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Original Article

Effect of Repeated Administration of Cefquinome on Biochemical and Hematological Parameters in Buffalo Calves

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ABSTRACT

Aim: Cefquinome, a fourth generation of cephalosporins have been developed for use in animals. Similar to other species, it may also have some adverse reactions in buffalo calves at therapeutic dosage. In the present study, effect of repeated administration of cefquinome on biochemical and hematological parameters was studied in buffalo calves. **Materials and Methods:** Animals were divided into two groups having three animals in each group. Group 1 was kept as control and animals of Group 2 were given cefquinome at dose rate of 2 $mg.kg^{-1}$ body weight by intramuscular route for continuously 7 days. Blood samples were collected daily and 3 days post treatment. **Results:** The values of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGTP), and alkaline phosphatase (ALKP) in control animals were in the range of 127.7–148.3 IU/L,49.0–55.6 IU/L, 14.0–17.3 IU/L, and 111.0–134.3 IU/L, respectively. The repeated administration of cefquinome did not influence the plasma activities of AST, ALT, GGTP, and ALKP in treated animals. The level of blood urea nitrogen (BUN) and creatinine before treatment was 14.3 ± 0.88 mg/dl and1.70 ± 0.04 mg/dl, which significantly increased on 3rd day (21.0 ± 1.53 mg/dl) and 2nd day (2.33 ± 0.07 mg/dl), respectively. Among hematological parameters, there was significant variation in levels of hemoglobin (Hb), total erythrocyte count (TEC), erythrocyte sedimentation rate (ESR), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) in treated animals. No abnormal clinical symptoms were observed in any animal. **Conclusion:** The results revealed that clinically, the therapy of cefquinome may be continued up to 7 days.

Key words: Biochemical effects, buffalo calves, cefquinome, hematological effects

INTRODUCTION

Many drugs may cause adverse or side-effects. The side-effects can be classified as pharmacological, biochemical, pathological, genotoxic, and allergic reactions. Biochemical side-effects are generally considered harbingers of pathological side-effects.[1] The cephalosporins of the third and fourth generation are used because of their relative cost in veterinary medicine. For this reason, there is a little knowledge about side-effects resulting from the veterinary use of these cephalosporins.[2] Cephalosporins are

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considered as safe group of drugs, but they may cause few side effects. The common side effects like hypersensitivity reactions and nephrotoxicity are less common with these drugs. Although eosinophilia and thrombocytosis are commonly reported, but these are considered as signs of healing of the infections treated, rather than its adverse reactions. Other reversible hematological reactions have been reported in some patients. Cefquinome, an aminothiazolyl cephalosporin and a member of the fourth generation of cephalosporins, developed especially for use in animals, has a very broad spectrum of activity against many bacteria. For judicious use of antibiotics, a rational dosage regimen is prerequisite, but it is not axiomatic to recommend the dose of an antibiotic without studying its adverse/side effects on the host at the recommended dosages schedule. So the present study was planned to know the adverse effects produced by cefquinome in buffalo calves at recommended dosage regimen.

MATERIALS AND METHODS

The experiment was performed in six healthy male buffalo calves of 6–12 months age and weighing between 100 and 120 kg. The animals were acclimatized in the animal shed of department under uniform conditions for 4 weeks before the start of experiment. During this period these animals were subjected to regular clinical examination. The animals were maintained on green fodder and wheat straw. Water was provided *ad libitum*. All animals were healthy at the time of experiment. They did not receive any drug treatment before the study. For monitoring adverse effects of cefquinome in buffalo calves, animals were divided into two groups having three animals in each group. Group 1 was kept as control and animals of Group 2 were given cefquinome at dose rate of 2 mg.kg^{-1} body weight[3] by intramuscular route for continuously 7 days. The animals were examined daily during the experimental period. Blood samples were collected daily and 3 days post treatment. Blood biochemical parameters viz. aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGTP), alkaline phosphatase (ALKP), blood urea nitrogen (BUN), and creatinine; and hematological parameters viz. packed cell volume (PCV), hemoglobin (Hb), total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), erythrocyte sedimentation rate (ESR), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), bleeding time, and clotting time were estimated by standard techniques. Student's *t*-test was used to test the significance of differences.

RESULTS

No abnormal clinical symptoms were observed in any animal. The results of biochemical and hematological parameters are shown in Tables 1-4. In this investigation, the values of BUN was significantly ($P < 0.05$) increased to 21.0 ± 1.53 mg/dl when compared to the corresponding value (14.3 ± 1.76 mg/dl) of healthy animals on 3rd day. Similarly, the values of creatinine were significantly ($P < 0.05$) increased to 2.33 ± 0.07 mg/dl on 2nd day when compared with the corresponding values (1.78 ± 0.12 mg/dl) of healthy ones.

The values of TEC were decreased significantly ($P < 0.01$) from 6.82 ± 0.51 to 4.45 ± 0.29 million/mm^3 on 6th day when compared with the corresponding values of healthy animals. Similarly, the value of Hb was decreased significantly ($P < 0.05$) from 14.1 ± 0.21 to 12.5 ± 0.64 g% on 3rd day when compared with the values of healthy animals. Also, the values of packed cell volume (PCV) were significantly ($P < 0.05$) decreased from 39.3 ± 0.67 to

Table 1: Effect of cefquinome (2 mg.kg^{-1}) administered continuously for 7 days on biochemical parameters in healthy and treated buffalo calves

Days	AST (IU/L)		ALT (IU/L)		GGTP (IU/L)		ALKP (IU/L)		BUN (mg/dl)		Creatinine (mg/dl)	
	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment
0	128.3±3.53	131.7±9.77	49.3±3.71	49.3±0.88	17.3±2.33	14.7±1.76	129.7±4.67	131.0±3.51	11.7±0.67	14.3±0.88	1.61±0.12	1.70±0.04
1	127.7±8.19	132.0±17.3	55.6±6.36	54.3±2.33	14.3±2.03	12.0±2.52	130.3±9.96	137.3±8.29	14.3±4.33	15.0±2.65	1.82±0.18	1.92±0.20
2	134.0±9.54	133.7±7.13	55.3±5.21	56.7±14.52	15.3±0.88	15.7±2.33	134.3±7.88	129.7±13.8	13.0±2.08	19.0±4.51	1.78±0.12	2.33±0.07**
3	144.3±5.36	146.7±3.84	55.3±6.12	61.7±1.67	15.7±0.88	15.0±1.00	128.0±4.36	134.0±22.7	14.3±1.76	21.0±1.53*	1.65±0.09	2.03±0.25
4	144.7±2.33	151.3±7.54	49.0±4.58	49.3±4.67	16.7±1.76	17.3±3.76	123.7±8.65	128.0±9.50	14.7±1.20	21.7±0.67**	1.90±0.16	1.95±0.18
5	148.3±2.73	160.7±4.70	49.6±6.94	54.0±2.65	14.0±2.08	14.3±2.67	113.7±8.19	120.3±2.91	12.7±1.76	20.7±4.63	1.80±0.10	2.08±0.15
6	139.7±5.49	147.7±3.18	50.3±4.63	54.3±2.33	15.0±1.53	16.7±1.33	114.7±8.19	115.7±5.78	13.0±1.00	21.0±2.08*	1.95±0.14	2.04±0.24
7	140.3±98	144.0±4.16	50.0±3.79	52.3±3.71	14.0±1.15	15.7±2.96	111.3±6.12	110.7±6.64	13.3±1.08	14.7±0.88	1.87±0.12	2.05±0.16
8	140.7±13.7	146.0±5.03	49.0±1.53	51.0±4.16	14.7±0.33	17.0±1.73	111.0±5.51	118.7±8.74	14.7±1.47	14.0±1.53	1.89±0.10	1.94±0.15
9	136.0±12.8	143.0±3.51	50.6±2.60	51.3±3.53	14.0±1.00	17.3±2.33	112.0±8.54	119.0±8.08	15.0±0.58	15.7±1.45	1.90±0.14	2.01±0.17

The values given are mean±SE of results obtained from three animals. AST = Aspartate aminotransferase, ALT = Alanine aminotransferase, GGTP = Gamma-glutamyl transpeptidase, BUN = Blood urea nitrogen, ALKP = Alkaline phosphatase, SE = Standard error. *Significantly (P<0.05) different as compared to the corresponding values of healthy animals,**significantly (P<0.01) different as compared to the corresponding values of healthy animals

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Table 2: Effect of cefquinome (2 mg.kg^{-1}) administered continuously for 7 days on BT, CT, TEC, and TLC in healthy and treated buffalo calves

Days	BT (min)		CT (min)		TEC (10^6/mm^3)		TLC (10^3/mm^3)	
	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment
0	5.40±0.72	4.17±0.60	5.62±0.69	4.33±0.58	6.38±0.60	5.97±0.13	11.8±0.85	10.2±0.16
1	3.63±0.33	4.26±0.14	3.83±0.33	4.55±0.28	5.08±0.30	5.95±0.18	10.5±0.29	11.3±0.39
2	4.50±0.45	4.77±0.90	4.62±0.44	5.00±0.95	6.57±0.80	5.53±0.94	10.0±0.13	11.2±0.64
3	4.50±0.32	4.69±0.78	4.70±0.31	5.00±0.81	5.15±0.41	4.36±0.55	10.4±0.35	11.4±0.93
4	4.33±0.07	4.33±0.44	4.69±0.21	4.83±0.34	5.02±0.18	4.26±0.84	10.6±0.21	10.3±0.39
5	3.86±0.43	4.52±0.32	4.22±0.55	4.88±0.34	4.96±0.29	5.50±0.53	10.8±0.68	11.2±0.77
6	4.66±0.54	4.33±0.12	4.99±0.40	4.66±0.27	6.82±0.51	4.45±0.29**	10.5±0.37	10.8±0.59
7	4.72±0.58	4.38±0.10	4.85±0.63	4.71±0.25	5.20±0.21	5.94±0.77	10.5±0.31	10.9±0.59
8	4.72±0.36	4.67±0.22	4.88±0.32	5.21±0.05	5.39±0.24	4.27±0.21*	10.8±0.92	11.0±0.38
9	4.33±0.15	4.64±0.25	4.77±0.30	4.92±0.20	4.28±0.25	4.23±0.23	10.6±0.70	10.2±0.29

The values given are mean±SE of results obtained from three animals. BT = Bleeding time, CT = Clotting time, TEC = Total erythrocyte count, TLC = Total leukocyte count, SE = Standard error. *Significantly (P<0.05) different as compared to the corresponding values of healthy animals,**significantly (P<0.01) different as compared to the corresponding values of healthy animals

Table 3: Effect of cefquinome (2 mg.kg^{-1}) administered continuously for 7 days on DLC in healthy and treated buffalo calves

Days	Neutrophils (%)		Lymphocytes (%)		Monocytes (%)		Eosinophils (%)		Basophils (%)	
	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment
0	52.3±3.84	40.0±4.62	41.3±0.67	57.3±2.67**	2.50±0.5	0.00	5.00±2.0	6.00	2.00±1.0	2.00
1	40.7±6.36	37.3±2.67	56.7±6.77	61.3±1.33	2.00	2.00	2.00	2.00	2.00	0.00
2	38.7±4.81	37.3±3.71	59.3±3.71	59.3±3.33	4.00	1.00	2.00	3.00±0.58	0.00	0.00
3	28.7±3.71	30.7±3.33	67.3±4.06	64.0±5.03	2.00	3.00±1.53	3.00	6.00±2.00	2.00±1.0	2.00
4	36.7±3.33	30.7±5.81	60.7±5.21	68.0±6.43	2.00	2.00	4.00	2.00	2.00	0.00
5	45.3±3.53	37.3±9.40	50.0±2.31	61.3±9.68	3.00±1.0	0.00	3.50±1.5	0.00	1.50±0.5	2.00
6	45.0±0.58	27.3±8.88	54.0±1.53	71.7±8.88	0.00	1.00	3.00	0.00	3.00	1.00
7	48.7±1.33	36.0±6.51	50.7±1.67	63.3±6.84	1.00	0.00	0.00	0.00	0.00	1.00
8	42.7±2.91	29.7±2.60*	56.0±2.00	68.7±2.33**	2.00	1.50±0.5	1.00	0.00	1.00	2.00
9	42.0±3.06	32.3±7.22	55.7±3.38	65.0±5.77	2.00	2.00	1.00	2.00±1.00	2.00	0.00

The values given are mean±SE of results obtained from three animals. DLC = Differential leukocyte count, SE = Standard error. *Significantly (P<0.05) different as compared to the corresponding values of healthy animals, **Significantly (P<0.01) different as compared to the corresponding values of healthy animals

Table 4: Effect of cefquinome (2 mg.kg^{-1}) administered continuously for 7 days on Hb, PCV, ESR, MCV, MCH, and MCHC in healthy and treated buffalo calves

Days	Hb (g%)		PCV (%)		ESR (mm/60 min)		MCV (fl)		MCH (pg/dl)		MCHC (g/dl)	
	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control	Treatment
0	10.0±0.61	10.0±0.40	41.7±1.45	37.7±0.88	95.3±4.41	108.3±4.41	66.2±4.84	63.2±2.81	15.8±0.54	16.8±1.03	24.1±1.02	26.6±0.92
1	10.8±0.16	10.8±0.50	39.3±0.67	36.7±0.67*	98.7±4.48	116.7±13.3	77.9±3.45	61.7±1.32**	21.5±1.00	18.1±0.82	27.6±0.06	29.4±1.64
2	12.8±0.55	13.2±0.93	41.3±1.67	36.7±1.67	95.0±4.04	104.0±7.81	64.3±5.60	70.9±14.4	19.9±1.55	25.8±5.80	31.0±0.36	36.0±1.66
3	14.1±0.21	12.5±0.64*	42.7±1.33	38.0±1.53	93.3±6.89	109.0±13.6	83.6±4.98	89.4±8.62	27.8±2.21	29.7±4.63	33.3±1.51	33.0±2.25*
4	12.5±1.08	13.3±0.68	41.7±2.19	36.7±0.88	84.0±13.3	110.0±4.16	82.9±2.18	94.3±20.7	25.0±2.21	34.8±9.50	30.4±3.55	36.3±2.53
5	13.3±0.23	12.2±0.48	38.3±1.20	33.3±1.67	84.3±3.48	110.3±9.84	77.6±3.47	61.2±3.14*	26.9±1.26	22.4±1.39	34.7±0.50	36.5±0.40*
6	13.5±0.62	11.8±0.44	38.3±1.67	34.0±1.53	85.3±2.73	119.0±13.01*	56.5±1.94	76.8±4.89**	19.9±0.86	26.7±2.34*	35.3±0.86	34.7±1.18
7	13.5±0.61	11.8±0.38	36.0±0.58	35.7±0.88	74.3±11.0	120.0±5.29**	69.5±3.21	61.8±6.79	26.2±2.26	20.4±1.78	37.6±1.51	33.2±1.01
8	12.4±0.27	12.5±0.56	37.3±1.86	36.3±0.88	74.3±14.5	81.7±18.4	69.3±2.68	85.5±5.23*	23.1±0.59	29.5±±2.53*	33.4±1.10	34.3±0.85
9	12.7±0.64	13.8±0.70	38.3±1.20	38.0±1.00	68.7±2.96	78.3±14.1	89.8±2.53	90.5±6.75	29.7±1.92	33.0±3.32	33.0±1.69	36.3±0.96

The values given are mean±SE of results obtained from three animals. *Significantly (P<0.05) different as compared to the corresponding values of healthy animals. **Significantly (P<0.01) different as compared to the corresponding values of healthy animals. Hb = Hemoglobin, PCV = Packed cell volume, ESR = Erythrocyte sedimentation rate, MCV = Mean corpuscular volume, MCH = Mean corpuscular hemoglobin, MCHC = Mean corpuscular hemoglobin concentration, SE = Standard error

36.7 ± 0.67% on day 1 when compared with the values of control animals. Neutrophils were significantly ($P < 0.05$) decreased from 42.7 ± 2.91 to 29.7 ± 2.60% on day 8 when compared with healthy animals. The values of lymphocytes were increased significantly ($P < 0.01$) from 56.0 ± 2.0 to 68.7 ± 2.33% on 8th day.

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Similarly the values of ESR were increased significantly ($P < 0.01$) from 74.3 ± 11.0 to 120 ± 5.29 mm/h on 7th day when compared with the values of healthy ones. There was a significant ($P < 0.05$) increase in the values of MCV, MCH, and MCHC from 69.3 ± 2.68 fl, 23.1 ± 0.59 pg/dl, and 34.7 ± 0.50 g/dl to 85.5 ± 5.23 fl, 29.5 ± 2.53 pg/dl, and 36.5 ± 0.40g/dl on day 8, 8, and 5, respectively, when compared with the corresponding values of healthy animals. There was no alteration in rest of the parameters.

DISCUSSION

Both BUN and creatinine are indicators of renal tubular necrosis. High BUN and serum creatinine and low serum Na^+, K^+, Mg^{2+}, Ca^{2+}, and PO_4^{3-} occur due to proximal tubular damage.[4] Bone marrow and peripheral blood cells may be adversely affected by drugs. Neutropenia, thrombocytopenia, hemolytic anemia, aplastic anemia, and macrocytic anemia are the commonest effects, in that order. Adverse effects may be produced by a direct toxic action of the drug or its metabolites on the bone marrow or, less often, on circulating cells.[5] It has been reported that the other cephalosporins (cefprozil, cefminox, and ceftriaxone) cause an increase in serum ALT and ALKP levels in humans.[6,7] Cefquinome causes increase in ALT, ALKP, MCHC, HCO_3A, and tCO_2 levels in dogs.[2]

Significant reduction of Hb content during investigation could be due to decrease synthesis of red blood cells in bone marrow[8] or reduced biosynthesis of heme in bone marrow[9] or as a result of increased rate of destruction. Increased activity of bone marrow or hemolysis could lead to impaired HB synthesis, which resulted in hypochromic anemia.[10] PCV is the most accurate, simple, and inexpensive method for the detection of degree of anemia. The decrease in PCV could be attributed to the decrease in TEC. One of the most important factors to be considered in reduction of TEC is the production of the hormone erythropoietin.[11] Since there is decrease in PCV and TEC, erythrocytes move down without hindrance quickly as compared to normal healthy group erythrocyte.

On the basis of information gathered from the present study, it is concluded that repeated administration of cefquinome did not influence the plasma activities of AST, ALT, GGTP, and ALKP; however, there was significant increase in levels of BUN, creatinine, TEC, ESR, and MCV. The results revealed that clinically, the therapy of cefquinome may be continued upto 7 days. It can be concluded that cefquinome, the first fourth generation cephalosporin, have some adverse effects on biochemical and hematological variables at a dose of 2 $mg.kg^{-1}$ in buffalo calves. Further to elucidate the margin of safety in buffalo calves, further studies are required with more number of animals.

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Conflicts of interest

There are no conflicts of interest.

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