Journal of Animal Research: v.5 n.1, p. 183-187. April. 2015

DOI Number: 10.5958/2277-940X.2015.00029.7

Comparative Efficacy of Nitazoxanide and Sulphadimidine in the Treatment of Cryptosporidiosis in Bovine Calves

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Received: 20 February, 2015 **Accepted:** 12 March, 2015

ABSTRACT

The present study was undertaken to assess the therapeutic efficacy of oral Nitaxoxanide and Sulphadimidine treatment against *Cryptosporidium* infection in bovine calves reared under field conditions. A total of 18 diarrhoeic calves naturally infected with *Cryptosporidium* infection were evaluated. Nitazoxanide was found to be very effective on the basis of disappearance of clinical signs, restoration of altered haemato-biochemical parameters to their normal level and 78.89% reduction in *Cryptosporidium* oocysts shedding. On the other contrary, sulphadimidine was found almost ineffective in the treatment of cryptosporidiosis in calves. Intravenous infusion of Ringer's lactate and 5% Dextrose used as adjunct therapy for correction of fluid and electrolyte losses fastened the recovery.

Keywords*: bovine calves, Cryptosporidium infection, nitazoxanide, sulphadimidine*

Calf diarrhoea is one of the prime concerns towards the neonatal calf mortality and the economic losses in dairy industry as livestock production becomes more intensified (Radostits *et al.*, 2007). The economic losses associated with cryptosporidiosis are due to calf mortality and the retarded growth of calves, the cost of drugs, veterinary assistance and the increased labour involved. The indirect losses are associated with reduction in milk production from dam. Two species of *Cryptosporidium* with significant biological differences infect cattle: *C. parvum* and *C. andersoni* (Santin *et al.,* 2004). But *C. parvum* is ubiquitous, zoonotic and has potential for environmental contamination. To date, many compounds including coccidiostats, broad spectrum antibiotics and other chemicals have been evaluated against *Cryptosporidium* infection in man and animals but have been found to be only partial effective. Therefore the present study aimed to assess the therapeutic efficacy of oral Nitaxoxanide and Sulphadimidine treatment against *Cryptosporidium* infection in bovine calves under field condition.

MATERIALS AND METHODS

A total of 18 diarrhoeic bovine calves naturally infected with *Cryptosporidium* were divided into 3 groups, viz. A, B and C, each comprising 6 calves in each group. Calves of group A received nitrothiazole benzidamide compound, Nitazoxanide tablet (Zoxakind™500) @ 30 mg/kg b.wt. in two divided doses daily, orally, for 3 days whereas calves of group B received antimicrobial agent Sulphadimidine tablet (Sulphadimidine® 5g) @ 140mg/kg b.wt. in two divided doses daily, orally, for 3 days. Calves of both groups received Intravenous infusion of Ringer's lactate and 5% Dextrose each @ 30 ml/kg b.wt. in two divided doses (as supportive measure depending on degree of dehydration). Calves of group C received no treatment and served as infected control. Therapeutic efficacy of two drugs was evaluated on the basis of disappearance of clinical signs, absence, or reduction of oocysts shedding and restoration of altered haemato-biochemical parameters of infected calves following

Table I. Effect of different therapeutic regimens on haematological and biochemical parameters (Mean* ± SE) in *Cryptosporidium* infected bovine calves

Parameter (unit)	Group	Observation period post treatment		
		Day 0	Day 4	Day 11
TEC (10^6/µl)	A	^{y}7.27±0.22	^{y}7.78±0.22 ^{a}	^{x}8.47±0.21 ^{a}
	B	^{x}7.29±0.25	^{xy}6.97±0.26 ^{b}	^{y}6.43±0.24 ^{b}
	C	^{x}7.21±0.22	^{xy}6.73±0.21 ^{b}	^{y}6.15±0.19 ^{b}
Hb (gm %)	A	^{y}9.0±0.22	^{y}9.53±0.16 ^{a}	^{x}10.23±0.16 ^{a}
	B	8.83±0.19	9.03±0.2 ^{b}	9.17±0.23 ^{b}
	C	^{x}9.07±0.15	^{x}8.7±0.16 ^{b}	^{y}8.03±0.2 ^{c}
PCV (%)	A	^{x}42.5±0.76	^{y}39.83±0.87 ^{b}	^{z}37.0±0.97^{c}
	B	42.33±0.67	41.33±0.88 $^{a b}$	40.67±1.11 ^{b}
	C	^{y}42.0±0.82	^{xy}43.5±0.85 ^{a}	^{x}45.5±1.02 ^{a}
TLC (10^3/µl)	A	^{x}10.33±0.21	^{xy}9.75±0.24 ^{b}	^{y}9.12±0.21 ^{c}
	B	10.07±0.19	9.85±0.2 ^{b}	9.98±0.27 ^{b}
	C	^{y}10.19±0.23	^{xy}10.75±0.27 ^{a}	^{x}11.38±0.25 ^{a}
Lymphocyte (%)	A	^{y}56.33±1.05	^{xy}58.5±1.18	^{x}61.0±1.24 $^{a b}$
	B	57.33±0.88	57.5±0.96	57.83±1.08 ^{b}
	C	^{x}57.17±0.79	^{x}56.17±0.79	^{y}53.33±0.67 ^{c}
Neutrophil (%)	A	^{x}36.0±0.73	^{xy}34.5±0.76	^{y}32.67±0.8 ^{b}
	B	35.33±0.67	34.67±0.76	34.0±0.86 ^{b}
	C	36.0±0.58	36.5±0.62	38.0±0.73 ^{a}
Eosinophil (%)	A	3.83±0.31	4.17±0.31	3.67±0.21 ^{b}
	B	4.33±0.33	4.83±0.31	5.0±0.45 ^{a}
Total serum protein (g/dl)	C	^{y}4.17±0.31	^{xy}4.5±0.56	^{x}5.67±0.33 ^{a}
	A	^{y}5.68±0.14	^{xy}5.85±0.10	^{x}6.12±0.12 ^{a}
Serum albumin (g/dl)	B	5.55±0.14	5.53±0.15	5.58±0.21 ^{b}
Serum globulin (g/dl)	C	5.70±0.12	5.54±0.16	5.40±0.18 ^{b}
Serum glucose (mg/dl)	A	^{y}2.71±0.09	^{xy}2.85±0.10 $^{a b}$	^{x}3.07±0.10 ^{a}
	B	2.68±0.08	2.62±0.09 ^{b}	2.78±0.13 $^{a b}$
Serum sodium (mEq/l)	C	2.75±0.09	2.67±0.10 $^{a b}$	2.59±0.11 ^{b}
	A	2.96±0.06	3.00±0.06	3.1±0.10
Serum potassium (mEq/l)	B	2.87±0.06	2.89±0.07	2.92±0.09
	C	2.95±0.07	2.90±0.06	2.82±0.11
Serum chloride (mEq/l)	A	^{z}91.44±0.59	^{y}95.48±0.33 ^{a}	^{z}98.82±0.63 ^{a}
	B	^{y}91.71±0.66	^{x}94.19±0.45 ^{a}	^{x}95.60±0.47 ^{b}
	C	^{z}91.63±0.75	^{y}88.49±0.56 ^{b}	^{x}85.77±0.36 ^{c}
	A	^{z}131.73±0.87	^{y}138.18±1.03 ^{a}	^{x}142.73±0.98 ^{a}
	B	^{z}132.73±1.0	^{y}135.49±0.87 ^{b}	^{x}138.0±0.34 ^{b}
	C	^{x}132.96±1.1	^{y}127.91±0.74 ^{c}	^{z}125.32±0.65 ^{c}
	A	4.34±0.16	4.61±0.13	4.74±0.10 ^{a}
	B	4.45±0.15	4.54±0.09	4.56±0.09 ^{a}
	C	^{x}4.62±0.17	^{xy}4.40±0.08	^{y}4.15±0.07 ^{b}
	A	^{z}88.47±1.02	^{y}94.0±0.79 ^{a}	^{x}98.14±0.92 ^{a}
	B	^{y}88.87±0.70	^{x}90.26±0.87 ^{b}	^{x}92.03±0.47 ^{b}
	C	^{x}88.66±0.71	^{y}86.28±0.63 ^{c}	^{z}83.96±0.54 ^{c}

*Mean values with different superscripts in the column (a, b and c) and row (x, y and z) represent significant (P<0.05) difference.

treatment. Clinical observation, faecal examination, and haemato-biochemical study were carried out on day 0, 4 and 11 post- treatment. The hematological parameters were studied following standard methods as described by Jain (1986). The biochemical parameters were estimated by the standard procedure using diagnostic kit in semi-autoanalyser. Faecal smear, stained with modified Ziehl-Neelsen stain for visualization of *Cryptosporidium* oocysts were examined microscopically. Oocysts were counted per microscopic field semi-quantitatively and the mean of oocysts count in 20 randomly selected fields at 1000x magnification was calculated. The percent reduction in mean *Cryptosporidium* oocysts count in faeces of calves infected with cryptosporidiosis as compared to pre-treatment value was calculated using the formula described by Coles *et al*. (1992) with slight modification. The percent therapeutic efficacy of a drug against cryptosporidiosis calves as compared to untreated control was calculated using the formula described by Moskey and Harwood (1941) with slight modification. The data were analyzed statistically by Completely Randomized Design (CRD) and approximate 't' test following the standard procedure as outlined by Snedecor and Cochran (1967).

RESULTS AND DISCUSSION

Clinical recovery in respect to altered demeanour, general appearance, diarrhoea and dehydration was marked in nitazoxanide treated calves. Present findings corroborated the earlier reports of Rossingol *et al.* (2001), Amadi *et al.* (2002) and Bailey and Erramouspe (2004) who also recorded significantly reduced duration and improved resolution of diarrhoea in nitazoxanide treated calves. On the other hand, sulphadimidine treated calves did not show significant improvement in regard to diarrhoea, appetite and appearance. Group C infected control calves did not show any improvement and rather there was deterioration of condition of calves.

Nitazoxanide treatment resulted gradual restoration of altered haematological parameters towards normal level by day 11th post treatment (table-1). However, calves of group B, that received sulphadimidine, did not show improvement in respect to normalization of altered parameters. The improvement in all haematological parameters recorded might be attributed to the elimination of *Cryptosporidium*, cessation of inflammation and haemorrhage if any, in the intestine. However, due to paucity of literature on effect of nitazoxanide and sulphadimidine treatment on haematological parameters, present findings could not be compared.(10^6/µl).

Likewise nitazoxanide treatment resulted in gradual restoration of all altered biochemical parameters to their normal level by day 11th post treatment where as in sulphadimidine treated animals altered biochemical parameters did not restore towards their normal level. The treatment with nitazoxanide eliminated the infection resulted in better appetite, feed conversion efficiency, increased availability and absorption of dietary nutrients and electrolytes. Fluid therapy provided as an adjunct therapy to the calves of all treated groups might have brought the altered level of electrolytes to their normal level. However, due to paucity of data on effect of nitazoxanide and sulphadimidine treatment on biochemical parameters, present findings could not be compared.

Assessment of oocysts shedding in faeces of *Cryptosporidium* infected bovine calves

The effect nitazoxanide and sulfadimidine treatment on *Cryptosporidium* oocysts count per microscopic field in faeces of bovine calves at 1000x magnification has been presented in table-2. Nitazoxanide treatment brought significant (P≤0.05) decrease in mean oocyst count on day 4th and 11th post treatment as compared to pre-treatment value. The present finding in respect to nitazoxanide is in agreement with reports of Rossignol *et al.* (2001).

Table 2. Effect of different therapeutic regimens on *Cryptosporidium* oocysts count (Mean±SE) per field in faeces of bovine calves at 1000x magnification

Group of animals	Pre-treatment day	Day 4th post treatment	Day 11th post treatment
Gr. A (nitazoxanide treated)	^{x} 8.67±0.88	^{y} 5.50±0.76 ^{a}	^{z} 1.83±0.65 ^{a}
Gr. B (sulfadimidine treated)	8.50±0.85	7.83±0.79 ^{b}	6.83±0.79 ^{b}
Gr. C (infected control)	8.50±0.85	8.67±0.49 ^{b}	7.33±0.28 ^{b}

Mean values with different superscripts in the column (a, b) and row (x, y and z) represent significant (P≤0.05) difference and mean values with common superscripts in the column (a, b) and

row (x, y and z) represent non-significant (P<0.05) difference.

However, there was non-significant decrease in oocyst count in group B as compared to pre–treatment value. When compared among groups at different intervals, there was significant (P≤0.05) decrease in mean oocyst count value in group A which received nitazoxanide, than group B which received sulphadimidine. On the other hand, group C calves did not show any significant change in mean oocyst count during study period.

Percent reduction in mean *Cryptosporidium* oocysts counts in faeces and percent therapeutic efficacy of drugs against cryptosporidiosis in bovine calves

The percent reduction in mean *Cryptosporidium* oocysts count in faeces of bovine calves as compared to pre-treatment value and percent efficacy of drugs as compared to untreated control calves in cryptosporidic calves have been presented in table-3. Nitazoxanide treatment in group A resulted 36.56% reduction in oocysts shedding on day 4th post treatment and 78.89% reduction on day 11th post treatment. But, sulphadimidine treated calves showed 7.88% and 19.65 % reduction in oocysts shedding on day 4th and 11th post treatment respectively which corroborated the reports by Fayer (1992).

Table 3. Percent reduction in mean *Cryptosporidium* oocysts count and percent efficacy of drugs against cryptosporidiosis in bovine calves

Group	Percentage reduction in mean oocysts count as compared to pre-treatment value		Percentage therapeutic efficacy as compared to untreated control	
	Day 4th post treat-ment	Day 11th post treat-ment	Day 4th post treat-ment	Day 11th post treatment
Gr. A (nitazoxanide treated)	36.56	78.89	36.56	75.03
Gr. B (sulfadi-midine treated)	7.88	19.65	9.68	6.82

On the contrary, Das *et al.* (2006) reported that sulphadimidine combined with furazolidone and fluid therapy showed 71.40% recovery in the treatment of cryptosporidiosis affected calves. The percent therapeutic efficacy was high in nitazoxanide treated group and it was found to be 75.03% by day 11th post treatment. Rossingol *et al*. (2001), Amadi *et al.* (2002) and Bailey and Erramouspe (2004) reported that nitazoxanide had good therapeutic efficacy against cryptosporidiosis. However, sulphadimidine treated calves showed comparatively lower efficacy i.e., 9.68% and 6.82% on day 4th and 11th post treatment, respectively. Similar to present finding, Fayer (1992) also found that sulfadimethoxine did not significantly improved symptoms and oocysts shedding in calves suffering from cryptosporidiosis.

The results on percent reduction in *Cryptosporidium* oocysts count per field in faeces and percentage therapeutic efficacy of different therapeutic regimens clearly indicated that nitazoxanide was superior to sulphadimidine in treating cryptosporidiosis in calves. Fluid therapy given as adjunct therapy hastened the recovery in the treated groups in respect to correction of fluid and electrolyte losses.

ACKNOWLEDGEMENTS

The authors are highly thankful to the Dean, College of Veterinary Sci and A.H. Anjora, Durg, Chattisgarh for providing necessary facilities and support required for the research.

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