Hypocalcemia in Fresh Cows- It’s More Than Just Milk Fever

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Goal of the Presentation

- To raise awareness of the profound effects subclinical hypocalcemia has on the post-partum performance of dairy cows.
Presentation Outline

• Compare and contrast milk fever vs. subclinical hypocalcemia
• Review the physiology of hypocalcemia
• Discuss preventative measures to minimize the impact of hypocalcemia at the herd level
• Compare the sources and physical forms of available oral Ca supplements
• Review IV treatment and oral Ca supplementation protocols for individual cows and discuss hypophosphatemia
• Detail Bovikalc® strategies for herds and for individual cows
Clinical Milk Fever

- Nonfebrile disease of 2nd and greater lactation cows
- In U.S., ~ 5% of cows develop milk fever each year
- Caused by an acute calcium (Ca) deficiency
- Occurs just before calving to 48 hours post-calving
- Clinical signs are obvious because Ca is essential for muscle and nerve function

Photo courtesy of Dr. Ken Nordlund – UW Madison SVM

Stages of Clinical Milk Fever

Normal Blood Ca = 8.6-10.4 mg/dL

Stage 1: Blood total Ca ~5.5 to 8.6 mg/dl
- Excitability, nervousness, shuffling of rear feet
- Droopy, cool extremities, off-feed, ↓rumen function
- Standing but may be wobbly, muscle tremors

Stage 2: Blood total Ca ~3.5 to 6.5 mg/dl
- Down in sternal recumbency, head towards flank, partial paralysis, moderate bloat
- ↓Stroke volume ↓cardiac output, ↑heart rate, cold extremities, moderate depression

Stage 3: Blood total Ca ~1.0 to 3.5 mg/dl
- Lateral recumbency, completely paralyzed
- Severely bloated, comatose, rapid, weak heart rate
- If untreated, death due to suffocation or CV collapse

Subclinical Hypocalcemia (SCH)

- Defined as low blood calcium without oblivious clinical signs
- "New normal" regarding hypoCa
- Nonfebrile disease that can affect cows in any lactation
- Most often, affects > 50% of 2\textsuperscript{nd} and greater lactation cows even if using anionic salts pre-fresh
- Target disease that often goes unrecognized on a dairy

Physiology of Milk Fever
(Why does hypocalcemia occur?)

• Start of each new lactation challenges a dairy cow’s ability to maintain normal blood Ca concentrations
  – A sudden Ca outflow occurs
  – Colostrum /milk very rich in Ca
  – Cows draw on bone Ca to survive

• This negative Ca balance continues for first 3-4 months of lactation

• Most cows experience a drop in blood Ca around calving

Even cows without clinical milk fever are often hypocalcemic around calving. Initiation of lactation is a challenge.

**Plasma Ca Around Calving**

*Fresh cows with (n=8) or without (n=19) milk fever*

A cow does not have to be down to be negatively affected by hypocalcemia.

Plasma total Ca, mg/dL

-7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

A cow does not have to be down to be negatively affected by hypocalcemia.

**Data from Kimura et al., J. Dairy Sci. 89:2588, 2006**
Physiology of Hypocalcemia

• Cows must quickly shift their priorities to adjust to this sudden Ca outflow
• Most cows are able to compensate for this sudden Ca drain within 48 hours
• If able to, cows secrete parathyroid hormone (PTH) in response to low blood Ca
• “A little hypocalcemia is good”

Physiology of Hypocalcemia

• PTH secretion signals the cow to:
  – Mobilize Ca from bone
  – Increase efficiency of Ca uptake from the intestine
  – Reduce urinary loss of Ca

• Occasionally, PTH homeostatic mechanisms of Ca regulation fail
  – Cow risk factors
  – Dietary risk factors

Cow Risk Factors for Hypocalcemia

- **Age (lactation number or parity)**
  - Age related disease (#1 risk factor)
  - 9% ↑ risk with each successive lactation
  - Rare in 1st calf heifers (growing skeleton)

- **High producers**
  - Due to increased milk production

- **Breed predilection**
  - Jersey/Guernsey/Swedish Red & White/Norwegian Red > Holstein/Brown Swiss > Ayrshire/Milking Shorthorn

- **Cows with a prior history of hypoCa**

- **Lame cows**

- **Twins, stillbirths, dystocia**

- **Body condition score**
  - BCS >3.5 – over-conditioned cows 3.3X greater odds

- **Hormonal factors**
  - Estrogen ↑ at end of gestation
  - Effects Ca mobilization from bone

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Dietary Risk Factors for Hypocalcemia

- Acid–base status at parturition
  - Alkalotic rations promote hypoCa
    - Rations high in sodium (Na+) and potassium (K+) create metabolic alkalosis
      - Impairs activity of PTH
    - Excessive dietary potassium (K+) impairs active transport of Mg across rumen wall
  - Acidic rations prevent hypoCa
    - Use of anionic salts or mineral acids (DCAD diets)
    - Stimulate PTH actions

- Excessive dietary phosphorous
  - High P diets decrease intestinal absorption of Ca

- Hypomagnesemia
  - Close-up or early lactation rations can be low in magnesium (Mg)
    - Mg necessary for PTH secretion
    - Hypomagnesemia reduces tissue sensitivity to PTH

Hypocalcemia occurs when:

- Ca leaves the bloodstream to enter the mammary gland faster than it can be replaced by intestinal Ca absorption and bone Ca resorption
- Cows that fail to maintain normal blood Ca concentrations develop milk fever or SCH

Physiology of Hypocalcemia

- Milk fever and SCH are gateway diseases that predispose cows to a variety of disorders and clinical complications
  - Key associated problems:
    - Decreased dry matter intake post-calving → ↓ milk yield
    - ↑Risk of secondary diseases
    - ↑Risk of early herd removal

Early Postpartum Hypocalcemic Cascade

HYPOCALCEMIA (clinical or subclinical)

↓ Smooth muscle function  ↓ Skeletal muscle function  ↑ Stress

A cow does not necessarily have to be down to be negatively affected by hypocalcemia

↑ Displaced Abomasum  ↓ Dry matter intake  ↓ Immune Function  ↑ Metritis

↑ Ketosis

↓ Potential Milk Yield  ←→  ↑ Removal Risk

Seifi et al., Vet J 188:216-220, 2011
Kimura et al., J. Dairy Sci. 89:2588, 2006
Minimizing the Impact of Hypocalcemia at the Herd Level

• High losses associated with hypocalcemia emphasize the need for prevention

• Two approaches to prevention
  1. Acidification of the pre-fresh diet
  2. Oral calcium supplementation post-calving

Termed dietary cation–anion difference or DCAD diets

Diets are made acidogenic by selecting inherently acidogenic feedstuffs and/or by use anionic salts or mineral acids
  - Creates a systemic metabolic acidosis in the cow

Evoking an acidic response in the cow prior to calving reduces the risk for hypocalcemia after calving

Dietary acidification makes cow’s tissues more responsive to PTH at calving so they can mobilize blood calcium at this critical timeframe

Oral Calcium Supplementation

- Oral Ca supplements are not all created equal
  - Oral Ca supplements use a variety of different Ca sources
  - The source of Ca greatly influences blood Ca absorption and responses
    - The Ca source must be soluble in digestive fluids to be effective
      - Creates concentration gradient
    - Ca passively diffuses into the blood between rumen and intestinal cells

Photo courtesy of Dr. Jesse Goff, Iowa State University CVM

Ca sources in Oral Calcium Supplements

• Calcium chloride
  • Acidogenic salt
    • Greatest ability to support blood Ca concentrations
    • Preferred Ca source - most soluble (bioavailable) of the Ca salts
    • Causes the cow to mobilize additional Ca from her skeleton
    • Caustic to lungs if inhaled; typically packaged to contain 40-54 g per dose

• Calcium propionate
  • Neutral salt
    • Need about 100 g of elemental Ca (1 lb.)
    • Is also glucogenic – provides precursors to blood glucose- slows GI motility

• Calcium carbonate
  • Alkaline salt
    • Regarded as insoluble in digestive fluids, does not raise blood Ca
    • Not suitable as oral Ca supplement - not soluble enough to induce rapid rise in blood Ca
Preferred Oral Ca Source = Boluses

- Bovikalc® oral Ca nutritional supplement
  Fat-coated bolus offers safety, convenience and effectiveness

- 43 g elemental Ca
  - 71% from calcium chloride (2 H₂O)
  - 29% from calcium sulfate (0.5 H₂O)

- Store at or below 86° F
Bovikalc® Offers Cow Safety

- The physical form of oral Ca has important implications for cow safety
  - Hypocalcemic cows have poor swallowing and gag reflexes
  - Do not drench with thin liquids
    - Risk of aspiration pneumonia
    - Calcium chloride is very caustic to upper respiratory tissues

Personal communication with Dr. Gary Oetzel – UW-Madison SVM
Bovikalc® Offers Cow Safety

• **Bovikalc® advantages:**
  - Little if any risk of aspiration pneumonia
  - No unpleasant taste to the cow
  - Little to no wastage
  - More prolonged release of the oral Ca
  - No irritation to oral cavity
  - Avoids inadvertent drowning that can occur with stomach tubes or esophageal pumps

*Photo courtesy of Dr. Jesse Goff, Iowa State University CVM*

Bovikalc® Offers Convenience

- Bovikalc® is vital for her and easy for you
  - A bolus is the easiest and most convenient form of oral Ca to administer
  - Saves end user time and labor
  - No wastage of the oral calcium
  - Exterior fat coating for easier swallowing

Bovikalc® is easy for you
Bovikalc® Offers Effectiveness

- Immediacy is critical when cows are hypocalcemic
  - Bovikalc® reaches peak blood concentrations in 60 minutes
  - Rapid rise in blood Ca concentrations helps prevent hypocalcemic standing cows from going down
  - Bovikalc® invokes an acidogenic response in the cow

Bovikalc® provides a rapid boost in blood calcium concentrations

Two Bovikalc® boluses results in sustained improvement in blood Ca concentrations for 24 hours

Sampson et al., Vet Ther. 10:131, 2009
Timing and Rationale for Supplementing Standing Cows (a minimum of two Bovikalc® boluses are needed)

Giving only one Bovikalc® bolus at calving leaves the cow without support when her blood calcium concentrations are naturally the lowest (nadir occurs at 12-24 h post-calving)

Blood Ca data from 5 studies reporting blood Ca concentrations around calving

Bovikalc® administration schedule from Oetzel and Miller, J. Dairy Sci., 95:7051, 2012

Bovikalc® label

Bovikalc® study, 2012

PREVENTION WORKS.
Individual Cow Supplementation

- Oral Ca supplementation is the best approach for standing cows with signs of hypocalcemia
- Still modest use of oral Ca by the dairy industry
  - Often a lack of veterinary involvement in designing Ca treatment protocols
  - IV Ca administration is glamorous
  - IV Ca shows short-term benefit but may do long-term harm

Photo courtesy of Dr. Gary Oetzel-UW-Madison SVM

Personal communication with Dr. Gary Oetzel – UW-Madison SVM
Individual Cow Supplementation

• 23% Calcium Gluconate is the preferred IV Ca solution for down cows
  – No added glucose
  – Added electrolytes of no value
    • Mg (magnesium) – already elevated
    • P (phosphorous)
      – will self-correct
      – unavailable hypophosphite
    • K (potassium) - negligible
  – Total body deficit ~ 6g Ca
    • 1 bottle is enough

IV Calcium Treatment Has Risks

adapted from data presented by Dr. Jesse Goff while at the USDA-ARS, Ames, Iowa


-very high blood calcium
-normal calcium mobilization stops
-risk of cardiac complications

~25-40% of cows treated favorably with IV calcium will relapse in 12-18 hours

Clinical milk fever
Treated with 10.5 grams Ca IV

normal blood calcium = 8.6 to 10.4 mg/dL

Hypocalcemic again
Individual Cow Supplementation

- Reducing relapses following IV calcium treatment to down cows
  - Following IV treatment – give 2 doses of Bovikalc®
  - 1st dose once cow is up and able to swallow
  - 2nd dose 12 hours later
    - Reduces relapse risk to 5-10%

Why is Bovikalc® the Correct Choice for Standing Cows with Signs of Hypocalcemia?

- IV Ca administration causes calcitonin release and rebound hypocalcemia post-administration.
- This reverses the beneficial effects of PTH:
  - Decreases bone mobilization of Ca and intestinal Ca absorption.
  - Increases urinary Ca excretion.
- These effects are negative to a cow struggling to maintain normal Ca levels at the start of lactation.

Photo courtesy of Dr. Gary Oetzel - UW-Madison SVM

Personal communication with Dr. Gary Oetzel – UW- Madison SVM
Why is Bovikalc® the Correct Choice for Standing Cows with Signs of Hypocalcemia?

- Oral Ca such as Bovikalc® does not impair the beneficial effects of PTH.
- Total body Ca deficit is ~6 g for a cow with milk fever.
- Of the 43g of Ca within Bovikalc®, ~4-6 g is absorbed.
- Corrects the deficit without altering PTH secretion.

Because Bovikalc® is more slowly absorbed than IV Ca, it does not shut down PTH secretion or activate calcitonin like IV Ca does!

Personal communication with Dr. Gary Oetzel – UW- Madison SVM
Blood Ca Levels in Standing Cows Given IV Ca Were Lower Than Control Group at 24 Hours

IV calcium extends the period of hypocalcemia post-calving when given to standing cows!
What About Low Phosphorous (P) Cows?

- Clinical relevance is subject to conjecture and debate
- Many vets include P supplementation for repeat milk fever cows
  - Either oral or IV P therapy
- Most cows with milk fever will also be hypophosphatemic (low P) due to elevations in circulating PTH and lactational drain of P
  - PTH secretion results in:
    - Loss of P via the saliva and urine

Normal P Levels = 5.6 to 6.5 mg/dL

Photo courtesy of Dr. Jesse Goff, Iowa State University CVM

Personal communication with Dr. Gary Oetzel – UW- Madison SVM
What About Low Phosphorous (P) Cows?

- Usually P will self-correct when the hypocalcemia is corrected.

- For unknown reasons, some cows are unable to restore normal blood P concentrations after Ca is corrected:
  - Irreversible musculoskeletal damage?

- Field treatments:
  - **IV**: 30g of sodium monophosphate in 300 ml of distilled water (Fleet® enema)
  - **Oral**: ½ # of sodium monophosphate in ~ 2 gallons of warm water
A Bovikalc® Supplementation Strategy for Herds

• Herds at high risk for hypocalcemia (high clinical milk fever rate, no anionic salts, Jerseys, or high prevalence of measured hypocalcemia)
  – Blanket supplement all 2+ lactation with 2 doses of Bovikalc®
    • (1st supplement at calving, 2nd supplement the next day)

• Herds without hypocalcemia problems
  – Supplement lame and high previous lactation milk production cows with two doses of Bovikalc®
    • A recent study suggested the 2nd bolus can be given at lock-up the next day
      – (1st supplement at calving, 2nd supplement the next day)

A Bovikalc® Supplementation Strategy for Individual Cows

• Hypocalcemic cows that are still standing
  – Cold ears, wobbly, triceps muscle tremors, poor GI motility, within 48 hours of calving
  – 1 dose now, one dose 12 h later

• Off-feed early lactation cows
  – Reduced intake and GI stasis; both can cause hypocalcemia

• After successful IV treatment of down cows
  – Prevent hypocalcemic relapses
  – One dose after cow is up and swallowing, one dose ~12 hours later

• Cows with a prior history of milk fever

• Non-parturient hypocalcemia cases
  – Following digestive upsets, estrus, toxic conditions
Bovikalc® Product Caution Statements

- **Caution**
  - Follow label instructions carefully. Incorrect use or handling may cause serious side effects.
  - User assumes risk of use or handling contrary to instructions, or under abnormal conditions or conditions not reasonably foreseeable.
  - Bovikalc should not be used for initial treatment of milk fever.
  - **Do not use Bovikalc® for cows lying down or showing signs of milk fever.**
  - Do not use excessive force when giving the bolus to the cow.
  - **Do not use the bolus if broken.**
  - Keep out of reach of children
Take Home Messages

• Subclinical hypocalcemia is the target disease or “new normal” when speaking of hypocalcemia in dairy cows
• Not all oral calcium sources are created equal
• A minimum of 2 doses of oral Ca are needed when supplementing cows with stage 1 milk fever or SCH
• Oral Ca like Bovikalc® is the correct choice for standing cows with signs of hypocalcemia
• Reserve IV Ca for down cows
Thank You and
What Questions
do You Have??