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Comparative study on 3 oral potassium formulations for treatment of hypokalemia in dairy cows

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Abstract

Background: Hypokalemia is of clinical relevance in cattle. Different mostly empirical treatment options are suggested.

Hypothesis/Objectives: To evaluate if oral administration of potassium influences the plasma concentration, the intracellular concentration in erythrocytes and in muscle, renal excretion of potassium, and to assess if there are differences in the efficacy of the potassium formulations.

Animals: Thirty cows with hypokalemia (plasma concentration <3.5 mmol/L) were systematically allocated to 3 treatment groups (10 cows/group).

Methods: The cows received 52 g of potassium in different formulations: group B—potassium chloride bolus (release over 12 hours); group G—potassium propionate gel (release over 2 hours); and group S—potassium chloride solution (immediately available). Potassium concentrations were repeatedly measured in plasma, erythrocytes, muscle, and urine using ICP-OES.

Results: Plasma potassium concentrations for all preparations increased within 30 minutes and the increase lasted for 12 hours. The concentrations of potassium in the erythrocytes and in the muscle, renal potassium excretion, and total urine volume were not affected by administration of any product. There were no differences between the treatments groups. The feed intake increased in 50% of cows within 2 hours after potassium application, which may contribute to the increase of plasma potassium concentration.

Conclusions and Clinical Importance: All the studied potassium formulations are equally effective to treat hypokalemia in dairy cows for over 12 hours but do not influence intracellular concentration or renal excretion of potassium. The plasma potassium concentration should be reevaluated after 12 hours.

KEYWORDS
erythrocyte potassium, muscle potassium, serum potassium

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1 | INTRODUCTION

Because of their potassium-rich diet, cows typically absorb excessive potassium which has to be excreted via the kidneys. However, a sudden decrease of feed intake may lead to hypokalemia as renal excretory mechanisms are not able to reduce the potassium excretion rapidly, and a basic renal excretion of potassium is mandatory.[1] Further possible reasons for decreased plasma potassium concentrations are alkalemia, hyperinsulinemia, and aldosterone release.[2-5] Hypokalemia can be of clinical importance especially in disease conditions like retained placenta, clinical mastitis, hepatic lipidosis, and abomasal displacement[4-8] and might be caused by concurrent partial or total anorexia, third space loss or diarrhea as well as by a shift into the intracellular compartment.[1] The physiological potassium concentration in blood plasma of cows ranges between 3.9 and 5.8 mmol/L.[9] Some studies have considered that the measurement of intracellular potassium may be even more relevant than the usually measured extracellular potassium concentration to assess the total potassium balance.[1,5,10,11]

Oral potassium administration has been recommended for the treatment of hypokalemic cows. The recommendations on the amount and application frequency for oral potassium treatment range widely between 60 and 300 g of potassium chloride per day.[5,9,12] However, the total daily doses of potassium chloride should not exceed 0.5 mEq/kg/h of body weight (BW) because this results in diarrhea, convulsions, muscular tremor, excessive salivation, and death.[13] Potassium chloride dissolves in water easily and is readily available for absorption within a short time period. There may be benefits (eg, longer lasting effect, lower treatment frequency) if devices or formulations release potassium over a more protracted period of several hours after placement in the rumen. Additionally, it seems that the efficacy of different formulations to increase plasma potassium concentration and the effects of potassium on intracellular potassium concentration and potassium excretion via urine are less well known in cows with naturally occurring hypokalemia with concurrent diseases than in experimentally induced hypokalemia in otherwise healthy cows.[5]

The objectives of the study were to evaluate if oral administration of potassium has an effect on plasma potassium concentration of cows with decreased feed intake and decreased plasma potassium levels and to assess if there are differences in the efficacy of different oral potassium formulations with different solution characteristics (bolus, gel, and solution). Intracellular potassium in erythrocytes and in muscle tissue and renal excretion of potassium were measured to assess further compartments of potassium metabolism.

The first hypothesis was that different oral potassium formulations have effects on magnitude and duration of plasma K concentration. Because of the expected faster absorption of the potassium chloride solution, it was hypothesized that the concentration peaks earlier with and higher in comparison to potassium propionate gel and potassium chloride bolus. In contrast, the slow release of formulations propionate gel and potassium chloride slow release bolus were assumed to result in an increased plasma potassium concentration over a prolonged time. Furthermore, it was expected that the intracellular

potassium concentrations are simultaneously increased and that different formulations result in variable potassium excretion via the kidney.

2 | MATERIAL AND METHODS

All used protocols and procedures concerning animal treatment have been approved by the Institutional Ethics Committee and the governmental animal protection authority according to national legislation (GZ 68.205/0145-II/3b/2013). Additionally, the owners had given permission to include their animals in the study. This was done either by signing a consent form or in cases when the owners were not personally present at the veterinary hospital by phone and documented in the medical records of the animals.

2.1 | Animals

Thirty lactating Austrian Fleckvieh cows (Simmental) between 2 and 6 lactation were recruited from the cases referred to the University Clinic for Ruminants at the Vetmeduni Vienna. The cows were enlisted in the study after their admittance at the clinic over a period of 7 months. The lactation status of the cows differed substantially between 6 and 234 days in milk (median 56 days), similarly milk yield also varied widely between 0 and 24 L/d (median 9.4 L/d). Body weight at admission varied between 670 and 810 kg. However, there were no differences in the parameters (days in milk $P = .67$; daily milk yield $P = .82$; BW $P = .89$) between the study groups.

Sample size calculation was impractical as no information was available on differences in absorption kinetics for different formulations. The sample size has been identified empirically comparing to similar studies.[5,11]

The main inclusion criterion was a plasma potassium concentration <3.5 mmol/L at the beginning of the study (time: −2, −1, and 0 hour). The study was started shortly after the admission at the hospital and the initial physical examination (16 cows) or later during the stay at the hospital (14 cows, between days 3 and 6 after admission). Furthermore, no obstructions of the gastrointestinal system or the urinary tract were found when the experimental procedure was started (cows were able to urinate and defecate). The cows have been assigned to treatment groups in an alternating order after their admission at the veterinary hospital. The cows were referred to the veterinary hospital for further treatment by private practitioners without any preselection. The primary disease conditions of the cows were: 8 cows suffered from a systemic febrile infection resulting in decreased feed intake, 7 cows suffered from endometritis/metritis (2 of them with retained fetal membranes), 11 cows underwent surgery for abdominal conditions (5 cows left displacement of the abomasum, 3 abomasal volvulus, 3 cecum dilatation) at least 2 days before potassium application, and 4 cows had other diagnoses (rumen alkalosis, abomasal ulcer, lameness because of a white line disease, indigestion). From the 11 cows which had surgery, 3 were assigned to group B, 3 in group G, and 5 in group S. Considering the postoperative hypomotility of the gastrointestinal tract,

these cows were included in the study not earlier than 48 hours after surgery. Eighteen cows received an antibiotic treatment (amoxicillin) and 13 cows were treated with ketoprofen (3 mg/kg BW) at the time of the study.

The cows of all 3 groups received the same amount of potassium using 3 different formulations.

2.2 | Potassium form and dosage

- Group B (bolus) was treated with a bolus (volume 120 mL) containing 100 g of potassium chloride (52 g potassium) which releases 55% of the potassium within 6 hours and 100% within 12 hours after placed in the rumen. The bolus consists of a mineral calcium-magnesium matrix.
- Group G (gel) received 500 mL gel containing 52 g of potassium as potassium propionate. The thixotrope gel releases potassium over a 2 hour period.
- Group S (solution) was treated with 100 g of potassium chloride (52 g potassium) solved in a 1 L tap water. Potassium chloride dissociated almost completely in water.

During the study, the animals were monitored from 3 hours before to 24 hours after the application of potassium. A physical examination (assessment of: behavior and general appearance, posture, eating and appetite, body temperature, respiratory rate, heart rate, respiration, rumination, defecation, and urination) was performed every 2 hours. The cows were fed a standard ration twice daily consisting of 50% hay and 50% grass silage at an amount of 20 kg dry matter per day and 3 kg pelleted concentrate per day. Feed intake was scored hourly by visual appraisal (0, no feed intake; 1, minimal feed intake, less than 1/3 of the ration consumed; 2, intermediate feed intake, 1/3 to 2/3 of the ration consumed, 3, good feed intake,

more than 2/3 of the ration consumed). Before the new feeding, the refusals were visually compared to the amount the animals were fed.

2.3 | Samples

An indwelling intravenous catheter (Intraflon 2, 12xG; 80 mm length; Hohenwallner, Leonding, Austria) was placed for blood sampling in the jugular vein. Before each sampling, a volume of 5 mL of blood was taken from the catheter and discarded. A lithium heparin (2 mL LHp, VACUETTE blood collection system, Greiner Bio-One GmbH, Kremsmünster, Austria) syringe was used to obtain venous blood samples for potassium measurement in plasma and in erythrocytes. Potassium concentration in plasma was measured every hour before potassium was administered (time −1 and 0). After potassium supplementation, blood samples were obtained every 30 minutes for 3 hours and again every hour until 6 hours post treatment. Finally, potassium in blood plasma was measured 12 and 24 hours after the oral potassium treatment. Potassium in erythrocytes was measured at the following time points: −2, 2, 6, 12, and 24 hours. Blood gas analysis and muscle biopsy were performed before the experiment and 6, 12, and 24 hours after potassium treatment. After each sample, the catheter was flushed and filled with a 5 mL of heparinized NaCl solution. Blood sampling started 2 hours before potassium administration (time point −2). Time points and sampling are presented in Table 1.

The total amount of urine was measured by catheterizing the urine bladder and collected the urine in a container. The urine volumes were measured every hour and samples were collected from these collections hourly beginning 2 hours before to 6 hours after the potassium treatment for analysis.

For the muscle biopsy, the gluteal muscle was chosen as biopsy site. The biopsy was obtained using a commercially available suction-muscle biopsy needle (modified Bergstrom needle, 5 mm diameter, Walter Veterinär-Instrumente e.K., Baruth, Germany) as described

TABLE 1 Overview on type and time of sample taking during the study, time 0 hour represents the time of application of potassium formulation

Time (h)	Plasma	Urine	Erythrocytes	Blood gas analysis	Muscle biopsy
-2	√	√	√	√	√
-1	√	√			
0	√	√			
0.5	√				
1	√	√			
1.5	√				
2	√	√	√		
2.5	√				
3	√	√			
4	√	√			
5	√	√			
6	√	√	√	√	√
12	√		√	√	√
24	√		√	√	√

recently.[11] The skin was clipped and surgically prepared. Subsequent to a local anesthesia (procaine hydrochloride, 5 mL of 2% solution), a stab incision through skin and subcutaneous fat was created allowing to insert the Bergstrom needle into the muscle tissue. A muscle tissue sample (approximately 200 mg) was obtained and the skin was closed.

2.4 | Sample preparation and laboratory analysis

The sample preparation and analyses have also been described in detail in a previous study.[11] The blood samples at time −2, −1, and 0 hour were analyzed using a blood gas analyzer (VetStat Electrolyte and Blood Gas Analyzer, IDEXX Laboratories, Westbrook, Maine) at the clinics for ruminants immediately after the sample had been obtained. The point-of-care test was used to decide immediately if the cow complies with the inclusion criterion (K < 3.5 mmol/L) and can be introduced in the study. The blood gas analyzer measured the potassium concentration in plasma by ion sensitive electrode (dynamic range 1–10 mmol/L, resolution 0.01 mmol/L, coefficient of variation 2.0%). Serum potassium concentrations of all samples taken during the complete study period (−2 to 24 hours; Table 1) were determined using a laboratory-based automatic analyzer (Varian Inc, Agilent Technologies, Waldbronn, Germany, coefficient of variation <1.5%); to maintain consistency, only these measurements were used for all further statistical analyses and figures. The hematological parameters were measured using an automatic analyzer (Hematology System, Siemens Healthcare GmbH, Erlangen, Germany, coefficients of variation for measured parameters between 0.77 and 4.1%).

The potassium in tissue and in the erythrocytes were measured in a specialized laboratory by 1 of the authors (A. Müller) using inductively coupled plasma optical emission spectroscopy (Vista-PRO, Varian Inc, Agilent Technologies, coefficient of variation <1.5%). For the analysis, 1 mL of heparinized blood was mixed with physiological NaCl solution and centrifuged. The supernatant was discarded. This procedure was repeated 3 times. Then, the samples were dried over night at 70°C, afterward weighed, mixed with 1 mL of HNO_3 suprapur (Merck KgaA, Darmstadt, Germany) and dried (at 70°C). To allow comparison, the values were corrected to a theoretical hematocrit of 100%, as described by Rasmusen et al.[14] The muscle samples were weighed, mixed with HNO_3 suprapur, and thermally processed. Finally, the diluted samples were analyzed also using inductively coupled plasma optical emission spectroscopy with emission line 766.491 nm.[11]

Every hour, creatinine (Crea) and potassium concentration has been measured both in blood samples and in the urine samples. Fractional clearance (FC) for potassium was calculated using the formula FC_K (%) = (K_{urine}/K_{plasma}) × 100: ($Crea_{urine}/Crea_{plasma}$).

2.5 | Statistical analysis

The data were analyzed using IBM SPSS v24 (IBM Corp, Armonk, New York). Normal distribution was tested applying Kolmogorov-Smirnov test. Data which were not normally distributed were log-transformed before further analysis. Plasma potassium concentrations of cows which had surgery before versus cows which had no surgery were compared applying the Mann-Whitney U test. The impact of the factors (independent variables), treatment (group), and time points on each parameter (dependent variables: potassium concentration in plasma, erythrocytes, and muscles cells) was analyzed using linear mixed-effects models where group and time points were added as fixed factors and the animal was modeled as a random factor. Because of correlated error terms within each subject, a block diagonal matrix where each block is a first-order autoregressive (AR1) covariance matrix was chosen as error covariance. Restricted maximum likelihood was used as estimation method. In addition, the interaction term treatment × time point was also added to the model. Differences between groups or time points were analyzed using Sidak's alpha-correction procedure as a post hoc analysis with P values <.05 considered to indicate statistical differences. Additionally, a residual analysis has been performed applying 2 procedures. First, a visual assessment of a Tukey-Anscombe plot (residuals versus fitted values) has been used and secondary correlations between z-standardized potassium concentrations and z-standardized residuals have been calculated. Both procedures did not indicate any deviation from homoscedasticity assumption (homogeneity of variance).

3 | RESULTS

3.1 | Feed intake

Feed intake increased by at least 1 score within 2 hours after potassium application in 15 of 30 cows. This was observed equally in all groups (5 animals of each group). Otherwise the general condition of the cows remained unchanged; there was no effect on heart and respiratory rate or body temperature.

3.2 | Potassium in plasma

The plasma potassium concentrations of all 3 groups were low (3.23 ± 0.81 mmol/L) before the administration of the potassium formulation (0 hour). As described above, a point of care device (ion-sensitive electrode) was used to measure plasma potassium concentrations at time −2, −1, and 0 hour to decide immediately if the cows fulfill the inclusion criterion of the study (K < 3.5 mmol/L). For all figures and statistical analyses, the measurements of the automatic analyzer for the complete study period have been used. There were some deviations between the measurements devices. In 12 out of the 90 blood samples taken before oral potassium supplementation (time: −2, −1, and 0 hour), the automatic analyzer measured plasma potassium concentration is equal or higher than 3.5 mmol/L (between 3.5 and 3.8 mmol/L); although using the point of care device, the potassium concentration in these samples were measured to be below 3.5 mmol/L.

Within 30 minutes, a significant increase of plasma potassium concentrations (P < .01) could be observed in all 3 groups independently from the applied potassium formulations (Figure 1). Compared to the concentration before application, the plasma potassium concentration remained increased over a period of 12 hours. There were no differences between the 3 groups over time (P = .73). There were
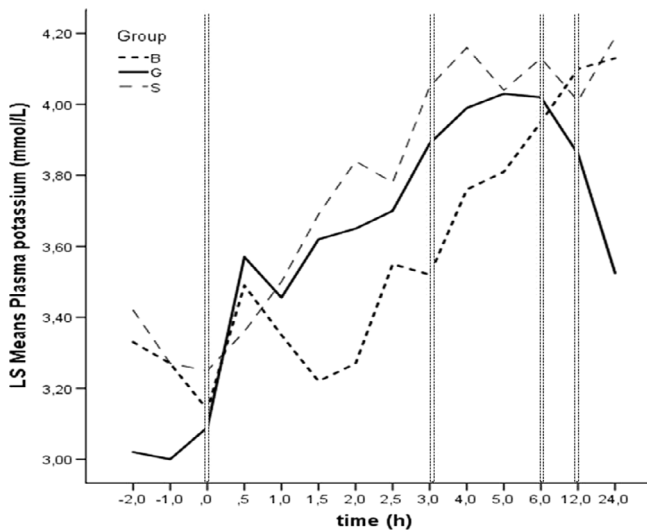
FIGURE 1 Least square means of plasma potassium concentrations (all measurements measured using laboratory method) of the groups (B, bolus; G, gel; S, solution) before and after oral potassium application at time 0 hour (caused by different time scales the curves and x-axis are interrupted)

no differences in cows which had surgery and cows which did not have surgery before (P = .81).

However, there were substantial individual variations in cows of all groups (Table 2). In 6 cows (2 cows per group), the potassium application did not result in a plasma potassium concentration increase of 3.5 mmol/L or higher during the study period of 24 hours.

3.3 | Potassium in erythrocytes

The concentration of potassium measured in the erythrocytes (Figure 2) varied very widely and ranged from 3758 to 27 592 mg/kg, with a mean value of 7916 mg/kg. The administration of potassium had no effect on the potassium concentration in the erythrocytes (P = .54). Group C showed significantly (P = .02) lower potassium values in the erythrocytes than in groups A and B. This difference already existed before the potassium administration and remained different over the complete measurement period.

3.4 | Potassium in muscle tissue

The measured potassium values in the muscle tissue also showed a very high variability between single animals and ranged from 887 to 14 115 mg/kg before potassium application. There were no differences between the 3 groups (P = .59). Potassium administration did not influence the intracellular potassium in muscle tissue as there was no difference (P = .60) between the examined points of time (Figure 3).

3.5 | Renal potassium clearance

Administration of potassium had no influence on the excretion of potassium via the urine: total volume of urine per hour (P = .61; Figure 4),

TABLE 2 Plasma potassium concentrations (mmol/L,) potassium concentration (mmol/L) before and after oral potassium application at time 0 hour with 3 different formulations containing 52 g of potassium (groups: B, bolus; G, gel; S, solution) (data given as median/1st/3rd quartiles)

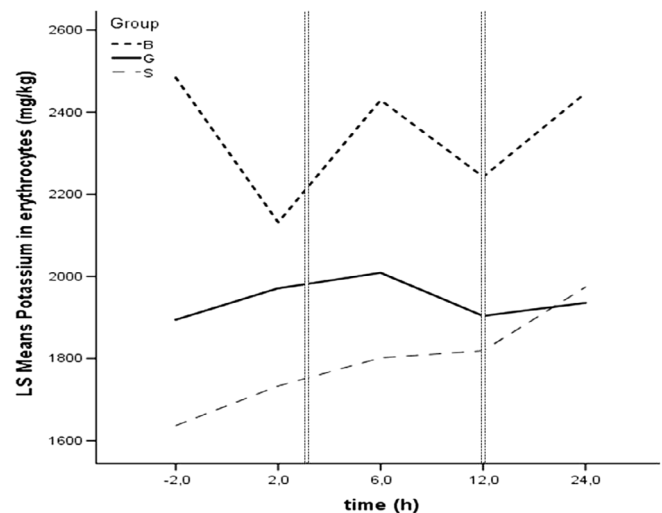|	Plasma potassium concentration (mmol/L)		
Time (h)	Group B (n = 10)	Group G (n = 10)	Group S (n = 10)
−2.0	3.3/3.1/3.6	3.0/2.6/3.5	3.3/3.1/3.7
−1.0	3.3/3.2/3.5	3.1/2.5/3.6	3.3/3.1/3.5
0	3.2/3.0/3.4	3.0/2.7/3.5	3.3/3.2/3.4
0.5	3.4/3.3/3.5	3.6/2.9/3.9	3.4/3.2/3.6
1.0	3.4/3.1/3.5	3.2/2.6/4.3	3.6/3.3/3.7
1.5	3.3/3.2/3.4	3.5/3.0/4.2	3.7/3.6/4.0
2.0	3.4/3.3/3.6	3.6/3.0/4.3	3.8/3.5/4.4
2.5	3.4/3.3/3.6	3.6/2.9/4.4	3.7/3.5/4.4
3.0	3.5/3.3/3.7	3.9/3.1/4.4	4.0/3.6/4.6
4.0	3.7/3.5/4.3	4.0/3.6/4.7	4.2/3.8/4.6
5.0	3.8/3.6/4.1	4.0/3.6/4.7	3.9/3.7/4.5
6.0	4.0/3.8/4.2	4.1/3.5/4.6	4.2/3.8/4.5
12.0	4.1/3.8/4.5	4.0/3.6/4.2	4.1/3.7/4.3
24.0	4.2/3.8/4.6	3.7/3.2/3.8	4.2/3.7/4.6

FIGURE 2 Least square means of potassium concentrations in erythrocytes (mg/kg dry weight) of the groups (B, bolus; G, gel; S, solution), before and after potassium application at time 0 hour (caused by different time scales the curves and x-axis are interrupted)

urine potassium concentration (P = .45; Table 3), and FC of potassium (P = .95; Figure 5) did not change during the treatment.

4 | DISCUSSION

An all-embracing finding of the present study was that oral administration of 52 g of potassium per animal resulted in a significant increase in plasma potassium concentration in all groups within 30 minutes after medication. Contrary to 1 of our hypothesis, there
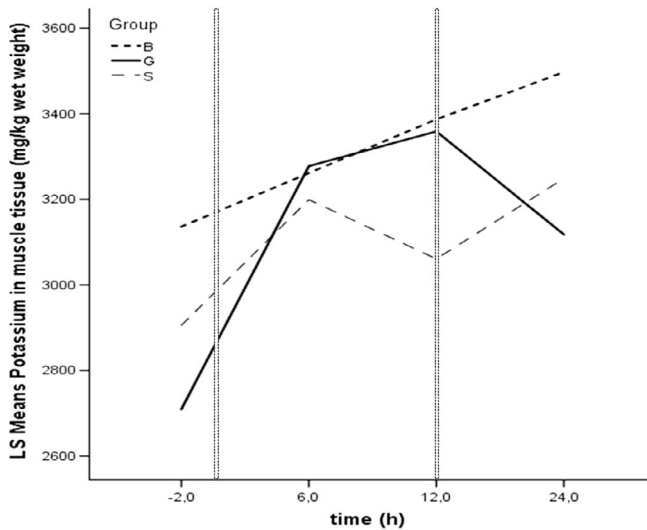
FIGURE 3 Least square means of potassium concentration in muscle tissue (mg/kg wet weight) of the groups (B, bolus; G, gel; S, solution) before and after potassium application at time 0 hour (caused by different time scales the curves and x axis are interrupted)
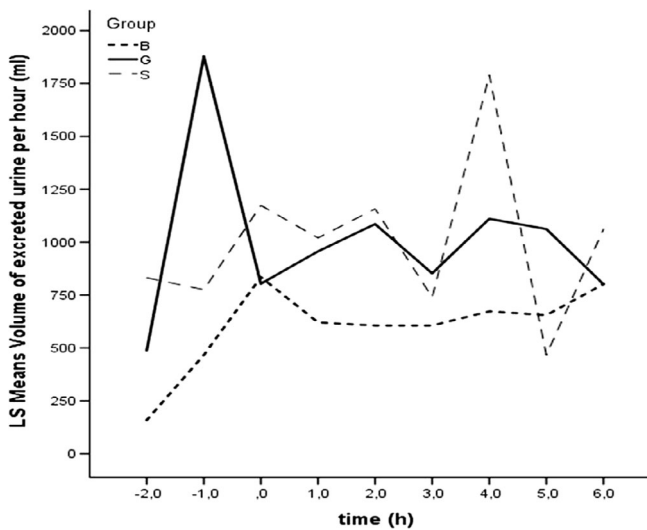
TABLE 3 Urine potassium concentration (mmol/L) before and after oral potassium application at time 0 hour with 3 different formulations containing 52 g of potassium (groups: B, bolus; G, gel; S, solution) (data given as median/1st/3rd quartiles)

Time (h)	Urine potassium concentration (mmol/L)		
	Group B (n = 10)	Group G (n = 10)	Group S (n = 10)
−2.0	91/68/132	67/34/101	55/45/102
−1.0	100/86/136	69/30/105	47/30/96
0	101/83/123	73/43/96	48/28/114
1.0	99/69/127	78/50/156	55/24/101
2.0	108/60/128	84/44/164	68/30/109
3.0	99/65/137	88/54/159	88/57/154
4.0	88/64/134	90/55/165	89/42/178
5.0	101/80/163	88/52/177	105/59/167
6.0	102/80/164	104/65/196	90/60/144

FIGURE 4 Least square means of urine volume (mL) excreted per hour during 8 hours of the study (2 hours before and 6 hours after potassium application) in the groups (B, bolus; G, gel; S, solution)
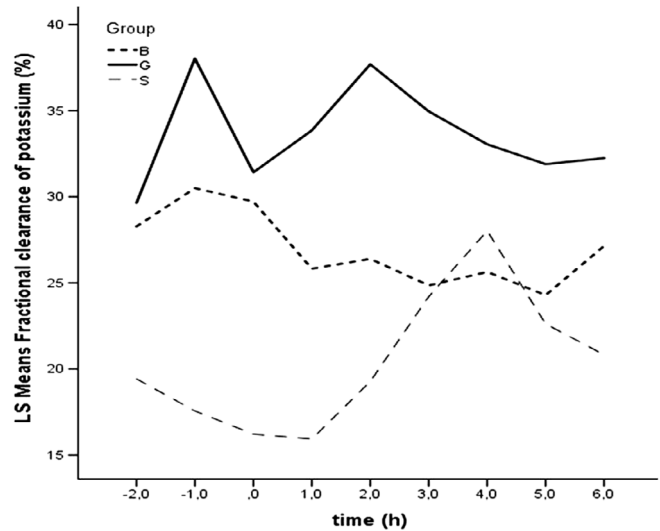

FIGURE 5 Least square means of fractional clearance of potassium (%) via urine during 8 hours of the study (2 hours before and 6 hours after potassium application) in the groups (B, bolus; G, gel; S, solution)

were no differences between the concentration/time characteristics of potassium in the plasma, although the formulations were reputed to release potassium differently over time. As the bolus releases sufficient amount of potassium to increase the plasma concentration within 30 minutes, it seems reasonable to prefer this method of administration as the application is convenient and safe, suffering no loss of volume or inadvertent aspiration which may occur when a solution is given OP. Furthermore, potassium chloride is irritating for mucosal membranes which can be avoided when given as a coated bolus. Potassium propionate has the advantage over potassium chloride that it is an energy-rich organic compound and propionate is the precursor for glucose synthesis and may result similar to propylene glycol in insulin secretion.[15] The clinical relevance of propionate in this formulation is unknown. We are aware that other factors like costs of the products or convenience of application may also influence the choice of the product.

However, it was observed in the present study that 50% of the cows started to increase their feed intake within 2 hours after the treatment. This "adverse effect" is known from previous studies that described the association between potassium deficiency and reduced feed intake.[16,17] Although feed intake was assessed only by visual appraisal which therefore is subjective to a certain degree, increasing appetite and feed intake is generally considered a clinical sign which might indicate treatment success in cattle.

Although hypokalemia occurs in cows with LDA and AV,[8] abomasal impaction,[7] and also in calves with neonatal diarrhea,[18] it seems likely that the condition is underdiagnosed because until recently no

point of care test had been available. A recent study found that low-cost instruments which are widely available now are suitable for use in "cow-side" and produce reliable measurements.[19] These new tools offer the potential to apply measurements of plasma potassium concentration frequently to adjust the volume and frequency of oral potassium application.

The intracellular potassium levels in erythrocytes and muscle tissue showed a very high variability and were not influenced by the oral potassium administration. However, it can be concluded that the oral potassium application of 52 g of potassium per animal primarily influences the extracellular plasma concentrations. Similar to Schneider et al,[11] the present study found the potassium concentration in erythrocytes to be very variable, supporting the opinion that this parameter is of limited usefulness to assess potassium in cattle. The internal potassium balance is very complex and many factors can cause a shift of potassium from the blood plasma into the cells. Secretion of aldosterone decreases plasma potassium not only by a shift of the ion into the cells, but also by enhancing the renal excretion and increasing the gastrointestinal secretion of potassium.[9] Treatment of ketosis with glucose and isoflupredone acetate also leads to a potassium shift into the cells.[20] Regarding the present study, it cannot be defined whether the hypokalemia was caused by potassium depletion or by a shift of potassium from the extracellular compartment into the cells. To our best knowledge, there are no reference ranges for the intracellular potassium in the muscle cells; however, the concentration found in the present study are similar to the results of a recent study in cows with decreased feed intake using identical methods.[11]

Field studies like the present study have certain limitations. One might be that the animals in the study were rather diverse according their primary disease conditions. Various mechanisms and disease pathological conditions may influence gastrointestinal motility and absorption. These effects are complex, hardly to avoid, and difficult to assess. As stated, the animals which had surgery were allowed at least 48 hours between surgery and potassium application to avoid bias caused by the postoperative hypodynamic ileus of the gastrointestinal tract. In general, we are aware of these shortcomings which are typical for field studies; however, the study aimed to test the substances under the field practice conditions and not in experimentally induced hypokalemic cows. This is different to the study where hypokalemia had been induced experimentally in otherwise healthy animals by increasing renal potassium excretion[5] and hence reducing the variable conditions of the animals. On the other hand, the cows of the present study represent the situation in practice a clear advantage for the practical relevance of the study.

Another point worthy of discussion is that only a decreased plasma potassium concentration was applied as an inclusion criterion. This parameter is easily obtainable and there is an established reference range which is not the case for intracellular muscle tissue or erythrocyte potassium.[9] Hypokalemia can be aggravated by a third space loss and alkalosis, for example, in cows suffering from a partial or complete ileus.[1] The changes of intracellular potassium concentration after oral potassium application might be too small to measure.

The main route of potassium excretion is via urine. Therefore, urine has been collected to measure the total amount of urine and calculate fractional potassium clearance. The applied amount of potassium increased the plasma potassium concentration effectively without resulting in an increased renal excretion which can be considered an ideal situation. Higher dosages or repeat doses may result in increased potassium and subsequent water excretion which might not be desirable in animals which are frequently dehydrated. The FCs of potassium varied substantially but were within the reference range from 21 to 56%.[21]

Similar to Constable et al,[5] the present study suggests that the potassium application results in an increased plasma potassium concentration for only 12 hours which results in the recommendation to repeat the application after that time until the feed intake has been returned to normal. As already mentioned, as there are point-of-care measurements available, the plasma potassium concentration should be used for decision on further treatments.

CONFLICT OF INTEREST DECLARATION

The Austrian Buiatric Association provided a grant covering the living expenses of Dr S. Schneider, and laboratory costs providing the potassium formulations by Chevita GesmbH. Dr. Wolf is affiliated with Chevita GesmbH. Chevita GesmbH did not influent the outcome of the study.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

All used protocols and procedures concerning animal treatment have been approved by the institutional ethics committee and the governmental animal protection authority according to national legislation (GZ 68.205/0145-II/3b/2013).

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REFERENCES

1. Sattler N, Fecteau G. Hypokalemia syndrome in cattle. *Vet Clin North Am Food Anim Pract*. 2014;30:351-357.

2. Grünberg W, Morin DE, Drackley JK, Barger AM, Constable PD. Effect of continuous intravenous administration of a 50% dextrose solution of phosphorus homeostasis in dairy cows. *J Am Vet Med Assoc*. 2006;229:413-420.

3. Constable PD, Grünberg W, Carstensen L. Comparative effects of two oral rehydration solutions on milk clotting, abomasal luminal pH, and abomasal emptying rate in suckling calves. *J Dairy Sci*. 2009;92:296-312.

4. Constable PD, Grünberg W, Staufenbiel R, Stämpfli HR. Clinicopathologic variables associated with hypokalemia in lactating dairy cows with abomasal displacement or volvulus. *J Am Vet Med Assoc*. 2013;242:826-835.

5. Constable PD, Hiew MWH, Tinkler S, Townsend J. Efficacy of oral potassium administration in treating lactating dairy cows with experimentally induced hypokalemia, hypochloremia and alkalemia. *J Dairy Sci*. 2014;97:1-14.

6. Smith GW, Constable PD, Morin DE. Ability of hematologic and serum biochemical variables to differentiate gram-negative and gram-positive mastitis in dairy cows. *J Vet Intern Med*. 2001;15:394-400.

7. Wittek T, Constable PD, Morin DE. Abomasal impaction in Holstein Friesian cows: 80 cases (1980-2003). *J Am Vet Med Assoc*. 2005;227:287-291.

8. Kalaitzakis E, Panousis N, Roubies N, Kaldrymidou E, Karatzias H. Macro mineral status of dairy cows with concurrent left abomasal displacement and fatty liver. *N Z Vet J*. 2010;58:307-311.

9. Goff JP. Macromineral disorders of the transition cow. *Vet Clin North Am Food Anim Pract*. 2004;20:471-494.

10. Johnson PJ, Goetz TE, Foreman JH, Vogel RS, Hoffmann WE, Baker GJ. Effect of whole-body potassium depletion on plasma, erythrocyte, and middle gluteal muscle potassium concentration of healthy, adult horses. *Am J Vet Res*. 1991;52:1676-1683.

11. Schneider S, Müller A, Wittek T. Concentration of potassium in plasma, erythrocytes, and muscle tissue in cows with decreased feed intake and gastrointestinal Ileus. *J Vet Intern Med*. 2016;30:679-685.

12. Sattler N, Fecteau G, Girard C, Couture Y. Description of 14 cases of bovine hypokalaemia syndrome. *Vet Rec*. 1998;143:503-507.

13. Peek SF, Divers TJ, Guard C, Rath A, Rebhun AC. Hypokalemia, muscle weakness and recumbency in dairy cattle. *Vet Ther*. 2000;1:235-244.

14. Rasmusen BA, Tucker EM, Ellory JC, Spooner RL. The relationship between the S system of blood groups and potassium levels in red blood cells of cattle. *Anim Blood Groups Biochem Genet*. 1974;5:95-104.

15. Maurer M, Peinhopf W, Gottschalk J, Einspanier A, Köller G, Wittek T. Effects of different dosages of propylene glycol in dry cows and cows in early lactation. *J Dairy Res*. 2017;84:375-384.

16. West JW, Coppock CE, Nave DH, Schelling GT. Effects of potassium buffers on feed intake in lactating dairy cows and on rumen fermentation in vivo and in vitro. *J Dairy Sci*. 1986;69:124-134.

17. Pradhan K, Hemken RW. Effect of potassium depletion in lactating bovine. *J Dairy Sci*. 1967;50:979.

18. 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.

19. Megahed AA, Hiew MWH, Grünberg W, Constable PD. Evaluation of 2 portable ion-selective electrode meters for determining whole blood, plasma, urine, milk, and abomasal fluid potassium concentrations in dairy cattle. *J Dairy Sci*. 2016;99:7330-7343.

20. Coffer NJ, Frank N, Elliot SB, Young CD, van Amstel SR. Effects of dexamethasone and isoflupredone acetate on plasma potassium concentrations and other biochemical measurements in dairy cows in early lactation. *Am J Vet Res*. 2006;67:1244-1251.

21. Itoh N. Fractional electrolyte excretion in adult cows establishment if reference ranges and evaluation of seasonal variations. *Vet Clin Pathol*. 1989;188:86-87.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.