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Effects of Hypertonic Saline Solution on Clinical Parameters, Serum Electrolytes and Plasma Volume in the Treatment of Haemorrhagic Septicaemia in Buffaloes

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ABSTRACT

This study was conducted to determine the efficacy of hypertonic saline solution (HSS) along with antibiotic (ceftiofur HCl) and non-steroidal anti-inflammatory drug (ketoprofen) in the treatment of haemorrhagic septicaemia in buffaloes. For this purpose, 50 buffaloes suffering from haemorrhagic septicaemia were randomly divided in two equal groups A and B. Group A served as control and was treated with ceftiofur HCl (IM) and ketoprofen (IV) @ 6 and 2 mg/Kg BW, respectively, for five days. Buffaloes of group B were administered with rapid intravenous infusion of hypertonic saline solution (7.5% NaCl) @ 4 ml/Kg BW once in combination with ceftiofur HCl and ketoprofen. Animals were monitored for 24 hours after initiation of treatment. Clinical parameters, serum electrolytes, plasma volume and survival index were recorded at different intervals after treatment. Survival rate (80%) in group B was significantly higher ($P<0.05$) than 48% in group A. The heart rate and respiration rate recovered more effectively in the buffaloes administered with treatment protocol B. Plasma volume was 98% which was almost normal within 24 hours after the infusion of hypertonic saline solution to the animals of group B. It was concluded from the study that hypertonic saline solution as an adjunct to antibiotic and a non-steroidal anti-inflammatory drug more efficiently improved respiration and heart rates and effectively restored plasma volume in resuscitating the buffaloes from haemorrhagic septicaemia than the conventional treatment.

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INTRODUCTION

In terms of morbidity and mortality, haemorrhagic septicaemia (HS) is one of the most important diseases of buffaloes and cattle in Pakistan (Raza *et al*., 2000). This disease is caused by a gram-negative bacterium *Pasteurella multocida* serotype B:2. The organism produces endotoxins which are responsible for all manifestations of the disease (Horadagoda *et al*., 2001). These endotoxins have severe effects on central circulation and lead to hypovolaemia. So, fluid administration is the corner stone for the management of patients suffering from septicaemia (Rivers *et al*., 2001).

Recent clinical data support the concept that an early restitution of the circulation is of great importance to improve oxygenation, maintain cardiac output and blood pressure and ultimately increase the survival rate (Somell *et al*., 2005, Somell *et al*., 2007). It is, therefore, of great value to restore the intravascular volume and thereby maintain an adequate cardiac output and oxygen delivery. Small volume resuscitation with hypertonic saline solution (HSS; 7-7.5% NaCl) promotes immediate plasma volume expansion due to mobilization of fluids from the intracellular compartments, thus restores cardiac output and regional blood flow and improves microcirculation, thereby decreasing inflammatory responses triggered by endotoxins (Kramer, 2003; Rocha-e-Silva and Poli-de-Figueiredo, 2005).

The aim of this study was to determine the efficacy of hypertonic saline solution as an adjunct to antibiotic (ceftiofur HCl) and non-steroidal anti-inflammatory (ketoprofen) therapy in the treatment of haemorrhagic septicaemia in buffaloes.

MATERIALS AND METHODS

Experimental animals

A total of 50 buffaloes of either sex aged from 1.5 to 2 years suffering from haemorrhagic septicaemia were selected from the areas in and around Faisalabad. The study period spanned from July to October during 2008 and 2009. The disease was diagnosed on the basis of clinical features i.e. sudden onset, high rise in body temperature, anorexia, depression, edematous swelling on throat, brisket and upper dewlap region, dyspnea, nasal discharge, salivation and reluctance to move (Carter and De Alwis, 1989; Radostits *et al*., 2007).

Treatment protocol

All the buffaloes suffering from the disease were randomly divided into two equal groups. Buffaloes in group A served as control and were treated with ceftiofur HCl (Inj. Excenel RTU®, Pfizer Animal Health Division, Pakistan) and ketoprofen (Inj. Ketoject®, Selmore Pharmaceuticals, Pakistan) @ 6 and 2 mg/kg BW, IM and IV, respectively. Animals in group B were treated with intravenous infusion of hypertonic saline solution (7.5% NaCl; 2400 mmol NaCl/L) @ 4 ml/Kg BW once in combination with ceftiofur HCl and ketoprofen at the same dosage as in group A. Hypertonic saline solution was administered once (only on the first day of treatment) in the buffaloes of group B, while ceftiofur HCl and ketoprofen were administered after every 12 and 8 hours, respectively, for five consecutive days in the both groups.

Measurement of parameters and analysis of samples

Body temperature, heart rate and respiration rate were recorded as clinical parameters. Rectal temperature was taken as body temperature. Heart rate was measured by means of thoracic auscultation, while respiration rate was measured by counting thoracic excursions. The venous blood samples with anticoagulant were used to determine haemoglobin (Hb) concentration and haematocrit (Hct) values, while the serum harvested from blood samples without anticoagulant after centrifugation was used to estimate serum sodium, potassium and chloride. The Hb concentration was determined by cyannmethaemoglobin method and Hct values were determined with microhaematocrit method as described by Benjamin (1978). Serum sodium (Na^+), potassium (K^+) and chloride (Cl^-) contents were determined with the help of Electrolyte Analyzer (Medica Corporation, Bedford, UK). Changes in relative plasma volume (rPV) were calculated from Hb concentration and Hct, using accepted formula (Greenleaf *et al*., 1979; Tyler *et al*., 1994). All the above parameters and survival index were recorded at baseline (before start of disease), 1, 3, 6, 12 and 24 hours after the start of treatment with or without hypertonic saline solution.

Statistical analysis

Statistical analyses were performed using student t-test. All analyses were performed using the Statistical Software Package (SPSS Version 11.5). Statistical significance was assigned at $P<0.05$.

RESULTS

As shown in Table 1, baseline values for the systemic parameters of both the groups differed non-significantly. After initiation of the respective treatments, the results were as under:

Clinical parameters

Buffaloes of group B showed significantly higher ($P<0.05$) survival rate (80%) as compared to 48% in group A at 24 h after HSS treatment (Table 1). Difference in survival index was evident between the two groups within 3 hours. Elevated body temperature was noted during the course of disease in animals of the both groups. After respective treatments, fall in the temperature was noted in the both groups but decline in rectal temperature was more rapid in animals of group B and it was near normal within 3 hours and was normal within 6 hours (Fig. 1). But in animals of group A, a fluctuating pattern was noted in the body temperature and it became normal after 12 hours.

There was difficult breathing in animals suffering from HS and lowered respiration rate was recorded. After treatment, mild change was observed toward normal in animals of group A, while the buffaloes of group B which were treated with HSS in combination with antibiotic and non-steroidal anti-inflammatory drug showed rapid improvement towards normal and respiration rate became normal within 12 hours (Fig. 2). After 24 hours, respiration rate was almost normal in animals of group A.

A sharp decrease in heart rate was recorded during the course of HS in all animals. After treating animals with HSS, it increased more rapidly in group B compared to its counterpart. In group A, a decreasing trend was recorded initially in heart rate after treatment. Although it increased later but could not achieve the normal values even after 24 hours. On the other hand, animals of group B showed good recovery and values became normal within 6 hours (Fig. 3).

Haematological parameters

Concentration of Hb in HS suffering animals was lower than the reference values. After instituting the respective treatments, animals of group B showed significant difference ($P<0.05$) in achieving the normal values (reference value: 12-15 g/dl) of Hb concentration within three hours when compared to group A (Table 1). Animals of group A achieved normal values within experimental time but group B showed better recovery and significant difference ($P<0.05$) over group A.

Haematocrit was also decreased than the normal values (reference value: 30-35%) in diseased buffaloes. After HSS treatment, the Hct values increased rapidly toward normal in group B and showed significant difference ($P<0.05$) over group A throughout the experimental period from 3rd hour. In group A, values of Hct increased slowly and attained the normal values up to 24 hours (Table 1). On the other hand, animals of group B achieved normal values within 3 hours, which were maintained for whole of the study period.

Animals suffering from HS showed decreased values of relative plasma volume (rPV). After initiation of treatment, rapid increase in rPV was recorded in animals

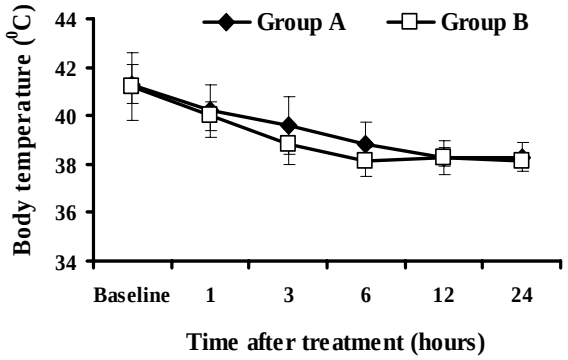

Fig. 1: Body temperature (^{0}C) in buffaloes suffering from haemorrhagic septicaemia before and after treatment (reference value: 38.3-38.5^{0}C).

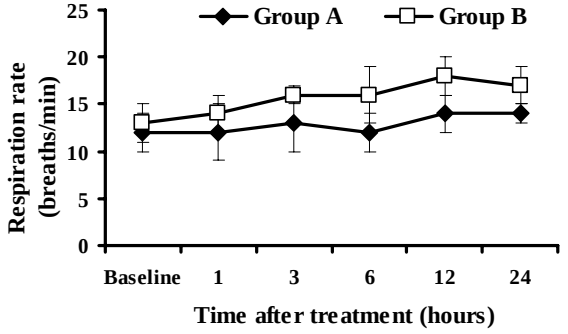

Fig. 2: Respiration rate in buffaloes suffering from haemorrhagic septicaemia before and after treatment (reference value: 15-20 breaths/ min).

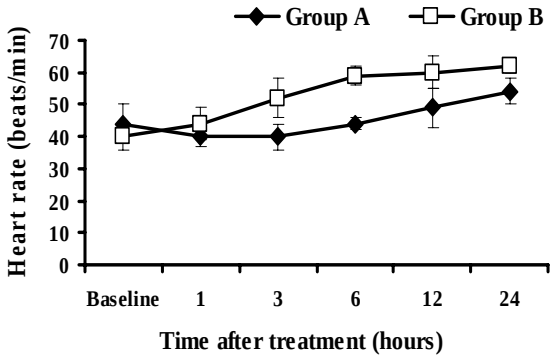

Fig. 3: Heart rate (beats/min) in buffaloes suffering from haemorrhagic septicaemia before and after treatment (reference value: 60-70 beats/min).

of group B which were treated with HSS along with ceftiofur HCl and ketoprofen, while a slow increasing trend was observed in animals of group A. The values of rPV were normal within 6 hours in group B, while it did not become normal throughout the study period in buffaloes of group A (Fig. 4).

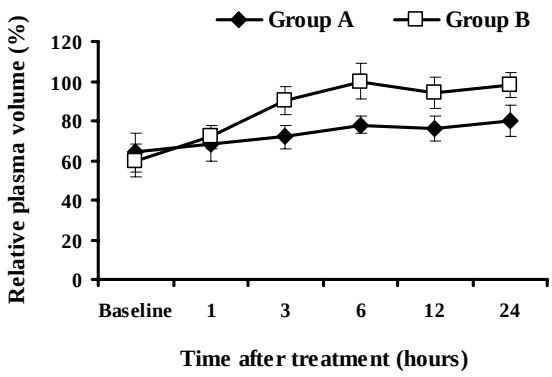

Fig. 4: Relative plasma volume (%) in buffaloes suffering from haemorrhagic septicaemia before and after treatment (reference value: 95-100%).

Serum electrolytes

Sodium ions (Na^+) concentration increased during disease in all the animals of the both groups than the normal (reference value: 130-135 mEq/L). After treatment, serum sodium concentration decreased in animals of group A ($P<0.05$) toward normal (Table 1), while group B showed increase in concentration of Na^+ ions during the first 3 hours when values reached up to 162 ± 3 mEq/L but after 3 hours, the trend became reverse and values decreased to reference values within 24 hours.

Chloride ions (Cl^-) concentration also showed the same trend as sodium ions. After instituting respective treatments, group A showed good recovery towards normal (reference value: 95-105 mEq/L) and significant differences ($P<0.05$) were observed over group B from 3rd to 12th hour of treatment (Table 1). In group B, rapid decrease in the Cl^- concentration was observed after 6th hour and became normal within the experimental period (Table 1).

A decrease was noted in the potassium ions (K^+) concentration during disease condition in all the animals. After administration of allotted treatments to the animals of both the groups, non-significant differences were observed at each observational time in recovering the values towards normal (reference value: 4-5 mEq/L: Table 1), and it never became normal within 24 hours in both the groups. So, there was non-significant difference between groups A and B regarding K^+ ions concentration.

DISCUSSION

Endotoxins have profound effects on the circulatory system including myocardial depression, pronounced vasodilatation and alterations in the endothelial barrier which result in hypovolaemia and decreased cardiac output. It is, therefore, of great importance to maintain an adequate cardiac output and blood pressure through restoration of intravascular volume. Thus, in addition to antibiotic therapy, fluid administration plays a pivotal role in the management of sepsis and septic shock (Gow *et al*., 1998; Zafar *et al*., 2009).

Table 1: Survival index, haematological parameters and serum electrolytes for samples obtained from buffaloes suffering from haemorrhagic septicaemia before and after treatment in both groups

Variables	Groups	Time after treatment (hours)					
		Baseline	1	3	6	12	24
Survival index	Group A	25	23	19	15	12	12
(No. of buffaloes)	Group B	25	25	24*	23*	20*	20*
Hb concentration	Group A	10.4 ± 0.8	10.2 ± 1.4	10.8 ± 1.2	11.2 ± 0.9	11.4 ± 1.3	12.8 ± 1.6
(g/dl)	Group B	9.80 ± 1.2	10.6 ± 0.8	12.2 ± 0.4*	12.8 ± 1.1*	14.2 ± 1.6*	14.4 ± 1.2*
Haematocrit (%)	Group A	26 ± 1.8	27 ± 2.0	27 ± 1.8	28 ± 1.1	29 ± 2.1	30 ± 2.8
	Group B	25 ± 1.4	28 ± 1.6	30 ± 2.2*	32 ± 1.8*	35 ± 2.6*	35 ± 1.8*
Sodium (mEq/L)	Group A	145 ± 6	145 ± 3*	142 ± 2*	140 ± 2*	136 ± 4*	138 ± 2
	Group B	142 ± 4	154 ± 4	162 ± 3	154 ± 2	146 ± 3	136 ± 3
Chloride (mEq/L)	Group A	110 ± 1.8	110 ± 2.0	107 ± 1.2*	105 ± 2.3*	106 ± 3.4*	104 ± 3.0
	Group B	112 ± 2.0	116 ± 1.4	120 ± 1.8	118 ± 2.8	114 ± 1.1	106 ± 2.4
Potassium (mEq/L)	Group A	3.2 ± 0.86	3.2 ± 0.88	3.3 ± 0.90	3.5 ± 1.0	3.7 ± 0.64	3.8 ± 0.66
	Group B	3.0 ± 0.98	2.9 ± 0.68	2.8 ± 1.10	3.2 ± 1.2	3.6 ± 0.88	3.8 ± 0.86

*Significantly different from other group ($P<0.05$).

In the present study, a treatment protocol was constructed in which animals were treated with the bolus intravenous infusion of 7.5% NaCl solution in combination with intramuscular administration of Ceftiofur HCl and intravenous administration of ketoprofen (non-steroidal anti-inflammatory drug). The survival rate among animals treated with protocol A and B was 48 and 80 percent, respectively. This higher (80%) recovery rate in group B was attributed to the addition of hypertonic saline solution in the treatment protocol. These findings are in agreement with the results reported by Raza *et al*. (2000).

Sodium (Na^+) concentration, if increased, is capable of elevating extracellular volume more than the transfused amount, so, it is of great importance to resuscitate the patient from septic shock (Constable, 1999). Hypertonic saline solution infusion to the septic shocked buffaloes induced significant increase in serum osmolality, however, animals were at risk of salt poisoning (Tyler *et al*., 1994; Ajito *et al*., 1999). In our study, the administration of 4 ml/Kg of HSS produced transient high sodium level that crossed the cut-off point of hypernatraemia (160 mM/l) for a short interval but after 3 hours its value became normal within 12 hours and no adverse effects were observed. These results are in line with the results reported by other scientists (Velasco *et al*., 1980; Tyler *et al*., 1994; Constable *et al*., 1996). Minor decrease in potassium concentration after HSS infusion has been observed previously (Constable *et al*., 1991; Suzuki *et al*., 1998), but was not considered clinically important.

Reduced plasma volume resulted in decreased cardiac output, with weak and declined heart rate. In group B, HSS rapidly increased Hct and Hb concentration and played a pivotal role in restoring plasma volume and also increased osmosis and ultimately blood pressure and heart rate (Constable *et al*., 1991; Tyler *et al*., 1994). As no fluid was administered in animals of group A, Hct and Hb concentration remained below the normal limits which ultimately resulted in decreased plasma volume and lowered heart rate. These observations strongly recommend that fluid administration is the basic tenet to resuscitate the patients from septic shock.

Higher recovery rate in animals of group B seems because of the administration of hypertonic saline solution, while buffaloes treated with the conventional treatment did not show satisfactory recovery rate because these animals were not administered with any fluid. Repetition of Ceftiofur HCl at 12 hour interval is the frequency recommended by manufacturer instead of 24 hours intervals because our own observations and those of Raza *et al*. (2000) have indicated that the HS cases respond temporarily with partaking of feed and water but worsened again if the repetition is deferred until 24 hours.

Conclusion

It was concluded from the study that hypertonic saline solution as an adjunct to antibiotic (ceftiofur HCl) and a non-steroidal anti-inflammatory drug (ketoprofen) efficiently improved respiration and heart rates and effectively restored plasma volume in resuscitating the buffaloes from haemorrhagic septicaemia than the conventional treatment.

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