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B Roopali
Department of Veterinary Medicine College of Veterinary Sciences & AH, Durg, Chhattisgarh, India

M Roy
Department of Biochemistry College of Veterinary Sciences & AH, Durg, Chhattisgarh, India

S Roy
Department of Veterinary Medicine College of Veterinary Sciences & AH, Durg, Chhattisgarh, India

Correspondence
B Roopali
Department of Veterinary Medicine College of Veterinary Sciences & AH, Durg, Chhattisgarh, India

Haemato-biochemical changes and therapeutic management of urinary tract infection in canines

B Roopali, M Roy and S Roy

Abstract
The present study was carried out to investigate the haemato-biochemical changes, urine analysis and treatment of urinary tract infection in canines. Seven female and three male dogs between 8-10 years old were presented to TVCC, Veterinary College, Durg and Private Clinic, Bhillai (Chhattisgarh) with a history of inappropriate urination like dysuria, stranguria, haematuria, or pollakiuria were included in the study. Blood samples were collected from the study group animals for the estimation of various haemao-biochemical parameters. Haemoglobin, PCV, TEC and lymphocytes were significantly reduced in affected dogs when compared to the healthy control group indicative of severe anaemia. TLC and neutrophil count were significantly increased in the affected animals compared to the control group suggestive of bacterial infection. There was significant elevation of BUN and creatinine along with significant decrease in the total protein, albumin and globulin in the affected dogs as compared to the healthy control group. For urinalysis, urine samples were collected by cystocentesis. Microscopic examination of urine sediment revealed pus cells suggestive of pyuria. Urine culture revealed the major presence of *E. coli* organism followed by *P. aerugenosa.* Hence, the affected dogs were diagnosed for urinary tract infection of bacterial origin and treated accordingly. The dogs were administered with tab prulifloxacin @ 600 mg orally once a day for 5 days along with other supportive treatment. Haemato-biochemical parameters were estimated on 6th day post treatment and were within normal physiological limits. Urine culture was found negative to microorganisms and microscopic examination of urine sediment was negative to pus cells on 6th day of treatment suggestive of absence of urinary tract infection.

Keywords: Prulifloxacin, urinary tract infection, *E. coli*, dogs

Introduction
Urinary tract infection refers to the microbial colonization of the urine or of any urinary tract organ (Greene, 2012) [4]. Urinary tract infection (UTI) of bacterial origin is the most common infectious disease of dogs, affecting 14% of all dogs during their lifetime. Most UTIs are the result of ascending bacteria from rectal or fecal contamination or from the distal urogenital tract. The infection is more prevalent in older dogs with a median age of 9 years (Passmore *et al.,* 2007) [16]. The causative pathogens in dogs suffering from UTIs of bacterial origin are diverse. Large, retrospective studies have documented the most common species of uropathogens in dogs and cats, with *Escherichia coli* being the single most common pathogen in both acute and recurrent UTIs (Sefton, 2000 and Oluoch *et al.,* 2001) [19, 15]. The other pathogens include *Staphylococcus, Proteus, Pseudomonas, Streptococcus* and *Klebsiella* spp. Unlike human patients, veterinary patients are often asymptomatic, and the UTI may be an incidental finding. Patients with signs of lower urinary tract disease or otherwise suspected of UTI should have a complete urinalysis performed on a fresh urine specimen, with emphasis on a detailed microscopic urine sediment examination. Culture of the bladder urine collected by cystocentesis is the definitive method by which UTIs are confirmed (Greene, 2012) [4]. This is especially important for patients with complicated UTIs. Antimicrobials are the cornerstone of UTI therapy and animals with recurring UTIs are managed empirically with repeated antibiotic courses. Fluroquinolones are often used to treat UTIs as first line of treatment because of there bactericidal activity with high urine concentration and penetrate urinary tract tissues (Oluoch *et al.,* 2001) [15]. The present paper reports the haemato-biochemical changes and successful therapeutic management of urinary tract infection of bacterial origin in dogs with prulifloxacin. To our best knowledge, this is the first report of successful treatment of urinary tract infection of bacterial origin with prulifloxacin in canines.

Materials and Methods

A total of seven female and three male dogs between 8-10 years age group presented to TVCC, Veterinary College, Durg and Private Clinic, Bhillai (Chhattisgarh) with a history of inappropriate urination like dysuria, stranguria, haematuria, or pollakiuria were included to access the therapeutic efficacy of prulifloxacin against urinary tract infections. The clinical diagnosis of the affected animals were made based on the characterstic clinical signs exhibited by the animals viz., dysuria, stranguria, haematuria, or pollakiuria and bladder urine analysis (microscopic and culture).

Haematolo-biochemical study

A total of of 5ml blood was collected on 0^{th} and 6^{th} day of treatment under aseptic conditions. 0.5 ml blood with disodium salts of EDTA as anticoagulant were used for estimation of haematological parameters and remaining 4.5 ml blood was processed for the exatraction of serum.

Haematological parameters (haemoglobin, packed cell volume, total erythrocyte count, total leucocyte count, differential leucocyte count and platelet count) were estimated with the help of fully automated haematology cell counter-Automatic Blood Cell Counter, Model PCE 210, Manufactured by ERMA Inc., Tokyo, Japan.

Serum samples were utilized for the estimation of biochemical parameters like blood urea nitrogen, creatinine, total protein, albumin, and globulin by ARTOS® semi automatic biochemical analyser using kits.

Urological Study

Urine samples from the affected animals were collected by cystocentesis and processed immediately. Urine specimen (10 ml) was centrifuged at room temperature for 20 minutes at 3,000 rpm. A drop of urine sediment was used for microscopic examination at low power (10X) and remaining urine sediment was inoculated into Blood agar and MacConkey agar plates using a sterile loop for bacterial isolation (Ling *et al.*, 2001) [11]. Single bacterial colonies were picked for identification of organisms by standard bacteriologic and biochemical procedures as mentioned by Carter (1990) [2].

Statistical Analysis

The haemato-biochemical values obtained in the affected group and control group were subjected to statistical analysis by one way ANOVA using Statistical Package For Social Sciences (SPSS) Version 20. Significance was set at 5 per cent ($p \leq 0.05$).

Results and Discussion

The haemato-biochemical parameters were evaluated in urinary tract infected dogs. A comparative analysis of haematological parameters are tabulated in Table (1). The haemogram (Haemoglobin, total erythrocyte count and PCV) in affected animals were significantly reduced ($p \leq 0.05$) when compared with healthy control group indicative of anaemia. The results of the present study were in close confirmation with Mrudula *et al.* (2005) [13] and Kralova *et al.* (2010) [9] that could be associated with the reduced renal erythropoisis, increased fragility of RBC or reduced RBC survival. There was a significantly elevation ($p \leq 0.05$) of total leucocyte count and neutrophils when compared to healthy control group along with significatant decrease ($p \leq 0.05$) in lymphocyte count. Similar findings were reported by Mrudula *et al.* (2005) [13] and Kralova *et al.* (2010) [9]. Leucocytosis, neutrophilia and lymphopenia might occur due to variable extent of stress induced by bacterial organisms in the urinary tract as well as a sign of manifestation of body defense mechanism against bacterial infection (Senior *et al.*, 1986) [17]. The mean values of eosinophils, basophils, monocytes and platelets showed insignificant change when compared to healthy control group and were within the normal physiological limits. All the haematological parameters were within normal physiological limits on 6^{th} day (post treatment).

The comparative analysis of biochemical parameters are tabulated in Table (2). The mean values of serum BUN and creatinine were significantly elevated ($p \leq 0.05$) in affected dogs compared to the healthy control group suggestive of uraemia, similar findings were reported by Jeong (2006) [7]. Creatinine is a resultant of muscle metabolism and its elevated level in blood indicated kidney disease. There was significant decrease in the serum total protein, albumin and globulin levels in the affected animals compared to the control group. Hypoprotenemia reported in the present study could be due to loss of protein in urine. Devaux (1996) [3] reported that patients with urinary tract infection had markedly reduced serum albumin levels due to increased urinary albumin levels. All the biochemical parameters were within normal physiological limits on 6^{th} day (post treatment).

In urinalysis, microscopic examination of urine sedimentent showed presence of pus cells indicative of pyuria. Neutrophils that migrate from blood vessels through tissue and cross the epithelial cell layer to enter the urinary space result in pyuruia (Greene, 2012) [4]. Altogether, 2 bacterial species were identified out of 10 suspected urine specimens sent for bacterial isolation and identification. Overall, *E. coli* was isolated from 8 (80.00%) samples and *P. aeruginosa* from 2 (20.00%) samples. Ling *et al.* (1979) [10]; Oluoch *et al.* (2001) [15] and Seguin *et al.* (2003) [18] reported that most urinary tract infection involve *E. coli* as the major causitive agent. Present study found the presence of two species in the urine samples of affected dogs (10) whereas Ling *et al.* (2001) [11] observed single bacterial species in more that 70% of the UTI cases in dogs.

The affected dogs were given tab prulifloxacin @ 600 daily once a day orally for 5 days, inj pantoprazole @ 40 mg IV for 5 days, inf D 5% 500ml IV for 5 days, inj lasix 1mg/kg BW IV for 5 days and inj Ondansetron 1mg/kg BW IV for 5 days. There are sufficient treatment options available for UTIs. However, Walker (1999) [20] and Hooper (2000) [6] found fluroquinolones to be effective in urinary tract infections. Fluroquinolones are often used to treat UTIs because they are bactericidal with high urine concentrations, effective against most *E. coli* organisms and penetrate the urinary tract tissues (Oluoch *et al.*, 2001) [15]. Among the fluroquinolones, Prulifloxacin is an oral fluoroquinolone specifically a lipophilic prodrug of ulifloxacin which has got broad spectrum antimicrobial activity against both gram positive and gram negative bacteria (Keam and Perry, 2004) [8]. It has been approved for the treatment of both complicated and uncomplicated lower urinary tract infections (Manjula *et al.*, 2014) [12]. Boothe *et al.* 2006 [1] found that enrofloxacin, ciprofloxacin and marbofloxacin given for 7-14 days to be the most effective quinolones against urinary tract infections caused by *E. coli* whereas, prulifloxacin used in the present study being an oral fluroquinolone administered once a day for 5 days was able to eliminate the urinary tract infection in canines. Hence, prulifloxacin was found to be efficacious in

eliminating urinary tract infection mainly caused by Gram negative organisms (*E. coli* and *P. aeruginosa*). Similar findings were reported by Noviello *et al.* (2006) [14] and Gulco *et al.* (2007) [5] in humans. Manjula *et al.* (2014) [12] reported that the prolonged and high urinary concentration following a single oral dose strongly supports use of prulifloxacin for the treatment of urinary tract infections and the broad spectrum antimicrobial activity of prulifloxacin allows its use in the empiric therapy of UTIs.

Table 1: Haematological changes in affected (0^{th} and 6^{th} day) and healthy control dogs

S. No	Parameter	Healthy dogs (n=10)	Affected dogs (n=10) 0^{th} day	Affected dogs (n=10) 6^{th} day
1.	Haemoglobin	$12.18^{a} \pm 0.04$	$9.52^{b} \pm 1.12$	$11.55^{a} \pm 1.22$
2.	Total erythrocyte count (x 10^6/µL)	$6.17^{a} \pm 0.05$	$4.12^{b} \pm 1.15$	$5.82^{a} \pm 0.11$
3.	Packed Cell Volume (%)	$42.49^{a} \pm 0.03$	$32.22^{b} \pm 1.36$	$40.89^{a} \pm 1.02$
4.	Total Leucocyte Count (x 10^3/µL)	$10.58^{a} \pm 0.17$	$17.76^{b} \pm 1.30$	$10.88^{a} \pm 0.11$
5.	Neutrophils (%)	$72.80^{a} \pm 0.18$	$79.55^{b} \pm 1.00$	$72.77^{a} \pm 0.06$
6.	Eosinophils (%)	2.01 ± 0.12	1.92 ± 0.02	$1.97^{a} \pm 0.01$
7.	Basophils (%)	0.48 ± 0.34	0.42 ± 0.05	0.45 ± 0.04
8.	Lymphocytes (%)	$21.12^{a} \pm 0.24$	$17.24^{b} \pm 1.52$	$20.87^{a} \pm 1.13$
9.	Monocytes (%)	2.16 ± 0.10	2.26 ± 0.10	2.22 ± 0.10
10.	Platelets (x 10^3/µL)	235.88 ± 18.74	215.00 ± 10.22	255.75 ± 15.26

Means bearing different superscripts differ significantly ($p \leq 0.05$)

Table 2: Biochemical changes in affected (0^{th} and 6^{th} day) and healthy control dogs

S. No	Parameter	Healthy dogs (n=10)	Affected dogs (n=10) 0^{th} day	Affected dogs (n=10) 6^{th} day
1.	BUN	$22.11^{a} \pm 0.11$	$54.18^{b} \pm 2.02$	$25.12^{a} \pm 0.28$
2.	Creatinine	$1.02^{a} \pm 0.12$	$4.12^{b} \pm 2.56$	$1.31^{a} \pm 0.02$
3.	Total protein	$6.52^{a} \pm 0.18$	$4.11^{b} \pm 1.84$	$6.82^{a} \pm 0.52$
4.	Albumin	$3.22^{a} \pm 0.22$	$1.53^{b} \pm 1.28$	$3.35^{a} \pm 0.51$
5.	Globulin	$3.3^{a} \pm 0.01$	$2.58^{b} \pm 0.2$	$3.47^{a} \pm 0.03$

Means bearing different superscripts differ significantly ($p \leq 0.05$)

Conclusion

The activity of prulifloxacin against urinary pathogens and its high and prolonged urinary concentration following a daily single oral dose for 5 days, suggest that prulifloxacin is an effective drug when compared to other fluoroquinolones for the treatment of urinary tract infections. To our best knowledge, this is the first report of successful treatment of urinary tract infection of bacterial origin with prulifloxacin in canines.

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