Kocatepe Vet J (2014) 7(1): 39-46
DOI: 10.5578/kvj.7375
Submittion: 12.03.2014
Accepted: 25.03.2014

RESEARCH ARTICLE

ARAŞTIRMA MAKALESİ

The Time Dependent Effects of Intravenous Administration of Isotonic Sodium Bicarbonate On Venous Acid-Base Status and Renal Function In Neonatal Calves with Acute Diarrhea#

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Key Words
Blood gases
Dehydration
Hyperkalemia
Kidney
Metabolic acidosis

Anahtar Kelimeler
Kan Gazları
Dehidrasyon
Hiperkalemi
Böbrek
Metabolik Asidoz

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#This study was performed with the permission of; Afyon Kocatepe University, Experimental Animals Local Ethic Committee at the date of 14.06.2012 and the number of 195 and supported by AKU BAPK (Project No: 2.SAG.BIL.14). It collected from graduate school thesis of Suleyman Zeybek.

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S U M M A R Y

This study investigates time-dependent effects of intravenous administration of isotonic sodium bicarbonate on venous acid-base status and renal function in neonatal calves with acute diarrhea. The etiologic diagnosis was not taken into consideration in this study. The material consists of 10 neonatal calves (1-30 days old) which were accepted to the clinic with complaints of acute diarrhea. Following the intravenous administration of calculated total sodium bicarbonate on the calves in the form of isotonic solution blood samples were collected pre-treatment and post-treatment: 15th min, 30th min, 1st hrs, 2nd hrs, 3rd hrs, 4th hrs, 6th hrs, 12th hrs and 24th hrs later. Based on the intra-group assessments at different measurement times, the study results revealed a statistically significant difference in pH, bicarbonate (HCO_3^-), basicity (BE), partial carbondioxide pressure (PCO_2), total carbondioxide concentration (TCO_2), potassium (K^+) and AST blood levels of the calves with diarrhea. A numerical decrease was determined in the post-treatment period despite the absence of a significant difference in serum concentrations of urea and creatinine as shown by the intra-group statistical assessments conducted in line with measurement times. The obtained data revealed that primary simple metabolic acidosis occurring in calves in relation to acute diarrhea can be treated successfully with the administration of intravenous isotonic sodium bicarbonate. According to the results, renal function deterioration should be considered along with the metabolic acidosis during the determination of treatment protocol and prognosis. The submitted study emphasizes the importance of hours 12 and 24 post-treatment for blood acid-basis status and renal function, respectively.

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Akut İshalli Neonatal Buzağılarda İntravenöz İzotonik Sodyum Bikarbonat Uygulamasının Venöz Asit-Baz Durumu ve Renal Fonksiyon Üzerine Zamana Bağlı Etkileri

ÖZET

Sunulan araştırmada akut ishalli neonatal buzağılarda intravenöz izotonik sodyum bikarbonat uygulamasının venöz asit-baz durumu ve renal fonksiyon üzerine zamana bağlı etkileri araştırıldı. Çalışmada etiyolojik tanı dikkate alınmamıştır. Materyali; yaşları 1-30 gün arasında değişen akut ishal şikayeti ile kliniğe başvuran 10 neonatal buzağı oluşturdu. Çalışma kapsamında, hesap edilen total bikarbonat ihtiyacı izotonik solüsyon tarzında intravenöz yolla buzağılara verildikten sonra, tedavi sonrası; 15. dakika, 30. dakika, 1. saat, 2. saat, 3. saat, 4. saat, 6. saat, 12. saat ve 24. saatte kan örnekleri toplandı. Çalışma sonuçları, ishalli buzağılarda, farklı ölçüm zamanları arasında gerçekleştirilen grup içi değerlendirmede; pH, bikarbonat, baz durumu, parsiyel karbondioksit basıncı, total karbondioksit konsantrasyonu, potasyum ve aspartat amino transferaz kan düzeylerinde istatistiki açıdan önemli derecede bir farkın olduğunu ortaya koydu. Üre ve kreatinin serum konsantrasyonlarında ise ölçüm zamanlarına göre gerçekleştirilen grup içi istatistiki değerlendirmede önem arz eden bir fark belirlenmemesine rağmen, tedavi sonrası dönemde numerik bir azalma belirlenmiştir. Elde edilen veriler, neonatal buzağılarda akut ishale bağlı gelişen primer basit metabolik asidozun intravenöz izotonik sodyum bikarbonat uygulaması ile başarılı bir şekilde tedavi edilebileceğini ortaya koydu. Sonuçlara göre, neonatal buzağı ishallerinde tedavi protokolünün belirlenmesi ve prognozun tayininde, metabolik asidozun yanı sıra renal fonksiyondaki bozulmanın da göz önünde bulundurulması gerektiği değerlendirildi. Sunulan çalışma, buzağılarda neonatal akut ishallerde kritik değişim noktası olarak, kan asit-baz durumu için; tedavi sonrası 12. saatin ve renal fonksiyon için ise tedavi sonrası 24. saatin önemli olduğuna vurgu yapmaktadır.

INTRODUCTION

Diarrhea is one of the leading causes of calf deaths (Constable 2004). Neonatal calf diarrhea is generally occurs in 1-10 day old calves and commonly between 12th-18th hours after birth (Hunt 1993). Regardless of the etiologic reason, metabolic changes in calves due to neonatal diarrhea are similar (Ocal et al. 2006). These significant changes include dehydration, acidosis, electrolyte imbalance, negative energy balance, hyperkalemia, renal and cardiovascular system disorders (Constable et al. 2005). In calves with acute diarrhea, dehydration and also metabolic acidosis which is primarily due to fecal bicarbonate and sodium loss. Thus, fluid electrolyte acid- base treatment is very crucial in neonatal diarrhea (Constable 1999).

In this study, the time dependent effects of intravenous isotonic sodium bicarbonate administration over venous acid-base status and renal function in mildly dehydrated neonatal calves with acute diarrhea were investigated. Presented study data shows authenticity as it reveals the time dependent critical change points in blood acid-base status and renal function This study also states crucial findings in terms of prognosis determination in such patients.

MATERIALS and METHODS

a. Animal Material

The animal material of this study was consisted of 10 neonatal calves (n=10) from various stock and gender, in the ages between 1-30 day old (13.00±1.90 days; mean±SE), presented to Kocatepe University, Veterinary Internal Medicine clinic (Afyonkarahisar, Turkey) with the complaints of acute diarrhea (1-3 days).

In those sample animals, clinically, skin turgor was recorded as diminished mildly in four animals, moderately in six animals, eyes were sunken into orbit mildly in five animals and moderately in five, sucking reflex was weak in six and disappeared in four.

As the material of this study, neonatal calves with acute diarrhea was selected in which the primary disturbance was metabolic and those were diagnosed with primary simple metabolic acidosis– without respiratory/mixed acid base disorder accompanying to metabolic acidosis based on the blood gas measurements at 0th hour. PCO_2 values in those calves were recorded in the ranges that calculated with PCO_2 formula (PCO_2=[(1.5x$HCO3^-$)+8]±2) (Narins and Emmett 1980, Morganroth 1990a, Morganroth 1990b, Rutecki and Whittier 1998).

b. Sampling and Blood Analysis

In calves which selected as suitable for the study according to zero hour blood gas measurements, following administration of calculated total sodium bicarbonate need as isotonic IV solution, blood samples were drawn respectively at 15th minute, 30th minute, 1st hour, 2th hour, 3th hour, 4th hour, 6th hour, 12th hour and 24th hour.

Blood gas analysis was performed instantaneously bedside with disposable kits in portable blood gas analyzer (Epoc Portable Vet). Total blood count was done with automatic hemocell counter (Mindray BC-2800 Vet) and biochemical analysis with autoanalyzer (Mindray BS-120 Vet).

Based on zero hour blood gas measurement trace; HCO_3^- need in all sampled calves was calculated with=(Negative BEx0.6xCA)/12 formula (Suzuki et al. 2002).

In this study, calculated total HCO_3^- need of sample calves; were given as 1.3% $NaHCO_3$ isotonic solution in 0.9% isotonic NaCl solution. First 13 gram of calculated total HCO_3^- need was given in 1 liter isotonic NaCl solution, as 1.3% isotonic $NaHCO_3$ solution within 1st hour; remaining amount of $NaHCO_3$ need, was given as slow infusion, as isotonic solution (% 1.3 $NaHCO_3$) in following 2 hours (Coskun et al. 2010).

Plasma volume change between sampling periods was calculated based on 0th hour serum total protein concentration (TP_0) and measurement time serum total protein concentration (TP_m) with the formula of Plasma volume change=(TP_0–TP_m)x100/TP_m (Van Beaumont et al. 1972).

Sampled calves were not given any oral fluids and/or food until 12th hour sampling time. All calves were given UHT sterilized milk in amount of 10% of their body weight with feeding bottle within first hour following 12th hour of study. These calves weren't given any different parenteral fluid regimen until the end of 24 hour sampling period except for the procedure mentioned above.

The investigation was concluded following required maintenance parenteral fluid/electrolyte, acid-base and etiologic/support treatments were performed in all calves based on 24th hour measurement data.

c. Statistical analysis

Statistical difference between different measuring times was determined by ANOVA test (One-Way ANOVA and Tukey test). Difference analysis between zero value and measuring times was

done with Paired samples t-test (SPSS Inc). Data was given as Mean ± Standard error (SE) ($p<0.05$).

RESULTS

Study findings were summarized in Fig. 1-5 and Table 1

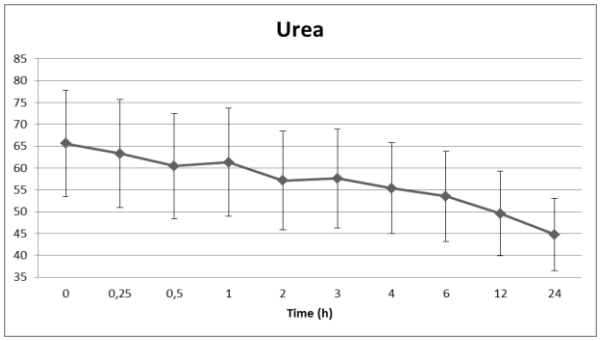

Fig 1: Time-dependent changes in serum urea concentration.

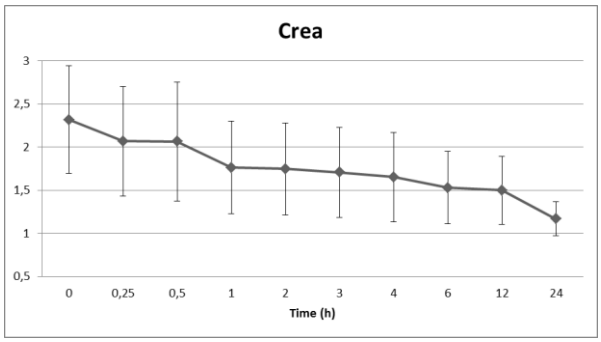

Fig. 2: Time-dependent changes in serum creatinine concentration.

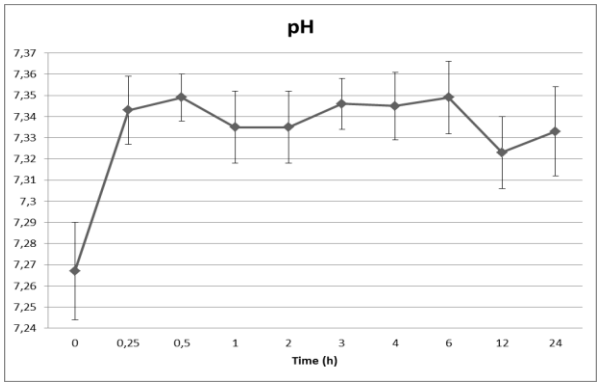

Fig. 3: Time-dependent changes in serum pH level.

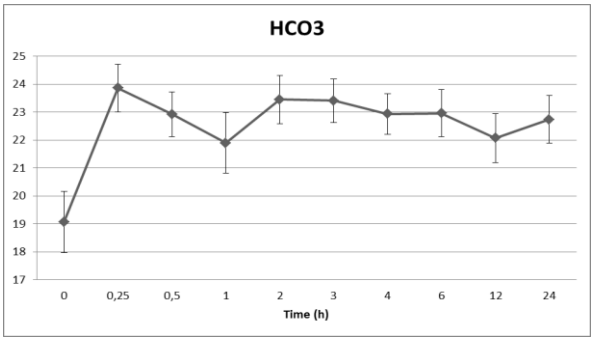

Fig. 4: Time-dependent changes in serum bicarbonate level.

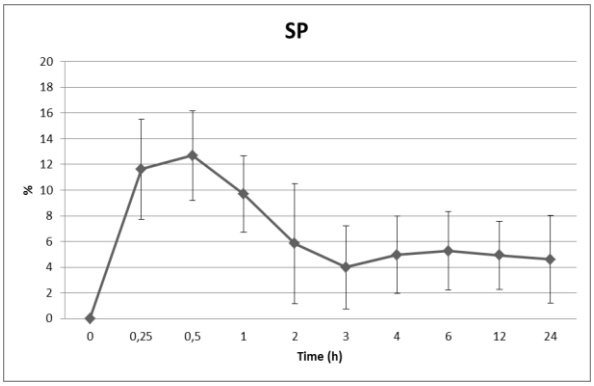

Fig. 5: Time-dependent changes in plasma volume.

a. Clinical Findings

Mean age of sample calves in this study was recorded as 13.0±1.9 days and the mean live weight was 39.00±2.65 kg (mean±SE). During the study, pulse (HR), respiratory rate (RR) and rectal temperatures (TEMP) of all calves were recorded; no statistical difference was detected on comparison within group (Table 1). Calves responded positively to applied treatment procedure and were ambulatory discharged. No death was observed during study and within 2 week after procedure.

b. Hematologic Analysis Findings

Based on hematologic measurement results; WBC, RBC, PLT, LYM, GRAN, HB, HCT, MCV and MCHC were evaluated, no statistical difference were detected on in-group evaluation (Table 1).

Table 1: Hematologic, Biochemical and Blood gas analysis findings and clinical examination data before and after treatment (mean±SE).

	Time (h)										
Parametrers	**0**	**0.25**	**0.5**	**1**	**2**	**3**	**4**	**6**	**12**	**24**	**p**
pH	7.267±0.023^{b}	7.343±0.016^{ab}	7.349±0.011^{a}	7.337±0.019^{ab}	7.335±0.017^{ab}	7.346±0.012^{a}	7.345±0.016^{ab}	7.349±0.017^{a}	7.323±0.016^{ab}	7.333±0.021^{ab}	0.044
HCO_3^- (mmol/L)	19.060±1.097^{b}	23.860±0.858^{a}	22.920±0.794^{ab}	21.890±1.082^{ab}	23.450±0.860^{a}	23.410±0.776^{a}	22.930±0.736^{ab}	22.960±0.833^{ab}	22.070±0.873^{ab}	22.740±0.857^{ab}	0.019
BE (mmol/L)	-7.480±1.380^{b}	-1.670±1.016^{a}	-2.160±0.765^{a}	-3.730±1.139^{ab}	-2.120±1.008^{a}	-2.060±0.911^{a}	-2.350±0.937^{a}	-2.410±0.971^{a}	-3.690±1.057^{ab}	-3.000±1.022^{ab}	0.008
pCO_2 (mmHg)	36.740±1.305^{b}	44.320±1.486^{a}	41.750±1.073^{ab}	40.960±2.011^{ab}	44.200±1.664^{a}	42.750±0.979^{ab}	42.480±0.806^{ab}	41.840±1.451^{ab}	42.570±1.139^{ab}	42.870±1.841^{ab}	0.026
TCO_2 (mmol/L)	20.220±1.124^{b}	25.190±0.877^{a}	24.170±0.798^{ab}	23.110±1.126^{ab}	24.750±0.883^{a}	24.570±0.834^{a}	24.250±0.764^{ab}	24.200±0.857^{ab}	23.330±0.903^{ab}	24.030±0.886^{ab}	0.021
K^+ (mmol/L)	5.470±0.287	4.480±0.264	4.260±0.225	4.170±0.211	4.150±0.213	4.310±0.216	4.170±0.137	4.380±0.121	4.140±0.209	4.360±0.187	0.001
Na^+ (mmol/L)	128.4±2.663	132.8±2.662	132.1±2.536	132.3±2.604	132.7±2.654	132.3±2.646	132.5±2.187	132.6±2.509	131.2±2.525	131.5±2.509	NS
Cl^-(mmol/L)	102.6±3.170	102.2±3.101	103.8±2.928	105.0±3.461	103.1±2.953	102.7±2.848	103.8±2.097	104.6±2.986	103.0±2.890	103.0±2.781	NS
Ca^{++} (mmol/L)	0.883±0.058	0.881±0.049	0.817±0.032	0.795±0.057	0.862±0.031	0.910±0.059	0.854±0.065	0.779±0.053	0.921±0.050	0.916±0.061	NS
SP (%)	-	11.622±3.907	12.703±3.487	9.691±2.986	5.833±4.690	3.996±3.326	4.954±3.007	5.259±3.065	4.918±2.629	4.597±3.413	NS
HB (g/dL)	10.043±0.925	8.986±0.393	10.343±1.161	9.314±0.340	9.243±0.356	9.329±0.352	9.286±0.385	9.514±0.378	9.657±0.488	9.457±0.412	NS
HCT (%)	29.371±3.064	27.186±1.602	30.957±3.441	27.586±1.367	28.029±1.466	28.100±1.395	28.043±1.516	28.657±1.594	28.257±2.047	27.329±1.525	NS
WBC (x 10^9/L)	8.750±0.797	8.760±0.865	9.150±0.900	8.690±0.779	9.730±0.929	9.800±0.979	9.580±0.771	10.490±0.743	10.090±0.814	9.690±0.845	NS
RBC (x 10^{12}/L)	7.741±0.604	7.356±0.381	8.125±0.658	7.585±0.446	7.630±0.362	7.640±0.323	7.567±0.329	7.670±0.320	7.467±0.398	7.384±0.369	NS
LYM (x10^9/L)	2.371±0.541	3.371±0.666	3.300±0.728	2.929±0.617	3.529±0.565	2.543±0.641	2.643±0.564	3.000±0.598	3.057±0.757	3.743±0.531	NS
GRAN (x10^9/L)	5.857±0.883	5.200±0.636	6.114±0.587	5.771±0.609	6.129±0.898	6.671±1.139	6.343±0.954	6.900±0.813	6.171±0.525	5.257±0.797	NS
MCV (fL)	39.071±0.711	39.114±0.827	39.229±0.789	38.986±0.796	38.929±0.820	38.857±0.792	38.843±0.789	38.414±1.070	38.386±0.950	38.157±0.968	NS
MCHC (g/dL)	34.700±1.028	33.229±0.632	33.400±0.409	33.871±0.516	33.071±0.477	33.286±0.440	33.229±0.467	33.343±0.588	34.443±0.807	34.700±0.620	NS
PLT (x10^9/L)	707.1±95.578	711.1±79.188	845.6±1.782	727.0±68.719	737.0±74.693	729.7±75.160	717.7±81.722	751.7±68.757	754.3±81.743	739.1±78.665	NS
ALT (U/L)	9.400±1.335	9.500±1.167	9.000±1.116	9.800±1.181	10.100±1.149	10.900±1.159	11.700±1.383	11.600±1.293	12.300±1.550	13.600±1.701	NS
AST (U/L)	49.600±3.397^{a}	48.400±3.433^{a}	49.300±3.426^{a}	51.300±3.760^{a}	53.100±4.231^{a}	58.000±4.282^{a}	61.000±4.437^{a}	60.200±4.638^{a}	64.200±4.136^{a}	65.400±4.761^{a}	0.013
GGT (U/L)	132.59±37.113	111.84±29.743	112.81±30.990	115.27±30.918	113.23±30.486	116.99±30.912	116.19±30.497	114.95±30.134	110.58±29.177	101.70±25.650	NS
LDH (U/L)	622.15±40.789	580.47±33.486	585.36±41.527	604.25±35.955	620.83±39.862	651.68±39.428	669.30±40.622	658.95±39.753	682.15±45.368	684.56±40.495	NS
GLU (mg/dL)	89.600±5.027	89.800±6.780	90.100±7.589	93.600±9.631	93.300±8.313	96.500±7.370	96.200±5.869	93.200±3.434	89.900±4.658	83.500±5.833	NS
LACT (mmol/L)	1.756±0.221	1.608±0.373	1.387±0.278	1.763±0.510	1.495±0.378	1.372±0.234	1.248±0.263	1.203±0.153	1.133±0.118	1.053±0.182	NS
TP (g/dL)	6.741±0.456	6.018±0.315	5.967±0.336	6.122±0.334	6.380±0.366	6.463±0.350	6.387±0.325	6.364±0.309	6.389±0.335	6.410±0.305	NS
ALB (g/dL)	3.046±0.154	2.789±0.119	2.738±0.104	2.840±0.115	2.817±0.110	2.942±0.117	2.955±0.113	2.917±0.117	2.966±0.112	3.001±0.123	NS
CK (U/L)	276.91±50.793	288.45±62.384	306.96±68.141	304.33±65.669	327.14±80.224	362.63±78.518	450.99±1.058	317.80±55.342	303.48±51.896	259.39±48.748	NS
UREA (mg/dL)	65.630±12.153	63.290±12.368	60.420±12.034	61.310±12.392	57.150±11.344	57.600±11.345	55.380±10.446	53.540±10.325	49.580±9.635	44.770±8.286	NS
CREA (mg/dL)	2.316±0.624	2.067±0.637	2.064±0.692	1.764±0.533	1.746±0.533	1.706±0.519	1.653±0.517	1.529±0.418	1.498±0.397	1.167±0.197	NS
RR	41.300±3.138	40.500±3.374	42.600±2.638	41.700±2.793	40.100±2.923	40.200±2.973	40.600±3.038	44.500±3.882	46.400±3.113	45.400±2.864	NS
HR	102.7±4.477	105.3±1.950	105.2±2.476	108.0±3.283	106.0±3.483	105.8±2.674	108.9±2.378	108.8±3.502	109.0±3.162	109.6±2.810	NS
TEMP	38.400±0.296	38.420±0.148	38.440±0.099	38.570±0.165	38.580±0.183	38.690±0.192	38.910±0.158	38.710±0.102	38.560±0.138	38.650±0.081	NS

c. Serum Biochemical Analysis Findings

Statistical changes were detected in serum ALT, AST, GGT (gamma-glutamyltransferase), LDH (lactate dehydrogenase), TP (total protein), ALB (albumin), CK, GLU (glucose), LACT (lactate), UREA and CREA (creatinine) levels between different measuring times. Time dependent change in serum urea and creatinine concentrations was given in Fig. 1-2.

d. Blood gas analysis findings

Statistical change in venous blood pH, pCO_2, HCO_3^-, BE, TCO_2, K^+, Na^+ (sodium), CI^- (chlorine), Ca^{++} (calcium) and SP (plasma volume) levels between different measuring times were evaluated. Based on blood gas measuring results; no statistical difference was detected between blood pH and HCO_3^- levels in in-group evaluation. Changes in blood pH and HCO_3^- levels were given in Fig. 3-4.

During in-group evaluation for measured K^+ concentrations in this study no significant difference was detected. Blood Na^+, CI^- and Ca^{++} values also did not show any statistically significant difference. Furthermore, no significant difference was detected for in-group statistical analysis between different measuring times in terms of plasma volume change ($SP_{\%}$) (Table 1). Besides, in the comparison based on measuring made following the completion of IV fluid electrolyte and acid/base treatments and 0th hr measurements; 11.622±3.907% increase in plasma volume at 15th min and 12.703±3.486% increase at 30th min were detected. In the comparison of 1st 2nd and 3rd hrs measuring data and 0th hrs, plasma volume, was recorded high respectively in rates of; 9.691±2.986%; 5.833±4.690% and 3.996±3.236%. In terms of SP, based on calculations with 0th hrs measuring data, in comparison of 3rd and 4th hrs measuring data; respective increase in plasma volume was seen at 4th hour and this increase continued till 6th hrs. After 6th hrs, a decline in plasma volume was seen (Fig. 5).

DISCUSSION

In this study, in-group comparison between measuring times, the statistical difference between pH, HCO_3^- and BE levels were respectively, p=0.044; p=0.019 and p=0.008. Pretreatment levels of pH, HCO_3^- and BE were lower than reference levels. This result was parallel to the findings of different study groups (Karademir and Sendil 2001, Ocal et al. 2006).

Comparison of pre-treatment measurement data showed that blood pH increased in all measuring times following treatment. This situation was found related to parenteral treatment. The highest pH value was recorded at 30th min (7.349±0.011) and at 6th hrs (7.349±0.017) The lowest pH level following treatment was at 12th hour (7.323±0.016). pH level at 24th hrs was compared to 12th hrs measuring, and respective increase was seen. This increase in pH might be related to initiation of oral intake in calves after 12th hrs.

Kasari (1999), in their study, reported that pH level under 7.28 and HCO_3^- level under 20 mmol/L in neonatal calves is related to metabolic acidosis. In human, pH<7.38 and PCO_2<40 mmHg and/or HCO_3^-<24 mmol/L are defined as *primary metabolic acidosis* (Rutecki and Whittier 1998). The decline in these parameters reflects metabolic acidosis (Constable et al. 2005). Similarly, in our study, pre-treatment pH, HCO_3^- and PCO_2 levels were also respectively 7.267±0.023; 19.060±0.016 and 36.740±1.305. These data shows *primary simple metabolic acidosis*.

Metabolic acidosis developed in calves with diarrhea are explained with fecal bicarbonate loss (Kasari and Naylor 1984). Measured bicarbonate levels, similar to blood pH levels, decreased at 12th hour and increased at 24th hour comparing to 12th hour measuring level. This increase can be related that all calves had milk 10% of their body weight following 12th hour of study. Time dependent changes in BE concentration were similar to changes in blood pH and HCO_3^- levels. Ocal et al. (2006) reported that post-tretment levels of pH, HCO_3^-, BE reach back to reference levels in neonatal calves. In parallel, in this study, pH, HCO_3^- and BE levels increased following treatment. This situation is the indicator of success in treatment of acidosis.

In evaluation of metabolic acidosis, other than aforementioned parameters, PCO_2 level is also beneficial (Groutides and Michell 1990b). PCO_2 decreased in calves with diarrhea following treatment (Kalinbacak 2003). Ocal et al. (2006) reported that non-significant increase in post treatment partial carbondioxide pressure was seen. In-group comparison, we showed statistically significant change in PCO_2 level dependent to measurement time. Increase in post-treatment PCO_2 levels, was detected as compared to 0th hrs measuring.

Calves with diarrhea also develop hyperkalemia (Groutides and Michell 1990a). As the HCO_3^- loss increase, serum K^+ concentration also increases (Ocal et al. 2006). Similarly, in this study, blood K^+ level (0th hrs) was higher. Kalinbacak (2003) reported that pre-treatment high K^+ levels in calves with diarrhea decreased and approached to normal levels following treatment. In our investigation, in group comparison, K^+ levels showed significant differences.

Similar to the study results, Coskun et al. (2010), showed that they investigated the time dependent effects of IV isotonic $NaHCO_3^-$ administrations over venous acid/base status in dehydrated calves with diarrhea, that blood pH and HCO_3^- concentrations increase, K^+ levels decrease in first 4th hrs after bicarbonate treatment in acidemic calves comparing to zero level and PCO_2 levels were measured within references range at all times.

The study data proved that there was statistically significant difference in serum AST concentrations in in-group evaluation. When compared with first measurement value post-treatment AST serum levels were higher. Proportional increase in serum levels with measuring times was detected. Differing from these study findings, Sendil and Karademir (2001) described an increase in AST before treatment and reported that this increase reversed after fluid/electrolyte treatment. Baser and Civelek (2013) reported that AST level in neonatal calves with acute diarrhea is high. When compared with post treatment measuring values, serum AST levels being low at 0th hrs can be explained by sample calves being presented in clinic in acute period and before development of liver damage (Karademir and Sendil 2001) due to toxemia.

In our study, in-group comparison between measuring times did not show any statistical difference for serum ALB and TP. Seifi et al. (2006) reported that there is a statistically significant increase in serum TP levels in neonatal calf diarrheas. Baser and Civelek (2013) reported that, there was no statistically significant difference in serum ALB concentrations in neonatal calves with diarrhea when compared to control group. Uzlu et al. (2010) noted statistically significant increase in serum TP levels and numerical decrease in ALB levels in calves with diarrhea when compared with control group.

Increase in blood lactate levels in calves with diarrhea is the leading cause of metabolic acidosis (Naylor 1989). High lactate levels in calves with diarrhea have been reported in various studies (Sing et al. 1992). In this study, while there was no statistical difference, pre-treatment serum lactate level was numerically higher than post-treatment all levels.

In this study, there was no statistical difference in serum UREA and CREA concentrations between different measuring times for in-group comparison. Nevertheless, when compared to zero value, on measurement of serum urea concentrations; at 15th min, 30th min, 1st hr, 2nd hr, 3rd hr, 4th hr, 6th hr, 12th hour measuring values; p=0.000 and between 0th and 24th hour measuring values p=0.05 level significance was described. Similarly, Seifi et al. (2006) reported that blood urea and creatinine concentrations significantly increased in neonatal calves with diarrhea. Baser and Civelek (2013) also reported significantly increase in urea and creatinine concentrations in neonatal diarrhea. Increase in serum urea and creatinine levels in calves with diarrhea, occurs as a result of decrease in renal perfusion rate which develops due to dehydration (Groutides and Michell 1990a). In comparison with creatinine, strong increase in urea concentration is more typical finding for prerenal insufficiency and dehydration (Groutides and Michell 1990a). In this study, when compared to pre-treatment, linear decline was detected in serum urea and also creatinine concentrations measured following treatment (Fig. 1 and 2). It was thought that this situation is associated to fluid-electrolyte treatment.

In this study, no statistical difference was seen in Na^+ concentrations in neonatal calves for in-group comparison. As the dehydration level in calves increase, hyponatremia, hypochloremia and hyperkalemia also aggravate (Dratwa-Chalupnika et al. 2012). When compared to post-treatment period, non-existence of significant decrease in zero hour blood Na^+ levels, although being measured under reference interval, might be related to early term referrals to clinic. Sampling only the animals with primary simple metabolic acidosis in this study is another indicator of being not complicated of selected cases. Baser and Civelek (2013), in their study, reported no statistical difference in serum Na^+ levels in neonatal calves with acute diarrhea when compared with control group. Seifi et al. (2006), also mentioned that hyponatremia was seen in neonatal calf diarrhea. However, this study was performed on animals which had diarrhea and/or recovered and died of diarrhea (Seifi et al. 2006).

As mentioned above, as known in general, calves with diarrhea are hypochloremic (Grove-White 1994). In this study, no statistical difference was detected in CI^- concentrations. With this aspect, presented study findings are parallel to the one done by Boyd et al. (1974).

In this study, there was no statistical difference in Ca^{++} concentrations in neonatal calves with acute diarrhea between different measuring times for in-group comparison. Uzlu et al. (2010) also reported similar results. On the contrary, there are also studies that reported decrease in plasma Ca^{++} levels in calves with diarrhea (Michell et al. 1992, Grove-White and Michell 2001). Decrease in blood Ca^{++} concentrations in calves with diarrhea is found related to the role of calcium in tamponization of acidosis as an important component of the system. (Ocal et al. 2006).

Deprivation in fluid-electrolyte balance in calf diarrhea causes hematologic and metabolic changes. Carbohydrate storages empty and glucose concentration declines (Dratwa-Chalupnik et al. 2012). Investigators reported that serum GLU level in calves with diarrhea is lower (Groutides and Michell 1990a, Seifi et al. 2006). Besides, it was also reported that serum glucose concentrations do not change in calf diarrhea (Kasari et al. 1985, Baser and Civelek 2013). In this study, there was no statistical difference in GLU concentrations between different measuring times.

When we look at the plasma volume changes between different measuring times based on first measurement value, the highest change in SP% after parenteral fluid-electrolyte and acid-base treatment was recorded at 30th min (~%13). The required and calculated amount of total HCO_3^- for sampled calves; was given in 0.9% $NaCl^-$ solution and first 13 grams within the first hour and remaining in two hours as isotonic solution. It was detected that plasma volume was higher in all measuring times compared to pre-treatment value, besides, while being higher compared to zero level, 30th min plasma volume decreased and at 3th hrs measuring, based on zero level, it reduced approximately back to +4% level. This situation can be explained by the transition of IV fluid to extracellular and intracellular compartments which were emptied due to dehydration. Similar to these findings, Coskun et al. (2010) also reported in their study, that plasma volume increased in the first two hours in calves which parenteral isotonic $NaHCO_3^-$ was applied. Although all calves were fed with oral milk 10% of their body weight after 12th hrs, no increase was observed in plasma volume at 24th hrs measuring. Expected increase might not be detected since the interval between 12th and 24th hrs measuring was 12th hrs. To efficiently restore and maintain the plasma volume in neonatal calves with acute diarrhea, oral nutrition should be kept and supported.

This study, showed that mild primary metabolic acidosis (BE>-10 mmol/L) (Koch and Kaske 2008) and mild/moderate dehydration due to acute diarrhea in neonatal calves can be successfully treated with IV isotonic $NaHCO_3$ administration. Study findings pointed out that, in determination of treatment procedure and diagnosis in neonatal calves with acute diarrheal, along with metabolic acidosis, deterioration in renal functions should also be considered. Obtained data, as a critical change point, mentions post-treatment 12th hrs for blood acid-base status, 24th hrs for renal functions and 30th min, 3rd hrs and 24th hrs for blood acid-base status; following isotonic IV solution infusion of calculated bicarbonate need in neonatal calves with acute diarrhea and mild primary simple metabolic acidosis.

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