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Comparison of a small volume of hypertonic saline solution and dextran 40 on hemodynamic alternations in conscious calves

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The hemodynamic effects of rapid intravenous (IV) administration of 10% dextran 40 in saline solution (D40) and 7.2% hypertonic saline solution (HSS) in calves were compared. Calves received isotonic saline solution (ISS), HSS or D40 (3 calves/group) and were monitored of blood pressure, and cardiac output (CO) for 180 min. HSS and D40 infusions induced a significant increase in relative plasma volume reaching 134.9 ± 2.8 and 125.0 ± 1.9%, respectively at the end of fluid infusion. In the HSS group, CO, cardiac index (CI) and stroke volume (SV) remained constant at low levels after 90 minutes despite the maximal values of CO, CI and SV at the end of infusion, reaching 21.0 ± 6.3 l/min (p<0.05), 177.8 ± 14.2 ml/min/kg (p < 0.001) and 0.20 ± 0.03 l/beat (at t = 10 min, p < 0.001), respectively. In contrast, CI and SV in the D40 group showed significant increases to 14.7 ± 2.9 l/min and 153.5 ± 17.2 ml/min/kg, respectively, at the end of fluid infusion. And those values remained constant at higher levels than those of the before infusions values throughout the experimental periods. Positive effects for hemodynamic alternations of D40 in calf practice were milder and longer than those of HSS. Therefore, the D40 infusion should be explored as a possible treatment for dehydrated calves, since rapid infusion of D40 may be safe and more beneficial for rehydrating more than HSS treatment.

Key words: calf, cardiac output, dextran, hemodynamic, hypertonic saline

Calf diarrhea remains a major cause of economic loss to cattle industry [1]. The cost-effective use of electrolyte containing oral rehydration solution for treatment of diarrheic calves is popular and widely accepted, despite progress in the understanding of the pathophysiology of the disease, [1,14]. If treatment with oral fluids is not successful, intravenous restoration of circulation volume is preferred. The goal of intravenous fluid therapy in dehydrated calves is to correct extracellular dehydration and restore circulating plasma volume.

The colloidal solutions, such as albumin, dextran, and hetastarch, are extremely effective volume expanders [4] and used for fluid resuscitations in hypovolemic patients [6], horses [9] and dogs [17]. Increasing colloidal osmotic pressure (COP) with colloidal products has remained an attractive theoretical premise for volume resuscitation. Especially, dextran has considerable advantage over other types of colloids for initial hypovolemia treatment due to its antithrombotic properties whereby cell aggregability is prevented and the incidence of system complications is convincingly reduced [6]. Van Den Broke *et al*. [20] suggested that dextran 40 (D40) can be recommended as a plasma substitute due to its higher initial increase in circulating plasma volume for humans, its moderate duration of effect and its low incidence of anaphylactic reaction.

Therefore, administration of a small-volume of D40 should be checked for safety and efficacy of hemodynamic responses before being recommended for the treatment of hypovolemic calves. The purposes of this study were to compare effects of rapid intraveneus infusion (IV) of a small volume of D40 and those of IV infusion of an equivalent volume of 7.2% hypertonic (HSS) and 0.9% isotonic saline solutions (ISS) on plasma volume and hemodynamic status of calves.

Materials and Methods

All procedures were in accordance with the National Research Council on Guide for the Care and Use of Laboratory Animals [13]. Experiments were performed on 9 healthy 3-month-old Holstein calves weighing 106.1 ± 26.0

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kg. Healthy calves were selected on the basis of physical examination, electrocardiography and hematological analysis. A well-balanced growth diet consisting of pelleted concentrated ration and mixed grass hay and free access to fresh water were provided until the day before the experiment.

The day prior to the experiment, all calves were sedated with an IV infusion of xylazine hydrochloride (Seduluck-2%; Nippon Zenyaku, Japan) as a dose of 0.2 mg/kg of body weight. An 8-F introducer (Fast-Cath; Nihon Koden, Japan) was placed in the left jugular vein. A 14-gauge, 40-cm length arterial and 15-cm length venous catheters (Sefelet Catheter NCKP-14; Nipro, Japan) were inserted in the right femoral artery and vein, respectively. After 24 h of catheterization, infusion of resuscitated fluid was initiated. Approximately 1 hour before fluid infusion, 16-gauge catheter (Sefelet Catheter NSL-16WOT; Nipro, Japan) was implanted percutaneously into the right jugular vein for fluid infusion. A balloon-tipped, flow directed thermo-dilution catheter (TC-704; Nihon Koden, Japan), which was used for measurement of cardiac output (CO) and pulmonary arterial pressure (PAP), was inserted through the introducer into the left jugular vein. This catheter was positioned with the proximal port in the right atrium and the distal port and thermistor in the pulmonary artery. Various pressures (systemic, central venous pressure (CVP) and PAP) were measured, using the bedside monitoring system (BP-308ETI; Nihon Koden, Japan) with a strain-gauge transducer (DX-360; Nihon Koden, Japan) positioned at the level of the point of the shoulder. All catheter positions were confirmed by the evidence of characteristic pressure waveforms. The transducers were calibrated with a water manometer before use. A base-apex electrocardiograph was continuously monitored throughout the experiment to detect any arrhythmias. Food and water were withheld from calves during the experiment.

After preparations, calves were monitored for 15 min to ensure hemodynamic stability. Calves were randomly divided into 1 of 3 groups (n = 3/group). Calves in each group were assigned to receive 5 ml/kg of ISS, HSS or D40 infusion at a flow rate of 20 ml/kg/hr via the right jugular vein catheter using infusion pump (PRS-25; Nikkiso, Japan). All calves were then monitored for 180 min. Arterial and venous samples were collected at time 0 (pre), and 5, 10, 15, 30, 45, 60, 90, 120, 150 and 180 minute after initiation of fluid infusion. Before collection of each blood sample, systolic (SAP), diastolic (DAP) and mean systemic pressure (MAP), mean PAP and CVP, heart rate (HR) and abnormal signs were recorded. Immediately after the recording was completed, CO was determined after ice-cold isotonic dextrose (5 ml) was injected into the right atrium at end-expiration of the ventilatory cycles using a bedside moritoring system. All CO measurements were performed in triplicate, and a mean value was determined for the 3 values. Cardiac index (CI: CO/body weight, l/min/kg), stroke volume (SV: CO/HR, l/beat), systemic vascular resistance (SVR: [MAP/CO] × 80, mmHg/l/min) and pulmonary vascular resistance (PVR: [PAP/CO] × 80, mmHg/l/min) were calculated [14].

Venous samples were collected at each recording point and used to determine hemoglobin concentration (Hb) and hematocrit values (Ht) using an automatic cell counter (MEK-6248; Nihon Koden, Japan). Other blood samples were centrifuged, and plasma was collected and stored at –20°C until assay. Changes in relative plasma volume (rPV) were calculated from Hb and Ht [18,19]. Plasma sodium, potassium and chloride concentrations were analyzed by electrode methods, using an automatic analyzer (Model 644; Bayer Medical, Japan). Plasma osmolarity was determined by use of the freezing point depression method using an osmometer (One-Ten Osmometer; Fiske, USA).

To test changes with time, data for each group were analyzed by repeated-measures ANOVA followed by the Bonferroni test. To test differences among groups, data for each time point were analyzed by one-way ANOVA and the Bonferroni test. Data represent as mean ± SD. For all analyses, values of $p < 0.05$ were considered significant [15].

Results

All calves were verified as clinically normal before the experiment based upon the assessment of their vital signs, attrition, food and water intake, and urine and feces production. Clinical signs, such as moist rales on ausculation, moist cough, jugular vein congestion, ophthalmoptosis, salivation or arrhythmia were not observed throughout the experiment. Sequential change in rPV was monitored in calves given D40 infusion (Fig. 1). There was a slight increase in the rPV of the ISS group, reaching 107.3 ± 3.1%. For the HSS and D40 groups, a progressive and significant increase in rPV was observed, reaching 134.9 ± 2.8% and 125.0 ± 1.9%, respectively, at the end of fluid infusion. These increases were greater than that for the ISS group. The pre-values of HR, SAP, MAP, DAP, PAP and CVP were 86.7 ± 15.9 bpm, 129.3 ± 8.6, 99.2 ± 5.1, 74.7 ± 5.7, 24.1 ± 4.3 and 0.7 ± 2.0 mmHg, respectively (Table 1). There was slight increase in the CVP of the ISS group, reaching 2.7 ± 0.6 mmHg at the end of fluid infusion. For the HSS and D40 groups, a progressive and significant increases in CVP were observed, reaching 6.0 ± 0.0 and 5.3 ± 0.6 mmHg, respectively, at the end of fluid infusion. The CVP increase of the HSS group was significantly greater than that for the other groups ($p < 0.05$). The mean values of HR, SAP, MAP, DAP and PAP were not affected by ISS, HSS or D40 infusion and remained constant throughout the experiment in all groups

The mean values of CO, CI, SV, SVR and PVR before infusion were 11.5 ± 1.7 l/min, 113.6 ± 8.6 ml/min/kg, 0.14

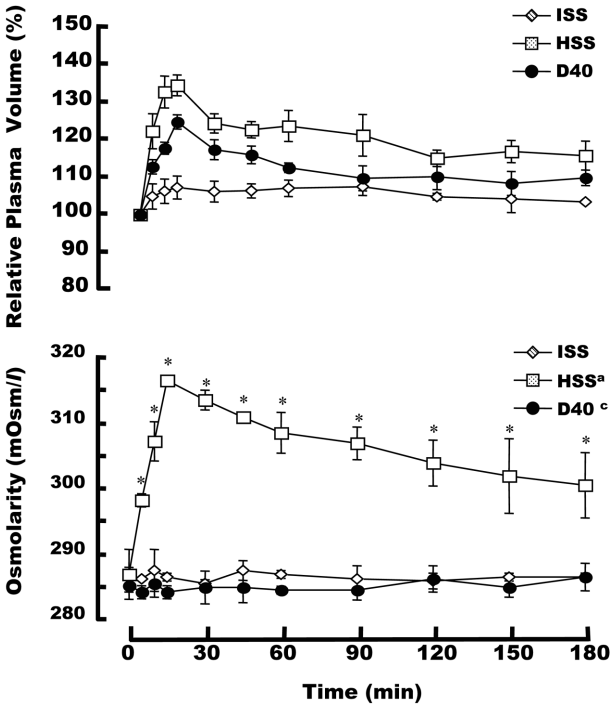

Fig. 1. Graphs depicting the relative plasma volume (rPV) and osmolarity in calves given 10% dextran 40 in saline or 7.2% hypertonic saline solution. Levels of significance (p<0.05) indicated: a: ISS versus HSS, b: ISS versus D40, c: HSS versus D40 and asterisk: versus pre-values by Bonferroni test.

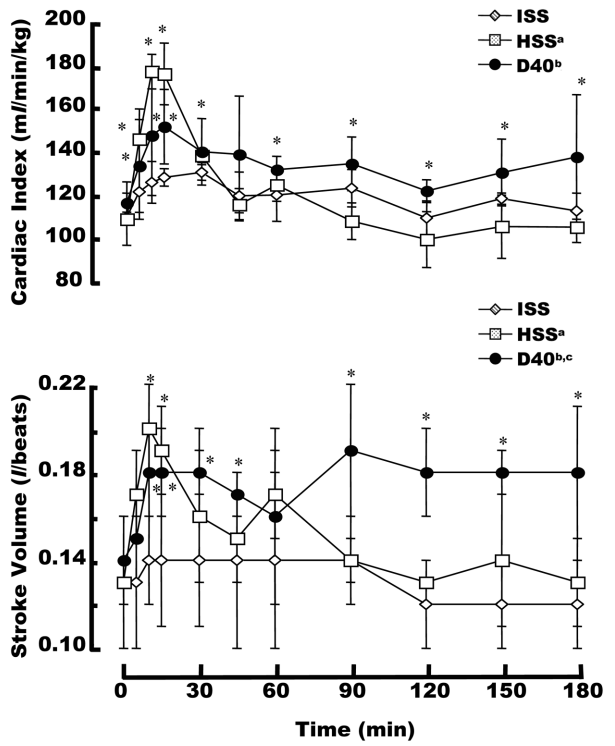

Fig. 2. Graphs depicting the cardiac index (CI) and stroke volume (SV) in calves given 10% dextran 40 in saline or 7.2% hypertonic saline solution.

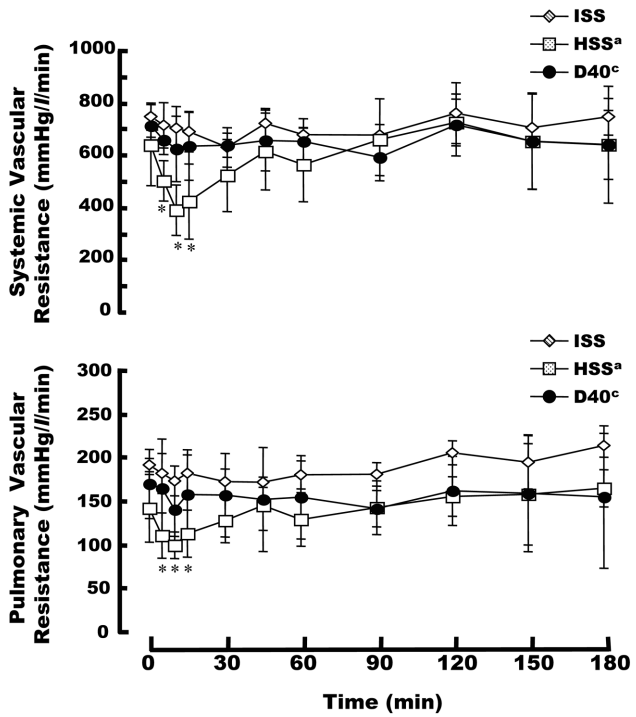

Fig. 3. Graphs depicting the systemic (SVR) and pulmonary vascular resistance (PVR) in calves given 10% dextran 40 in saline or 7.2% hypertonic saline solution.

± 0.03 l/beat, 700.4 ± 96.6 and 170.2 ± 35.9 mmHg/l/min, respectively. Those values in ISS group were slightly increased from the pre-values until the end of fluid infusion. In the HSS group, CO, CI and SV remained constant at low levels after 90 min despite the increasing maximal values of CO, CI and SV at the end of infusion, reaching 21.0 ± 6.3 l/min ($p < 0.05$), 177.8 ± 14.2 ml/min/kg ($p < 0.001$) and 0.20 ± 0.03 l/beat (at t = 10 min, $p < 0.001$), respectively (Fig. 2). In contrast, CI and SV in the D40 group showed significant increases to 14.7 ± 2.9 l/min and 153.5 ± 17.2 ml/min/kg, respectively, at the end of fluid infusion. Those values remained constant at higher levels than those of the pre-values throughout the experiment.

The SVR and PVR in ISS and D40 groups were not affected by ISS or D40 infusion and remained constant throughout the experiment (Fig. 3). However, SVR and PVR in the HSS group were progressively and significantly decreased from the pre-values, reaching 393.3 ± 95.8 and 100.8 ± 15.5 mmHg/l/min at 10 minutes, respectively. SVR and PVR were significantly ($p < 0.001$) lower than the other groups during HSS infusion.

The mean values of plasma sodium, potassium and chloride concentrations, and osmolarity were 139.8 ± 2.0, 4.38 ± 0.27 and 102.3 ± 3.0 mEq/l, and 285.7 ± 2.2 mOsm/l, respectively. Those values remained without changes after administration of ISS or D40, and remained constant throughout the experiment. However, plasma sodium and

Table 1. Hemodynamic and plasma electrolytes alternations of 10% dextran 40 in saline (D40) or 7.2% hypertonic saline solution (HSS) administered IV in calves (mean±SD)

	0	5	10	15	30	45	60	90	120	150	180
Heart Rate (bpm)											
ISS	86.7±19.1	93.0±20.9	90.7±24.0	92.7±19.3	91.7±8.9	85.2±23.2	86.7±22.1	83.7±12.5	89.0±17.3	97.0±23.5	94.0±24.3
HSS	95.7±10.7	102.7±10.1	105.7±13.1	111.3±13.9	100.3±11.5	90.3±15.0	88.7±16.7	89.7±15.3	90.7±18.6	89.7±15.7	91.3±11.6
D40	77.7±16.9	84.7±16.7	78.0±16.1	81.7±18.1	78.3±19.9	78.7±16.3	83.0±7.8	72.0±15.4	73.0±23.9	69.7±11.2	74.0±17.3
Cardiac Output (l/min)											
ISS	10.6±0.5	11.6±0.9	12.1±0.8*	12.3±0.8*	12.5±0.1*	11.5±1.3	11.5±1.0	11.8±0.5	10.5±0.5	10.5±0.9	11.4±0.3
HSS[a]	12.8±2.4	17.1±3.4	20.9±5.1*	21.0±6.3*	16.4±4.3	13.7±3.2	14.7±3.5	12.7±2.7	11.7±2.7	11.7±2.5	12.5±3.3
D40[b,c]	10.6±2.4	12.8±1.0	14.2±2.6	14.7±2.9*	13.5±1.8	13.3±2.2	12.8±2.3	13.1±2.5	11.9±2.5	11.9±2.4	12.7±3.0
Systolic Arterial pressure (mmHg)											
ISS	128.0±9.5	131.7±12.7	133.3±10.8	131.0±13.2	126.0±16.1	134.0±11.4	128.0±18.2	129.0±11.3	125.0±13.1	126.3±4.2	123.7±5.5
HSS	126.3±6.0	130.0±2.0	122.7±5.9	127.3±4.6	127.3±2.5	127.3±3.1	127.3±7.2	129.0±10.1	131.3±7.5	125.0±10.1	123.7±9.9
D40	134.0±10.8	136.0±9.6	136.3±11.2	138.7±9.3	137.7±3.5	137.3±12.2	132.0±13.1	129.7±13.1	135.0±5.6	133.3±9.6	132.3±16.1
Mean Arterial Pressure (mmHg)											
ISS	98.7±5.5	103.7±9.7	105.7±5.9	106.0±8.2	98.7±12.5	103.3±4.6	97.7±10.1	100.0±6.2	99.3±9.3	100.3±2.9	100.7±0.6
HSS	99.0±3.6	105.3±7.6	98.7±8.1	104.0±6.1	102.7±4.2	101.3±3.1	100.0±5.2	101.7±8.3	104.3±11.0	97.0±9.6	96.7±8.3
D40	100.0±7.8	105.0±9.8	108.7±10.0	114.0±6.1	107.7±12.7	107.7±8.6	103.0±10.3	95.7±9.8	104.3±4.5	100.0±6.6	101.3±12.6
Diastolic Arterial Pressure (mmHg)											
ISS	75.7±2.1	79.7±8.1	81.3±1.5	81.7±3.5	75.0±11.5	80.7±0.6	73.3±8.1	76.3±6.4	76.0±7.8	82.0±5.6	75.3±0.6
HSS	73.7±4.9	82.3±9.1	72.7±11.7	76.3±9.7	78.7±4.2	77.3±5.5	76.3±4.0	81.7±9.9	84.3±2.2	75.0±10.1	74.0±6.2
D40	74.7±10.0	81.0±14.2	84.3±9.5	88.0±3.5	84.3±16.1	84.3±9.3	79.0±7.2	73.3±8.5	79.3±5.5	73.3±12.2	79.3±14.0
Pulmonary Arterial Pressure (mmHg)											
ISS	25.7±1.5	26.7±1.5	26.3±2.9	28.3±2.9	27.3±0.4	25.0±2.0	26.3±3.8	27.0±1.0	27.3±1.5	28.0±3.6	29.3±2.3
HSS	22.3±4.5	23.3±4.2	25.7±3.5	28.7±4.7	26.0±3.0	24.7±5.5	23.7±6.4	22.7±5.5	23.0±6.1	23.7±6.4	25.7±5.0
D40	24.3±6.4	26.3±7.6	24.7±2.5	28.3±4.5	26.3±5.5	24.7±5.5	24.7±6.1	23.3±4.7	24.0±5.0	24.3±5.5	24.0±5.6
Central Venous Pressure (mmHg)											
ISS	0.7±2.3	1.0±1.7	1.3±3.1	2.7±0.6	1.3±2.1	-1.0±4.4	-0.7±2.5	0.0±2.0	0.3±1.2	0.3±0.6	-0.3±2.1
HSS[a]	0.3±0.6	4.3±4.0*	4.0±1.0*	6.0±0.0*	4.3±2.1*	4.7±1.5*	5.0±2.6*	2.7±2.1	3.3±3.2	1.7±3.1	1.0±2.6
D40[b,c]	0.7±2.0	1.7±1.5	4.0±1.0*	5.3±0.6*	4.3±1.2*	3.3±1.5	2.3±1.5	1.7±0.6	2.0±1.7	1.7±1.5	1.7±0.6
Sodium (mEq/l)											
ISS	140.3±2.1	140.0±2.0	140.0±2.0	140.0±2.0	140.3±2.1	140.3±2.1	141.7±0.6	141.7±0.6	142.0±1.0	142.0±1.0	142.0±1.0
HSS[a]	139.3±0.6	145.7±1.5*	150.7±2.5*	155.7±1.5*	153.7±1.2*	152.7±1.2*	151.7±1.2*	150.7±1.2*	149.7±1.2*	149.3±1.5*	149.0±2.0*
D40[c]	139.7±3.2	139.7±3.2	139.3±3.1	139.3±2.9	139.7±3.2	139.7±3.2	140.0±3.6	140.7±3.2	141.0±3.6	141.0±3.6	141.0±3.6
potassium (mEq/l)											
ISS	4.30±0.14	4.24±0.15	4.21±0.28	4.18±0.17	4.20±0.10	4.25±0.29	4.34±0.24	4.28±0.31	4.41±0.29	4.28±0.20	4.50±0.26
HSS[a]	4.40±0.18	4.05±0.09*	3.80±0.07*	3.61±0.14*	3.83±0.06*	3.94±0.06*	3.94±0.05*	3.98±0.14*	3.93±0.12*	3.98±0.19*	4.02±0.13*
D40[c]	4.45±0.48	4.24±0.42	4.20±0.44	4.23±0.44	4.30±0.43	4.19±0.42	4.33±0.55	4.32±0.50	4.24±0.43	4.29±0.31	4.27±0.34
Chloride (mEq/l)											
ISS	103.7±0.6	104.7±1.5	105.7±1.5	105.7±1.5	105.7±1.5	106.7±0.6	106.0±1.0	107.0±1.0	107.7±0.6	109.0±1.0	108.0±1.0
HSS[a]	100.3±4.0	109.3±5.0*	115.7±5.5*	121.3±5.0*	118.3±3.5*	117.3±3.5*	115.7±3.1*	114.0±2.6*	113.3±2.3*	113.3±2.3*	112.7±2.9*
D40[c]	103.0±3.0	104.0±2.0	105.0±2.0	104.7±2.5	104.7±2.5	105.0±2.0	103.7±2.5	104.0±2.6	105.3±2.1	105.3±2.1	106.0±1.7

Levels of significance indicated ($p < 0.05$) a: ISS vs HSS, b: ISS vs D40, c: HSS vs D40, *: vs pre-value by Bonferroni test.

chloride concentrations (Table 1), and osmolarity (Fig. 1) in HSS group were progressively and significantly increased from the pre-values until the end of HSS infusion, reaching 155.7 ± 1.5 and 121.3 ± 5.0 mEq/l, and 316.3 ± 0.6 mOsm/l, respectively ($p < 0.001$). The sequential changes in plasma sodium and chloride concentrations, and osmolariy in the HSS group were significantly greater than those in the other groups ($p < 0.001$). In the HSS group, plasma potassium concentrations were progressively and significantly decreased from the pre-values until the end of HSS infusion, reaching 3.61 ± 0.14 l/min (Table 1, $p < 0.001$).

Discussion

Intravenous infusion of a small volume of 10% dextran 40 in saline or 7.2% hypertonic saline solutions to normal, 3-months old Holstein calves were found to be effective in increasing plasma volume. Although the increase in rPV of D40 group was lower than that of HSS group at the end of the fluid infusion, the increases in rPV remained up to 10%

higher than pre-values in the D40 group throughout the experiment. While IV infusion of HSS induced the dramatically altering hemodynamic status, the positive effects of HSS were not persistent. In contrast, the positive effects of D40 were mild but persistent, since increases in CI and SV caused by D40 infusion remained higher than the pre-values until the end of the experiment. It is suggested that D40 infusion should be explored as a treatment for dehydrated calves since rapid infusion of D40 may be safer and more beneficial for rehydrating calves than HSS treatment. In addition, as HSS travels through the pulmonary artery, a variety of reflexes are stimulated which result in increased CO and renal perfusion [1-3,18,19,21]. A number of studies [1-3,21] have documented clinical benefits of HSS resuscitation on severely hypovolemic calves with diarrhea. However, because of an induced natriuresis and rapid redistribution of sodium molecules, the positive effects of HSS are short-lived [11]. In this study, while IV infusion of HSS induced the dramatically altering hemodynamic status, the positive effects of HSS are short-lived. Although correcting dehydration with rapid administration of a small volume of HSS, which successfully restores the circulating plasma volume of the dehydrated calf, HSS should not be used in the initial stabilization if dehydration is moderate or severe. Because it pulls fluid from the interstitial and the interstitial is already depleted [12] in this dehydrated animals.

Colloids are clearly more efficient than crystalloids in attaining resuscitation endpoints as judged by the need for administration of a far smaller fluid volume. Colloid solutions have been developed and used over the past 70 years as expanders of the intravascular space [16]. Colloid containing solutions seem superior to crystalloid solutions due to efficient re-expansion of circulating plasma volume and enhancement of capillary blood flow [7]. Therefore, colloids can be considered in hypovolemic calves with diarrhea resulting from plasma loss, because the fluid resuscitation of hypovolemia with colloidal solutions increases COP and requires less volume of resuscitative fluid. In addition, colloids may be combined with crystalloids to obviate administration of large crystalloid volumes [5]. Hiippala and Teppo [8] demonstrated that dextran produced greater plasma volume expansions than hydrocyethyl starch, and volume effect of Ringer's solution was clearly exceeded by both colloids. Van Den Broke *et al*. [20] suggested that D40 can be recommended as a plasma substitute due to its higher initial increase in circulating plasma volume, its moderate duration of effect and its low incidence of anaphylactic reaction. Therefore, administration of a small-volume D40 should be confirmed for safety and efficacy of hemodynamic responses before being recommended for the treatment of hypovolemic calves.

More than three times the volume of crystalloids had to be substituted as compared to Dextran solution for maintenance of plasma volume and left ventricular filling pressure [10]. In addition, CO remained higher in the treatment with D40 than that with Lactated Ringer's [10]. In the present, D40 infusion induced significant increases in CO, CI and SV, reaching 14.7 ± 2.9 l/min, 153.5 ± 17.2 ml/min/kg and 0.18 ± 0.04 l/beat, respectively at the end of the fluid infusion. And those values remained constant at higher levels than those of pre-values throughout the experimental periods. Although the increases in plasma volume caused by the 5 ml/kg D40 infusion were lower than that by HSS infusion, CO and SV remained constant higher during the experimental periods. In the present, we demonstrated that the positive effects for hemodynamic alternations of D40 in calf practice were milder and longer than those of HSS. Therefore, D40 infusion should be explored as a treatment for dehydrated calves, since rapid infusion of D40 may be safer and more beneficial for rehydrating calves than HSS treatment.

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