs to be assessed before it is recommended for clinical application in treatment of infections caused by sensitive organism. So present study was planned to investigate the clinical impact of single intramuscular administration of lincomycin on biochemical and hematological parameters to exclude possibilities of adverse reactions associated with its use in goats and to recommend safe use among field veterinarians.

2. Materials and Methods

2.1 Experimental Animals

The present study was conducted on six healthy female goats weighing 38-56 kg. The study protocol was approved by the animal ethics committee. Animals were procured

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from Department of Livestock Production Management, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana and housed in separate pan. All animals were maintained on standard ration, and water was provided *ad libitum*. All animals were acclimatized for period of 15 days and observed clinically daily to rule out presence of any disease.

2.2 Drugs and Chemicals

Lincomycin Injection (Lynx 30%, Wallace, Ahmedabad) and lincomycin standard (Lincomycin hydrochloride, CDH, Delhi) were procured commercially. Autopak kits for enzyme estimation were purchased from Bayer (Siemens Medical Solutions Diagnostics Ltd., Baroda). All other chemicals/reagents used in this study were of analytical grade, obtained from reputed companies.

2.3 Experimental Design and Drug Administration

All the six animals were treated with Lincomycin at a dose rate of 10.0 mg/kg body weight after intramuscular administration in deep gluteal muscle. All animals were observed daily for any side effects or clinical abnormalities throughout the period of experiment. Safety assessment was carried out by monitoring haematological and biochemical parameters in goats. Blood samples were collected at day 0 (before administration of drugs), and on 6th day from jugular vein into sterile tubes with tri-potassium ethylene diamine tetra-acetic acid for haematological and in sterile heparinizd test tubes for biochemical analysis. Plasma was separated after centrifugation of blood samples at 2500 rpm for 15 minutes and stored at 2-8°C until assayed for enzyme estimation. The biochemical parameters of Alkaline Phosphatase (ALKP), Acid Phosphatase (ACP), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate Dehydrogenase (LDH), Gamma-Glutamyl Transpeptidase (GGT), Total proteins, albumin, creatinine, Blood urea nitrogen, Cholesterol, Total bilirubin and Direct bilirubin were analyzed by using automatic Clinical Analyzer (Systronics). Haematological parameters like White Blood Cell (WBC) count, Red Blood Cell count (RBC), hemoglobin (HGB) concentration, Packed cell volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH and Mean Corpuscular Hemoglobin Concentration (MCHC) were analyzed immediately after collection. The statistical analysis was performed using student's t-test using SPSS software (Version 16.0). Statistical differences were considered at $p \leq 0.05$.

3. Results and Discussion

The mean values of Alkaline Phosphatase (ALKP), Acip Phosphatase (ACP), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate Dehydrogenase (LDH), Gamma-Glutamyl Transpeptidase (GGT), Total proteins, albumin, creatinine, Blood urea nitrogen, Cholesterol, Total bilirubin and Direct bilirubin are presented in Table 1 and 2. The mean values of White Blood Cell (WBC) count, Red Blood Cell count (RBC), hemoglobin (HGB) concentration, Packed Cell Volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH and mean Corpuscular Hemoglobin Concentration (MCHC) are presented in Table 3. During the experimental period, none of the animal of study group revealed any clinical symptoms and mortality attributable to the 5 days intramuscular administration of lincomycin.

Table 1. Biochemical parameters (mean± SE) before and after single dose intramuscular administration of lincomycin in goats. (Mean ± SE; n=6)

Day	Biochemical Parameters							
	ALT (IU)	AST (IU)	ALKP (IU)	ACP (IU)	LDH (IU)	GGT (IU)	BUN (mg/dl)	Cretinine (mg/dl)
0	28.83± 3.19	19.33± 1.33	233.50± 27.96	224.39± 11.47	634.3± 71.96	16.83± 1.53	35.0± 4.6	0.65± 0.13
6	28.50± 2.00	20.0± 2.13	264.167± 39.58	219.39± 3.31	1196.0*± 78.86	18.00± 1.71	40.67± 4.3	1.37*± 0.14

*Values in treatment groups are significantly different ($p<0.05$) when compared to control (0 day).

Table 2. Biochemical parameters (mean± SE) before and after single dose intramuscular administration of lincomycin in goats. (Mean ± SE; n=6)

Day	Biochemical Parameters				
	Totalprotein (IU)	Albumin (IU)	Cholesterol (IU)	Total bilirubin (IU)	Direct bilirubin (IU)
0	5.167±0.36	3.30±0.47	90.0±9.30	0.67 ±0.42	1.00±0.45
6	5.05 ±0.23	3.50±0. 30	84.33±5.42	1.00±0.45	0.67 ±0.42

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

Table 3. Haematological parameters (mean± SE) before and after single dose intramuscular administration of lincomycin in goats (Mean ± SE; n=6)

Day	Haematological Parameters						
	TLC ($x10^3/\mu l$)	TEC ($x10^6/\mu l$)	Hb (g/dl)	PCV (%)	MCV (fl)	MCH (pg/dl)	MCHC (g/l)
0	14.46± .59	8.96± 1.03	7.57±0.43	13.97±2.68	16.60±1.03	8.67± 0.99	42.97±4.97
6	13.02±1.12	8.37± .66	7.22± 0.36	11.47±2.04	19.20± 7.57	11.43±1.89	42.40±4.73

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

The safety study of lincomycin in large animal has not been reported but safety profile of some fluoroquinolones like ciprofloxacin, enrofloxacin and levofloxacin was investigated in different species of domestic animal by different research group (Bhavsar *et al.,* 2004; Khargharia *et al.,* 2007; Patel *et al.*, 2009). In this study, it has been demonstrated that lincomycin at the dose of 10.0 mg/kg of body weight in goats does not cause significant biochemical alteration in most of the biochemical parameters except for the significant elevation in lactate dehydrogenase and Creatinine levels. Lactate dehyrogenase is an intracellular enzyme, which is widely distributed throughout the body and is found at high levels in tissues that utilize glucose for energy. It is therefore a non-specific indicator of tissue injury and is not related to any specific organ. As a result, an increase in LDH can reflect damage to any of different tissues like skeletal or cardiac muscle, kidney and liver (More, 2006). Increase in creatinine levels indicates renal tubular necrosis and nephron damage (Brar *et al.,* 2000).

Fluoroquinolones like ciprofloxacin when given repeated in calves at intramuscular dose in calves did not cause any significant alteration in the values of biochemical parameters (Bhavsar *et al.,* 2004). The same conclusion was also obtained for enrofloxacin in yak (Khargharia *et al.,* 2007) and levofloxacin in layer birds (Patel *et al.,* 2009).

Safety of lincomycin single given at the rate of 10.0 $mg.kg^{-1}$ of body weight in goats consequently for five 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) and Total Leukocyte Count (TLC). 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.

On the basis of observation of various hematological and biochemical parameters, multiple intramuscular administration of lincomycin (10.0 mg/kg) will have moderate affect on hepatic as well as renal functioning. This suggests that intramuscular administration of lincomycin at least for 5 days is found safe in goats.

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