



Original Research

Comparison of Therapeutic Efficacy of Ceftriaxone-Tazobactam with Amoxicillin- Clavulanic Acid in Dogs Suffering From Urinary Tract Infection

Manisha Punia*, Dinesh Gulia, Ashok Kumar and Gaurav Charaya

Department of Veterinary Medicine, College of Veterinary Sciences, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar-125004, Haryana, INDIA

*Corresponding author: manishapunia8@gmail.com

Rec. Date:	May 01, 2018 03:21
Accept Date:	Jun 14, 2018 17:30
DOI	10.5455/ijlr.20180501032116

Abstract

The present study was conducted to evaluate the therapeutic efficacy of ceftriaxone-tazobactam and amoxicillin-clavulanic acid in dogs suffering from urinary tract infection. Out of 22 dogs diagnosed with urinary tract infection, 12 dogs were administered antibiotics based on antibiotic sensitivity pattern. Two groups were made each having six dogs. In group A, ceftriaxone-tazobactam was administered @20 mg per kg BW once daily by IM route for 5 days and in group B amoxicillin-clavulanic acid was administered @20 mg per kg BW twice daily by oral route for 7 days. Therapeutic efficacy was determined on the basis of remission of clinical signs and effect on haemato-biochemical parameters. Sampling for evaluation of haemato-biochemical alteration was done on day 0 and 3 of the treatment. Results of therapy revealed group A therapy to be more effective as compared to group B therapy on the basis of remission of clinical signs. Blood urea and creatinine values decreased significantly in group A whereas non-significant alteration was seen in group B dogs. However, normalization of phosphorous values was significant in both the groups.

Key words: Amoxicillin-Clavulanic Acid, Ceftriaxone-Tazobactam, Haemato-Biochemical Alterations, Therapeutic Efficacy

How to cite: Punia, M., Gulia, D., Kumar, A., & Charaya, G. (2018). Comparison of Therapeutic Efficacy of Ceftriaxone-Tazobactam with Amoxicillin- Clavulanic Acid in Dogs Suffering from Urinary Tract Infection. International Journal Of Livestock Research, 8(11), 88-93. doi: 10.5455/ijlr.20180501032116

Introduction

Urinary tract infection (UTI) refers to the microbial colonization of the urinary tract or any urinary tract organ, except the distal urethra, which has a normal bacterial flora. UTI is thought to be the most common infectious disease in dogs and is believed to be a major reason for antibiotic prescription in small animal practice. The origin of UTI can be bacterial, fungal, algal, protozoal and very rarely viral. Bacterial urinary tract infections are most common and are responsible for affecting 14% of all dogs during their lifetime and infections with a single bacterial species are more prevalent than mixed infections (Ettinger and Feldman,





2010; Westdropp *et al.*, 2012). Most common bacteria causing infection are *Escherichia coli*, *Proteus* spp., *Pseudomonas* spp., *Staphylococcus* spp. and *Streptococcus* spp. The patient with UTI may show a number of clinical signs like pollakiuria, dysuria, stranguria, urinary incontinence, haematuria, frequent licking of the vulvar or preputial area, dribbling of urine and various systemic signs like fever, depression, anorexia, renal pain and vomiting.

For treatment, a range of antimicrobial agents have been used to control UTIs such as penicillins, cephalosporins, tetracyclines, chloramphenicol, aminoglycosides and fluoroquinolones. Despite UTI being a common condition, the management of UTIs in dogs has become more complicated as the prevalence of antibiotic resistant strains of various pathogens has increased (Jessen *et al.*, 2015). Inadvertent antimicrobial use whether, therapeutic or otherwise exposes bacterial pathogens to varying concentration of antimicrobial drugs leading to emergence of resistance and abundance of the resistant bacteria. Hence, prudent use of antimicrobials is an important step in reducing the emergence of antimicrobial resistance and microbiological culture combined with susceptibility testing is the cornerstone of UTI diagnosis and serves as the best instrument for guiding treatment decisions in individual dogs.

Extended Spectrum Beta Lactamases (ESBLs) which are capable of conferring resistance to these agents, has compromised the effectiveness of the third generation cephalosporins in clinical practice. However, combinations of β -lactamase inhibitors have proved useful in treating infections caused by ESBL producing bacteria (Maddux, 1991). Therefore, the present study was conducted to compare the therapeutic efficacy of ceftriaxone-tazobactam with amoxicillin- clavulanic acid in dogs suffering from urinary tract infection.

Materials and Methods

Study Area, Design and Animals

Out of 22 dogs diagnosed to be affected with UTI at VCC, LUVAS, Hisar, 12 dogs on the basis of antibiotic sensitivity pattern done were selected for the present investigation. The selected dogs of Group A (n=6) were administered ceftriaxone-tazobactam @20 mg per kg BW once daily by IM route for 5 days while the dogs of Group B (n= 6) were administered amoxicillin- clavulanic acid @20 mg per kg BW twice daily by oral route for 7 days. The dosage for ceftriaxone – tazobactam combination and amoxicillin –clavulanic acid combination was given as per Thirunavvukarasu *et al.*, 2010 and Weese *et al.*, 2011, respectively.

Therapeutic Efficacy

Therapeutic efficacy was determined on the basis of remission of clinical signs and near normalization of the haemato-biochemical values. Blood samples were collected on day 0 and day 3rd of the treatment and analyzed for haemato-biochemical alteration for determining the effect of therapy.



Hematological Parameters

The blood samples collected in vials coated with potassium EDTA were immediately analyzed for complete hematological examination using fully automated haematology cell counter (MS4s, Melet Schloesing Laboratoires, France). The erythrocytic indices measured were haemoglobin (Hb) in g/dl, total erythrocyte count (TEC) in million/mm³ and hematocrit (Hct) in %. The leucocytic indices measured were total leucocyte count (TLC) in 10³/mm³, differential leukocyte count (DLC), lymphocytes (L) in %, monocytes (M) in %, neutrophils (N) in %, eosinophils (E) in % and basophils (B) in %. The thrombocytic indices measured were thrombocyte count (THR) in 10³/μl.

Serum Biochemistry

Serum analysis was done for calculating blood urea, creatinine, phosphorous, total protein, albumin, globulin, sodium, potassium, chloride glucose, AST, ALT and calcium. Fully automated Random Access Clinical Chemistry Analyzer (EM 200TM Erba Mannheim–Germany) was employed for estimation of biochemical parameters using kits procured from Transasia Biomedical Limited.

Statistical Analysis

Results obtained for different parameters were analysed statistically by two way anova with repeated measure using SPSS 20 software.

Results and Discussion

Amoxicillin-clavulanic acid was chosen because this antibiotic is approved for treatment of UTI in dogs, has a spectrum of activity against common uropathogens, reaches high concentrations in the urine, and is commonly prescribed by primary care veterinarians (Westdropp *et al.*, 2012). Moreover, Amoxicillin-clavulanic acid combination is recommended to be used for the first line treatment of UTI (Weese *et al.*, 2011; Pleydell *et al.*, 2012). Ceftriaxone-tazobactam combination was selected as the efficacy of the combination has been evaluated in certain animal models (Georgopoulos *et al.*, 1999) and for certain bacterial species which was found to be effective in treating UTI affected dogs. In six dogs of group A treated with ceftriaxone-tazobactam, there was a significant difference in the day 0 and day 3 mean values of blood urea, creatinine and phosphorus whereas values of calcium, total protein, albumin, glucose, sodium, potassium and chloride didn't differ significantly before and after the treatment as is evident from Table 1. Mean values of blood urea decreased from 69.78±12.0 mg/dl to 50.91±10.89 mg/dl, creatinine from 1.67±0.12 mg/dl to 1.20±0.15 mg/dl and phosphorous from 4.53±0.23 mg/dl to 3.81±0.28 mg/dl on day 3 of treatment. On haematological examination, we found that there was a significant reduction in the mean values of neutrophils, lymphocytes, eosinophils, basophils and the percent neutrophils decreased from 72.50±3.42 to 66.00±2.46 as shown in Table 2.

Table 1: Comparison of biochemical alterations before and after treatment in group A (Ceftriaxone-tazobactam) and group B (Amoxicillin-clavulanic acid) treated dogs

Biochemical Parameters	Group A		Group B		Reference Values
	0 hr	72hrs	0 hr	72 hrs	
Blood urea (mg/dl)	69.78±12.0 ^{aA*}	50.91±10.89 ^{bA*}	71.5±22.25 ^{aA}	66.2±20.14 ^{aA}	15 (10-20) mg/dl
Creatinine (mg/dl)	1.67±0.12 ^{aA*}	1.20±0.15 ^{bA*}	1.52±0.23 ^{aA}	1.41±0.21 ^{aA}	1 (0.5-1.5) mg/dl
Phosphorus (mg/dl)	4.53±0.23 ^{aA*}	3.81±0.28 ^{bA*}	5.94±1.18 ^{aA*}	4.65±0.86 ^{bA*}	4.1 (2.9-5.3) mg/dl
Calcium (mg/dl)	7.75±0.54 ^{aA}	7.83±0.62 ^{aA}	7.43±0.67 ^{aA}	7.2±0.55 ^{aA}	10.4 (9.1-11.7) mg/dl
Sodium (mmol/L)	138.95±2.00 ^{aA}	141.2±2.56 ^{aA}	143.91±3.74 ^{aA}	146.53±3.65 ^{bA}	147 (142-152) mmol/L
Potassium (mmol/L)	5.14±0.73 ^{aA}	4.35±0.17 ^{aA}	5.50±0.64 ^{aA}	4.84±0.083 ^{aB}	4.5 (3.9-5.1) mmol/L
Chloride (mmol/L)	117.48±0.51 ^{aA}	117.63±2.32 ^{aA}	117.56±4.43 ^{aA}	119.41±4.09 ^{bA}	117 (110-124) mmol/L
Total protein (g/dl)	7.42±0.788 ^{aA}	6.905±0.73 ^{aA}	7.36±0.384 ^{aA}	6.99±0.246 ^{aA}	6.45 (5.4-7.5) g/dl
Albumin (g/dl)	2.965±0.41 ^{aA}	2.79±0.49 ^{aA}	3.29±0.25 ^{aA}	3.133±0.209 ^{aA}	2.7 (2.3-3.1) g/dl
Globulin (g/dl)	4.46±0.48 ^{aA}	4.11±0.60 ^{aA}	4.07±0.30 ^{aA}	3.86±0.015 ^{aA}	3.4 (2.4-4.4) g/dl
Glucose (mg/dl)	69.33±5.30 ^{aA}	77.85±6.90 ^{aA}	83.35±11.8 ^{aA}	90.13±7.42 ^{aA}	97.5 (76-119) mg/dl

Means bearing different superscripts in a row differ significantly ($p < 0.05$); Small alphabetical letter indicates comparison within the group and capital alphabetical letters indicates the comparison between the groups; * indicates the values differs significantly

However, there was non-significant increase in the values of Hb, PCV, TEC, platelets and non-significant decrease in the values of TLC which showed that there was improvement in the clinical cases. The decrease in neutrophil count may be attributed to the effectiveness of antibiotics whereas decrease in blood urea and creatinine is attributed to fluid therapy and restriction of damage caused by bacteria to kidney by effect of antibiotics on the microorganisms.

Table 2: Comparison of haematological alterations before and after treatment in Group A (Ceftriaxone-tazobactam) and Group B (Amoxicillin-clavulanic acid) treated

Haematological Parameters		Group A		Group B		Reference Values
		0 hrs	72 hrs	0 hrs	72 hrs	
Hemoglobin (g/dl)		10.67±1.23 ^{aA}	11.25±1.10 ^{aA}	12.00±0.89 ^{aB}	12.27±0.45 ^{aA}	15.5 (12-19)
TLC ($10^3/\text{mm}^3$)		10.67±1.61 ^{aA}	9.47±1.37 ^{aA}	14.00±3.47 ^{aA}	12.79±1.94 ^{aA}	9.55 (5-14.1)
DLC (%)	N	72.50±3.42 ^{aA}	66.00±2.46 ^{bA}	75.33±1.82 ^{aA}	71±2.11 ^{bA}	71.5 (58-85)
	L	20.33±2.44 ^{aA}	27±2.44 ^{bA}	20±1.46 ^{aA}	23.50±1.82 ^{bA}	14.5 (8-21)
	E	1.17±0.40 ^{aA}	2.83±0.48 ^{bA}	2.17±0.31 ^{aA}	2.33±0.49 ^{aA}	4.5 (0-9)
	B	1.83±0.40 ^{aA}	0.67±0.21 ^{bA}	0.50±0.22 ^{aA}	0.83±0.31 ^{aA}	0.5 (0-1)
	M	4.17±0.60 ^{aA}	3.50±0.34 ^{aA}	2.00±0.58 ^{aA}	2.33±0.42 ^{aB}	6 (2-100)
TEC ($10^6/\text{mm}^3$)		5.50±0.85 ^{aA}	5.50±0.74 ^{aA}	5.50±0.34 ^{aA}	5.91±0.35 ^{aA}	6.45 (5-7.9)
PCV (%)		38.17±5.26 ^{aA}	38.45±4.50 ^{aA}	39.67±3.25 ^{aA}	40.48±2.13 ^{aA}	46 (35-57)
Platelets (10^3)		249.50±96.62 ^{aA}	275.50±63.36 ^{aA}	250.67±43.54 ^{aA}	303.33±52.42 ^{aA}	416 (211-621)

(N= Neutrophils; L= Lymphocytes; E= Eosinophils; B= Basophils; M= Monocytes); Means bearing different superscripts in a row differ significantly ($p < 0.05$); Small alphabetical letter indicates comparison within the group and capital alphabetical letters indicates the comparison between the groups.

Inappetance, fever, weakness in hind legs and stranguria were the major clinical symptoms shown by the dogs affected with UTI. Recovery was evaluated on the basis of remission of clinical signs after three days

of treatment. The remission was seen in all the six dogs treated with ceftriaxone-tazobactam combination. The dogs of group B treated with amoxicillin-clavulanic acid combination showed significant reduction in the mean values of phosphorous and DLC. The mean phosphorous values decreased from 5.94 ± 1.18 mg/dl to 4.65 ± 0.86 mg/dl on day 3 and neutrophil count decreased from $75.33 \pm 1.82\%$ to $71 \pm 2.11\%$ on day 3, respectively. Values of calcium, total protein, albumin, glucose, sodium, potassium and chloride didn't differ significantly before and after the treatment whereas non-significant decrease in values of blood urea and creatinine was seen on day 3rd. Moreover, there was non-significant increase in the values of Hb, PCV, TEC, platelets and non-significant decrease in the values of TLC which showed that there was improvement in the clinical cases. Out of six dogs treated with amoxicillin-clavulanic acid, 5 recovered clinically and one showed recurrence of clinical signs of UTI after the treatment.

Remission of clinical signs was seen in all the dogs in group A whereas one dog in group B did not show complete remission of clinical signs as a consequence of which relapse was seen. There was significant reduction in the day 0 and day 3 mean values of blood urea, creatinine and phosphorous in group A while in group B, significant reduction was seen only in mean values of phosphorous. As the blood urea, creatinine and phosphorous are the indicators of renal functions, decrease in values of blood urea, creatinine and phosphorous in group A as compared to group B suggested ceftriaxone-tazobactam combination to be more effective than amoxicillin-clavulanic acid. The percent efficacy of treatment has been recorded on the basis of remission of clinical signs and near normalisation of the haemato-biochemical values. Thus, it was seen that recovery in dogs of group A was 100% while it remained 83.3% in group B as one case was presented again in clinics with signs of UTI (Table 3).

Table 3: Comparative therapeutic efficacy of antibiotics in UTI

Groups	No. of Cases Treated	Antibiotic Treatment Given	Re occurrence of Infection	Recovery %
A	6	Ceftriaxone- tazobactam	0/6	100%
B	6	Amoxicillin- clavulanic acid	6-Jan	83.33%

Percent efficacy of ceftriaxone-tazobactam in our study is in accordance with the findings of Thirunavukkarasu *et al.* (2010) who has also reported 100 % efficacy. In our study efficacy of amoxicillin-clavulanic acid has been found to be 83.3 % which is in conformity with that of Westdropp *et al.* (2012) and Cotard *et al.* (1995) who observed the clinical cure rates of 87.9% and 69.7%, respectively. The overall findings of our study are similar to the findings of Payne *et al.* (1994) who have shown tazobactam to be more effective and active β -lactamase inhibitor than clavulanic acid. However our recommendation is to use the antibiotics for UTI based on antibiotic sensitivity testing results for getting 100% efficacy and for complete recovery it is suggested to continue the antibiotic till complete remission of clinical signs.



Conflicting Interest

The authors have none to declare.

References

1. Cotard, J.P., Gruet, P., Pechereau, D., Moreau, P., Pages, J.P., Thomas, E. & Deleforge, J. (1995). Comparative study of marbofloxacin and amoxicillin-clavulanic acid in the treatment of urinary tract infections in dogs. *Journal of Small Animal Practice*, 36:349–353.
2. Ettinger, S.J. & Feldman, E.C. (2010). Diseases of the dog and cat. In: Textbook of Veterinary Internal Medicine. 7th edn. Vol-I. W.B. Saunders, Philadelphia.
3. Georgopoulos, A., Buxbaum, A. & Graninger, W. (1999). Efficacy of β -lactam and inhibitor combinations in a diffusion chamber model in rabbits. *J. Antimicrob. Chemother.* 43:497-01.
4. Jessen, L. R., Sorensen, T.M., Bjornvad, C. R., Nielsen, S. S. & Guardabassi, L. (2015). Effect of antibiotic treatment in canine and feline urinary tract infections: A systematic review. *The Veterinary Journal*, 203:270–277.
5. Maddux, M. (1991). Effects of β -lactamase mediated antimicrobial resistance: the role of β -lactamase inhibitors. *Pharmacotherapy*.11:40-50.
6. Payne, D.J., Cramp, R., Winstanley, D.J. & Knowles, D.J.C. (1994). Comparative activities of clavulanic acid, sulbactam and Tazobactam against clinically important β -Lactamases. *Antimicrob Agents Chemother.*38:767-72.
7. Pleydell, E., Souphavanh, K., Hill, K., French, N. & Prattley D. (2012). Descriptive epidemiological study of the use of antimicrobial drugs by companion animal veterinarians in New Zealand. *New Zealand Veterinary Journal*, 60:115–22.
8. Thirunavukkarasu, P. S., Srinivasan, S. R., Vijayalakshmi, P., Vijaykumar, G., Nambi, A. P., Vairamuthu, S. & Prathaban, S. (2010). Clinical evaluation of ceftriaxone and tazobactam in canine urinary tract infection. *Intas Polivet*, 11(1):84-85.
9. Weese, J.S., Blondeau, J.M., Boothe, D., Breitschwerdt, E.B., Guardabassi, L., Hillier, A., Lloyd, D.H., Papich, M.G., Rankin, S.C., Turnidge, J.D. & Sykes, J.E. (2011). Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases. *Vet Med Int.* 263768.
10. Westdropp, J.L., Sykes, J.E., Irom, S., Daniels, J.B., Smith, A., Keil, D., Settje, T., Wang, Y. & Chew, D. J. (2012). Evaluation of the efficacy and safety of high dose short duration enrofloxacin treatment regimen for uncomplicated urinary tract infections in dogs. *J. Vet. Intern. Med.*, 26:506-512.