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Safety assessment of cefquinome following multiple intramuscular administration regarding haematology of cow calves

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Abstract

The present study was carried out to investigate haematological alterations induced after repeated intramuscular administration of cefquinome at the dose rate of 2 mg.kg^{-1} body weight in five healthy male cow calves. Blood samples were collected before administration of the drug which served as control (day 0). After administration of drugs, blood samples were collected at day 1st, 2nd, 3rd, 4th, 5th and 6th from jugular vein into Ethylene Diaminetetraacetic Acid Tripotassium Salt (K_3EDTA) coated vacutainers for haematological parameters (Hemoglobin, Packed cell volume, total leukocyte count and differential leukocyte count) analysis. The results of the study clearly demonstrated that repeated intramuscular administration of cefquinome in therapeutic doses produced non-significant difference ($p<0.05$) in values of haematological parameters in cow calves when compared with control values (0 day). Lack of clinical signs of adverse reactions and absence of significant difference in haematological parameters following intramuscular administration, may open a new avenue for insight into the strategy for clinical treatment of various bacterial diseases in cow calves.

Keywords: Cefquinome, Cow calves, Safety study, Cephalosporin, Antibiotic.

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Introduction

Cefquinome is the first animal dedicated, semi-synthetic, fourth generation cephalosporin antibiotic, having broad spectrum of activity. It is effective against a wide range of bacteria and is highly resistant to β-lactamase. The *in vitro* and *in vivo* efficacy of this drug is against a wide range of gram-negative and gram-positive bacterial pathogens and many anaerobic bacteria. It is resistant to the actions of β-lactamases which inactivate many other cephalosporins, including ceftizoxime and ceftazidime. Cefquinome is active against many strains of methicillin-resistant staphylococci (MRSA) and enterococci [5, 6, 10, 2, 12]. Cefquinome is relatively safer antibacterial having fewer adverse effects than other cephalosporins. Owing to its high efficacy, broad spectrum of activity, rapid tissue penetration, high safety and very low development of bacterial resistance, cefquinome is gaining popularity among the practitioners. However, the data on safety of multiple intramuscular administration of cefquinome in cow calves are scarce. The haematological 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 used 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 haematological alterations induced after multiple intramuscular administration of cefquinome in cow calves.

Material and Methods

Experimental animals

The present study was carried out on five healthy male cow calves of Gir breed (6-12 months of age and between

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70 to 120 kilograms of body weight) at Instructional Dairy Farm, College of Veterinary Science and Animal Husbandry, Mhow, Nanaji Deshmukh Veterinary Science University, Jabalpur (M.P.). The calves were housed in experimental calf pen, two weeks prior the experiment for acclimatization. The animals were fed concentrates, green fodder and roughage and had free access to water. All essential and standard managemental measures were adopted to keep the calves free from stress. The animals were observed for any clinical abnormalities during the period of experiment. The study was approved by the Institutional Animal Ethics Committee (IAEC), College of Veterinary Science and Animal Husbandry, Mhow.

Drugs and chemicals

Cefquinome was gifted by Wellcon Animal Health Pvt. Ltd., Agra,, India. Reagents kits for haematological analysis were purchased from Diatron MI Zrt., Budapest, Táblás u. 39, 1097 Hungary.

Experimental design

Five healthy male cow calves were employed to assess the safety of intramuscular administration of cefquinome (2 $mg.kg^{-1}$ b.wt., repeated at 24 hours interval) for 5 days. Blood samples were collected before administration of the drug which served as control (day 0). After administration of drugs, blood samples were collected at day 1st (24 h), 2nd (48 h), 3rd (72 h), 4th (96 h), 5th (120 h) and 6th (144 h) from jugular vein into Ethylene Diaminetetraacetic Acid Tripotassium Salt (K3EDTA) coated vacutainers for haematological analysis. Blood smears for determination of differential leukocyte count (DLC) were prepared from fresh blood at the time of blood collection. Blood samples collected in test tubes with K_3EDTA and blood smears prepared at predetermined time intervals during course of experiment were used to evaluate following haematological parameters viz. Haemoglobin (Hb), Packed cell volume (PCV), Total leukocyte count (TLC) and Differential leukocyte count (DLC: neutrophils, lymphocytes, basophils, eosinophils and monocytes). All these haematological parameters (Hb, PCV and TLC) were estimated by using semi-automatic haematology analyzer (Abacus 380, Diatron MI PLC, Hungary) except DLC which was estimated as per method described by Schalm [9].

Statistical analysis

The data generated from the safety profile study were compared by Least Square Difference test using SPSS software (version 12.0.1).

Results

Values of the haematological parameters (haemoglobin, packed cell volume, total leukocyte count and differential leukocyte count (neutrophils, lymphocytes, basophils, eosinophils and monocytes) before and after intramuscular administration of cefquinome (2 $mg.kg^{-1}$ b.wt., repeated at 24 h interval) for 5 days in cow calves are presented in Tables 1. No significant alterations ($p>0.05$) in haemoglobin level, packed cell volume, total leukocyte count, and differential leukocyte count have been observed in the study when compared with control values (0 day) following daily intramuscular administration of cefquinome for 5 days in cow calves. All animals were not exhibited any local or systemic adverse reactions after daily intramuscular administration of cefquinome.

Table 1. Effect of intramuscular administration of cefquinome (2 $mg.kg^{-1}$ body weight, repeated at 24 hours interval) for 5 days on haematological parameters in healthy cow calves

Parameters	Mean ± S.E.						
	0th Day	1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day
Haemoglobin ($g.dl^{-1}$))	10.89 ± 0.38	10.73 ± 0.55	11.08 ± 0.46	10.81 ± 0.40	10.84 ± 0.27	10.83 ± 0.34	10.84 ± 0.36
PCV (%)	32.06 ± 0.42	32.07 ± 0.60	33.02 ± 0.53	33.01 ± 0.69	32.08 ± 0.63	32.06 ± 0.22	32.05 ± 0.22
TLC ($\times 10^3.cmm^{-1}$)	9.22 ± 0.21	9.31 ± 0.19	9.24 ± 0.25	9.32 ± 0.20	9.31 ± 0.20	9.31 ± 0.21	9.30 ± 0.24
Neutrophil (%)	25.57 ± 0.74	25.79 ± 0.66	24.83 ± 0.05	24.82 ± 0.12	25.19 ± 0.41	24.90 ± 0.32	24.87 ± 0.54
Lymphocyte ($\times 10^3.cmm^{-1}$)	62.91 ± 0.97	63.23 ± 0.51	62.83 ± 0.83	63.13 ± 0.45	62.70 ± 0.54	63.90 ± 1.09	63.02 ± 0.45
Basophil (%)	0.75 ± 0.07	0.68 ± 0.06	0.69 ± 0.03	0.73 ± 0.05	0.73 ± 0.03	0.69 ± 0.03	0.71 ± 0.04
Eosinophil (%)	2.14 ± 0.26	2.47 ± 0.24	2.69 ± 0.32	2.32 ± 0.30	1.94 ± 0.15	1.94 ± 0.28	1.87 ± 0.11
Monocyte (%)	2.32 ± 0.23	2.28 ± 0.18	2.06 ± 0.08	2.19 ± 0.13	2.29 ± 0.24	2.22 ± 0.21	2.23 ± 0.19

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

Discussion

Antimicrobial therapy is usually employed to cure bacterial infection or to prevent the secondary bacterial infections. Prolonged therapy or high dosage regimen implemented during the treatment may exhibit the toxic effect, if any. Considering this fact, safety study of a drug is indeed necessary to notify any alteration in the physiological or biochemical parameters of the body fluid and tissue along with therapeutic effects. If alterations are very minor, the drug is relatively safe and if severe, then adverse effects of such drug will be observed. The effects of long term cefepime therapy on body systems were extensively evaluated in rats and dogs [3, 4]. In the present study, safety of multiple intramuscular doses of cefquinome (2 mg.kg^{-1} body weight) repeated at 24 hours interval in healthy cow calves was monitored by studying various haematological evaluations. The haematology included determination of haemoglobin (Hb), packed cell volume (PCV), total erythrocytes count (TEC), total leukocyte count (TLC) and differential leukocyte count (DLC: neutrophil, lymphocyte, basophil, eosinophil and monocyte). The results suggest that multiple intramuscular doses of cefquinome (2 mg.kg^{-1} body weight) repeated at 24 hours interval in healthy cow calves did not alter the haematological parameters. It indicates that repeated long term administration of cefquinome was well tolerated in in cow calves.

In agreement to the present findings, no significant alteration in all haematological parameters following single intramuscular administration of cefquinome (2 mg.kg^{-1} b.wt., repeated at 24 h interval) along with intramuscular administration of tolfenamic acid (2 mg.kg^{-1} body weight) in sheep has been reported [8]. Similarly, it has been reported that multiple intramuscular doses of cefquinome (20 mg.kg^{-1} b.wt. repeated at 12 h) along with meloxicam (0.2 mg.kg^{-1} b.wt. repeated at 24 h) for 7 days in goats did not alter the haematological parameters [11]. No significant changes in haematological parameters following repeated intramuscular cefepime administration (20 mg kg^{-1}) in sheep [7]. There was no significant changes in haematological parameters following repeated intramuscular administration of cefpirome in combination with intramuscular administration of ketoprofen in goats has been reported [1]. However, slight decrease in the average value of relative lymphocyte counts and a slight increase in the average value of relative segmented neutrophil counts following multiple administration of cefepime (20 mg kg^{-1}) has been reported in dogs [4].

On the basis of observations of various haematological parameters, it is concluded that multiple intramuscular administration of cefquinome did not adversely affect cow calves. This suggests that long term intramuscular administration of cefquinome is safe in cow calves. Thus it is advisable to use cefquinome at recommended dosage for treatment of infections not responding to conventional antibacterial drugs

Conflict of Interest: None Declared

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