Pharmacokinetics and adverse reactions to fentanyl transdermal patches in healthy and hospitalized calves

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Introduction

Fentanyl is a mu opioid receptor agonist that has been used for analgesia in multiple species. One of the more common routes of administration of fentanyl is the transdermal route. There have been multiple reports of the use of Fentanyl Transdermal Patches (FTP) in large animal practice as a longer-term method of analgesia. The use of the patches has been described for analgesia in horses, sheep, goats, pigs, and llamas, but there is no data available for the use of this extended-release formulation in cattle.

Materials and Methods

The primary objectives of this study were to determine the pharmacokinetics (PK) and effect of fentanyl transdermal patches in healthy and hospitalized bovine calves.

Results

Three patient calves and 5 healthy calves had fentanyl patches applied as described for sheep. Six out of the 8 calves exhibited episodes of tachycardia, tachypnea, bellowing, and ataxia. These signs resolved within 2 to 6 hours in 6 calves when the patches were removed, and a commercial opioid antagonist was administered to 2 calves. Maximum concentration ranged from 0.726 to 3.292 ug/mL, and a time to maximum concentration ranged from 4 to 10 hours at the time of patch removal due to clinical presentation.

Significance

The adverse effects of the administration of fentanyl patches in calves requires more research to determine an appropriate clinical regimen and environment for this sustained-delivery therapy.

Comparison of ionized calcium concentrations using an Abaxis Vetscan iSTAT with a Horiba LAQUAtwin calcium meter in dairy cows fed low, medium, and high calcium DCAD rations and challenged with EGTA

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Introduction

Prepartum feeding of a negative dietary cation-anion difference (-DCAD) ration has proved to be an effective method of preventing hypocalcemia. However, the optimum Ca concentration to feed with -DCAD rations has not been determined. We conducted an experiment to assess the implications of feeding a low, medium, and high concentration Ca -DCAD ration on the ability of a cow to respond to an induction of hypocalcemia.

Materials and Methods

Three groups of non-lactating, non-pregnant Holstein cows were fed -DCAD rations (15.1 mEq/100 g DM) for 21 d with low (LC = 0.45% Ca; n=5), medium (MC = 1.13% Ca; n=6) or high (HC = 2.02% Ca; n=6) concentrations of dietary Ca and then subjected to a controlled induction of hypocalcemia to determine the ability of cows to respond to the challenge based on dietary Ca. On d 22, 23, and 24 hypocalcemia was induced using an intravenous infusion of 5% ethylene glycol

tetraacetic acid (EGTA). During infusion, blood samples were collected every 15 min until 60% of pre-infusion iCa concentrations were achieved. Samples were collected post-infusion at 0, 2.5, 5, 10, 15, 30, and every 30 min thereafter until 90% of pre-infusion iCa was reached.

Results

We utilized a likelihood ratio to determine whether the variances of the 2 meters were equal when measuring iCa concentrations during EGTA challenge and recovery period. Variance for the iSTAT was 0.02745, while variance for the Horiba meter was 0.14447. The chi-square value was significant ($P<0.0001$). These results indicate that the Horiba meter is more variable when measuring blood iCa concentration and produces values that are significantly higher than values obtained from the iSTAT ($P<0.001$).

Significance

The Horiba LAQUAtwin meter is less likely to accurately identify a cow with clinical or subclinical hypocalcemia than the Abaxis Vetscan iSTAT.

Effect of prepartum energy balance on neutrophil function following pegbovigrastim treatment in periparturient cows

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Introduction

Treatment with granulocyte colony stimulating factor (G-CSF) increases neutrophil (PMN) count and enhances PMN function in the periparturient cow. It was hypothesized that prepartum undernutrition might reduce the effect of a commercial recombinant bovine G-CSF product (pegbovigrastim; Imrestor (IMR), Elanco) on PMN count and function. Hence the objective of this study was to test the effect of undernutrition for 1 month prior to calving on the response to IMR.

Materials and Methods

Cows (n=99) on pasture in a research herd in New Zealand were blocked by expected calving date and BCS and randomly assigned in a 2 by 2 factorial design to be fed to exceed energy requirements prepartum (FULL), or restricted to approximately 85% of prepartum energy requirements (RES). At approximately 7 d before expected calving and on the day of calving, half the cows in each feed group were injected with the labelled dose of IMR while the remaining half were injected with saline. Blood samples were collected pre-and post-calving for complete blood count, biochemistry and in vitro assessment of PMN function including phagocytosis, myeloperoxidase (MPO) release, and oxidative burst.

Results

Energy restriction prepartum resulted in lower body weight (96 ± 0.4% vs 101 ± 0.5% of initial body weight for RES vs FULL cows at calving; $P < 0.001$), and a higher proportion of cows with elevated concentrations (>0.4 mmol/L) of fatty acids (NEFA) in blood (35/41 (85%) vs 23/41 (56%) elevated for RES vs FULL cows at 7 d before calving; $P < 0.001$).

Treatment with IMR increased PMN count from 6 days before to 21 days after calving (9.8 ± 0.2 vs. 3.9 ± 0.2 x 10^9/mL; $P < 0.001$). There was a time by IMR interaction ($P < 0.001$) for proportional release of MPO by PMN, with higher release at 4 d post-calving in IMR cows (0.80 (95% CI = 0.72 to 0.88) vs 0.59 (95% CI = 0.53 to 0.64), $P < 0.05$). There was no effect of prepartum energy restriction, nor energy restriction by IMR interactions for any of the white blood cell counts or functional tests.

Significance

It is concluded that IMR treatment results in significant increases in PMN count, and enhances PMN function as indicated by increased MPO release. The response to IMR was not affected by restricted pre-partum energy intake.