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Measurement of abomasal conditions (pH, pressure and temperature) in healthy and diarrheic dairy calves using a wireless ambulatory capsule

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\textbf{ABSTRACT}

This study investigated abomasal luminal parameters in healthy and diarrheic calves by using a wireless ambulatory capsule (WAC). The acetaminophen absorption test (APAT) was used to determine abomasal emptying rate. Four healthy and five diarrheic female Holstein-Friesian calves (age < 14 days) were included in the study. For APAT, calves were fed 2 L of milk replacer containing 50 mg acetaminophen/kg body weight, and blood samples were taken during a 12-h period afterward. Concomitantly, a WAC in the abomasum continuously measured luminal pH, pressure, and temperature. Five hours post suckling, intraluminal temperature was significantly higher in diarrheic calves than in healthy calves. Abomasal pH and pressure were not significantly different, but intraluminal pressure was always numerically lower in diarrheic calves. During APAT no significant differences in maximum acetaminophen concentrations (C\textsubscript{max}) and time to reach maximum acetaminophen concentration (T\textsubscript{max}) were observed. Nonlinear regression findings revealed a longer acetaminophen half-time (AAP t\textsubscript{1/2}) in diarrheic calves compared to healthy calves [564 ± 96 min vs. 393 ± 84 min, respectively; \textit{P} = 0.04] and lower area under the concentration curve values (\textit{e.g.,} 60 min postprandial AUC\textsubscript{60} 681 ± 244 (µg min)/mL vs. 1064 ± 23 (µg min)/mL, respectively; \textit{P} = 0.04). In conclusion, abomasal luminal conditions were different between diarrheic and healthy calves. Impaired abomasal motility may induce enhanced bacterial fermentation processes as indicated by a higher abomasal temperature in diarrheic calves, which should be considered in management of their feeding.

\section{1. Introduction}

Neonatal diarrhea is the main cause of death during the first 2 weeks of life in calves (Torsein et al., 2014). Furthermore, diarrhea results in poor growth performance and increases the susceptibility to other infections (Windeyer et al., 2014). Kirchner et al. (2015) recently reported that neonatal diarrhea affects abomasal motility, which consequently delays the abomasal emptying rate (AER) after milk intake. Impaired abomasal motility may increase bacterial fermentation and the production of short-chain fatty acids (SCFAs) (Nouri and Constable, 2006), and luminal temperature may rise as a result of bacterial fermentation. The production of SCFAs contributes to the inhibition of abomasal motility by affecting chemoreceptors in the abomasal epithelium (Leek, 1977; Crichlow and Leek, 1986; Crichlow, 1988). In addition, growth of gas-producing bacteria such as Clostridium perfringens, Sarcina ventriculi, and Lactobacillus spp. is considered to be a predisposing factor for abomasal tympany ( Marshall, 2009). SCFAs have been found to impair the sodium transport system of the gastric mucosa of equines under in vitro conditions (Nadeau et al., 2003), leading to an osmotic influx of water into the cells and swelling and degradation of the mucosa (Argenzio, 1999; Carney et al., 1981). Abomasal conditions can be characterized by several intraluminal...
parameters such as pH, temperature, and abomasal pressure. As previously described, intraluminal pH is determined by invasive methods such as cannulation or through post-mortem study (Rachmann et al., 2009; Constable et al., 2009). A noninvasive wireless ambulatory capsule (WAC) for intraluminal pH, pressure, and temperature measurements has been already described in ponies (Stokes et al., 2012), dogs (Boillat et al., 2010), and humans (Koziolek et al., 2015). To our knowledge, noninvasive WAC measurements have not been described in calves. To investigate the AER, a variety of methods have been used, such as the acetaminophen absorption test (APAT, Constable et al., 2009), d-xylose absorption test (Wittek et al., 2005a, 2005b), scintigraphic evaluation (Marshall et al., 2005), and ultrasonographic measurements (Sen et al., 2006; Wittek et al., 2005a). In particular, the APAT has been evaluated as an appropriate nonradioactive method in cows (Wittek et al., 2009), heifers (Ehsani-Kheradgerdi et al., 2011), and healthy calves (Constable et al., 2009; Marshall et al., 2005; Sen et al., 2006). Acetaminophen (AAP) is absorbed in the proximal small intestine (Prescott, 1980), and it serves as an accurate parameter of gastric emptying (Snyder et al., 2014) or abomasal emptying in healthy animals (Marshall et al., 2005; Nouri and Constable, 2006; Sen et al., 2006).

However, to our knowledge data about diarrheic calves and the AER are lacking.

The aim of the study was to investigate abomasal conditions (abomasal pH, luminal pressure temperature and emptying rate) in healthy and diarrheic calves using WAC tool and APAT. We hypothesized that abomasal emptying is delayed in diarrheic calves compared to healthy calves. In consequence abomasal conditions differ with respect to abomasal pH, temperature, and luminal pressure.

2. Materials and methods

2.1. Animals

Nine Holstein-Friesian suckling calves [female; 4–14 days old, mean age (± SD): 7.7 ± 3.5 d; mean body weight (BW ± SD): 43.7 ± 6.3 kg] from one farm were used in this study; four were healthy, and five were diarrheic. The calves were housed in individual stalls from birth until 14 days postpartum (length × width × height: 1.90 m × 1.14 m × 1.35 m) andbeded on straw. Except for the experimental day the animals were fed twice daily with 4 L of combined skimmed milk and whey protein milk replacer containing ingredients as labeled: crude protein, 20.0%; crude fat, 17.0%; crude ash, 7.2%; phosphorus, 0.7%; calcium, 0.8%; sodium, 0.6% (FOK TOP, Alpuro Breeding). The animals had free access to water except for the day of the measurements.

This study was approved by the State Department of Agriculture, Food Safety and Fisheries of Mecklenburg-Western Pomerania, Germany (AZ 7221.3-1-018/15) and followed the guidelines for Animal Experiments of University Leipzig.

2.2. Experimental design

The study was performed in subsequent order including healthy calves as controls and calves with naturally occurring diarrhea. Inclusion criteria for the healthy group were a fecal score ≤ 1 on a scale of 0–3 according to Walker et al. (1998) A score of 0–1 indicated well-formed feces up to abnormal feces that tend to be pasty. Inclusion criteria for the diarrhea group were a fecal score ≥ 2 on a scale of 0–3. A score of ≥ 2 describes pasty feces, mainly liquid with solids up to liquid feces. Calves had diarrhea for 24 h before the experimental day.

Animals suffering from other diseases such as pneumonia or omphalitis (see clinical examination) were excluded from the study. After the experimental day diarrheic calves were treated with oral rehydration solutions, state of diarrhea improved without any medical intervention.

Calves were equipped with a WAC to determine abomasal pH, pressure, and temperature. The APAT was performed in each animal to analyze AER.

2.3. Clinical assessment

In the morning before sampling all calves were weighed on an electronic scale. Clinical examinations included the measurement of heart rate and lungs (auscultation), respiratory rate (counting) and rectal temperature (electronic thermometer). Calves were manually checked for omphalitis.

2.4. Acetaminophen absorption test

After a fasting period of 12 h calves were fed 2 L of a milk replacer by a bucket with a teat according to the protocol previously published by Marshall et al. (2005). Healthy calves were fed with 49.1 ± 4.4 mL/kg BW, and diarrheic calves were fed with 44.6 ± 4.4 mL/kg BW (amount of feeding per kg BW: p = 0.31). Fifty milligrams acetaminophen (AAP)/kg BW (Pracetam, Animedica) was mixed into the milk replacer. The mean (± SD) milk replacer temperature was 12.7 ± 2.9 °C when provided to the animals.

2.5. Feces collection

Rectal fecal samples were collected once during APAT.

2.6. Blood collection

Before the animals were fed, an indwelling catheter [14 G, 6.4 cm (2.5 in.)] was inserted into the right or left jugular vein after the skin was shaved and disinfected. The catheter was flushed with physiological saline after each blood sampling. Blood samples were collected 30 min before the test meal was fed to the calves and then at 30-min intervals for 8 h and at 60-min intervals for another 4 h. Blood was collected into tubes containing lithium heparin (10 mL Monovette, Sarstedt). Immediately after blood collection, lithium heparin tubes were centrifuged at 3000g for 10 min. Plasma was removed and stored at −20 °C until analysis. Additionally one venous blood sample was taken 30 min preprandially into a 3-mL syringe (PICO 50, Radiometer) containing heparin for oxymetric analysis.

2.7. Administration of WAC

Before administration of a WAC, the ventral abdominal region of each calf was shaved. All capsules (13 mm × 26 mm) were calibrated with a buffer solution containing citric acid (pH 6.0) and activated by the appropriate software tool (MotiliGI, SmartPill Corp). The pH, temperature and pressure sensors in the WAC send data at 434 MHz and, according to the manufacturer's information, the WAC measures pH from 0.5 to 9.0 pH units with an accuracy of ± 0.5 units; pressure from 0 to 350 mmHg with an accuracy of ± 5 mmHg; and temperature from 25 to 49 °C with an accuracy of ± 1 °C. In the case of pressure, the software provided a baseline correction. In our study we used the temperature compensated data as these data considered real values measured in the animal (Koziolek et al., 2015). The capsule was administered to the calves with a modified pill applicator before feeding them the milk replacer. A data receiver was fixed on the left side of each calf with an elastic bandage (CoFlex Vet, Andover). The successful placement of the capsule into the abomasum was verified by ultrasonographic imaging using a 3.5-Hz sector probe (A6Vet Sonoscope, Sonoring, see Supplementary file 1) 30 min after WAC application and afterwards at 60-min intervals for at least 12 h after milk intake. Approximately every 30 s the integrated antenna of the WAC sent pH, temperature, and pressure sensor information to the receiver. According to the manufacturer's information, the pH sensor took measurements every 5 s in a range of 0.5–9 units with an accuracy of ± 0.5 units. The temperature was measured every 20 s in a range from 25 to 49 °C, with an accuracy of ± 1 °C. Pressure data were taken at a frequency of 2 Hz in a range from 0 to 350 mm Hg.
(±5 mm Hg). The pressure data are expressed in kilopascals. Artificial pressure peaks due to manipulations of the examiner were marked by pressing the ‘Event’ button on the data receiver. These data were excluded from the statistics. 90% of the collected data were measured during a lying position of the calf.

2.8. Feces analysis

Feces were analyzed for Rota virus, Corona virus, Escherichia coli, and Cryptosporidium parvum by a commercial enzyme-linked immunosorbent assay (Fassisi BodiA, Fassisi).

2.9. Blood analysis

Blood plasma was analyzed by liquid chromatography–mass spectrometry analysis to determine AAP concentration.

The maximum AAP concentration (Cmax) and time to maximum AAP concentration (Tmax) after oral AAP application are primarily dependent on the AER correlating with a faster rate of absorption compared with the rate of elimination. An AAP time curve was generated by using the first derivative of Siegel’s modified power exponential equation as follows:

\[ C(t) = \frac{A}{(k t + 1)} \]

where \( C \) is the calculated AAP concentration (µg/mL) depending on the time \( t \) (time from the start of suckling in minutes). The constant \( m \) is the total cumulative recovery of AAP when the time is infinite; the constant \( k \) is the estimated rate of abomasal emptying (min\(^{-1}\)), and constant \( b \) is an estimate of duration of the lag phase before the exponential emptying phase is reached. All constants were determined through nonlinear regression analysis. Acetaminophen abomasal half-time was calculated by applying the generated constants into following equation:

\[ \text{AAP}_{1/2} = \left( -1 \right) \ln \left( \frac{1}{2} \right) \]

This pharmacokinetic model was validated and recommended by Marshall et al. (2005) as providing the most accurate abomasal emptying indices in calves.

Area under the curve (AUC) data were determined from the AAP concentration–time plot from 0 to 60 min, 0–120 min, 0–240 min, and 0–720 min calculated by the trapezoidal method using the following equation as previously described (Marshall et al., 2005):

\[ \text{AUC}_{(0-t)} = \sum_{i=0}^{n-1} \left( t_{i+1} - t_{i} \right) \left( \frac{C_{i} + C_{i+1}}{2} \right) \]

where \( C_i \) is the AAP concentration at the post-suckling time \( t_i \).

Before calves were fed, venous blood samples were analyzed oximetrically by a blood gas analyzer (corrected to rectal temperature, ABL80 Flex, Radiometer). The following parameters were measured: pH, partial pressure of carbon dioxide (pCO2) and oxygen (pO2), sodium, chloride, potassium, calcium, and hematocrit (Hct). Bicarbonate (HCO3\(^-\)) was calculated according to the equation of Hasselbalch. Anion base excess and anion gap were calculated by a blood gas analyzing device.

Total plasma protein (TPP) was analyzed by refractometry (Euromax).

2.10. Statistical analysis

Data analysis was performed with a statistical software program (Statistica 7.1, StatSoft). Data were assessed for normal distribution by the Kolmogorov–Smirnov test. Outlier tests were performed, and data were excluded when they were assumed to be an error of assessment.

Normally distributed data were subjected to unpaired t-test. In case of nonnormal distribution of data, the data were subjected to Mann–Whitney U test. To calculate AAP half-time, AAP concentration data were analyzed by nonlinear regression. Data are expressed either as mean ± standard deviation (SD) considering normal distribution or as median, 25 and 75 percentiles in case of nonnormal distribution. Statistical significance was accepted at \( P < 0.05 \). A trend was postulated at \( P < 0.10 \).

3. Results

3.1. Feces and vital parameters

All healthy calves were tested negative for diarrhea-causing pathogens. Calves with diarrhea were tested positive for Rota virus and Cryptosporidium parvum. Three of the five diarrheic calves were infected with Corona virus, and Escherichia coli was found in two of five fecal samples (see Supplementary file 2).

Vital parameter findings were not significantly different between healthy and diarrheic calves. Mean (±SD) rectal temperature 39.0 ± 0.26 °C and 38.8 ± 0.53 °C for diarrheic and healthy calves, respectively. Mean (±SD) heart rate and mean (±SD) respiratory rate were similar for diarrheic and healthy calves: 105 ± 16 bpm vs. 125 ± 9 bpm, and 45 ± 20 bpm vs. 41 ± 4 bpm.

3.2. APAT

The mean (±SD) maximum AAP concentration for diarrheic calves was 45 ± 12 µg/mL (range, 29–51.5 µg/mL), which was not significantly different from that for healthy calves (59.5 ± 8 µg/mL; range, 50.7–66.4 µg/mL; \( P = 0.13 \); Fig. 1). Times to reach maximum AAP concentration \( (T_{\text{max}}) \) were similar in both groups (Table 1). Within the 720 min of the observation period, AAP concentrations did not reach basal values measured before milk replacer intake. The calculated AAP abomasal half-time \( (\text{AAP}_{1/2}) \) was longer in diarrheic calves than in health calves (245 ± 42 min vs. 171 ± 36 min, respectively; \( P = 0.04 \)). The AUCs were significantly higher in healthy calves than in diarrheic calves (Table 1).

3.3. Blood gas analysis

Blood pH, hematocrit, electrolytes, and anion gap were not significantly different between the two groups of calves (Table 2). Lower bicarbonate concentrations were observed in diarrheic calves (27.7 ± 3.4 mmol/L) compared to healthy calves (32.7 ± 2.6 mmol/L; \( P = 0.04 \)). Furthermore, the anion base excess was lower in diarrheic calves (2.7 ± 3.8 mmol/L) than in healthy calves (7.8 ± 1.9 mmol/L; \( P < 0.05 \).

Fig. 1. Acetaminophen concentrations(µg/mL); \( O \) = healthy calves (H); \( \Delta \) = diarrheic calves (D); dashed line – nonlinear regression curve of H; straight line – nonlinear regression curve of D, time \( P < 0.001 \), diagnosis \( P = 0.208 \), time*diagnosis \( P = 0.127 \) (data are expressed as means ± SD).
3.6. Abomasal temperature

Abomasal temperature was 1.95 ± 0.77°C in healthy calves and 1.89 ± 0.63°C in diarrheic calves. The mean time (± SD) to reach pH < 2 was similar in both groups after test meal intake (data are expressed as means ± SD).

3.3.1. TPP

Within 14–24 days after WAC application, the capsules were still found in the abomasum as confirmed by ultrasonic imaging. However, further monitoring was not in the target of the study.

4. Discussion

In the present study we used calves that appeared to be in an early phase of neonatal diarrhea as reflected by similar results for hematocrit and electrolytes compared to healthy calves but with significant lower bicarbonate concentrations and a lower base excess. Diarrheic calves were positively evaluated by clinical signs (fecal score) and diarrhea-causing pathogens. Only calves with voluntary feed intake were included to ensure an adequate milk intake of 2 L in all calves for APAT. All calves tolerated the administration of the WAC by a pill applicator well. The WAC was inserted after calves suckled a small amount of milk in order to avoid an excessive milk intake, which provoked the reticular groove retractor well. The WAC was inserted after calves suckled a small amount of milk in order to avoid an excessive milk intake, which provoked the reticular groove retractor well.

In all calves, the median abomasal pressure values were generally different between the two groups. One hour postsuckling, the median pressure was −2.8 kPa (−3.5/−1.7) in healthy calves and −3.1 kPa (−5.3/−2.7) in diarrheic calves. The median pressure continuously decreased until reaching −4.7 kPa (−6.1/−2.9) at 600 min in healthy calves and −6.0 kPa (−10.0/−4.0) in diarrheic calves.

3.7. Abomasal pressure

The median abomasal pressure was −4.1 kPa (−5.6/−3.1; 25th and 75th percentile) and ranged from −11.5 kPa at 658 min to 13.1 kPa at 530 min. During the whole observation period (0–720 min postprandial) abomasal pressure data were not significantly different between the two groups. One hour postsuckling, the median pressure was −2.8 kPa (−3.5/−1.7) in healthy calves and −3.1 kPa (−5.3/−2.7) in diarrheic calves. The median pressure continuously decreased until reaching −4.7 kPa (−6.1/−2.9) at 600 min in healthy calves and −6.0 kPa (−10.0/−4.0) in diarrheic calves.

3.7.1. WAC excretion

Within 14–24 days after WAC application, the capsules were still found in the abomasum as confirmed by ultrasonic imaging. However, further monitoring was not in the target of the study.

In the present study we used calves that appeared to be in an early phase of neonatal diarrhea as reflected by similar results for hematocrit and electrolytes compared to healthy calves but with significant lower bicarbonate concentrations and a lower base excess. Diarrheic calves were positively evaluated by clinical signs (fecal score) and diarrhea-causing pathogens. Only calves with voluntary feed intake were included to ensure an adequate milk intake of 2 L in all calves for APAT. All calves tolerated the administration of the WAC by a pill applicator well. The WAC was inserted after calves suckled a small amount of the test meal, which provoked the reticular groove reflex. Fasting values of abomasal pH, temperature, and pressure were therefore not measured.

The appearance of the WAC in the abomasum of each calf was confirmed by ultrasonography at intervals of 60 min. Interestingly, based on ultrasonography, the WAC was not transported from the abomasum into the small intestine within 24 days after application, in contrast to humans (Koziolek et al., 2015) and ponies (Stokes et al., 2012).

In all calves, the median abomasal pressure values were generally described as subatmospheric, with a minimum abomasal pressure of −11.5 kPa. In ponies a mean minimum gastric pressure of 0.0 kPa has been reported (Stokes et al., 2012). In calves, a maximum pressure of 13.1 kPa (98.3 mm Hg) was similar to the mean maximum gastric pressure reported in ponies (126 ± 36 mm Hg; Stokes et al., 2012). Maximum pressure peaks up to 50 kPa were identified as the capsule passed from the stomach into the duodenum in dogs (Boillat et al., 2010), ponies (Stokes et al., 2012), and humans (Koziolek et al., 2015). In our study we did not observe similar maximum pressure peaks because the capsule was not passed from the abomasum into the small intestine during the observation period of 720 min or at more than 24 days after WAC application (Fig. 5). However, the median intraluminal pressure tended to be lower in diarrheic calves than in healthy calves; however, the difference was not significant, probably because of the low number of subjects.

Maximum pH was obtained immediately after feeding and steadily decreased until 12 h postprandial. The pH values measured by WAC were similar to postprandial pH values obtained in other studies using calves with an abomasal cannula that were fed either milk or milk replacer (Constable et al., 2005; Sen et al., 2006) or oral rehydration...
solutions (Sen et al., 2006; Bachmann et al., 2009). The time to pH < 2
was not significantly different in healthy or diarrheic calves. However,
times to pH < 2 have been confirmed by other studies in calves fed milk
replacer (Sen et al., 2006). It must be emphasized that pH variations
depend on the location of the WAC in the abomasum. WACs that are
close to the abomasal wall are primarily located in whey and probably
experience lower pH values than WACs located in the middle of the
chyme, particularly in the curd formation. Furthermore, McLauchlan
et al. (1989) found pH differences in the gastric body and antrum in
humans due to varied buffering effects of the chyme. The WAC presence
in the abomasum was always confirmed by ultrasonography, but the
exact location of the WAC in each term was not documented in our
study. However, the WAC can be speculated to have been close to the
abomasal mucosa in the xiphoidal region given the similar pH trends
during the observation period in both groups. Related to the location of
the WAC, pH measurements may reflect continuous hydrochloric acid
production by the parietal cells of the mucosa and the acidification by
the whey. In that context, Constable et al. (2005) reported lower pH
values after the intake of cow’s milk, which was either a result of the
clotting process by the extrusion of low whey pH or by a fast AER,
among other possibilities. In the present study, AER was delayed in
diarrheic calves, and therefore the location of the WAC in the acidifying
whey near the abomasal mucosa might be a possible explanation.
The low temperatures at the beginning of the observation period
were probably related to the low temperature of the milk fed to the
calves, but the abomasal temperature increased within the first 3 h after
milk intake. Afterward, the mean abomasal temperature was higher
than the mean rectal temperature in both groups. However, the abo-
masal temperature of diarrheic calves steadily increased until a mean
maximum temperature of 39.6 °C was reached 9 h postprandial. Higher
temperatures were found in diarrheic calves than in healthy calves 7 h
after milk replacer intake. One explanation for the higher intraluminal
temperatures might be related to fermentation processes in the

![Fig. 2. Representative WAC data from a diarrheic calf, abomasal
temperature (dashed line), pH (straight gray line), and pressure
(straight black line) against time.]

![Fig. 3. Abomasal temperature data against time; O – healthy calves; Δ – diarrheic calves;
* data were significantly different (P < 0.05), (data are expressed as means ± SD).]

![Fig. 4. Box plots of abomasal pressure data against time at each hour
after the test meal; clear boxes – healthy calves; banded boxes –
diarrheic calves (bottom and top of the box correspond to 25th and
75th percentiles).]
abomasum. In that context pH-tolerant mucosa-associated Lactobacilli ssp. were recently found by Hund et al. (2014) in the abomasum in calves. One consequence of bacterial fermentation is the production of SCFAs. SCFAs were reported to cause cell edema by interrupting the sodium transport under in vitro conditions in horse gastric tissue (Nadeau et al., 2003). A similar impairment of the sodium transport might also occur in the abomasum; however, data are lacking in the calf. If cell edema impairs the functionality of the abomasal movement, it may lead to delayed abomasal emptying. In addition, we detected pathogens such as Cryptosporidium parvum, Rota virus, and Corona virus in all diarrheic calves, and these pathogens are known for their mucosainjuring potential (Tzipori, 1983; Tzipori et al., 1983).

Another likely explanation for the higher intraluminal temperatures in the abomasum might be related to dehydration in diarrheic calves. With respect to dehydration a decreased heat loss has been described by Walker et al. (1998) due to impaired peripheral perfusion in experimentally induced diarrhea in neonatal calves. As TPP and other parameters such as electrolytes and hematocrit were similar between healthy and diarrheic calves, it can be speculated that calves did not suffer under severe dehydration. However, from our study it remained open whether fermentation processes or a decreased heat loss impaired intraluminal temperature in the abomasum.

APAT data confirm the results of Kirchner et al. (2015) who reported delayed abomasal emptying measured by ultrasonography in diarrheic calves. The AAP half-time was nearly 3 h faster in healthy calves (393 ± 84 min) than in diarrheic calves (564 ± 96 min). However, no significant differences in Cmax and Tmax were observed between the two groups of calves. The AUC values of diarrheic calves were about 25% lower compared to those of healthy calves, which could also be explained by malabsorption processes in the small intestine. More severely injured small intestine might alter AAP indices more noticeably. A validation of APAT with other methods of assessment (scintigraphy, ultrasonography) is necessary.

Interestingly, serum AAP curve showed an initial increase until 90 min postprandial, followed by a decrease 120 min postprandial, and a second rise in serum AAP in the following in both groups. In recent research it has been discussed that the abomasal emptying might be influenced by initial insulin and glucagon-like peptide-1 response in the early stage of glucose absorption (Stahel et al., 2016, MacPherson et al., 2016) which may explain the early postprandial fluctuations.

Considering WAC and APAT data, we confirmed our hypothesis that abomasal conditions differ between healthy and diarrheic calves. However, we emphasize that we used calves with mild symptoms of diarrhea without any impairment of suckle reflex and hydration or electrolyte status. Changes in abomasal luminal conditions and abomasal emptying could be more substantial in calves with severe diarrhea.

5. Conclusion

WAC is a tool to assess intraluminal pH, temperature, and pressure data. A slower AER and bacterial fermentation processes should be considered in the feeding management of diarrheic calves. In particular, smaller meal sizes might decrease the risk for fermentation processes in the abomasum. Based on the second finding that WAC was not transported from the abomasum into the small intestine within 24 days after application, the capsule might offer a new therapy tool in applying drugs with a constant flow of agents (e.g. buffering substances or trace elements such as selenium for calves on pasture) over several days or weeks.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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Appendix A. Supporting information

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References

Argenzio, R.A., 1999. Comparative pathophysiology of nonglandular ulcer disease: a review of experimental studies. Equine Vet. J. 19–23.
Bachmann, L., Homeier, T., Arth, S., Brueckner, M., Ravel, H., Deiner, C., Hartmann, H., 2009. Influence of different oral rehydration solutions on abomasal conditions and the acid-base status of sucking calves. J. Dairy Sci. 92, 1649–1659.
Boillat, C.S., Gaschen, F.P., Gaschen, L., Stout, R.W., Hosgood, G.L., 2010. Variability
associated with repeated measurements of gastrointestinal tract motility in dogs obtained by use of a wireless motility capsule system and scintigraphy. Am. J. Vet. Res. 71, 903–908.

Carney, C.N., Orlando, R.C., Powell, D.W., Dotson, M.M., 1981. Morphologic alterations in early acid-induced epithelial injury of the rabbit esophagus. Lab. Invest. a J. Tech. Methods Pathol. 45, 198–208.

Constable, P.D., Grünberg, W., Castensen, L., 2009. Comparative effects of two oral rehydration solutions on milk clotting, abomasal luminal pH, and abomasal emptying rate in suckling calves. J. Dairy Sci. 92, 309–316.

Crichlow, E.C., 1988. Ruminal lactic acidosis: forestomach epithelial receptor activation by undissociated volatile fatty acids and rumen fluids collected during loss of reticuloruminal motility. Res. Vet. Sci. 45, 364–368.

Crichlow, E.C., Leek, B.F., 1986. Forestomach epithelial receptor activation by rumen fluids from sheep given intraruminal infusions of volatile fatty acids. Am. J. Vet. Res. 47, 1015–1018.

Ehsani-Kheradgirdi, A., Sharifi, K., Mohri, M., 2011. Evaluation of a modified acetaminophen absorption test to estimate the abomasal emptying rate in Holstein-Friesian heifers. Am. J. Vet. Res. 72, 1600–1606.

Hund, A., Dzieciol, M., Schmitz-Esser, S., Wittek, T., 2014. Characterization of mucosa-associated bacterial community in abomasal ulcers by pyrosequencing. Vet. Microbiol. 177, 132–141.

Kirchner, D., Schwedhelm, L., Weitschies, W., 2015. Intragastric pH and pressure profiles in calves with left displaced abomasum or abomasal volvulus. Am. J. Vet. Res. 76, 213–220.

Koziolek, M., Schneider, F., Grimm, M., Mode, C., Seekamp, A., Roustom, T., Siegmund, W., Weitschies, W., 2015. Intragastric pH and pressure profiles after intake of the high-caloric, high-fat meal as used for food evaluation studies. J. Control. Release 220, 71–78.

Leek, B.F., 1977. Abdominal and pelvic visceral receptors. Br. Med. Bull. 33, 163–168.

MacPherson, J.A.R., Berends, H., Leal, L.N., Cant, J.P., Martin-Tereso, J., Steele, M.A., 2016. Effect of plane of milk replacer intake and age on glucose and insulin kinetics and abomasal ampying in female Holstein Frisian dairy calves fed twice daily. J. Dairy Sci. 99, 8007–8017.

Marshall, T.S., 2009. Abomasal ulceration and tympany of calves. Vet. Clin. North Am.: Food Anim. Pract. 25, 209–220.

Marshall, T.S., Constable, P.D., Crochik, S.S., Wittek, T., 2005. Determination of abomasal emptying rate in suckling calves by use of nuclear scintigraphy and acetaminophen absorption. Am. J. Vet. Res. 66, 364–374.

McLauchlan, G., Fullarton, G.M., Crean, G.P., McColl, K.E., 1989. Comparison of gastric body and antral pH: a 24 h ambulatory study in healthy volunteers. Gut 30, 573–578.

Nadeau, J.A., Andrews, F.M., Patton, C.S., Argenzio, R.A., Mathew, A.G., Saxton, A.M., 2003. Effects of hydrochloric, salicylic, and other volatile fatty acids on pathogenesis of ulcers in the non glandular portion of the stomach of horses. Am. J. Vet. Res. 64, 413–417.

Nouri, M., Constable, P.D., 2006. Comparison of two oral electrolyte solutions and route of administration on the abomasal emptying rate of Holstein-Friesian calves. J. Vet. Intern. Med. / Am. Coll. Vet. Intern. Med. 20, 620–626.

Prescott, L.F., 1980. Kinetix and metabolism of paracetamol and phenacetin. Br. J. Clin. Pharmacol. 10, 2916–2985.

Sen, I., Constable, P.D., Marshall, T.S., 2006. Effect of suckling isotonic or hypertonic solutions of sodium bicarbonate or glucose on abomasal emptying rate in calves. J. Chem. Inf. Model. 53, 1689–1699.

Snyder, A., Koehler, G., Seiwert, B., Abraham, G., Schusser, G.F., 2014. Influence of laxatives on gastric emptying in healthy warmblood horses evaluated with the acetaminophen absorption test. Berl. und Münch. Tierärztl. Wochenschr. 127, 170–175.

Stabel, P., MacPherson, J.A.R., Berends, H., Steele, M.A., Cant, J.P., 2016. Short communication: parameters of abomasal emptying and glucose-insulin dynamics in Holstein-Friesian calves at 2 ages and 2 levels of milk replacer intake. J. Dairy Sci. 100, 1–5.

Stokes, A.M., Lovie, N.L., Keown, M.L., Gaschen, L., Gaschen, F.P., Barthel, D., Andrews, F.M., 2012. Evaluation of a wireless ambulatory capsule (SmartPill®) to measure gastrointestinal tract pH, luminal pressure and temperature, and transit time in ponies. Equine Vet. J. 44, 482–486.

Torsein, M., Janszon-Mork, M., Lindberg, A., Halfén-Sandgren, C., Berg, C., 2014. Associations between calf mortality during days 1 to 90 and herd-level cow and production variables in large Swedish dairy herds. J. Dairy Sci. 97, 6613–6621.

Tzipori, S., 1983. Cryptosporidiosis in animals and humans. Microbiol. Rev. 47, 84–96.

Tzipori, S., Smith, M., Halpin, C., Makin, T., Krautil, F., 1983. Intestinal changes associated with Rotavirus and enterotoxigenic Escherichia coli infection in calves. Vet. Microbiol. 8, 35–43.

Walker, P.G., Constable, P.D., Morin, D.E., Drackley, J.K., Foreman, J.H., Thurmon, J.C., 1998. A reliable, practical, and economical protocol for inducing diarrhea and severe dehydration in the neonatal calf. Can. J. Vet. Res. = Rev. Can. De. Rech. Vét. 62, 205–213.

Windrey, M.C., Leslie, K.E., Godden, S.M., Hodgins, D.C., Lissemore, K.D., LeBlanc, S.J., 2014. Factors associated with morbidity, mortality, and growth of dairy heifer calves up to 3 months of age. Prev. Vet. Med. 113, 231–240.

Wittek, T., Constable, P.D., Marshall, T.S., Crochik, S.S., 2005a. Ultrasonographic measurement of abomasal volume, location, and emptying rate in calves. Am. J. Vet. Res. 66, 537–544.

Wittek, T., Schreiber, K., Füll, M., Constable, P.D., 2005b. Use of the o-xylene absorption test to measure abomasal emptying rate in healthy lactating Holstein-Friesian cows and in cows with left displaced abomasum or abomasal volvulus. J. Vet. Intern. Med. / Am. Coll. Vet. Intern. Med. 19, 905–913.

Wittek, T., Locher, L.F., Alkaassem, A., Constable, P.D., 2009. Effect of surgical correction of left displaced abomasum by means of omentopexy via right flank laparotomy or two-step laparoscopy-guided abomasopexy on postoperative abomasal emptying rate in lactating dairy cows. J. Am. Vet. Med. Assoc. 234, 652–657.