Post Mortem Investigation of Possible Mucosal Damages in Dairy Cows Following Four Oral Administrations at 12 Hour Intervals of a Calcium Chloride Paste Formulation

Nicolai Agger, *DVM*
Company KRUUSE
Byvej 35, 5290 Marslev
Denmark
Kurt Lomborg, *DVM*
Kjeldbjergvej 34, 7800 Skive
Denmark
Niels Zangenberg, *MScChemEng*
Royal Danish School of Pharmacy
Universitetsparken 2, 2100 Copenhagen
Denmark

Introduction

It is well-known that the incidence of milk fever in dairy cows can be significantly reduced when gut absorption of approximately 50g calcium takes place 4 times with 12 hour intervals around calving.[1,2,3] There are several different oral calcium formulations available containing different calcium salts, e.g., chloride, propionate, formiate, oxide, and carbonate. The amount of absorbed calcium following oral administration, however, is dependent on water- solubility of the different salts.[4] Calcium chloride is the most readily absorbed salt. The bioavailability of calcium propionate and formiate are inferior to calcium chloride. Consequently, a higher amount of administered calcium salts like calcium propionate or formiate is needed in order to get approximately 50g calcium absorbed from the gut. Calcium oxide and calcium carbonate are not water-soluble and therefore poorly absorbed.

It is also well-known that due to its caustic effect, calcium chloride in water or watery gel causes serious mucosal damages in the pharynx, esophagus, forestomachs and abomasum.[5,6] Several of these products in Europe are withdrawn from the market due to the caustic effect of calcium chloride on the mucosa. A calcium chloride bolus with a protective layer of fat surrounding it is available in Scandinavia. However, serious consequences are reported following administration of the calcium bolus to calving cows with impaired or absent mobility of the digestive tract. In these cases the bolus or boli lie directly on the mucosa in either rumen or reticulum, and the caustic calcium chloride would be in direct contact with the mucosa. A fatal case report is published in the Danish Veterinary Journal.[7]

A water-in-oil emulsion, where the caustic calcium chloride is dissolved in water and protected by oil, has been on the market during the past 6-7 years. The mucosal damages are minimized following administration. Maladministration into the lungs, however, has been observed due to the viscosity of the product.[8]

In cooperation with the Royal Danish School of Pharmacy, a calcium chloride paste formulation (BOVIVET® Calcium Paste, Jørgen Kruuse A/S) has been developed. In this paste formulation 180g calcium chloride and 6g magnesium chloride are distributed in and protected by a special two-component oil preparation and filled on to a 255ml cartridge. During the production of the paste formulation the dry materials are sticked together with the fat part of the oil which is then covered by rape seed oil.

This publication describes an investigation of possible mucosal damages of the tongue, pharynx, larynx, oesophagus, forestomachs and abomasum following oral administration of the calcium chloride paste formulation 4 times with 12 hours interval.

Materials and methods

Three clinically healthy, non-lactating and non-pregnant Friesian cows from one dairy herd were bought and confined in a farm without other animals.

Following an acclimatization period of 7 days, 1 cartridge of calcium chloride paste formulation was administered orally to the cows four times with 12 hour

This manuscript was received after the program was completed and in press.

intervals. The reaction of the cows to the administration was thoroughly observed and any abnormal reaction was registered. If any waste of paste formulation took place during the administration the amount wasted was registered.

In connection with the oral administration heparin stabilized blood samples were drawn from all 3 cows at the following time points:

Immediately before dosing, and 15, 30, 60, and 120 minutes post dosing.

Furthermore, an extra blood sample was drawn 240 minutes post first and third dosing.

The plasma samples were analyzed for total calcium on VetTest® 8008 (Idexx Labs, Inc.). In a Danish study VetTest® 8008 is described as user-friendly for dry chemical analyses in veterinary practice.[9] Duplicate analyses of all samples were performed.

Approximately 12 hours after the last administration the cows were slaghtered at a local abattoir.

The tongue, pharynx, larynx, oesophagus, rumen, reticulum, omasum, oesophageal groove, and abomasum were removed and inspected. All changes were photographed.

All handling and registrations were done by experienced large animal veterinarians.

Results

Administration of the paste formulation was uneventful. The cows hardly resisted the administration which lasted on average 30-40 seconds. In few cases, a small amount of paste (5-10 ml) fell out when the cartridge was withdrawn after the administration.

Increased salivation for approximately 1 minute was observed in almost all cows following administration, and one cow showed increased tear production immediately after dosing.

The average plasma concentrations of total calcium (mmol/l) for the three cows are given in figure 1.

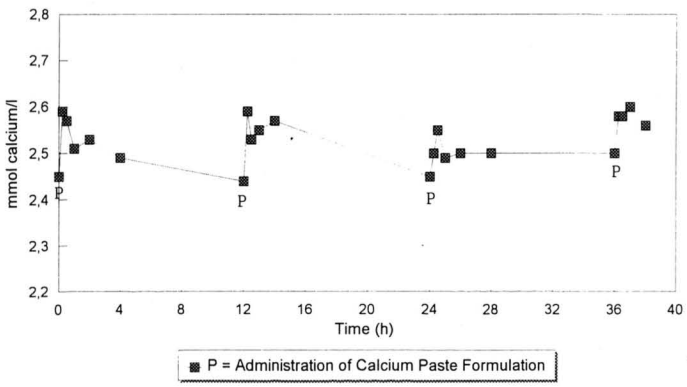

Figure 1. Calcium Conc. after 4 x Calcium Adm.

The clinical findings at post mortem are shown in table 1.

Table 1. Macroscopic changes of the cranial part of the digestive tract of three dairy cows 12 hours post 4th administration of a calcium chloride paste formulation.

	Cow A	Cow B	Cow C
Oral cavity	n.a.d.*	n.a.d.	n.a.d.
Tongue	n.a.d.	n.a.d.	scar at back of tongue
Pharynx	n.a.d.	n.a.d.	n.a.d.
Larynx	n.a.d.	n.a.d.	n.a.d.
Oesophagus	n.a.d.	n.a.d.	n.a.d.
Rumen	n.a.d.	n.a.d.	n.a.d.
Reticulum	n.a.d.	hyperaemia at the tip of the papillae	n.a.d.
Oesophageal groove	n.a.d.	slight hyperaemia	hyperaemia
Omasum	n.a.d.	n.a.d.	n.a.d.
Abomasum	small area with hyperaemia and oedema close to pylorus (not related to calcium chloride administration)	n.a.d.	n.a.d.

*n.a.d.= no abnormalities detected

Discussion

The uneventful administration of the paste formulation is a good sign of protection of the caustic calcium chloride. The wasted amount of paste formulation at the end of dosing is negligible and does not influence the effect of the preventive program.

Increased salivation is a known phenomenon following administration of calcium chloride formulations.

It appears from figure 1 that an increased absorption of calcium is registered immediately after each administration of the calcium paste formulation. This increased absorption of calcium takes place at two locations of the gut. Firstly, an instant peak absorption from the esophageal groove and abomasum within 15 minutes post administration and secondly, a slightly increased absorption of calcium across the small intestinal wall 1-2 hours later.

For this study non-lactating and non-pregnant cows were used. The normal homeostasis of calcium in non-calving cows is well functioning. Consequently, excessive amount of calcium given orally might only temporarily disturb the cow's own ability to regulate calcium absorption. The effect of calcium dosing on the absorption of calcium in calving cows with supressed calcium regulation is expected to last longer.

It can be seen in table 1 that the damaging effect on the mucosa is almost eliminated for this special formulation. A few hyperaemic area only in the mucosa of

the forestomachs are observed, i.e., at the tip of the papillae in the reticulum of one cow, and in the oesophageal groove of two cows. One cow was without any calcium chloride related changes at all.

The observed slight changes do not affect the cow and will heal in no time. Other observations registered are all occasional findings at slaughter and not related to this investigation.

The rapid peak concentration of plasma calcium around 15 minutes after dosing suggests that the calcium paste formulation passes by the rumen and is introduced directly into the oesophageal groove and abomasum.

Conclusion

This study has demonstrated that oral dosing of 1 cartridge of a newly developed calcium chloride paste formulation given 4 times with 12 hour intervals to 3 non-lactating and non-pregnant Frisian cows did not cause any resistance to the administration. Only a few small amounts of paste formulation were lost when the cartridges were withdrawn from the mouth after administration.

One cartridge of calcium paste formulation contains 180g calcium chloride and 6g magnesium chloride.

An increased concentration of calcium in plasma was seen within 15 minutes after each administration and this increase lasted for several hours.

The damaging effect of calcium chloride following administration of this newly developed paste formulation was reduced to slight hyperaemia at the tip of the papillae in the reticulum and in the oesophageal groove. These changes, however, are negligible. They do not disturb the well being of the cow and the changes heal instantly.

References

1. Jonsson, G. Milk fever prevention. *Vet. Rec.* 1978; 102: 165-169. 2. Schlütken, A. Untersuchungen über die wirksamkeit eines Gegärpareseprophylaxeverfahrens beim Rind und Erhebungen über das Gebärpareseaufkommen in Ostwestfalen-Lippe. *PhD Thesis, Justus-Liebig-Universität Giessen* 1993. 3. Wermuth, NC. New treatment of milk fever. *Proc., XVI World Buiatrics Congress* 1990; 525-528. 4. Goff, JP, and RL Horst. Oral Administration of Calcium Salts for Treatment of Hypocalcemia in Cattle. *J. Dairy Sci.* 1993; 76: 101-108. 5. Wentink, GH, and TSGAM v.d. Ingh. Oral Administration of Calcium Chloride containing Products: Testing for deleterious Side-effects. *Vet. Quart.* 1992; 14: 76-79. 6. Jørgensen, RJ, A Basse, and V Aslan. Sequelae to Oral Calcium Chloride gel Dosing og Cows. *Proc., XVI World Biuatrics Congress* 1990; 511-513. 7. Philipsen, JS. Bovikalc® kapsler - Calciumklorid - Aetsninger. *Dansk Vet. Tidsskrift* 1990; 73: 653-655. Rudebeck, K. Personal communication 1996. 9. Andersen, P. Afproevning af VetTest® 8008 paa plasma fra koer med maelkefeber. *Dansk Vet. Tidsskrift* 1996; 79: 527-530.