Journal of Veterinary Internal Medicine, 2026, 40(5), aalag215
https://doi.org/10.1093/jvimsj/aalag215
Original Research | Food & Fiber Animal Cardiology

Ability of intravenous small-volume hypertonic sodium bicarbonate, sodium chloride, and glucose solutions to rapidly reverse electrocardiographic abnormalities in hyperkalemic calves with neonatal diarrhea

Florian M. Trefz[1,*], Ingrid Lorenz[2], Peter D. Constable[3]

[1]Clinic for Ruminants with Ambulatory and Herd Health Services, Center for Clinical Veterinary Medicine, LMU Munich, Oberschleißheim, Germany
[2]Bavarian Animal Health Service (Tiergesundheitsdienst Bayern e.V.), Poing, Germany
[3]College of Veterinary Medicine, University of Illinois Urbana-Champaign, Urbana, IL, United States
[*]Corresponding author: Florian M. Trefz, Clinic for Ruminants with Ambulatory and Herd Health Services, LMU Munich, Sonnenstraße 16, 85764 Oberschleißheim, Germany (Florian.Trefz@lmu.de).

Abstract

Background: **Hyperkalemia is common in dehydrated calves with neonatal diarrhea and can result in life-threatening cardiac conduction abnormalities.**

Hypothesis/Objectives: **Compare the effects of IV small-volume hypertonic solutions of $NaHCO_3$, NaCl, and glucose in correcting electrocardiographic abnormalities.**

Animals: **Twenty-two neonatal diarrheic calves with plasma potassium concentrations (*c*K) > 5.8 mmol/L.**

Methods: **Prospective randomized clinical trial. Calves randomly received either 8.4% $NaHCO_3$ (6.4 mL/kg; $n = 7$), 7.5% NaCl (5 mL/kg; $n = 8$), or 46.2% glucose (5 mL/kg; $n = 7$) IV over 5 min and were subsequently allowed to suckle 2 L of an oral electrolyte solution. Lead II ECG variables were determined before the infusion, during infusion, and 7, 15, 30, 60, 90, and 120 min after the start of infusion.**

Results: **Seven minutes after initiation of infusions, administration of hypertonic sodium solutions but not glucose resulted in a significant ($P < .05$) increase in heart rate and ST segment duration as well as a decrease in heart rate variability, QRS duration, and T wave amplitude. Generalized linear mixed model analysis identified *c*K, the interaction between *c*K and plasma sodium concentrations, or both, as significant predictors of most electrocardiographic variables. Posttreatment increase in *c*K in 2 calves in group NaCl was associated with the loss of P waves, prolonged QRS duration, and increased T wave amplitude.**

Conclusions and clinical importance: **Hypertonic sodium solutions allow for a rapid reversal of the cardiotoxic effect of hyperkalemia. Hypertonic $NaHCO_3$ should be preferred over hypertonic NaCl or glucose.**

Keywords calves, electrocardiography, intravenous fluid therapy, potassium, sodium

Abbreviations *c*K, plasma potassium concentrations; *c*Na, plasma sodium concentrations

Introduction

Hyperkalemia is a common and clinically relevant electrolyte imbalance in neonatal diarrheic calves, with a reported prevalence of 28%-34% in study populations of severely affected animals.[1–3] Traditionally, hyperkalemia was thought to result from acidemia-induced shifts of potassium ions between the intracellular and extracellular compartments.[4] However, more recent studies suggest that the development of hyperkalemia in these calves depends primarily on the type of acidosis present[1,2] and that acidemia per se is not associated with depletion of intracellular potassium stores.[5] Notably, plasma potassium concentrations (*c*K) are most strongly associated with clinical and laboratory indicators of dehydration, suggesting that decreased glomerular filtration rate plays a central role in the pathogenesis of hyperkalemia.[1,2,6]

The clinical consequences of hyperkalemia are primarily related to impaired neuromuscular excitability, which can manifest

Received: December 13, 2025. **Revised:** August 19, 2026. **Accepted:** August 25, 2026
© The Author(s) 2026. Published by Oxford University Press on behalf of the American College of Veterinary Internal Medicine.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

as muscle weakness and cardiac conduction abnormalities.[1,3] These effects may be exacerbated by concurrent hyponatremia and acidemia because of strong ion acidosis[7,8]—conditions that commonly coexist in hyperkalemic neonatal diarrheic calves.[2,3] Early ECG changes in response to increasing *c*K include increased voltages of the P, Ta, S, and T waves.[3] With more severe hyperkalemia, ECG abnormalities can progress to include P wave disappearance (atrial standstill), QRS widening, ST segment elevation, ventricular escape rhythms, and arrhythmias.[3,4,9,10]

Furthermore, the clinical picture of hyperkalemic diarrheic calves is characterized by severe clinical dehydration, cyanosis, impaired ability to stand, and affected calves frequently are presented with signs of shock.[1] Consequently, acute hyperkalemia in diarrheic calves should be considered an emergency and treatment should focus on rapid resolution of clinical signs and stabilization of affected animals.[11] The treatment of hyperkalemia should focus chronologically on antagonizing the effect of increased *c*K on excitable tissues, redistributing extracellular potassium into cells, and finally on enhancing elimination of potassium from the body.[12] In theory, those treatment recommendations can be readily achieved in neonatal diarrheic calves by rapid IV administration of hypertonic sodium salt solutions such as 7.2% NaCl or 8.4% $NaHCO_3$ because those solutions induce rapid plasma volume expansion and have the potential to enhance the redistribution of potassium ions into the cells.[13,14] More importantly, the resulting sodium load of those infusion solutions is of therapeutic usefulness because the cardiotoxic effects of hyperkalemia can be rapidly reversed by increasing plasma sodium concentrations (*c*Na) as demonstrated for hypertonic NaCl in studies involving humans, dogs, and a single diarrheic calf.[8,15,16]

Hyperkalemia in humans is commonly treated by IV administration of insulin and dextrose to stimulate intracellular uptake of potassium ions.[7,12] Intravenous administration of a hypertonic glucose solution therefore might represent an alternative option in the initial treatment of hyperkalemic diarrheic calves, because hypertonic glucose solutions induce endogenous insulin release that promotes intracellular uptake of potassium ions by stimulating Na^+/K^+-ATPase activity.[17] We previously reported that hypertonic $NaHCO_3$ infusions have advantages in rapid and sustained restoration of potassium homeostasis when compared with a hypertonic NaCl or glucose solution.[14] In that study, infusions of a 7.5% NaCl solution produced a short-term decrease in *c*K. We also reported that a delayed potassium-lowering effect, lack of alkalinizing capacity, and decreased *c*Na represented potential disadvantages of hypertonic glucose solution over the use of sodium bicarbonate-containing infusion solutions.[14] Our current study is based on the analysis of ECG findings that were recorded during the previous study, with the main objective being to explore the potential ability of IV small-volume hypertonic sodium bicarbonate, sodium chloride, and glucose solutions to reverse ECG abnormalities in hyperkalemic diarrheic calves. A secondary aim was to assess associations between clinicopathologic findings and changes in ECG variables over time. Based on our previous findings, we aimed to explore whether IV administration of small-volume hypertonic $NaHCO_3$ infusions may be associated with a clinically relevant treatment advantage in correcting hyperkalemic ECG abnormalities compared with hypertonic NaCl or glucose solutions.

Materials and methods

A detailed description of materials and methods used is provided in the Appendix. In brief, this prospective randomized clinical study enrolled 22 neonatal diarrheic calves ($\leq$ 21 days old) with hyperkalemia (*c*K $>$ 5.8 mmol/L) admitted to a university hospital for treatment. Most calves belonged to the German Fleckvieh breed. After clinical examination and placement of a jugular vein catheter, calves were randomly allocated to 1 of 3 treatment groups.

Calves in the sodium bicarbonate group (NaBic; n = 7) received 8.4% sodium bicarbonate (6.4 mL/kg over 5 min), providing the same sodium load as in the NaCl group. The saline group (NaCl; n = 8) received 7.5% sodium chloride (5 mL/kg over 5 min). The glucose group (Gluc; n = 7) received a 46.2% glucose solution (5 mL/kg over 5 min) prepared to match the osmolarity of the hypertonic saline. At 20 min after the start of infusion, all calves were offered 2 L of an oral electrolyte solution; any unsuckled volume was tube fed after 10 min.

Electrocardiograms were recorded at baseline, during infusion (2.5 min), and at 7, 15, 30, 60, 90, and 120 min after the initiation of the infusion. During the trial, calves were monitored clinically, and a detailed analysis of recorded ECGs was performed at a later point in time. Amplitudes and durations of ECG complexes were determined using the bipolar limb lead II from a 32-s averaged recording.[3] Irregularities in RR intervals were defined as $>$ 10% variation between consecutive intervals.[18] Heart rate variability (HRV) was assessed by calculating the standard deviation of RR intervals[19,20] (HRV-SDRR) and the coefficient of variation of RR intervals[21] (HRV-CV), derived from the 32-s ECG recordings.

Samples for venous blood gas and electrolyte analyses were collected at corresponding time points (except at 2.5 min during infusion), and plasma total protein concentrations were determined from the same samples after centrifugation.

Differences between treatment groups and over time were evaluated using a linear mixed-effects model analysis. The ECG variables were log-transformed if necessary. Associations between ECG changes and clinical pathology variables were analyzed using generalized linear mixed models with backward elimination; treatment group was retained as a fixed effect and the individual calf identified as a random effect. Segmented linear regression[3,22,23] was used to characterize the relationship of *c*K and the *c*K:*c*Na ratio with ECG variables using a mixed model approach. For all analyses, P-values $<$ .05 were considered statistically significant.

Results

A similar initial decrease in *c*K was observed in the NaBic and NaCl groups until 15 min. However, *c*K subsequently increased in the NaCl group, whereas it continued to decrease in the NaBic group until the end of the study period. Values for *c*K remained unchanged in group Gluc until 30 min. More detailed information concerning the observed changes of laboratory variables has been reported elsewhere.[14]

Baseline characteristics of specific ECG findings are reported in Table 1. Changes of lead II ECG measurements over the study period in the 3 treatment groups are presented in Table 2 and selected ECG findings are illustrated in Figures 1-3. Baseline imbalances existed across treatment groups: An irregular heart rhythm was evident at baseline in 3 calves in the NaBic group and 4 calves

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 1 Baseline characteristics of specific ECG findings in 22 hyperkalemic calves with diarrhea treated either with a hypertonic 8.4% sodium bicarbonate (n = 7; group NaBic), 7.5% NaCl (n = 8; group NaCl), or a 46.2% glucose solution (n = 7; group Gluc).

Finding	Treatment group		
	NaBic	NaCl	Gluc
Presence of arrhythmias	3/7	4/8	0/7
Presence of bradyarrhythmia	1/7	2/8	0/7
Missing P waves	2/7	2/8	1/7
Presence of tall and peaked T waves	4/7	4/8	5/7

As in a previous study,[3] tall and peak-shaped appearing T waves were defined as the presence of T wave amplitude $\geq$ 0.75 mV and a "peakedness index" $\geq$ 8.0 μV/ms, which was calculated by dividing T wave amplitude by T wave duration. Bradyarrhythmias were defined as the presence of arrhythmias and a heart rate $<$ 90 beats/min.

of group NaCl, of which 4 calves (2 calves each in the NaCl and NaBic groups) had an irregular rhythm with missing P waves and increased QRS duration (Figures 1 and 2). No arrhythmias were present in any calves of group Gluc. Administration of hypertonic sodium solutions resulted in restoration of regular heart rhythm and a significant decrease in HRV (Table 2).

At baseline, P waves were not detectable in 2 calves each in the NaBic and NaCl groups, both of which exhibited arrhythmias, and in 1 calf in the Gluc group, which showed no signs of arrhythmias. A return of P waves was detectable at 7 min in 1 calf of group NaBic and 2 calves of group NaCl, and at 30 min in the calf of group Gluc. No P waves were detectable in 1 calf of group NaBic throughout the 120-min study period. Associated with a renewed increase in *c*K, disappearance of P waves again was detected in 2 calves of group NaCl at 60 and 120 min, respectively. In one of these 2 calves, ventricular tachycardia was additionally observed at 60 and 90 min (Figure 2). Furthermore, an irregular ventricular escape rhythm recurred at 120 min. As shown in Figure 4, infusions with hypertonic NaBic and NaCl were associated with more pronounced shortening of QRS duration relative to baseline than infusions with the hypertonic glucose solution during the first 30 min of the trial.

Significant time effects were observed for all reported ECG measurements. A group $\times$ time effect was observed for heart rate, HRV-SDRR, P, Ta, S, and T wave amplitudes, as well as for QRS duration. A group effect was observed for S wave amplitude (Table 2). Effect sizes for between-group comparisons are reported in Table S1. As a sensitivity analysis addressing baseline imbalance in ECG severity, the mixed-effects models were repeated after exclusion of all calves presenting with arrhythmias at baseline (t = 0). In this restricted dataset, the effects of time and the group-by-time interaction remained significant across the analyzed outcomes.

Results of the generalized linear mixed modeling for the observed changes in heart rate, amplitudes of P, Ta, S, and T waves and the ST segment as well as for QRS duration, ST segment duration, and ST angle are presented in Table 3. Except for heart rate and ST segment duration, the interaction between *c*K and *c*Na was a significant predictor in all models. Also, the interaction of *c*K and *c*Na provided additional explanatory value beyond *c*K in the models for QRS duration and amplitudes of P wave, T wave, and ST segment.

Figures 5 and 6 illustrate the association between *c*K and changes of selected ECG findings. Seven ECG indices were characterized by 2 linear regression equations with different slopes and a different breakpoint at the stated mean *c*K, as shown in Table 4. Scatterplots illustrating the association between the *c*K:*c*Na ratio and selected ECG variables are shown in Figures S1 and S2.

After a mean duration of 12 $\pm$ 5 days of hospitalization, 21 of the 22 calves were discharged in a healthy state. One calf in the NaCl group was euthanized because of advanced pneumonia that progressed during its hospital stay.

Discussion

Central findings of this exploratory study suggest that IV administration of small-volume hypertonic sodium solutions allows for rapid reversal of the cardiotoxic effects of hyperkalemia in neonatal diarrheic calves. Notably, significant changes in ECG variables (including increased heart rate, decreased HRV and T wave amplitude, as well as shortened QRS duration) were observed during or immediately after administration of hypertonic NaBic or NaCl. These findings are consistent with previous reports in hyperkalemic humans, dogs, and a calf with diarrhea.[8,15,16,24]

Interestingly, resolution of ECG abnormalities occurred despite only minimal decreases in *c*K after infusion. This effect may be attributable to a decreased *c*K:*c*Na ratio, because an immediate improvement in ECG variables was not observed in the Gluc group, which received a sodium-free infusion. Instead, the respective dynamics of the *c*K:*c*Na ratio were associated with an increase in QRS duration (as an indicator of the duration of ventricular depolarization) in calves in this treatment group, whereas a shortening of QRS duration was noted in groups NaBic and NaCl (Figure 4). Hyperkalemia decreases the transmembrane potassium gradient, resulting in a less negative resting membrane potential and decreased activity of voltage-gated sodium channels.[17,25–28] This change leads to a decreased upstroke velocity during phase 0 of the cardiac action potential, slowing myocardial conduction of the action potential, and thereby increasing the QRS duration. Studies in isolated cardiomyocytes have demonstrated that increased extracellular sodium concentrations enhance phase 0 upstroke velocity,[29] likely because of increased sodium influx, thereby improving conduction abnormalities[26,27] and shortening the QRS duration.

Further support for the therapeutic value of lowering the *c*K:*c*Na ratio with hypertonic sodium solutions is provided by generalized linear mixed models that aimed to predict ECG changes over time. In most models, the interaction between *c*K and *c*Na was a significant predictor and added explanatory value beyond *c*K in the models for QRS duration and the amplitudes for P wave, T wave, and ST segment. In the latter models, regression coefficients indicated that *c*K $\times$ *c*Na was inversely associated with ECG abnormalities compared to *c*K alone, suggesting that calves with similar *c*K exhibited less severe ECG changes when *c*Na was increased.

In a previous study involving 130 neonatal calves with diarrhea and associated potassium balance disorders, we identified increased voltages of the P, Ta, S, and T waves as early ECG signs of hyperkalemia.[3] Moreover, segmented linear regression

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 2 Data for ECG measurements (lead II) and effect sizes for within-group comparisons in 22 neonatal diarrheic calves before and after administration of infusions with a hypertonic 8.4% sodium bicarbonate ($n = 7$; group NaBic), 7.5% NaCl ($n = 8$; group NaCl), or 46.2% glucose solution ($n = 7$; group Gluc) over a period of 5 min and subsequent suckling of an oral electrolyte solution.

		Time after start of treatment							*P*-value		
Variable	**0 min**	**2.5 min**	**7 min**	**15 min**	**30 min**	**60 min**	**90 min**	**120 min**	**Group**	**Time**	**Group × Time**
Heart rate (bpm)											
NaBic	106 (82/130)[a]	121 (98/144)[a]	118 (98/138)[a]	114 (95/134)[a]	121 (94/148)[a]	126 (108/144)[a]	119 (100/138)[a]	120 (101/139)[ab]	.35	<.001	.008
NaCl	92 (73/111)[a]	126 (99/154)[a]*	121 (100/142)[a]*	113 (87/138)[a]*	117 (94/140)[a]*	120 (92/148)[a]*	122 (84/160)[a]*	106 (84/128)[a]			
Gluc	124 (94/154)[a]	121 (94/154)[a]	129 (110/147)[a]	126 (105/148)[a]	134 (109/159)[a]	139 (113/166)[a]	142 (118/166)[a]	142 (120/165)[b]			
NaBic Δ 0 min	N/A	14.7 (0.4/29.0)	12.1 (−1.5/25.8)	8.4 (−8.2/25.1)	15.1 (−0.3/30.6)	20.0 (−0.5/40.5)	13.0 (−13.5/39.5)	14.0 (−0.9/29.2)			
NaCl Δ 0 min	N/A	33.9 (20.5/47.2)	29.0 (16.2/41.8)	20.3 (4.7/35.8)	24.5 (10.0/39.0)	27.6 (8.5/46.8)	29.5 (4.8/54.2)	13.9 (−0.2/28.0)			
Gluc Δ 0 min	N/A	−3.4 (−17.7/10.9)	4.7 (−8.9/18.4)	2.1 (−14.5/18.8)	10.0 (−5.4/25.5)	15.4 (−5.1/35.9)	18.3 (−8.1/44.7)	18.4 (3.4/33.5)			
HRV-SDRR (ms)											
NaBic	26 (6/105)[a]	18 (6/57)[a]	9 (2/33)[a]*	12 (3/45)[a]	6 (4/10)[a]*	5 (3/7)[a]*	5 (3/9)[a]*	6 (4/9)[a]*	.29	<.001	.04
NaCl	31 (14/69)[a]	14 (5/38)[a]*	5 (3/8)[a]*	8 (4/17)[a]*	8 (4/17)[a]*	9 (4/20)[a]*	9 (4/21)[a]*	10 (5/18)[a]*			
Gluc	8 (4/15)[a]	8 (5/13)[a]	5 (3/8)[a]	5 (3/10)[a]	7 (4/13)[a]	5 (3/9)[a]	6 (4/11)[a]	5 (3/8)[a]			
NaBic ratio 0 min	N/A	0.69 (0.31/1.56)	0.33 (0.16/0.71)	0.46 (0.19/1.14)	0.24 (0.10/0.58)	0.17 (0.06/0.47)	0.21 (0.07/0.58)	0.24 (0.10/0.55)			
NaCl ratio 0 min	N/A	0.44 (0.21/0.94)	0.15 (0.07/0.30)	0.25 (0.11/0.58)	0.25 (0.11/0.58)	0.28 (0.11/0.71)	0.30 (0.12/0.80)	0.31 (0.14/0.70)			
Gluc ratio 0 min	N/A	1.08 (0.48/2.44)	0.62 (0.29/1.32)	0.71 (0.29/1.73)	0.91 (0.37/2.24)	0.72 (0.27/1.95)	0.82 (0.29/2.31)	0.63 (0.27/1.48)			
HRV-CV (%)											
NaBic	4.4 (1.4/14.3)[a]	3.5 (1.3/9.2)[a]	1.7 (0.5/5.4)[a]*	2.3 (0.7/7.3)[a]	1.3 (0.8/1.9)[a]*	0.9 (0.7/1.2)[a]*	1.0 (0.7/1.6)[a]*	1.2 (0.9/1.6)[a]*	.39	<.001	.08
NaCl	4.7 (2.1/10.5)[a]	2.8 (1.1/7.1)[a]	0.9 (0.6/1.3)[a]*	1.5 (0.8/2.7)[a]*	1.5 (0.8/2.7)[a]*	1.7 (0.9/3.3)[a]*	1.8 (0.9/3.5)[a]*	1.7 (1.0/2.9)[a]*			
Gluc	1.5 (0.9/2.7)[a]	1.6 (1.0/2.7)[a]	1.0 (0.5/1.9)[a]	1.1 (0.6/2.1)[a]	1.5 (0.9/2.5)[a]	1.3 (0.8/1.9)[a]	1.5 (0.9/2.3)[a]	1.1 (0.8/1.6)[a]			
NaBic ratio 0 min	N/A	0.80 (0.36/1.77)	0.38 (0.18/0.79)	0.51 (0.22/1.19)	0.29 (0.13/0.65)	0.21 (0.09/0.50)	0.24 (0.10/0.57)	0.27 (0.13/0.60)			
NaCl ratio 0 min	N/A	0.60 (0.29/1.26)	0.19 (0.10/0.39)	0.30 (0.14/0.66)	0.31 (0.15/0.67)	0.36 (0.16/0.79)	0.39 (0.17/0.87)	0.36 (0.17/0.76)			
Gluc ratio 0 min	N/A	1.07 (0.49/2.36)	0.66 (0.32/1.36)	0.73 (0.31/1.69)	0.99 (0.44/2.25)	0.82 (0.35/1.92)	0.96 (0.40/2.29)	0.74 (0.34/1.62)			
P amplitude (mV)											
NaBic	0.17 (0.03/0.30)[a]	0.14 (0.04/0.23)[a]	0.15 (0.07/0.23)[a]	0.16 (0.07/0.26)[a]	0.19 (0.10/0.28)[a]	0.19 (0.10/0.28)[ab]	0.19 (0.10/0.28)[ab]	0.20 (0.11/0.28)[ab]	.33	<.001	<.001
NaCl	0.15 (0.06/0.23)[a]	0.15 (0.06/0.23)[a]	0.19 (0.15/0.23)[a]	0.18 (0.13/0.22)[a]	0.19 (0.13/0.24)[a]	0.16 (0.09/0.23)[a]	0.16 (0.09/0.23)[a]	0.15 (0.07/0.23)[a]			
Gluc	0.22 (0.11/0.33)[a]	0.21 (0.10/0.33)[a]	0.16 (0.06/0.25)[a]	0.17 (0.08/0.27)[a]	0.22 (0.17/0.28)[a]	0.28 (0.22/0.33)[b]	0.29 (0.20/0.37)[b]*	0.28 (0.21/0.34)[b]			
NaBic Δ 0 min	N/A	−0.03 (−0.06/0.0)	−0.02 (−0.06/0.03)	0.0 (−0.04/0.03)	0.02 (−0.03/0.07)	0.02 (−0.04/0.08)	0.03 (−0.03/0.08)	0.03 (−0.03/0.09)			
NaCl Δ 0 min	N/A	0.0 (−0.03/0.03)	0.04 (0.0/0.09)	0.03 (0.0/0.07)	0.04 (−0.01/0.09)	0.02 (−0.04/0.07)	0.01 (−0.04/0.06)	0.0 (−0.05/0.06)			
Gluc Δ 0 min	N/A	−0.01 (−0.04/0.02)	−0.06 (−0.11/0.02)	−0.05 (−0.09/−0.01)	0.0 (−0.05/0.06)	0.06 (0.0/0.12)	0.07 (0.01/0.12)	0.06 (0.0/0.12)			
Ta amplitude (mV)											
NaBic	−0.05 (−0.09/−0.02)[a]	−0.02 (−0.04/0.00)[a]*	−0.03 (−0.04/−0.01)[a]	−0.03 (−0.05/−0.01)[a]	−0.04 (−0.06/−0.02)[a]	−0.04 (−0.06/−0.02)[a]	−0.04 (−0.06/−0.02)[ab]	−0.04 (−0.07/−0.02)[a]	.08	.01	.03
NaCl	−0.05 (−0.07/−0.02)[a]	0.00 (−0.01/0.00)[a]*	−0.02 (−0.03/0.00)[a]*	−0.03 (−0.05/−0.01)[a]	−0.03 (−0.05/−0.01)[a]	−0.04 (−0.06/−0.02)[a]	−0.03 (−0.05/−0.01)[a]	−0.04 (−0.06/−0.01)[a]			
Gluc	−0.07 (−0.11/−0.02)[a]	−0.07 (−0.12/−0.01)[b]	−0.06 (−0.12/−0.01)[a]	−0.05 (−0.10/−0.00)[a]	−0.05 (−0.08/−0.02)[a]	−0.06 (−0.09/−0.03)[a]	−0.07 (−0.10/−0.04)[b]	−0.07 (−0.10/−0.04)[a]			
NaBic Δ 0 min	N/A	0.03 (0.01/0.05)	0.02 (0.0/0.05)	0.02 (0.0/0.04)	0.01 (−0.01/0.04)	0.01 (−0.01/0.03)	0.01 (−0.01/0.03)	0.01 (−0.01/0.03)			
NaCl Δ 0 min	N/A	0.04 (0.02/0.06)	0.03 (0.01/0.05)	0.02 (0.0/0.04)	0.02 (0.0/0.04)	0.01 (−0.01/0.02)	0.02 (0.0/0.03)	0.01 (−0.01/0.03)			
Gluc Δ 0 min	N/A	0.0 (−0.02/0.02)	0.0 (−0.02/0.03)	0.02 (0.0/0.04)	0.01 (−0.01/0.04)	0.0 (−0.02/0.02)	0.0 (−0.02/0.02)	0.0 (−0.03/0.02)			
S amplitude (mV)											
NaBic	−1.99 (−2.23/−1.74)[a]	−1.32 (−1.53/−1.10)[a]*	−1.42 (−1.67/−1.16)[a]*	−1.49 (−1.72/−1.25)[a]*	−1.58 (−1.84/−1.32)[a]*	−1.65 (−1.90/−1.39)[a]*	−1.65 (−1.90/−1.40)[a]*	−1.62 (−1.83/−1.41)[a]*	.044	<.001	.005
NaCl	−1.96 (−2.23/−1.68)[a]	−1.29 (−1.56/−1.02)[a]*	−1.33 (−1.52/−1.14)[a]*	−1.36 (−1.59/−1.13)[a]*	−1.52 (−1.81/−1.24)[a]*	−1.67 (−1.96/−1.38)[a]*	−1.64 (−1.96/−1.32)[a]*	−1.68 (−1.96/−1.39)[a]*			
Gluc	−2.09 (−2.41/−1.78)[a]	−1.86 (−2.18/−1.53)[b]*	−1.80 (−2.06/−1.55)[b]*	−1.69 (−1.97/−1.41)[a]*	−1.76 (−2.15/−1.37)[a]*	−2.02 (−2.40/−1.64)[a]	−2.07 (−2.49/−1.64)[a]	−2.11 (−2.47/−1.75)[b]			
NaBic Δ 0 min	N/A	0.67 (0.48/0.86)	0.57 (0.43/0.71)	0.50 (0.34/0.66)	0.40 (0.19/0.61)	0.34 (0.09/0.59)	0.34 (0.08/0.60)	0.37 (0.14/0.60)			
NaCl Δ 0 min	N/A	0.67 (0.49/0.84)	0.63 (0.50/0.76)	0.60 (0.45/0.75)	0.44 (0.24/0.63)	0.28 (0.05/0.52)	0.32 (0.07/0.56)	0.28 (0.07/0.50)			
Gluc Δ 0 min	N/A	0.24 (0.05/0.43)	0.29 (0.15/0.43)	0.40 (0.24/0.57)	0.34 (0.13/0.55)	0.08 (−0.17/0.32)	0.03 (−0.23/0.29)	−0.01 (−0.24/0.22)			

(*Continued*)

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 2 Continued

Variable	0 min	Time after start of treatment							*P*-value		
		2.5 min	7 min	15 min	30 min	60 min	90 min	120 min	Group	Time	Group × Time
T amplitude (mV)											
NaBic	0.95 (0.60/1.30)[a]	0.65 (0.39/0.92)[ab]*	0.52 (0.30/0.74)[a]*	0.60 (0.41/0.79)[a]*	0.66 (0.40/0.93)[a]*	0.72 (0.48/0.95)[a]	0.68 (0.48/0.89)[a]*	0.68 (0.51/0.85)[a]*	.75	<.001	.03
NaCl	0.93 (0.61/1.25)[a]	0.46 (0.19/0.73)[a]*	0.55 (0.23/0.88)[a]*	0.55 (0.28/0.82)[a]*	0.67 (0.38/0.96)[a]*	0.75 (0.40/1.11)[a]	0.74 (0.33/1.15)[a]	0.69 (0.35/1.03)[a]*			
Gluc	0.95 (0.78/1.12)[a]	0.89 (0.69/1.10)[b]	0.83 (0.61/1.04)[a]	0.72 (0.43/1.01)[a]	0.59 (0.21/0.98)[a]*	0.74 (0.34/1.15)[a]	0.74 (0.36/1.13)[a]	0.76 (0.41/1.10)[a]			
NaBic Δ 0 min	N/A	−0.30 (−0.5/−0.1)	−0.43 (−0.64/−0.23)	−0.35 (−0.55/−0.16)	−0.29 (−0.52/−0.05)	−0.23 (−0.48/0.01)	−0.27 (−0.51/−0.03)	−0.27 (−0.49/−0.06)			
NaCl Δ 0 min	N/A	−0.47 (−0.66/−0.28)	−0.38 (−0.57/−0.18)	−0.38 (−0.57/−0.19)	−0.26 (−0.48/−0.04)	−0.18 (−0.40/0.05)	−0.19 (−0.42/0.03)	−0.24 (−0.44/−0.03)			
Gluc Δ 0 min	N/A	−0.06 (−0.26/0.14)	−0.12 (−0.33/0.09)	−0.23 (−0.43/−0.03)	−0.35 (−0.59/−0.12)	−0.20 (−0.45/0.04)	−0.20 (−0.44/0.04)	−0.19 (−0.41/0.02)			
T to S amplitude ratio											
NaBic	−0.48 (−0.66/−0.30)[a]	−0.51 (−0.77/−0.26)[a]	−0.37 (−0.53/−0.21)[a]	−0.41 (−0.56/−0.26)[a]	−0.43 (−0.63/−0.23)[a]	−0.45 (−0.64/−0.27)[a]	−0.43 (−0.61/−0.26)[a]	−0.44 (−0.59/−0.28)[a]	.87	.006	.10
NaCl	−0.46 (−0.58/−0.34)[a]	−0.33 (−0.51/−0.16)[a]	−0.39 (−0.59/−0.20)[a]	−0.39 (−0.51/−0.26)[a]	−0.42 (−0.54/−0.30)[a]	−0.43 (−0.57/−0.29)[a]	−0.41 (−0.56/−0.26)[a]	−0.39 (−0.54/−0.24)[a]			
Gluc	−0.45 (−0.50/−0.41)[a]	−0.50 (−0.66/−0.33)[a]	−0.46 (−0.57/−0.35)[a]	−0.43 (−0.63/−0.24)[a]	−0.33 (−0.56/−0.09)[a]	−0.35 (−0.51/−0.20)[a]	−0.35 (−0.48/−0.21)[a]	−0.34 (−0.46/−0.23)[a]*			
NaBic Δ 0 min	N/A	−0.03 (−0.17/0.11)	0.11 (0.0/0.23)	0.07 (−0.04/0.18)	0.05 (−0.09/0.18)	0.03 (−0.07/0.13)	0.05 (−0.05/0.14)	0.05 (−0.03/0.13)			
NaCl Δ 0 min	N/A	0.13 (0.0/0.26)	0.07 (−0.04/0.18)	0.08 (−0.02/0.18)	0.05 (−0.08/0.17)	0.04 (−0.06/0.13)	0.05 (−0.04/0.14)	0.07 (0.0/0.15)			
Gluc Δ 0 min	N/A	−0.04 (−0.18/0.09)	−0.01 (−0.13/0.11)	0.02 (−0.09/0.13)	0.13 (−0.01/0.26)	0.10 (0.0/0.20)	0.11 (0.01/0.20)	0.11 (0.03/0.19)			
ST amplitude (mV)											
NaBic	0.09 (0.00/0.18)[a]	0.02 (0.00/0.06)[a]	0.03 (0.00/0.06)[a]	0.04 (0.01/0.07)[a]	0.04 (0.03/0.06)[a]	0.04 (0.02/0.06)[a]	0.04 (0.02/0.06)[a]	0.04 (0.02/0.05)[a]	.57	.04	.07
NaCl	0.13 (0.03/0.24)[a]	0.08 (0.00/0.17)[a]	0.06 (0.02/0.10)[a]*	0.04 (0.01/0.07)[a]*	0.06 (0.02/0.09)[a]*	0.06 (0.0/0.12)[a]	0.08 (−0.07/0.24)[a]	0.05 (−0.01/0.10)[a]*			
Gluc	0.08 (0.00/0.16)[a]	0.06 (0.00/0.13)[a]	0.01 (−0.07/0.10)[a]	0.05 (0.00/0.10)[a]	0.04 (0.00/0.07)[a]	0.04 (0.00/0.09)[a]	0.05 (0.02/0.09)[a]	0.06 (0.02/0.09)[a]			
NaBic Δ 0 min	N/A	−0.06 (−0.12/−0.01)	−0.06 (−0.13/0.01)	−0.05 (−0.12/0.02)	−0.04 (−0.12/0.03)	−0.05 (−0.11/0.02)	−0.05 (−0.14/0.04)	−0.05 (−0.12/0.02)			
NaCl Δ 0 min	N/A	−0.05 (−0.10/0.00)	−0.07 (−0.13/−0.01)	−0.09 (−0.15/−0.03)	−0.08 (−0.15/−0.01)	−0.07 (−0.13/−0.01)	−0.05 (−0.13/0.03)	−0.09 (−0.15/−0.02)			
Gluc Δ 0 min	N/A	−0.02 (−0.08/0.04)	−0.07 (−0.13/0.00)	−0.03 (−0.09/0.04)	−0.04 (−0.12/0.03)	−0.04 (−0.10/0.03)	−0.03 (−0.11/0.06)	−0.02 (−0.09/0.04)			
ST angle (°)											
NaBic	4 (2/11)[a]	1 (0/2)[a]*	1 (0/3)[a]	1 (0/4)[a]	2 (1/3)[a]	2 (1/3)[a]	2 (0/5)[a]	2 (1/3)[a]	.75	.003	.20
NaCl	3 (1/10)[a]	0 (0/2)[a]*	2 (1/6)[a]	2 (1/4)[a]	2 (1/6)[a]	2 (1/8)[a]	1 (0/8)[a]	1 (0/4)[a]			
Gluc	4 (2/10)[a]	3 (1/12)[a]	1 (0/8)[a]	1 (0/9)[a]	2 (1/7)[a]	2 (0/11)[a]	2 (0/11)[a]	2 (0/11)[a]			
NaBic ratio 0 min	N/A	0.17 (0.05/0.57)	0.20 (0.05/0.80)	0.30 (0.08/1.11)	0.47 (0.15/1.45)	0.48 (0.13/1.85)	0.38 (0.09/1.60)	0.50 (0.17/1.44)			
NaCl ratio 0 min	N/A	0.13 (0.04/0.39)	0.64 (0.18/2.29)	0.85 (0.25/2.90)	0.73 (0.24/2.09)	0.74 (0.21/2.59)	0.55 (0.14/2.11)	0.30 (0.11/0.81)			
Gluc ratio 0 min	N/A	0.68 (0.21/2.22)	0.39 (0.10/1.53)	0.34 (0.09/1.29)	0.69 (0.22/2.15)	0.40 (0.10/1.53)	0.40 (0.15/1.22)	0.42 (0.10/1.67)			
QRS duration (ms)											
NaBic	93 (70/121)[a]	71 (63/79)[a]*	72 (61/84)[a]*	74 (60/90)[a]*	74 (62/88)[a]*	74 (64/85)[a]*	73 (64/85)[a]*	72 (62/85)[a]*	.63	.002	<.001
NaCl	91 (79/104)[a]	73 (65/82)[a]*	72 (61/84)[a]*	76 (65/89)[a]*	77 (67/88)[a]*	81 (71/93)[a]	80 (67/96)[a]	83 (71/98)[a]			
Gluc	80 (64/101)[a]	88 (72/107)[a]	89 (72/110)[a]	84 (70/102)[a]	82 (72/92)[a]	77 (68/88)[a]	78 (73/84)[a]	74 (65/84)[a]			
NaBic ratio 0 min	N/A	0.76 (0.67/0.87)	0.77 (0.68/0.88)	0.79 (0.71/0.89)	0.80 (0.70/0.91)	0.80 (0.70/0.92)	0.79 (0.68/0.92)	0.78 (0.69/0.89)			
NaCl ratio 0 min	N/A	0.80 (0.71/0.90)	0.78 (0.69/0.89)	0.83 (0.75/0.92)	0.84 (0.74/0.96)	0.89 (0.78/1.01)	0.88 (0.76/1.02)	0.92 (0.81/1.03)			
Gluc ratio 0 min	N/A	1.10 (0.96/1.25)	1.11 (0.97/1.27)	1.05 (0.94/1.17)	1.02 (0.89/1.17)	0.96 (0.84/1.11)	0.98 (0.84/1.14)	0.92 (0.81/1.05)			
ST duration (ms)											
NaBic	49 (21/76)[a]	89 (64/114)[a]*	95 (62/128)[a]*	82 (53/112)[a]*	75 (46/105)[a]*	68 (51/84)[a]	77 (57/98)[a]*	74 (52/97)[a]*	.27	<.001	.16
NaCl	63 (41/85)[a]	120 (70/169)[a]*	105 (62/148)[a]*	103 (66/140)[a]*	87 (56/118)[a]	79 (46/111)[a]	79 (48/109)[a]	83 (48/118)[a]			
Gluc	52 (33/71)[a]	67 (50/83)[a]	60 (46/75)[a]	73 (49/97)[a]	71 (35/108)[a]	67 (39/94)[a]	64 (36/92)[a]	65 (40/89)[a]			
NaBic Δ 0 min	N/A	40.6 (17.3/63.8)	46.0 (23.1/68.9)	33.7 (12.4/55.0)	26.9 (2.0/51.7)	19.1 (−0.5/38.8)	28.9 (9.0/48.7)	25.7 (6.5/44.9)			
NaCl Δ 0 min	N/A	56.3 (34.5/77.9)	41.8 (20.3/63.2)	39.8 (19.8/59.7)	23.8 (0.5/47.0)	15.5 (−2.9/33.9)	15.3 (−3.3/33.8)	19.8 (1.8/37.7)			
Gluc Δ 0 min	N/A	14.3 (−9.0/37.5)	8.0 (−14.9/30.9)	20.9 (−0.4/42.1)	19.1 (−5.7/44.0)	14.3 (−5.4/34.0)	11.7 (−8.1/31.6)	12.3 (−6.9/31.5)			

Values for ECG variables are reported as geometric means (HRV-SDRR, HRV-CV, ST angle, and QRS duration) or means (all other variables) and associated lower and upper limits of the 95% CIs (in brackets). Different letters (eg, *a* vs *b*) indicate a statistically significant difference between groups at the respective time point ($P < .05$), whereas the same or overlapping letters (eg, *a* vs *a* or *a* vs *ab*) indicate no significant difference. Asterisks indicate values that are significantly different from 0 min ($P < .05$). Effect sizes for within-group comparisons are reported as mean differences from 0 min (Δ) or ratios to 0 min with associated 95% CIs (in brackets). Abbreviations: HRV-SDRR = heart rate variability based on standard deviation of RR intervals; HRV-CV = heart rate variability based on coefficients of variation of RR intervals; N/A = not applicable.

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

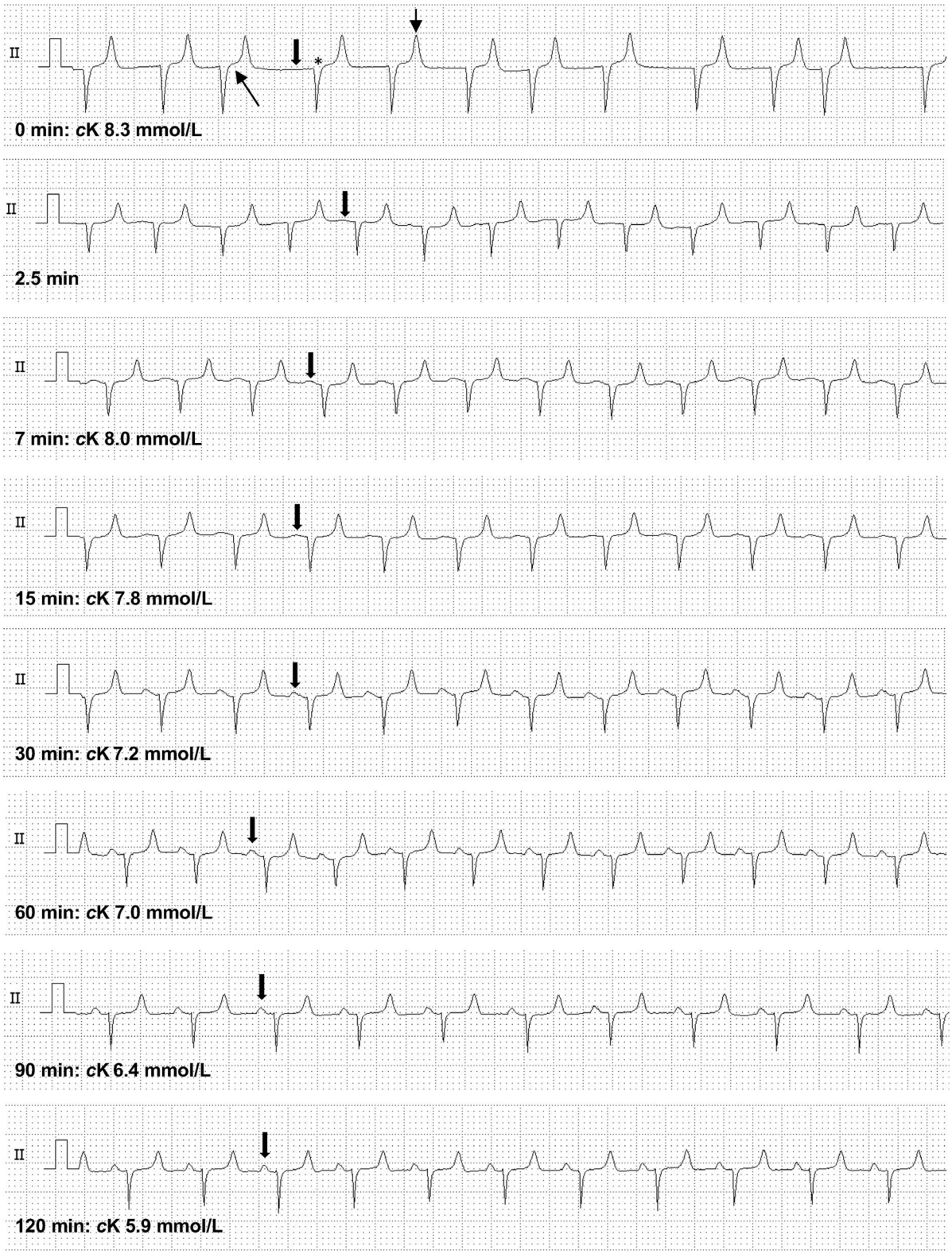


Figure 1 Electrocardiographic findings in a hyperkalemic neonatal diarrheic calf (25 mm/s, 5 mm/mV) before, during, and after intravenous administration of 8.4% sodium bicarbonate (6.4 mL/kg over 5 min) and subsequent suckling of an oral electrolyte solution. At initial presentation, plasma potassium concentration was 8.3 mmol/L, venous pH 7.19, and plasma sodium concentration 123.3 mmol/L. The baseline ECG revealed arrhythmias, absent P waves (thick arrow), increased QRS duration (asterisk), ST-segment elevation (thin oblique arrow), and tall symmetric T waves (thin straight arrow). Follow-up ECGs (2.5-120 min after infusion start) demonstrated rapid restoration of P waves (indicated by thick arrows) and normalization to sinus rhythm.

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

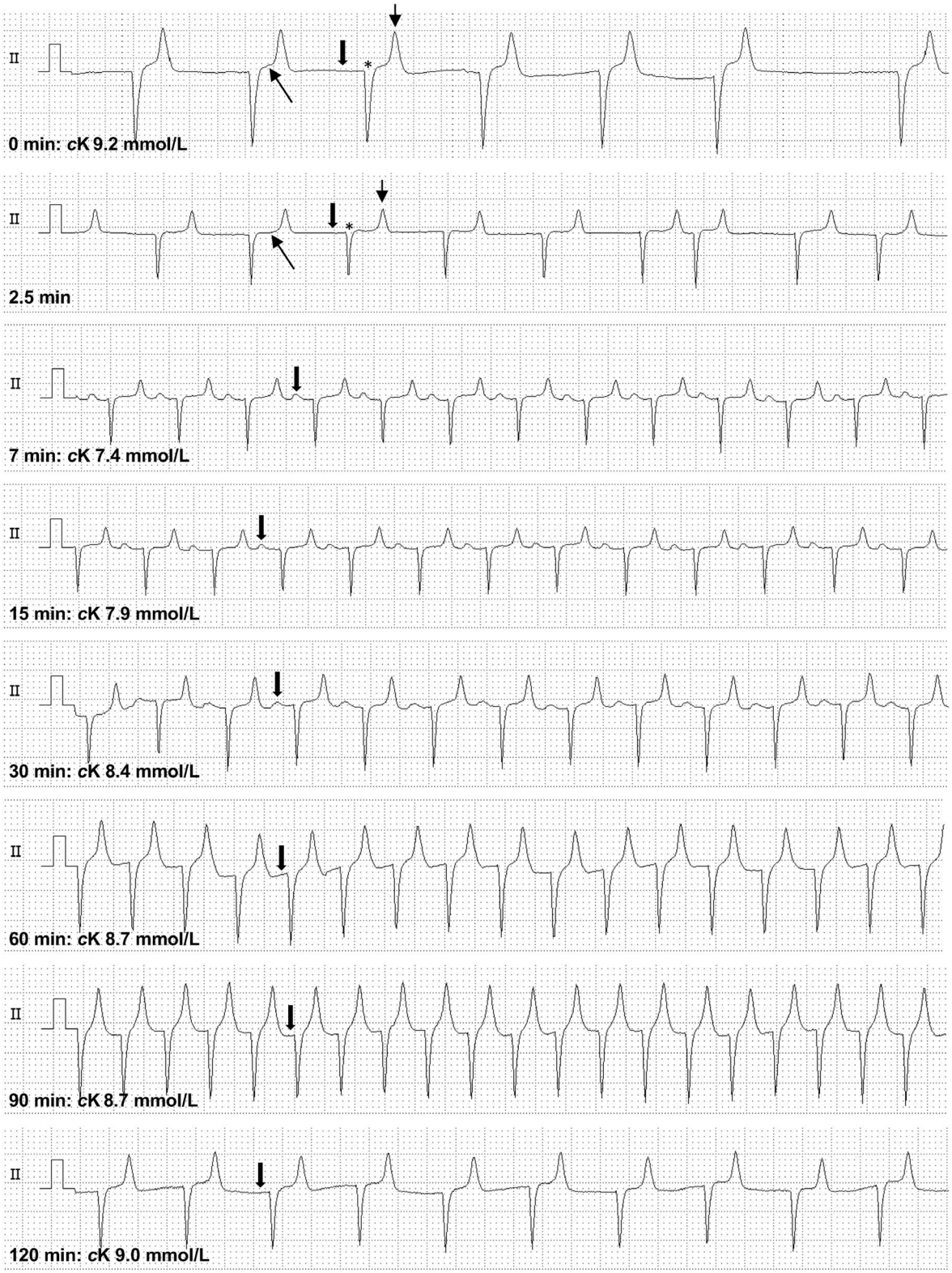


Figure 2 Electrocardiographic findings in a hyperkalemic neonatal diarrheic calf (25 mm/s, 5 mm/mV) before, during, and after intravenous administration of 7.5% hypertonic sodium chloride (5 mL/kg over 5 min) and subsequent suckling of an oral electrolyte solution. At initial presentation, plasma potassium was 9.2 mmol/L, venous pH 6.84, and plasma sodium 120.3 mmol/L. The baseline ECG showed arrhythmias, absent P waves (thick arrow), widened QRS complexes (asterisk), ST-segment elevation (thin oblique arrow), and tall symmetric T waves (thin straight arrow). The ECG at 2.5 min reveals decreased S and T wave amplitudes, ST segment flattening (thin oblique arrow) and decreased QRS duration (asterisk), but RR-irregularities and no P waves (thick arrow). A normal sinus rhythm and return of P waves (thick arrows) were evident at 7, 15, and 30 min. Further electrocardiograms at 60, 90, and 120 min revealed again a loss of P waves (thick arrows) and increased QRS duration, and tachycardia at 60 and 90 min.

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026



Figure 3 Electrocardiographic findings in a hyperkalemic neonatal diarrheic calf (25 mm/s, 5 mm/mV) before, during, and after intravenous administration of 46.2% glucose (5 mL/kg over 5 min) followed by oral electrolyte solution. At presentation, plasma potassium was 7.8 mmol/L, venous pH 7.19, and plasma sodium 122.3 mmol/L. The electrocardiogram at baseline reveals no P waves (thick arrow), increased QRS duration (asterisk), ST-segment elevation (thin oblique arrow), and large amplitude symmetric T waves (thin straight arrow). Further electrocardiograms were recorded at 2.5, 7, 15, 30, 60, 90, and 120 min after initiation of infusion of the hypertonic dextrose solution. Return of P waves (thick arrow), decreased QRS duration (asterisk), flattening of ST segment (thin oblique arrow), decreased T wave amplitudes (thin straight arrow), and less negative S wave amplitudes were observed at 30 min.

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 3 Generalized linear mixed models for predicting changes of selected ECG variables over time. ECGs were recorded in 22 neonatal diarrheic calves before and after administration of infusions with a hypertonic 8.4% sodium bicarbonate (NaBic; $n = 7$), 7.5% sodium chloride (NaCl; $n = 8$), or 46.2% glucose solution (Gluc; $n = 7$) over a period of 5 min and subsequent suckling of an oral electrolyte solution.

Model estimates					**Estimated marginal means (95% CI) for treatment groups**		
Variable	**Estimate**	**95% CI**	***P*-value**	**VIF**	**NaBic**	**NaCl**	**Gluc**
Heart rate							
Constant	205.1	11.9/398.3	.04	–			
Na	1.20	0.83/1.57	<.001	1.2			
pH	−30.96	−58.07/−3.86	.03	1.4			
Group (Ref. Gluc)				1.4			
NaBic	−22.00	−44.52/0.52	.06				
NaCl	−39.13	−60.82/−17.43	<.001		120.4 (104.4/136.4)	103.3 (88.6/118.0)	142.4 (126.9/157.9)
Heart rate variability (HRV-SDRR)							
Constant	−155.3	−368.0/57.4	.15	–			
K × Na	−0.25	−0.45/−0.04	.02	1.0			
Na	−0.41	−0.69/−0.12	.006	1.2			
pH	29.9	1.4/58.4	.04	1.4			
Group (Ref. Gluc)				1.4			
NaBic	−5.0	−13.9/3.9	.27				
NaCl	14.2	6.5/21.8	<.001		0.9 (−5.6/7.4)	20.0 (14.0/26.1)	5.9 (0.8/11.0)
P wave amplitude							
Constant	0.65	0.14/1.17	.01	–			
K	−0.03	−0.04/−0.02	<.001	1.1			
K × Na	0.0008	0.0002/0.0014	.009	1.1			
Na	0.003	0.001/0.004	<.001	1.3			
pH	−0.079	−0.156/−0.002	.04	1.5			
Plasma volume	−0.001	−0.001/−0.0004	<.001	1.0			
Group (Ref. Gluc)				1.5			
NaBic	−0.06	−0.13/0.01	.08				
NaCl	−0.085	−0.152/−0.017	.02		0.18 (0.13/0.23)	0.16 (0.11/0.20)	0.24 (0.19/0.29)
Ta wave amplitude							
Constant	−0.072	−0.094/−0.05	<.001	–			
K × Na	−0.0005	−0.0008/−0.0002	.003	1.0			
Plasma volume	0.0004	0.0001/0.0006	.002	1.0			
Group (Ref. Gluc)				1.0			
NaBic	0.024	−0.007/0.055	.13				
NaCl	0.036	0.006/0.066	.02		−0.04 (−0.06/−0.02)	−0.03 (−0.05/−0.01)	−0.07 (−0.09/−0.04)
S wave amplitude							
Constant	1.59	−1.62/4.79	.33	–			
K × Na	0.01	0.006/0.013	<.001	1.0			
Plasma volume	0.012	0.01/0.014	<.001	1.0			
pH	−0.528	−0.973/−0.084	.02	1.3			
Group (Ref. Gluc)				1.3			
NaBic	0.51	0.12/0.90	.01				
NaCl	0.26	−0.11/0.63	.16		−1.47 (−1.75/−1.19)	−1.72 (−1.97/−1.46)	−1.98 (−2.25/−1.71)
T wave amplitude							
Constant	0.36	0.04/0.69	.03	–			
K	0.085	0.046/0.123	<.001	1.0			
K × Na	−0.007	−0.010/−0.003	<.001	1.0			
Plasma volume	−0.006	−0.008/−0.004	<.001	1.0			
Group (Ref. Gluc)				1.0			
NaBic	−0.09	−0.42/0.24	.60				
NaCl	−0.08	−0.40/0.25	.65		0.68 (0.44/0.92)	0.70 (0.47/0.92)	0.77 (0.53/1.00)

(*Continued*)

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 3 Continued

Model estimates					Estimated marginal means (95% CI) for treatment groups		
Variable	**Estimate**	**95% CI**	***P*-value**	**VIF**	**NaBic**	**NaCl**	**Gluc**
QRS duration							
Constant	283.4	126.2/440.6	<.001	–			
K	4.30	2.17/6.42	<.001	1.1			
K × Na	−0.28	−0.44/−0.12	<.001	1.1			
Na	−0.38	−0.68/−0.09	.01	1.2			
pH	−25.0	−46.7/−3.4	.02	1.5			
Group (Ref. Gluc)				1.5			
NaBic	1.54	−9.48/12.56	.78				
NaCl	0.78	−10.15/11.7	.89		81.0 (72.9/89.1)	80.2 (72.8/87.7)	79.5 (72.0/86.9)
ST duration							
Constant	113.6	82.9/144.2	<.001	–			
K	−10.2	−14.2/−6.1	<.001	1.0			
Plasma volume	0.60	0.37/0.83	<.001	1.0			
Group (Ref. Gluc)				1.0			
NaBic	8.6	−19.6/36.8	.55				
NaCl	26.6	−1.1/54.3	.06		70.1 (50.0/90.3)	88.1 (69.3/106.9)	61.5 (41.4/81.7)
ST amplitude							
Constant	0.012	−0.043/0.067	.66	–			
K	0.009	0.0003/0.017	.04	1.0			
K × Na	−0.001	−0.002/−0.0004	.001	1.0			
Plasma volume	−0.001	−0.001/−0.0004	<.001	1.0			
Group (Ref. Gluc)				1.0			
NaBic	−0.012	−0.052/0.028	.55				
NaCl	0.009	−0.031/0.049	.65		0.04 (0.01/0.07)	0.06 (0.03/0.09)	0.05 (0.02/0.08)
ST angle							
Constant	50.5	14.6/86.3	.006	–			
K × Na	−0.051	−0.087/−0.014	.006	1.0			
pH	−6.58	−11.56/−1.58	.01	1.0			
Group (Ref. Gluc)				1.0			
NaBic	−0.32	−2.93/2.30	.81				
NaCl	−0.61	−3.00/1.78	.61		2.8 (0.9/4.7)	2.5 (0.8/4.2)	3.1 (1.4/4.8)

The interaction between *c*K and *c*Na was included in the models as a centered variable by multiplying the differences of each variable from its respective mean (*c*K = 6.32 mmol/L; *c*Na = 133.6 mmol/L). Abbreviation: VIF = variance inflation factor.

analysis identified distinct threshold values at which ECG variables changed: P wave amplitude decreased when *c*K exceeded 6.5 mmol/L; S wave amplitude decreased at *c*K > 7.4 mmol/L; QRS duration increased at *c*K > 7.8 mmol/L; and ST segment angle increased at *c*K > 9.1 mmol/L. Additionally, P wave amplitude was characterized by a second breakpoint at *c*K = 8.2 mmol/L, above which P waves were absent.[3]

These previously reported breakpoints were not confirmed in our present study (Table 4; Figures 5 and 6), likely because of greater variability in the underlying data, which may be attributable to confounding effects of different treatment interventions, particularly in *c*K:*c*Na. This interpretation is supported by the results of segmented linear regression analyses of *c*K:*c*Na with QRS duration, P wave amplitude, T wave amplitude, and the T-to-S wave amplitude ratio, which in part demonstrated a better model fit than analyses using *c*K alone (see Figures 5 and 6 compared with Figures S1 and S2). Notably, breakpoint estimates for several ECG variables were associated with narrow CIs. This finding is not unexpected in analyses involving repeated measurements from the same calf, particularly when the second slope differs markedly from the first, is of opposite sign, or when both slopes are substantially larger than zero (see Table 4).

Generalized linear mixed model analyses detected significant effects of treatment group in some of the models. However, these significant treatment effects should be interpreted with caution and do not necessarily indicate a clinically meaningful advantage of any specific intervention. The uneven distribution of calves with severe ECG alterations related to marked hyperkalemia across the 3 treatment groups, which is likely related to the small sample size, may have influenced the results. For example, at baseline, none of the calves in the Gluc group exhibited arrhythmias, whereas P wave amplitude alterations were more frequent in the NaBic and NaCl groups.

In our present study, smaller P wave amplitude or absence of P waves were associated with *c*K > 6.7 mmol/L. The absence of P waves, reflecting atrial standstill, is a hallmark ECG feature

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

Table 4 Results of segmented linear regression analyses evaluating the association between 7 ECG variables and *c*K as well as *c*K:*c*Na ratio in calves of the study population. The analyses were based on 154 observations obtained from 22 calves (7 measurements per calf) during a 120-min study period before, and after IV infusion of hypertonic 8.4% sodium bicarbonate ($n = 7$), 7.5% sodium chloride ($n = 8$), or a 46.2% glucose solution ($n = 7$).

Variable	Intercept	Slope 1	Slope 2	Breakpoint	95% CI for breakpoint
Analyses based on the plasma potassium concentration					
QRS duration	42.3	5.85	111.2	8.72	8.60-8.84
P wave amplitude	0.33	−0.02	−0.08	6.74	6.27-7.21
S wave amplitude	−2.74	0.22	−0.16	5.55	5.54-5.56
T wave amplitude	0.73	−0.04	0.20	5.65	5.64-5.66
T to S wave amplitude ratio	−0.28	−0.01	−0.08	5.67	4.80-6.54
ST angle	1.54	0.25	7.29	7.85	7.84-7.86
ST segment amplitude	−0.01	0.01	0.22	8.32	8.02-8.62
Analyses based on the plasma potassium to sodium ratio					
QRS duration	46.8	6.81	92.1	7.03	6.63-7.43
P wave amplitude	0.32	−0.03	−0.08	5.36	5.35-5.37
S wave amplitude	−1.83	0.04	−0.25	5.47	4.84-6.09
T wave amplitude	0.60	0.01	0.25	4.97	4.50-5.44
T to S wave amplitude ratio	−0.31	−0.02	−0.09	4.81	4.04-5.57
ST angle	4.79	−0.40	3.01	5.30	5.28-5.32
ST segment amplitude	0.05	−0.002	0.07	5.74	5.20-6.28

The potassium to sodium ratio was calculated by dividing potassium by sodium concentrations and multiplying the resulting value by 100 to improve readability.

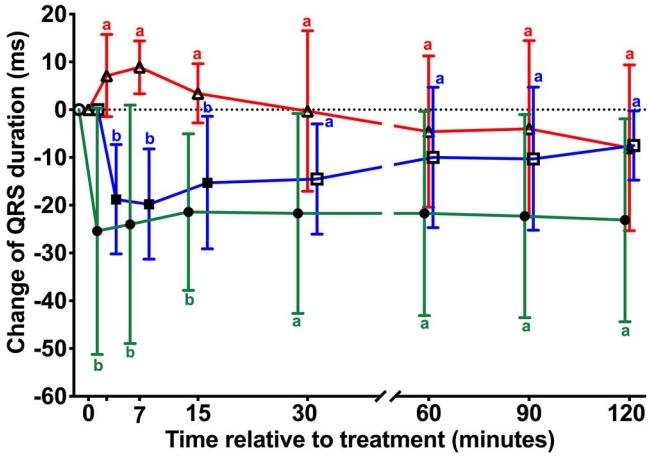


Figure 4 Changes of QRS duration relative to baseline in 22 neonatal diarrheic calves during and after injections of an 8.4% sodium bicarbonate solution in a dosage of 6.4 mL/kg body mass (green line and circles; $n = 7$), 7.5% sodium chloride solution in a dosage of 5 mL/kg body mass (blue line and squares; $n = 8$), or a 46.2% glucose solution in a dosage of 5 mL/kg body mass (red line and triangles; $n = 7$) over a period of 5 min and subsequent administration of an oral electrolyte solution. The x-axis is segmented to enhance visualization of early treatment effects, with higher temporal resolution during the first 30 min (0-30 min). Values with different lowercase letters differed significantly between groups ($P < .05$). Filled symbols indicate a statistically significant difference from baseline (0 min). Data are shown as means with upper and lower limits of the 95% CI. Values for groups NaBic and Gluc were slightly offset at each time point to improve readability.

of marked hyperkalemia and has been described previously in calves,[3,5,10,30,31] companion animals,[32–34] and humans.[35,36] This phenomenon can be explained by the higher sensitivity of atrial myocytes to hyperkalemia and sustained depolarization relative to other cardiac tissues, including sinoatrial and atrioventricular nodal fibers.[25,37,38]

Observed changes in *c*K during the 120 min study period suggested a treatment advantage of hypertonic sodium bicarbonate over the use of hypertonic NaCl and glucose solutions in terms of a more rapid and sustained restoration of potassium homeostasis. This conclusion is based on the observation that hypertonic NaCl was associated with a renewed increase in *c*K after an initial potassium-lowering effect. Furthermore, administration of hypertonic glucose resulted in a delayed decrease of *c*K associated with endogenous insulin release.[14] Of interest is our finding that these differences were not clearly reflected by between-group comparisons of most ECG variables (especially at later stages of the trial), which is likely related to small sample size and large variability of ECG findings. Baseline differences of specific ECG findings were present across treatment groups. Therefore, results of between-group comparisons must be interpreted cautiously. The large variability of ECG findings is, however, not unique to the present dataset, because considerable variability of ECG findings also was observed in our previous study in calves[3] and in studies in hyperkalemic dogs, cats, and humans.[34,39,40] Nevertheless, 2 min after completion of the infusion ($t = 7$ min), calves of group Gluc had shorter ST segment durations and significantly larger S wave amplitudes when compared with calves of groups NaBic and NaCl, as well as numerically larger T waves when compared with calves of group NaBic. In general, calves of group Gluc exhibited numerically or significantly larger S wave amplitudes compared with calves of groups NaBic and NaCl throughout the experiment. This finding also was reflected by a significant group effect in the linear mixed-effects model and the generalized linear mixed model analysis. The latter indicated that changes in plasma volume were positively associated with changes of S wave amplitude. This finding may be explained by the Brody phenomenon, which refers to the observation that an increase in ventricular volume

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

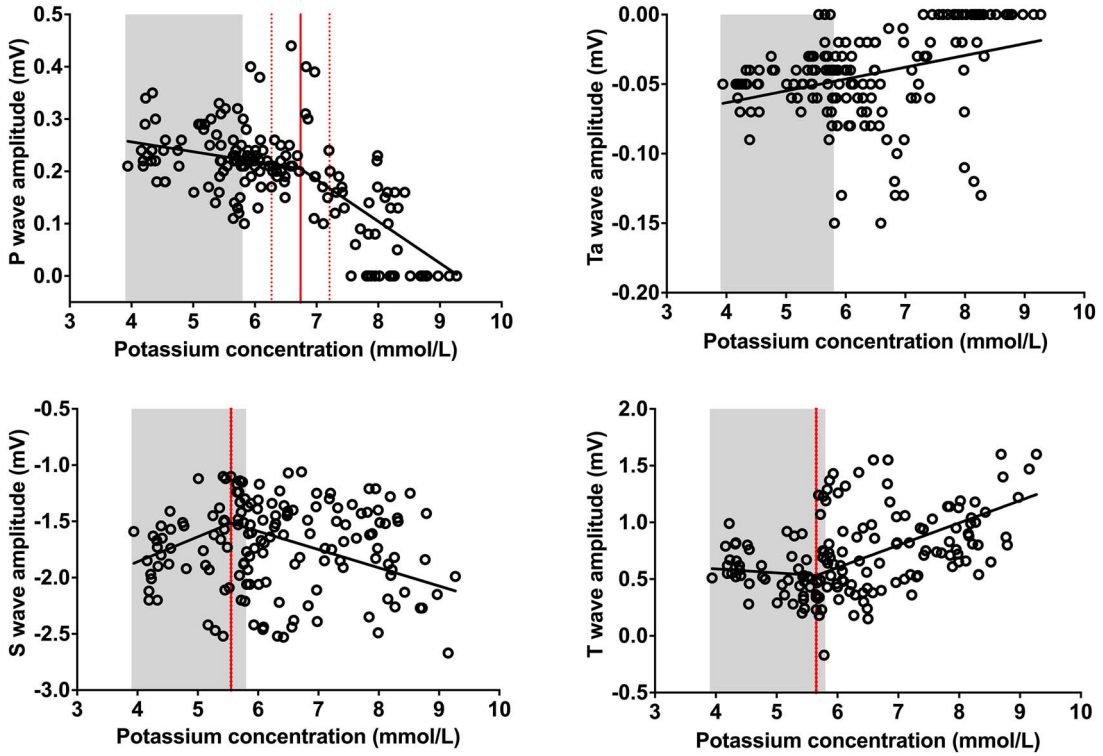


Figure 5 Scatterplots illustrating the association between plasma potassium concentration and P, Ta, S, and T wave amplitudes across the study period. A total of 154 observations obtained from 22 calves (7 time points per animal) are shown. The lines represent the results of segmented regression (P, S, and T amplitude) or simple linear regression analysis (Ta amplitude). Solid red vertical lines indicate statistically identified breakpoints from segmented regression; dashed red lines denote the corresponding 95% CIs. Gray-shaded areas represent the reference range for plasma potassium concentrations (3.9-5.8 mmol/L).

leads to an increase in QRS complex voltage.[41–43] This occurs because the larger intracavitary blood mass enhances the radial components while decreasing the tangential components of the cardiac dipole.[41] However, the Brody phenomenon only partially explains the observed group differences in S wave amplitude, because administration of the 46.2% glucose solution led to more pronounced plasma volume expansion only during the first 15 min of the trial. Administration of the sodium- and buffer-free infusion solution in the Gluc group may have been an additional contributing factor, because this intervention led to persistent acidemia and negatively affected the *c*K:*c*Na ratio. In both our present and a previous study,[3] acidemia was positively associated with increased S wave amplitude voltages.

Furthermore, the delayed potassium-lowering effect of hypertonic glucose was reflected in the ECG of the single calf that initially presented with absent P waves because of marked hyperkalemia (Figure 3). In some individual calves from the NaCl group, significant ECG abnormalities such as the loss of P waves and ventricular escape rhythms reappeared after initial improvement (Figure 2). This recurrence was associated with a renewed increase in *c*K. The absence of P waves indicates severe impairment of atrial depolarization,[10,44] a condition that may compromise ventricular filling and predispose to hemodynamic instability. Ventricular escape rhythms reflect advanced disturbances of impulse formation and conduction and generally are considered signs of myocardial electrical instability.[35,44] From a clinical perspective, these findings suggest that a rapid and sustained decrease of *c*K is important in the initial treatment of affected calves. In this context, the documented rapid and more sustained potassium-lowering effect of hypertonic sodium bicarbonate may provide a clinically relevant treatment advantage over the use of hypertonic sodium chloride in individual calves with advanced hyperkalemia. Although hypertonic sodium bicarbonate is already routinely administered to severely acidemic diarrheic calves in clinical practice, regardless of *c*K, our present study provides novel insight into the temporal ECG response to different hypertonic infusion solutions. Thus, the principal contribution of our study is not the identification of a new therapeutic approach but a better understanding of the mechanisms underlying the rapid reversal of hyperkalemia-associated cardiac conduction abnormalities and how rapid stabilization of affected calves can be achieved.

A deterioration in general condition was not noted during clinical monitoring of the calves with recurrence or incomplete reversal of ECG manifestations (which would have been an indication to stop the experiment); however, further IV fluid therapy was required immediately after the end of the 120-min study period in these calves because of ongoing clinical signs of marked dehydration. Severe clinical dehydration or even shock is a hallmark finding in hyperkalemic calves with neonatal diarrhea,[1,2,6] and the rehydration protocol was insufficient to correct the existing fluid deficit in most of the animals.

To the best of our knowledge, ours is the first randomized clinical trial evaluating the efficacy of different hypertonic infusion solutions for rapid reversal of ECG abnormalities in hyperkalemic animals with neonatal diarrhea and dehydration. However, our study had several limitations, primarily related to its exploratory nature and small sample size. Another potential limitation is the use of bipolar limb lead II for ECG analysis, which was chosen

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

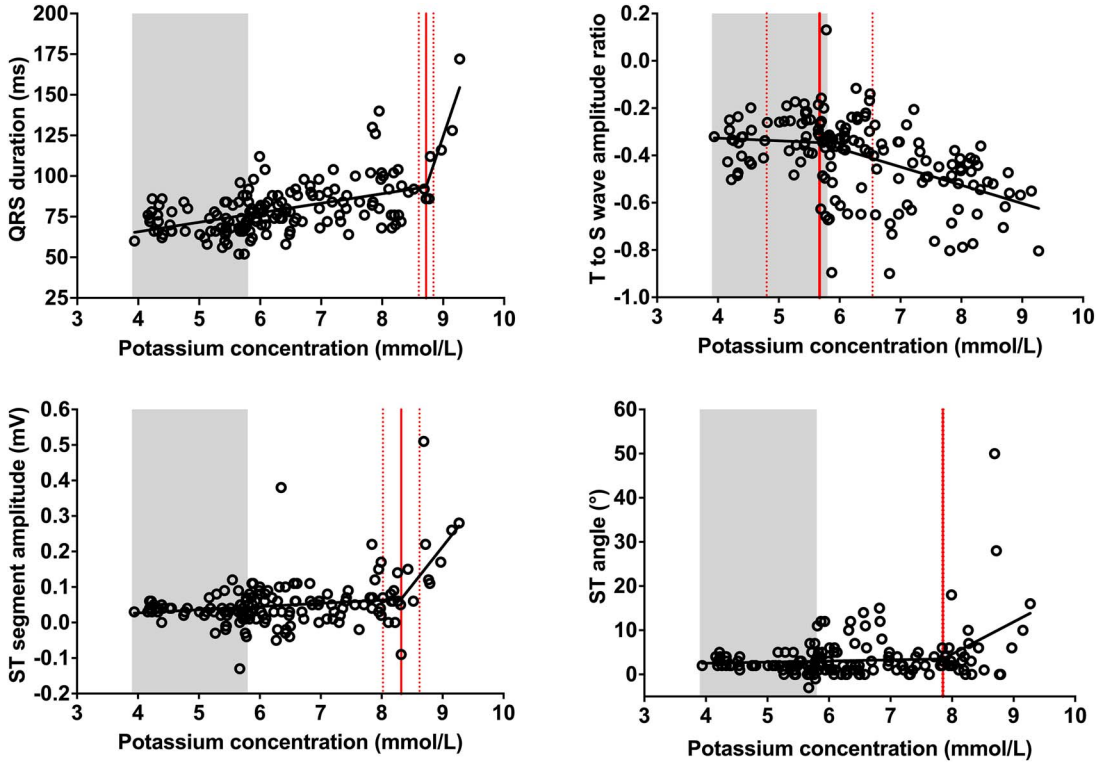


Figure 6 Scatterplots illustrating the association between plasma potassium concentrations during the study period and QRS duration, T to S wave amplitude ratio, ST segment amplitude measured at the start of the T wave, and ST angle. A total of 154 observations obtained from 22 calves (7 time points per animal) are shown. Vertical solid red lines mark the breakpoints identified by segmented regression and dashed red lines the corresponding 95% CIs. Gray-shaded areas represent the reference range for plasma potassium concentrations (3.9-5.8 mmol/L).

because it is a frequently used ECG lead in small animal medicine. A previous study evaluating ECG parameters in clinically healthy, lactating Holstein cows reported decreased amplitudes and increased waveform variability in limb lead recordings, including lead II, when compared to base–apex lead configurations.[45] However, a comparative analysis of limb lead II and base–apex lead using the same ECG system in our previous study in calves[3] did not identify major differences in amplitudes, durations, or variability of ECG variables. Still, we cannot exclude the possibility that the use of base–apex leads might have yielded more consistent results. In addition, the non-blinded evaluation of the ECG recordings may be regarded as a shortcoming, but the use of dedicated software ensured a standardized and consistent assessment of amplitudes and durations of the selected ECG variables.[3]

The short observation period also may be considered a limitation. However, the study was specifically designed to evaluate the effectiveness of various infusion solutions in rapidly stabilizing hyperkalemic calves, rather than assessing the full resuscitative response to a single hypertonic injection followed by oral electrolyte therapy. Future adequately powered studies with larger sample sizes are warranted to further investigate the clinical utility of different IV fluids in hyperkalemic calves. In particular, it should be determined whether combined administration of sodium bicarbonate and glucose offers a clinically meaningful therapeutic advantage in affected animals. A study in diarrheic calves has demonstrated that sequential administration of IV isotonic sodium bicarbonate and then IV 50% dextrose and insulin (0.25 IU/kg SC) resulted in a lower *c*K than in calves that did not receive dextrose and insulin.[46] Previous studies[47,48] have used a higher sodium bicarbonate dosage (10 mL/kg) than that administered in our present study for hypertonic rehydration purposes. Whether this higher dosage results in superior clinical outcomes compared with our protocol remains to be determined.

Conclusions

Our exploratory study suggests that small-volume IV administration of hypertonic sodium solutions can rapidly reverse the cardiotoxic effects of hyperkalemia in calves, including restoration of normal heart rhythm and atrial activity, shortening of the QRS duration, and decreases in S and T wave amplitude voltages. Because of their alkalinizing capacity and more sustained potassium-lowering effect when compared with hypertonic NaCl solutions, hypertonic sodium bicarbonate solutions appear to be a promising treatment option for a rapid stabilization of hyperkalemic calves.

Acknowledgments

The authors thank all staff members of the Clinic for Ruminants with Ambulatory and Herd Health Services (LMU Munich) who were involved in the clinical management of calves for their assistance.

Author contributions

Florian M. Trefz (Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

administration, Resources, Validation, Visualization, Writing—original draft, Writing—review & editing), Ingrid Lorenz (Supervision, Writing—review & editing), and Peter D. Constable (Conceptualization, Formal analysis, Methodology, Supervision, Writing—original draft, Writing—review & editing)

Supplementary material

Supplementary material is available at *Journal of Veterinary Internal Medicine* online.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

This work was financed by research grants (TR 1321/1-1 and TR 1321/3-1) of the German Research Foundation (Deutsche Forschungsgemeinschaft, Bonn, Germany).

Off-label antimicrobial declaration

The authors declare no off-label use of antimicrobials.

Institutional animal care and use committee or other approval declaration

Methods of this study were approved by the Animal Welfare and Ethics Committee of the government of Upper Bavaria (permit no. 55.2-1-54-2532-211-13). Written informed consent was obtained from the owners of calves before inclusion into the study.

Human ethics approval declaration

The authors declare human ethics approval was not needed.

Appendix

Detailed description of materials and methods

Calves

A prospective study was carried out involving 22 hyperkalemic neonatal diarrheic calves (age $\leq$ 21 days) with measured plasma potassium concentrations (*c*K) $>$ 5.8 mmol/L that were admitted to a university teaching hospital for treatment. Results of this study focusing on the observed dynamics of *c*K during the experiment have already been published previously and detailed information on the study population and exclusion criteria for calves can be found elsewhere.[14]

Experimental protocol

After weighing and an initial clinical examination, a catheter (Splittocan Infusionskatheter, 16-gauge, 150 mm, Walter Veterinär Instrumente, Baruth, Germany) was placed in a jugular vein and secured in place with suture material. Calves were randomly allocated to 1 of 3 treatment groups which was conducted by drawing a lot out of a pool of 3 possible lots representing each treatment group:

1. *Sodium bicarbonate group* (NaBic; *n* = 7): Calves received a commercially available 8.4% sodium bicarbonate solution (theoretical osmolarity 2000 mOsm/L; Natriumhydrogencarbonat, 8.4%, B. Braun Melsungen AG, Germany) at a dosage of 6.4 mL/kg over a period of 5 min. This dosage was chosen in order to provide the same sodium load as in calves of group NaCl.
2. *Sodium chloride group* (NaCl, *n* = 8): Calves received a commercially available 7.5% sodium chloride solution (theoretical osmolarity, 2566 mOsm/L; Hypertone Natriumchloridlösung, 7.5 g/100 mL, B. Braun Melsungen AG, Germany) at a dosage of 5 mL/kg body weight over 5 min. This provided a sodium load of 6.4 mmol/kg.
3. *Glucose group* (Gluc, *n* = 7): Calves received a 46.2% glucose solution in a dosage of 5 mL/kg over a period of 5 min. For this purpose, a commercially available 50% glucose solution (Glucose 500 mg/mL, Braun Melsungen AG, Germany) was diluted with sterile water (Ampuwa, Fresenius Kabi Deutschland GmbH, Germany) in order to provide an infusion solution that had a comparable osmolarity (2564 mOsm/L) to the hypertonic NaCl solution.

Fifteen minutes after completion of infusions, calves were allowed to suckle 2 L of a commercially available oral electrolyte solution (Effydral, Zoetis Deutschland GmbH, Berlin, Germany). This oral electrolyte solution contained 2.34 g NaCl (40 mmol), 1.12 g KCl (15 mmol), 6.72 g sodium bicarbonate (80 mmol), 3.84 g citric acid (20 mmol), 32.44 g lactose monohydrate (90 mmol), and 2.25 g glycine (30 mmol) per liter. The theoretical calculated osmolarity and effective strong ion difference of this solution was 410 mOsm/L and 80 mEq/L, respectively. If the respective volume of the solution was not suckled entirely within 10 min, the remainder of the solution was tube fed after blood sampling at 30 min after start of treatment. Administration of the oral electrolyte solution was only possible at 20 min after start of treatment because of the tight schedule associated with the infusion protocols, repeated blood sampling, and ECG recordings.

During the trial, calves were monitored clinically, and a detailed analysis of the recorded ECGs was performed at a later point in time. After the end of the study period at 120 min, calves were immediately treated according to clinic principles and received further infusions based on the current acid–base and clinical dehydration status.

Electrocardiographic examinations

An ECG examination was performed immediately before injection of the infusion solution (0 min), during infusion (2.5 min after start of infusion), and 7, 15, 30, 60, 90, and 120 min after the initiation of the infusion using a PC-based ECG system (PC-EKG 2000, Eickemeyer, Tuttlingen, Germany). As previously described,[3] ECGs were recorded in a standardized body position by placing calves in sternal recumbency with the legs positioned parallel to the long axis and folded normally at the carpal and tarsal joints. Electrocardiogram electrodes were attached to the skin using alligator clips over the olecranon on the caudal aspect of the forelimbs, over the patellar ligament on the cranial aspect of the hindlimbs, and at the eighth intercostal space of the left thorax close to the costochondral junction. For this purpose, a small area of the skin

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

was clipped, cleaned with alcohol (70% solution) and electrocardiographic gel applied. Amplitudes and durations of the ECG complexes were determined using the bipolar limb lead II from a software program that averaged the amplitude and duration of the complexes during a recorded 32-s period, thereby producing a single template of P, QRS, and T waves. Detailed information on the software-based analysis of ECG measurements and determination of the amplitudes and duration of selected ECG complexes have also been described elsewhere.[3] Analyses of ECG measurements could not be masked as clinical and laboratory examinations were performed by the same investigator. For the present analysis, RR irregularities were defined as a deviation of 2 consecutive RR intervals of more than 10%.[18] In order to quantify the extent of arrhythmias, heart rate variability (HRV) was assessed by calculating the standard deviation of RR intervals[19,20] (HRV-SDRR) and the coefficient of variation of RR intervals[21] (HRV-CV), derived from the 32-s ECG recordings.

Laboratory analyses

For the present analysis, venous blood pH, plasma sodium concentrations (*c*Na), and *c*K were determined at 0, 7, 15, 30, 60, 90, and 120 min relative to the onset of infusion from lithium-heparinized blood samples. These samples were anaerobically collected from the catheter using 2-mL polypropylene syringes and analyzed with a blood pH, gas, and electrolyte analyzer with ion-selective electrodes (Rapidpoint 405, Siemens Healthcare Diagnostics Inc., Tarrytown). The *c*K:*c*Na ratio was calculated by dividing potassium by sodium concentrations and multiplying values by 100 to improve readability.[3] After blood gas analysis, syringes were immediately refrigerated and centrifuged within 60 min after collection at 1500 × *g* for 10 min. Harvested plasma samples were assayed for concentrations of total protein with the biuret method using an automatic analyzing system (Cobas c311, Roche Diagnostics, Mannheim, Germany). Changes in plasma volume were extrapolated from changes in plasma total protein concentrations.[14,49]

Statistical analyses

At the time of study planning, no published data were available regarding the efficacy of different hypertonic infusion solutions for a rapid reversal of electrocardiographic abnormalities in hyperkalemic calves with neonatal diarrhea. Consequently, an a priori sample size calculation was not feasible, and the data obtained in the present study were analyzed in an exploratory manner. The study was therefore designed as an exploratory, hypothesis-generating investigation, and all statistical analyses and resulting inferences should be interpreted accordingly rather than as confirmatory evidence.

Commercially available software programs (SPSS, version 31.0, IBM, New York, USA; GraphPad Prism, version 10.1.1, GraphPad Software, Boston, Massachusetts, USA; SAS, version 9.4, SAS Inc., Cary, USA) were used for the statistical analysis of the results and *P*-values $< .05$ were considered significant. A normal distribution of data was assessed by the Shapiro–Wilk *W* test and visual inspection of QQ-plots. If necessary, ECG variables were log-transformed to achieve a normal distribution of respective variables. Values of non-normally distributed variables were back-transformed after statistical analysis to facilitate comparisons of values to previous studies and are reported as geometric means and respective 95% CIs. Values of untransformed ECG variables are reported as means and associated 95% CIs. A linear mixed-effects model was used to detect differences of ECG variables (heart rate, HRV-SDRR, HRV-CV, amplitudes of P, Ta, S, T, and ST segment as well as T to S amplitude ratio, QRS duration, ST angle, and ST segment duration) over time and between treatment groups. Outcomes were analyzed using time (0, 2.5, 7, 15, 30, 60, 90, and 120 min), group (NaBic, NaCl, and Gluc), and the interaction between them. *P*-values were corrected for multiple comparisons using the Benjamini–Hochberg procedure. To assess the impact of baseline ECG imbalance, a sensitivity analysis was performed excluding all calves with arrhythmias at baseline ($t = 0$). Linear mixed-effects models were then re-fitted using the same model structure as in the primary analysis.

In order to assess associations between changes in ECG variables (heart rate, heart rate variability, P, Ta, S, and T wave amplitude as well as QRS duration, ST segment duration, ST amplitude, and ST angle) and variables of clinical pathology over time, generalized linear mixed models were constructed. Independent predictors considered for model development were selected based on biological relevance and included venous blood pH, plasma volume expansion, *c*Na, *c*K, and the interaction between *c*K and *c*Na. The latter was included in the models as a centered variable by multiplying the difference from the mean of each variable. Multivariable modeling was performed using a backwards elimination procedure. The selection procedure was stopped when all included variables had a *P*-value $< .05$ except for the effect of group which was forced as a fixed effect into all models using group Gluc as reference group. The individual calf was identified as a random effect.

Segmented linear regression[3,22,23] was used to characterize the relationship between each ECG variable of interest and *c*K by sequentially modeling the ECG variable-plasma *c*K relationship using 3 models. Segmented linear regression was applied to identify potential clinically relevant breakpoints, as this approach allows data-driven estimation of changes in the slope of the relationship between a predictor and an outcome variable, particularly when threshold effects are suspected.[3,50] For example, electrolyte concentrations may exert minimal clinical effects within a certain range but may be associated with pronounced changes once a critical threshold is exceeded.

Segmented linear regression analyses required a mixed models approach because 7 data points were obtained from each of the 22 calves during treatment, producing a total of 154 data points with a correlated data structure. The first model used linear mixed model regression (PROC MIXED, SAS, Inc) to apply a linear regression equation to the data, such that $y = b_0 + b_1 \times [K]$. The second model used nonlinear mixed models regression (PROC NLMIXED, SAS Inc) to apply 2 sequential linear regression equations with different slopes and a common breakpoint ($[K]_1$) to the data, such that if $x \leq [K]_1$ then $y = b_0 + b_1 \times x$; if $x > [K]_1$ then $y = b_0 + b_1 \times [K]_1 + b_2 \times (x - [K]_1)$. The third model used nonlinear mixed models regression to apply 3 sequential linear regression equations with different slopes (the third was constrained to a slope = 0) and 2 common breakpoints ($[K]_1$, $[K]_2$) to the data, such that if $x \leq [K]_1$ then $y = b_0 + b_1 \times x$; if $[K]_1 < x \leq [K]_2$ then $y = b_0 + b_1 \times [K]_1 + b_2 \times (x - [K]_1)$, and if $x > [K]_2$ then $y = b_0 + b_1 \times [K]_1 + b_2 \times ([K]_2 - [K]_1)$. The last equation assumes that $y = 0$ when plasma $[K] > [K]_2$. When 1 or 2 breakpoints were identified by applying segmented regression, the estimated plasma *c*K for the breakpoint and the 95% CI for the estimate were calculated in order to characterize the sequence of

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

ECG changes as plasma *c*K increased. Nonlinear mixed models were fit by applying the adaptive Gauss–Hermite quadrature approximation for the marginal likelihood function and quasi-Newton optimization. Linearity of model fit was evaluated using residual plots. Furthermore, the Akaike information criterion (AIC) was used to compare models involving 1, 2, or 3 sequential linear regression equations, with the lowest AIC value indicating better relative model fit provided $\Delta AIC \geq 2$; when $\Delta AIC < 2$ for 2 models we selected the simplest model. We evaluated the final model fit using plots of actual and predicted values and residual plots and the width of the 95% CIs for breakpoint estimates.

References

1. Trefz FM, Lorch A, Feist M, Sauter-Louis C, Lorenz I. The prevalence and clinical relevance of hyperkalaemia in calves with neonatal diarrhoea. *Vet J*. 2013;195:350-356. https://doi.org/10.1016/j.tvjl.2012.07.002
2. Trefz FM, Constable PD, Sauter-Louis C, Lorch A, Knubben-Schweizer G, Lorenz I. Hyperkalemia in neonatal diarrheic calves depends on the degree of dehydration and the cause of the metabolic acidosis but does not require the presence of acidemia. *J Dairy Sci*. 2013;96:7234-7244. https://doi.org/10.3168/jds.2013-6945
3. Trefz FM, Lorenz I, Constable PD. Electrocardiographic findings in 130 hospitalized neonatal calves with diarrhea and associated potassium balance disorders. *J Vet Intern Med*. 2018;32:1447-1461. https://doi.org/10.1111/jvim.15220
4. Lewis L, Phillips R. Diarrheic induced changes in intracellular and extracellular ion concentrations in neonatal calves. *Ann Rech Vétér*. 1973;4:99-111.
5. Golbeck L, Cohrs I, Leonhard-Marek S, Grünberg W. Effect of dehydration and acidemia on the potassium content of muscle tissue and erythrocytes in calves with neonatal diarrhea. *J Dairy Sci*. 2018;101:9339-9349. https://doi.org/10.3168/jds.2018-14790
6. Trefz FM, Lorenz I. Plasma potassium concentrations in neonatal diarrhoeic calves are correlated with serum aldosterone concentrations but not with insulin concentrations. *Vet J*. 2017;230:41-44. https://doi.org/10.1016/j.tvjl.2017.09.005
7. Evans KJ, Greenberg A. Hyperkalemia: a review. *J Intensive Care Med*. 2005;20:272-290. https://doi.org/10.1177/0885066605278969
8. Garcia-Palmieri MR. Reversal of hyperkalemic cardiotoxicity with hypertonic saline. *Am Heart J*. 1962;64:483-488. https://doi.org/10.1016/0002-8703(62)90033-9
9. Özkan C, Altuğ N, Yüksek N, Kaya A, Akgül Y. Assessment of electrocardiographic findings, serum nitric oxide, cardiac troponins and some enzymes in calves with hyperkaliemia related to neonatal diarrhoea. *Revue Méd Vét*. 2011;162:171-176.
10. Weldon AD, Moise NS, Rebhun WC. Hyperkalemic atrial standstill in neonatal calf diarrhea. *J Vet Intern Med*. 1992;6:294-297. https://doi.org/10.1111/j.1939-1676.1992.tb00354.x
11. Lorenz I, Trefz FM. Diarrhea in calves. In: Gross JJ, ed. *Production Diseases in Farm Animals: Pathophysiology, Prophylaxis and Health Management*. Springer; 2024:211-221. https://doi.org/10.1007/978-3-031-51788-4_10.
12. Weisberg LS. Management of severe hyperkalemia. *Crit Care Med*. 2008;36:3246-3251. https://doi.org/10.1097/CCM.0b013e31818f222b
13. Constable PD, Grünberg W. Hyperkalemia in diarrheic calves: implications for diagnosis and treatment. *Vet J*. 2013;195:271-272. https://doi.org/10.1016/j.tvjl.2012.11.002
14. Trefz FM, Constable PD, Lorenz I. Effect of intravenous small-volume hypertonic sodium bicarbonate, sodium chloride, and glucose solutions in decreasing plasma potassium concentration in hyperkalemic neonatal calves with diarrhea. *J Vet Intern Med*. 2017;31:907-921. https://doi.org/10.1111/jvim.14709
15. Kaplan JL, Eynon CA, Dalsey WC, Braitman LE, Clas D, De Garavilla L. Hypertonic saline treatment of severe hyperkalemia in nonnephrectomized dogs. *Acad Emerg Med*. 2000;7:965-973. https://doi.org/10.1111/j.1553-2712.2000.tb02085.x
16. Constable PD. Hypertonic saline. *Vet Clin North Am Food Anim Pract*. 1999;15:559-585. https://doi.org/10.1016/s0749-0720(15)30164-x
17. Yeoh RN, Akiyama Y, Senzaki M, Kazama I. Insulin accelerates recovery from QRS complex widening in a frog heart model of hyperkalemia. *J Vet Med Sci*. 2021;83:1855-1859. https://doi.org/10.1292/jvms.21-0481
18. Pessoa RB, Batista CF, Santos KR, Bellinazzi JB, Della Libera AMMP, Larsson MHMA. Holter monitoring (24-h electrocardiography) of Holstein calves. *Acta Sci Vet*. 2016;44:1374. https://doi.org/10.22456/1679-9216.81081
19. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. *Front Public Health*. 2017;5:258. https://doi.org/10.3389/fpubh.2017.00258
20. Reed MJ, Robertson CE, Addison PS. Heart rate variability measurements and the prediction of ventricular arrhythmias. *QJM*. 2005;98:87-95. https://doi.org/10.1093/qjmed/hci018
21. Billman GE. The effect of heart rate on the heart rate variability response to autonomic interventions. *Front Physiol*. 2013;4:222. https://doi.org/10.3389/fphys.2013.00222
22. Robbins KR, Saxton AM, Southern LL. Estimation of nutrient requirements using broken-line regression analysis. *J Anim Sci*. 2006;84:E155-E165. https://doi.org/10.2527/2006.8413_supple155x
23. Gonçalves MA, Bello NM, Dritz SS, et al. An update on modeling dose-response relationships: accounting for correlated data structure and heterogeneous error variance in linear and nonlinear mixed models. *J Anim Sci*. 2016;94:1940-1950. https://doi.org/10.2527/jas.2015-0106
24. Schwarz KC, Cohen BD, Lubash GD, Rubin AL. Severe acidosis and hyperpotassemia treated with sodium bicarbonate infusion. *Circulation*. 1959;19:215-220. https://doi.org/10.1161/01.cir.19.2.215
25. Fisch C. Relation of electrolyte disturbances to cardiac arrhythmias. *Circulation*. 1973;47:408-419. https://doi.org/10.1161/01.cir.47.2.408
26. Robert T, Burbach M, Joseph A, Mesnard L. Sodium is the secret re-agent of bicarbonate therapy during hyperkalemia. *Kidney Int*. 2016;90:450-451. https://doi.org/10.1016/j.kint.2016.05.015
27. Dépret F, Peacock WF, Liu KD, Rafique Z, Rossignol P, Legrand M. Management of hyperkalemia in the acutely ill patient. *Ann Intensive Care*. 2019;9:32. https://doi.org/10.1186/s13613-019-0509-8
28. Weiss JN, Qu Z, Shivkumar K. Electrophysiology of hypokalemia and hyperkalemia. *Circ Arrhythm Electrophysiol*. 2017;10:e004667. https://doi.org/10.1161/circep.116.004667

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

29. Ballantyne F, Davis LD, Reynolds EW. Cellular basis for reversal of hyperkalemic electrocardiographic changes by sodium. *Am J Physiol*. 1975;229:935-940. https://doi.org/10.1152/ajplegacy.1975.229.4.935
30. Bergman EN, Sellers AF. Studies on intravenous administration of calcium, potassium, and magnesium to dairy calves. II. Some cardiac and respiratory effects. *Am J Vet Res*. 1954;15:25-35.
31. Basoglu A, Aydogdu U. Terminal atrial standstill with ventricular escape rhythm in a neonatal calf with acute diarrhea. *Turk J Vet Anim Sci*. 2013;37:362-365. https://doi.org/10.3906/vet-1202-27
32. Bakshi SP, Ajithkumar S, Sindhu OK, Madhavan Unny N, Sebastian R. Electrocardiographic changes associated with hyperkalaemia in domestic cats. *J Vet Anim Sci*. 2023;54:115-124. https://doi.org/10.51966/jvas.2023.54.1.115-124
33. El-Said BM, Abdelbaset-Ismail A, Mahmoud ARM, El-Maghawry S, Gouda SM. Electrocardiographic findings in healthy, hypokalemic and hyperkalemic dogs. *J Anim Health Prod*. 2021;9:20-25.
34. Tag TL, Day TK. Electrocardiographic assessment of hyperkalemia in dogs and cats. *J Vet Emerg Crit Care*. 2008;18:61-67. https://doi.org/10.1111/j.1476-4431.2007.00268.x
35. Mattu A, Brady WJ, Robinson DA. Electrocardiographic manifestations of hyperkalemia. *Am J Emerg Med*. 2000;18:721-729. https://doi.org/10.1053/ajem.2000.7344
36. Dittrich KL, Walls RM. Hyperkalemia: ECG manifestations and clinical considerations. *J Emerg Med*. 1986;4:449-455. https://doi.org/10.1016/0736-4679(86)90174-5
37. de Mello W, Hoffman BF. Potassium ions and electrical activity of specialized cardiac fibers. *Am J Physiol*. 1960;199:1125-1130. https://doi.org/10.1152/ajplegacy.1960.199.6.1125
38. Lemoine L, Le Bastard Q, Batard E, Montassier E. An evidence-based narrative review of the emergency department management of acute hyperkalemia. *J Emerg Med*. 2021;60:599-606. https://doi.org/10.1016/j.jemermed.2020.11.028
39. Montague BT, Ouellette JR, Buller GK. Retrospective review of the frequency of ECG changes in hyperkalemia. *Clin J Am Soc Nephrol*. 2008;3:324-330. https://doi.org/10.2215/CJN.04611007
40. Wrenn KD, Slovis CM, Slovis BS. The ability of physicians to predict hyperkalemia from the ECG. *Ann Emerg Med*. 1991;20:1229-1232. https://doi.org/10.1016/s0196-0644(05)81476-3
41. Brody DA. A theoretical analysis of intracavitary blood mass influence on the heart-lead relationship. *Circ Res*. 1956;4:731-738. https://doi.org/10.1161/01.res.4.6.731
42. Della Torre PK, Zaki S, Govendir M, Church DB, Malik R. Effect of acute haemorrhage on QRS amplitude of the lead II canine electrocardiogram. *Aust Vet J*. 1999;77:298-300. https://doi.org/10.1111/j.1751-0813.1999.tb10265.x
43. Ker J, Webb EC, Van Papendorp D. The Brody effect induced by premature ventricular complexes in the ovine heart. *Onderstepoort J Vet Res*. 2009;76:443-448. https://doi.org/10.4102/ojvr.v76i4.27
44. Ettinger PO, Regan TJ, Oldewurtel HA. Hyperkalemia, cardiac conduction, and the electrocardiogram: a review. *Am Heart J*. 1974;88:360-371. https://doi.org/10.1016/0002-8703(74)90473-6
45. DeRoth L. Electrocardiographic parameters in the normal lactating Holstein cow. *Can Vet J*. 1980;21:271-277.
46. Altuğ N, Yüksek N, Özkan C, et al. Serum potassium-lowering effects of insulin plus dextrose and adrenalin treatment that enhance intracellular potassium transitions in hyperkalemic diarrheic calves. *Pak Vet J*. 2016;36:140-144.
47. Koch A, Kaske M. Clinical efficacy of intravenous hypertonic saline solution or hypertonic bicarbonate solution in the treatment of inappetent calves with neonatal diarrhea. *J Vet Intern Med*. 2008;22:202-211. https://doi.org/10.1111/j.1939-1676.2007.0029.x
48. Coskun A, Sen I, Guzelbektes H, Ok M, Turgut K, Canikli S. Comparison of the effects of intravenous administration of isotonic and hypertonic sodium bicarbonate solutions on venous acid-base status in dehydrated calves with strong ion acidosis. *J Am Vet Med Assoc*. 2010;236:1098-1103. https://doi.org/10.2460/javma.236.10.1098
49. Van Beaumont W, Greenleaf JE, Juhos L. Disproportional changes in hematocrit, plasma volume, and proteins during exercise and bed rest. *J Appl Physiol*. 1972;33:55-61. https://doi.org/10.1152/jappl.1972.33.1.55
50. Hiew MWH, Megahed AA, Horstman LA, Constable PD. Clinical utility of plasma progesterone and blood and plasma glucose concentrations in predicting parturition in Holstein cows. *J Dairy Sci*. 2020;103:5575-5590. https://doi.org/10.3168/jds.2019-17800

Downloaded from academic.oup.com/jvim/article/40/5/aalag215/8996743 by guest on 04 November 2026

© The Author(s) 2026. Published by Oxford University Press on behalf of the American College of Veterinary Internal Medicine. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.
Journal of Veterinary Internal Medicine, 2026, 40, aalag215
https://doi.org/10.1093/jvimsj/aalag215
Original Research