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# Effect of dehydration and acidemia on the potassium content of muscle tissue and erythrocytes in calves with neonatal diarrhea

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## ABSTRACT

Disturbances of extracellular potassium (K) homeostasis in calves with severe neonatal diarrhea have been studied extensively. Although total body depletion of this predominantly intracellular electrolyte is generally thought to occur in diarrheic calves, the mechanisms through which K depletion occurs are poorly understood. The aim of this study was to investigate how intracellular K homeostasis is affected by dehydration and acidemia, the 2 most important metabolic disturbances in calves with naturally occurring diarrhea. Twenty-seven calves with naturally occurring neonatal diarrhea, pronounced dehydration, and acidemia, and 2 groups of 10 healthy control calves were included in this study. Blood samples and muscle biopsies were obtained immediately before initiation of treatment ($T_0$) and after complete rehydration and correction of acidemia ($T_1$) from diarrheic calves. Blood samples were used to perform blood gas, blood biochemical, and hematological analyses and to determine K content in erythrocytes. Muscle biopsies were used to determine muscle tissue K content and tissue dry matter. Controls were used to determine values for erythrocyte and muscle tissue K content in healthy neonatal calves for comparison with diarrheic calves. As defined by the inclusion criteria, diarrheic calves showed pronounced acidemia and dehydration at $T_0$. Mean muscle tissue K content and tissue dry matter remained unchanged between sampling times and did not differ from values measured in healthy control calves. Erythrocyte K content increased from 73.63 ± 13.73 to 77.64 ± 15.97 mmol/L (±standard deviation) but was associated with a concomitant decline in erythrocyte volume. Values measured at both sampling times in diarrheic calves did not differ from erythrocyte K measured in healthy control calves. The plasma K concentration (median [interquartile range]) decreased from 5.44 [4.76–6.17] to 4.16 [3.99–4.31] mmol/L between $T_0$ and $T_1$. Although changes in plasma [K] were associated with the degree of dehydration, neither dehydration nor acidemia was associated with changes of K content in muscle tissue or erythrocytes. In conclusion, severe dehydration and acidemia in diarrheic calves were not associated with notable changes in K content of muscle tissue or erythrocytes. These results do not support the concept of pronounced K depletion occurring in calves with neonatal diarrhea. Erythrocytes are a poor surrogate tissue in which to measure changes of intracellular K content in diarrheic calves because of concomitant changes in erythrocyte volume that complicate the interpretation of results.

**Key words:** calf, intracellular, potassium, depletion

## INTRODUCTION

Diarrhea remains one of the most common diseases and the most important cause of calf mortality in the first month of life (USDA, 2007; Medrano-Galarza et al., 2018). Neonatal diarrhea of calves is associated with several metabolic disturbances including dehydration, acidemia, hypoglycemia, and hyperkalemia (Smith and Berchtold, 2014). Disturbances of extracellular K balance in particular and the underlying causes have been studied in considerable detail (Trefz et al., 2013a, 2015a, 2017; Trefz and Lorenz, 2017). Hyperkalemia in diarrheic calves, occurring with an incidence of up to 34%, has been recognized as a potentially life-threatening sequela associated with bradycardia, arrhythmia, and, in severe cases, death of the affected patient (Groutides and Michell, 1990; Weldon et al., 1992; Trefz et al., 2013b). Dehydration (and the resultant decreased renal perfusion) and, to a lesser extent, acidemia (and the ensuing compartmental K shifts) have been identified as the most important driving forces behind observed changes in plasma K concentrations ([K]; Trefz et al., 2013a; Trefz and Lorenz, 2017). In contrast to extracellular K homeostasis, little is known about the potential effects of dehydration and acidemia on intracellular K homeostasis of diarrheic calves. Studies of the 1970s

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reported a pronounced depletion of intracellular K content in muscle tissue that occurred within hours in calves with experimentally induced neonatal diarrhea (Lewis and Phillips, 1972, 1973). However, the underlying mechanisms causing these important losses of K from the intracellular space, which accounts for approximately 98% of the total body K pool, have not been established. To better understand intracellular K homeostasis in diarrheic calves, the aims of this study were (1) to determine the intracellular K content on the example of muscle tissue and erythrocytes in calves affected by naturally occurring neonatal diarrhea before and after correction of dehydration and acidemia, (2) to compare them to values obtained in healthy calves, and (3) to identify factors contributing to the alteration of the intracellular K content in these animals. We hypothesized that acidemia and dehydration both have important effects on intracellular K homeostasis as described for extracellular K homeostasis.

## MATERIALS AND METHODS

### Animals

This study was approved by the Animal Welfare and Ethics Committee of the government of Lower Saxony, Germany (permit no 33,19-42502-05-16A019). Written consent was obtained from the owners of the animals participating in this study.

A prospective clinical study over the course of 1 yr (May 2016 to May 2017) was conducted on calves presented to the Clinic for Cattle, University of Veterinary Medicine Hannover, Foundation (Hanover, Germany), for the treatment of severe neonatal diarrhea. Main inclusion criteria were naturally occurring diarrhea, age between 3 and 21 d at the time of presentation, clinical signs of severe dehydration (eyeball recession over 3 mm, prolonged skin tenting), and a base excess (**BE**) lower than −10 mmol/L. To be able to standardize the initial therapy, we elected to exclude animals that did not require parenteral fluid therapy. Therefore, calves that were still ambulatory, had adequate suckle reflex, and thus were suitable for exclusive oral fluid therapy were excluded. Further exclusion criteria were a rectal temperature >40.0°C, clinical signs suggestive of septicemia, and concomitant diseases potentially impeding recovery (e.g., omphalitis or pneumonia) at the time of admission.

Established reference ranges for muscle tissue and erythrocyte K content in calves are not available; therefore, we included 2 groups of healthy age-matched control calves (10 animals in each group) to obtain an estimate of normal values for muscle tissue and erythrocyte K content. The sample size of the control groups was determined arbitrarily. Control calves for the determination of muscle K content and muscle tissue DM in healthy animals were chosen from the pool of clinically healthy neonates of the Clinic for Cattle obtained by C-section. Values of erythrocyte K content were obtained from an unrelated study conducted under field conditions that investigated the development of erythrocyte electrolyte content in healthy dairy calves in the first weeks of life. Samples from this data set were selected to match the age distribution of the group of diarrheic calves. Calves serving as control animals were determined to be healthy based on thorough physical examination.

### Housing and Feeding

Diarrheic calves were housed in individual calf stalls on rubber mats, copiously bedded with straw in a temperature-controlled facility. Control calves were housed in individual hutches located outside and copiously bedded with straw; calves had free access to water and were fed 2 L of whole milk 4 times daily.

Calves with diarrhea were offered 2 L of a commercial milk replacer (**MR**; Sprayfo Excellent, Sloten GmbH, Diepholz, Germany) from a nipple bucket 4 times per day. A custom-made oral electrolyte solution (**OES**) containing 20.1 g of dextrose, 3.9 g of NaCl, 3 g of $KHCO_3$, and 3 g of Na-propionate per L (strong ion difference = 74 mEq/L) also offered from a nipple bucket was accessible ad libitum between meals. Consumption of MR and OES was recorded. Clean water offered from a bucket was available at all times, and calves had ad libitum access to hay and water.

### Standard Procedures

At admission, calves underwent a complete physical exam, were weighed on an electronic scale, and were evaluated for inclusion and exclusion criteria. Blood was collected by venipuncture from a jugular vein (Strauss-Kanüle, 17G, Dispomed Witt oHG, Gelnhausen, Germany) in lithium heparin and $K_3$-EDTA tubes. Blood gas capillaries were filled by directly inserting the capillaries into the conus of the needle. Blood samples were processed as described below. Blood from calves serving as controls for the erythrocyte K content was obtained by venipuncture from a jugular vein as described for diarrheic calves.

An electrocardiogram (**ECG**, DIMEQ EKG 601, Bosch Healthcare Solutions, Waiblingen, Germany) was recorded by base-apex derivation as described earlier in ruminants (DeRoth, 1980; Grünberg et al., 2015).

Muscle biopsies were obtained from the vastus lateralis of the musculus quadriceps femoris using a