

Research Article

Comparative Evaluation of *per Os* and Parenteral Administration of Tribriksen™ in Equines Suffering from Bacterial Infections

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ABSTRACT

Equines including horses, donkeys and mules are very important for the economy of Pakistan. Contaminated injury wounds and contagious respiratory infections result in an adverse effect on health and performance of these species. Tribriksen™ is an antibacterial agent effective against a wide spectrum of bacterial pathogens. The current study was planned to determine the comparative efficacy of *per os* and parenteral administration of Tribriksen™ in equines suffering from bacterial infections. All the three species were randomly divided into 2 equal groups A and B. Tribriksen™ 48% at 1 mL 30 kg⁻¹ body weight was given parenterally to group A and *per os* to group B. Severity scores before and after five days of treatment were noted. All the forty animals showed highly significant decrease (P<0.01) in their severity score after five days of the treatment with Tribriksen™. All the three species exhibited significant decrease in their severity score post treatment with Tribriksen irrespective of the route. Group A revealed a highly significant decrease (p<0.01) in severity score in horses and donkeys after the treatment, whereas,

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mules had showed significant decrease. Severity scores were significantly low by *per os* treatment as well. It was noted that both the route were equally effective for the animals. Comparison of routes in individual species showed non-significant difference by the route of treatment.

INTRODUCTION

Many bacteria are capable of causing enteric, integumentary, urinary, and respiratory diseases in equines. Some bacteria only cause disease when viruses or other agents have first damaged these systems. Other bacteria are capable of producing disease independently.

Contagious respiratory infections in horses are major causes of both acute and chronic respiratory diseases resulting in impaired pulmonary functions and reduced performance. The chronic squeal of these infections are important to the horse industry and include bronchopneumonia, chronic obstructive pulmonary disease, and exercise induced hemorrhage (Wilson, 1993). These problems are commonly treated with parenteral antibiotics.

The basic nature of equine work seems to put them at risk for traumatic injuries. One of the most common reasons that clients present their horses to the veterinarian is trauma that results in skin and soft tissue wounds. Most often wounds occur on horse's limbs and are caused by harness, tacks, and foreign objects such as fences, gates, farm implements and building materials. Wounds on the distal limbs of horses can be especially difficult to manage because of poor circulation, joint movement and minimal soft tissue between skin and bone. There is also always the risk of contamination from the environment. Excessively exudative or contaminated wounds or wounds with bacterial colonization may require a wound dressing and/or use of antibiotics.

Tribrissen™ (Glaxo Smith Kline, Pakistan Ltd.) is an antibacterial agent effective against a wide spectrum of bacterial pathogens. Its generic name is

trimethoprim_sulphadiazine. Tribrissen™ is for use in horses where potent systemic antibacterial action against sensitive organisms is required such as in the control of acute strangles, respiratory tract infections, acute urogenital infections, wound infections and abscesses. Tribrissen™ is well tolerated by foals.

Tribrissen Oral Suspension™ is indicated (30 mg kg⁻¹ b.wt) for the treatment of horses with bacterial infections caused by sensitive bacteria including, gastro-intestinal infections, infections of respiratory tract, infections of urogenital tract, wound infections and cellulitis, salmonellosis and as prophylacticum for post-operative infections (Anonymous, 2008).

Tribrissen™ is commonly used in the form of injection of various doses in equines and though indicated but not commonly used orally against bacterial infections. For the owner/attendant of an equine suffering from a bacterial infection, oral administration of Tribrissen™ seems easier and more convenient than the parenteral administration of this drug. However, the oral use of this drug vis-a-vis its parenteral use has not been evaluated thus far in equines suffering from bacterial infections.

This study was planned to determine the comparative efficacy of *per os* and parenteral administration of Tribrissen™ in equines suffering from bacterial infections.

MATERIALS AND METHODS

A total of 40 equines suffering from bacterial infections of respiratory tract and skin (septic wounds) were selected from district Faisalabad, Punjab. Animals suffering from bacterial infections were selected on the basis of signs, symptoms and previous history of a respiratory infection or the skin wounds. They were divided into two groups (A and B) irrespective of the type of infection. Both the groups included mules, donkeys and horses in a random ratio.

All the relevant particulars like owner's profile, animal's profile, clinical signs, treatment and response to treatment were recorded on a proforma.

Group A was treated with inj. Tribriksen™ (containing trimethoprim 8% w/v and sulphadiazine 40% w/v) @ 1 mL 30 kg⁻¹ b.wt. intramuscularly. Whereas, Group B was given Tribriksen™ oral suspension (containing trimethoprim 8% w/v and sulphadiazine 40% w/v) @ 1 mL 30 kg⁻¹ b. wt. *per os*, for five days (Anonymous, 2008). Equines of neither group had previously been not treated with antibiotics /antibacterials.

Animals were evaluated for the response to treatments, on the basis of clinical signs and symptoms i.e. coughing, body temperature through rectum, feed intake, healing of wound.

The recording of these parameters was conducted for five days during treatment and on 10th day post treatment.

Data analysis: The data relating to severity score were analyzed by comparing means±SE through t-test (SAS, 2004).

The severity score ranges from 0-4 were assigned as under:

1. Healthy, 1 mildly sick, 2 Moderate sick, 3 severely diseased, 4 highly diseased
2. Odds Ratio of cure rates affected by treatment protocol A and protocol B were calculated by the formula given below (Collet, 1991):

	Number of animals recovered	No. of animals unrecovered
Group A	A	B
Group B	C	D

$$\text{Odds ratio} = \frac{P_1}{1-P_1} / \frac{P_2}{1-P_2} = \frac{ad}{bc}$$

Body weights of the equines were calculated by using following formula.

Caroll and Huntington, 1998; Rudman and Keiper, 1991.

$$\text{Estimated weight wt (kg} = [(\text{girth})^2 \times \text{length}] \div Y$$

Where Y = 11900

RESULTS

A total of 40 equines suffering from respiratory tract and wound infections and maintained under natural conditions were divided into group A and group B of 20 animals. Donkeys, horses and mules were included in both the groups.

1. **Group A:** parenteral (intramuscular) treatment with Inj. Tribriksen™ 48%
2. **Group B:** *per os* treatment with Tribriksen oral suspension™ 48%.

The animals were treated for 5 days and their severity scores were recorded. The response to either treatment was evaluated Table 1, 2.

Table 1: Proportion of equines cured by intramuscular administration of injection Tribriksen™ (Protocol A)

Group A	Treatment protocol	No. of animals recovered divided by the number of animals treated.
Horse	Inj. Tribriksen™ 48%	6/7
Donkey	Inj. Tribriksen™ 48%	6/7
Mule	Inj. Tribriksen™ 48%	4/6

Table 2: Proportion of equines cured by *per os* administration of Tribriksen oral suspension™ (Protocol B)

Group A	Treatment protocol	No. of animals recovered divided by the number of animals treated.
Horse	Tribriksen oral suspension™ 48%	6/7
Donkey	Tribriksen oral suspension™ 48%	6/7
Mule	Tribriksen oral suspension™ 48%	5/6
	Number of animals recovered	No of animals unrecovered
Group A	16 = a	4 = b
Group B	17 = c	3 = d

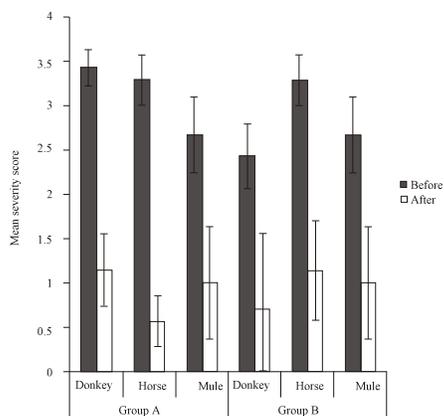


Fig. 1: Comparison of severity scores pre and post treatment with Tribriessen™ in equines suffering from bacterial infections of respiratory tract and wounds

Table 3: Effect of Tribriessen™ treatment (interamuscular/per os) in equines suffering from bacterial infections of respiratory tract and wounds

Groups	Timing of observation	Mean severity scores	n	SE	t-value
Overall	Before treatment	2.98	40	0.14	11.46**
	After treatment	0.93	40	0.18	
Group A	Before treatment	3.15	20	0.18	9.00**
	After treatment	0.90	20	0.25	
Group B	Before treatment	2.80	20	0.21	7.28**
	After treatment	0.95	20	0.27	

n= Number of observations, A= interamuscular injection of Tribriessen™
SE = Standard error, B= per os administration of Tribriessen oral
** = Highly significant (p<0.01), suspension™

$$\text{Odds ratio} = \frac{P_1}{1-P_1} / \frac{P_2}{1-P_2} = \frac{ad}{bc} = \frac{16 \times 3}{4 \times 17} = \frac{48}{68} = 0.706$$

Odd ratio less than 1 indicate that group A is approximately less effective than group B. Severity scores of all 40 equines significantly decreased (p<0.01) after the five days treatment with Tribriessen™ as shown in the Table 3 and Fig.1. Group A also showed highly significant decrease in severity scores at the termination of the treatment. A highly significant decrease in severity scores was observed after the end of treatment with Tribriessen™ (per os).

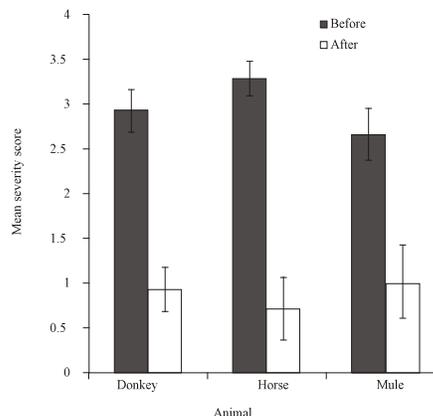


Fig. 2: Effect of Tribriessen™ treatment in equines suffering from bacterial infections of respiratory tract and wounds.

Table 4: Effect of Tribriessen™ (intramuscular/per os) treatment on clinical severity scores of equines suffering from bacterial infections of respiratory tract and wounds.

Equine species	Timing of observation with respect to treatment	Mean severity scores	N	SE	t-value
Donkey	Before	2.93	14	0.24	
	After	0.93	14	0.24	6.74**
Horse	Before	3.29	14	0.19	
	After	0.86	14	0.31	8.34**
Mule	Before	2.67	12	0.28	
	After	1.00	12	0.42	5.00**

n = Number of observations, SE = Standard error, ** = Highly significant (p<0.01)

A total of 14 donkeys were treated with Tribriessen™ (parenteral or per os) and were seen to have a highly significant decrease (p<0.01) in severity scores post treatment as given in the Table 4 and Fig. 2. Horses showed a highly significant decrease in severity scores post treatment with Tribriessen™. Mules also showed a highly significant decrease in their severity scores after the 5 days of Tribriessen™ treatment.

In the group A, the donkeys showed a highly significant decrease (p<0.01) in their clinical severity scores after the 5 days of treatment as shown in the Table 5 and Fig. 3. The horses also showed a highly significant decrease in mean

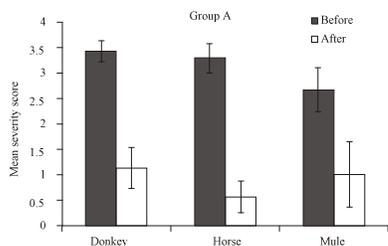


Fig. 3: Comparison of severity scores pre and post parenteral treatment (*I/m*) of Tribriissen™ in equines suffering from bacterial infections of respiratory tract and wounds.

Table 5: Comparison of severity scores pre and post parenteral treatment (*I/m*) of Tribriissen™ in equine species suffering from bacterial infections of respiratory tract and wounds

Equine species	Timing of observation with respect to treatment	Mean severity scores	N	SE	t-value
Donkey	Before	3.43	7	0.20	5.44**
	After	1.14	7	0.40	
Horse	Before	3.29	7	0.28	7.55**
	After	0.57	7	0.29	
Mule	Before	2.67	6	0.42	3.37*
	After	1.00	6	0.63	

n = Number of observations, SE = Standard error, * = Significant (p<0.05), ** = Highly significant (p<0.01)

severity scores post treatment. Mules showed significant decrease (p<0.05) in their severity scores post treatment with Tribriissen™.

In the group B, the donkeys showed a highly significant decrease (p<0.01) in their severity scores after the 5 days of treatment as shown in the Table 6, 7 and Fig. 4. The horses also showed a highly significant decrease in severity scores means post treatment. Mules showed significant decrease (p<0.05) in their severity scores post treatment with tribriissen™ given orally.

Groups A and B had clinical severity scores of 3.15±0.182 and 2.8±0.213, respectively before the start of treatment with Tribriissen™. Group A was given Tribriissen™ in injectable form and B was given Tribriissen™ in oral form. After the treatment of 5 days, the severity scores of group A and B were

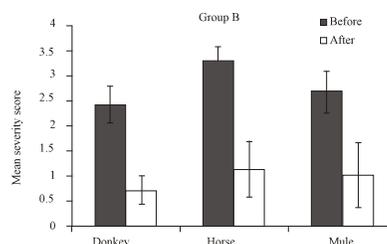


Fig. 4: Comparison of severity scores pre and post *per os* treatment of Tribriissen™ in equines suffering from bacterial infections of respiratory tract and wounds.

Table 6: Comparison of severity scores pre and post *Per os* treatment of Tribriissen™ in equine species suffering from bacterial infections

Equine species	Timing of observation with respect to treatment	Mean severity scores	N	SE	t-value
Donkey	Before	2.43	7	0.36	4.08**
	After	0.71	7	0.28	
Horse	Before	3.29	7	0.28	4.67**
	After	1.14	7	0.55	
Mule	Before	2.67	6	0.42	3.37*
	After	1.00	6	0.63	

n = Number of observations, SE = Standard error, * = Significant (p<0.05), ** = Highly significant (p<0.01)

Table 7: Comparisons of parenteral (*I/m*) and *per os* treatment of Tribriissen™ in equines suffering from bacterial infections of respiratory tract and wounds

Equine species	Timing of observation with respect to treatment	Mean severity scores	N	SE	t-value
Before	Group A	3.15	20	0.18	1.25 ^{NS}
	Group B	2.80	20	0.21	
After	Group A	0.90	20	0.25	0.13 ^{NS}
	Group B	0.95	20	0.27	

n = Number of observations, A= interamuscular injection of Tribriissen™, SE = Standard error, B= *per os* administration of Tribriissen oral, NS = Non-significant (P>0.05) suspension™

0.90±0.25 and 0.95±0.276, respectively. Severity scores comparison showed a non-significant (p>0.05) difference with both the routes of treatment.

Table 8 and Fig. 6, illustrates that the donkeys treated with either parenteral or oral form of

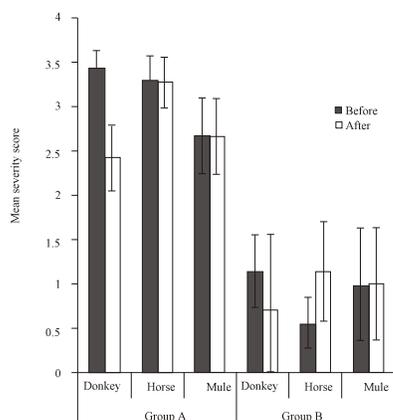


Fig. 5: Comparison of parenteral (*I/m*) and *per os* treatment of Tribriksen™ in equines suffering from bacterial infections of respiratory tract and wounds.

Table 8: Comparison of parenteral and *per os* treatment of Tribriksen™ in equine species suffering from bacterial infections of respiratory tract and wounds.

Species	Timing of observation with respect to treatment	Timing of observation with respect to treatment	Mean clinical severity scores	N	SE	t-value
Donkey	Before	Group A	3.43	7	0.20	2.38*
		Group B	2.43	7	0.36	
	After	Group A	1.14	7	0.40	
		Group B	0.71	7	0.28	
Horse	Before	Group A	3.29	7	0.28	0.00 ^{NS}
		Group B	3.29	7	0.28	
	After	Group A	0.57	7	0.29	
		Group B	1.14	7	0.55	
Mule	Before	Group A	2.67	6	0.42	0.00 ^{NS}
		Group B	2.67	6	0.42	
	After	Group A	1.00	6	0.63	
		Group B	1.00	6	0.63	

n = Number of observations, A= interamuscular injection of Tribriksen™, SE = Standard error, B= *per os* administration of Tribriksen oral, NS = Non-significant ($p>0.05$) suspension™

Tribriksen™ did not show a significant difference ($p>0.05$) in their clinical severity scores from the route of treatment. However, a significant difference in severity scores was there between the donkeys of group A and B. Horses were also showing a non-significant difference from the route of treatment.

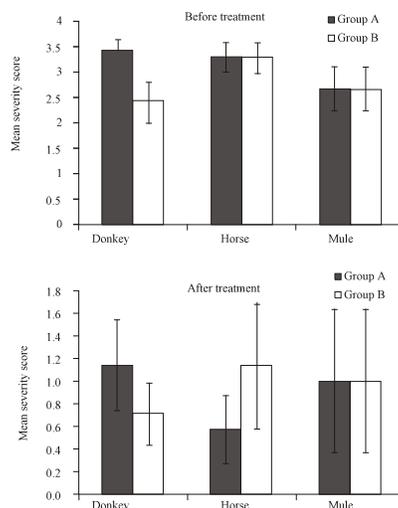


Fig. 6: Comparison of parenteral and *per os* treatment of Tribriksen™ in all equines suffering from bacterial infections of respiratory tract and wounds.

In the same way, mules were recovered by both the ways of treatment and a non-significant difference was there in the route of treatment.

DISCUSSION

Equines including horses, donkeys and mules very important for the economy of Pakistan. They suffer from traumatic injuries and respiratory infections every now and then because of nature of their work. Contamination of the injury wounds and contagious respiratory infections results in an adverse effect on health and performance of the equines. The squeal of these infections are very important as they are a lurking danger for the health and performance of the equines and their industry.

It is commonly used via parenteral route and its oral therapy is not in regular use. Therefore, the present study was designed to evaluate the

comparative efficacy of *per os* and parenteral administration of Tribriessen™ in equines suffering from bacterial infections.

The effect of Tribriessen™ on the respiratory infections (bacterial) and wounds was evaluated on the basis of clinical signs and symptoms. Extent of infection is elaborated by the clinical signs which can be interpreted on the basis of severity score (1-5) of the animals. Overall, all the 40 animals had a highly marked decrease ($P < 0.01$) in their severity score after five days of the treatment with Tribriessen™ 48% @ 1ml/30kg body weight. In a previous study, the use of Tribriessen™ PO & IV 6ml/100kg had resulted in cure of respiratory conditions, simple wounds, bone infections and urinary tract infections (Abunameh, 2009). Brumfitt and Miller (1993) observed that the Trimethoprim is a very good inhibitor of bacterial dihydrofolate reductase thus acting as a bacteriostatic.

Duijkeren *et al.* (1994) observed the trimethoprim/sulfonamide combinations (TMPS) are often used for antibacterial treatment in horses. Ensink *et al.* (1993) concluded that many bacteria are sensitive to trimethoprim/sulfonamide *in vitro* including *Streptococcus equi* sub sp. *zooepidemicus* (*S. zooepidemicus*), a highly pathogenic agent for horses.

A total of 14 donkeys in both the groups were treated via either injectable or oral form of Tribriessen™. They exhibited significant decrease in their severity score post treatment with Tribriessen™ than the pre treatment score. All the suffering horses (14) showed significant effect after the treatment with Tribriessen™. Same was true for the mules as well. Dargatz *et al.* (2000) and Wilson, (2001) reported that trimethoprim-sulfamethoxazole (SXT) and trimethoprim-sulfadiazine are used to treat respiratory infections in all equine species.

The results of parenteral treatment among three species were compared in this study. They revealed that a marked reduction ($p < 0.01$) in severity score

was observed in horses and donkeys, whereas, mules exhibited a marked decrease ($p < 0.05$) in clinical severity score of respiratory tract and wound infections.

The comparison of *per os* treatment of Tribriessen™ have shown highly significant ($p < 0.01$) effects by the treatment in horses and donkeys. Mules were having a significant effect ($p < 0.05$) of *per os* therapy. Kelly *et al.* (2003) noted that the administration of trimethoprim - sulfadiazine *per os* once daily for two weeks at the rate of 30 mg kg⁻¹ resulted in healing of wound at tracheotomy site and marked reduction in subcutaneous emphysema. Oral administration of Trimethoprim/sulfonamide is more convenient and this combination has broad spectrum of activity (Duijkeren *et al.*, 1994).

The group A (parenteral) and B (*per os*) were compared with each other for the effect of Tribriessen™ therapy. Pre and post treatment severity scores means of the 20 animals in each group were non-significantly different ($p < 0.05$). It meant that the both the route are equally effective for the animals. Furguson *et al.* (2007) reported that the problems of anorexia, weight loss in a 23- year old mare resolved within a 2- week course of oral trimethoprim and sulphadiazine combination. Oral trimethoprim-sulfamethoxazole is a successful therapy for primary prophylaxis against *Pneumocystis carinii* pneumonia in diseased persons (Hughes *et al.*, 1987; Olsen *et al.*, 1993). Parenteral combination of trimethoprim-sulfamethoxazole was used to prevent *pneumocystis carinii* pneumonia (Olsen *et al.*, 1993).

CONCLUSION

The current study led to the conclusion that Tribriessen™ is equally effective in either oral or injectable form for the treatment of respiratory and wound infections in the three equine species.

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