Relationship of Methods of Treatment to Relapse Rate and Serum Levels of Calcium and Phosphorous in Parturient Hypocalcaemia

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Introduction

Parturient hypocalcaemia (milk fever) is one of the top nine diseases of economic importance to the diaryman (7). Consequently, research continues not only to prevent this disease, but to find better means of treatment. A satisfactory response to initial treatment for parturient hypocalcaemia generally has been obtained by the intravenous administration of calcium borogluconate (8g of calcium). However, after this treatment a large number of cows relapse and require further attention. This not only adds to the cost of therapy but increases the possibility of injuries to the musculoskeletal system when cows become recumbent for a second time.

A trial was designed to determine if the type of drug used and the amount and method of its administration influenced serum levels of calcium, inorganic phosphorous and the relapse rate in parturient hypocalcaemia.

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[1]*Cal-Dextro #2, Fort Doge Laboratories Inc., Fort Dodge, Iowa 50501.*

[2]*Calcium Gluconate, Pitman-Moore Ltd., Don Mills, Ontario.*

[3]*Varian Instruments, Georgetown, Ontario.*

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Materials and Methods

A total of 100 Holstein cows which were recumbent with parturient hypocalcaemia were used for this trial. The cows were owned by 45 clients and were treated over a two year period by the Ambulatory Clinic, Ontario Veterinary College. These cases of parturient paresis occurred in all months of the year, since there is no seasonal calving period in dairy herds in this part of Ontario. Slightly more cows were treated during the winter feeding period than when cows were on grass. Immediately prior to treatment, each cow in the trial was given a complete clinical examination.

The cows were randomly divided into four treatment groups as the cases of parturient hypocalcaemia were received over the two year period. The treatment groups were:

1. 500 ml of calcium, phosphorous, magnesium and dextrose preparation, CADEX 1[1] (8.42g of calcium, 4.80g of phosphorous, 1.88g of magnesium and 82.50g of dextrose) given intravenously.
2. 500 ml of calcium borogluconate CAGLU 1[2] (8g of calcium) given intravenously.
3. 500 ml of a calcium, phosphorous, magnesium and dextrose preparation given intravenously and 500 ml given subcutaneously (CADEX 2).
4. 500 ml of calcium borogluconate given intravenously and 500 ml given subcutaneously (CAGLU 2).

All preparations were given with sterile equipment as aseptically as possible. The drugs given subcutaneously were administered at two injection sites, just behind the shoulders, 250 ml at each site.

All cows were recumbent with parturient hypocalcaemia before they were treated. Cows had to respond by getting up following treatment in order to remain on the trial. Cattle which did not get up, regardless of the reasons, were excluded from the trial. All clients were instructed not to milk out cows after treatment for 24 to 48 hours and to bathe the area in which the solutions had been administered

TABLE I

DIFFERENCES IN PROPORTION OF PARTURIENT HYPOCALCAEMIA RELAPSES BY TREATMENT GROUP IN HOLSTEIN COWS

Treatment[a]	Number Relapses	Number not Relapsing	Total	Proportion Relapsing	
CADEX 1	9	16	25	0.36	0.38
CAGLU 1	10	15	25	0.40	
CADEX 2	1	24	25	0.04	0.06
CAGLU 2	2	23	25	0.08	
Total	22	78	100	0.22	

Group 1 = CADEX 1 and CAGLU 1
Group 2 = CADEX 2 and CAGLU 2
Chi-Square (total) = 15.15 ($p \leq 0.005$)
Chi-Square for difference between Groups 1 and 2 = 14.92 ($p \leq 0.001$)
Chi-Square for difference within Group 1 = 0.1166 (not significant)
Chi-Square for difference within Group 2 = 0.1166 (not significant)
[a]CADEX 1 – Ca, P, Mg, dextrose preparation, 500 ml IV
CAGLU 1 – Ca borogluconate, 500 ml IV
CADEX 2 – Ca, P, Mg, dextrose preparation, 500 ml IV and 500 ml SC
CAGLU 2 – Ca borogluconate, 500 ml IV and 500 ml SC

TABLE II

CALCIUM LEVELS (mg %) BY TYPE OF TREATMENT FOR PARTURIENT HYPOCALCAEMIA AND TIME POSTTREATMENT IN HOLSTEIN COWS

Time	Treatment[a] CADEX 1	CADEX 2	CAGLU 1	CAGLU 2
Initial	3.88 (25)	4.13 (25)	4.30 (23)	3.86 (25)
+ 12 hours	5.20 (25)	7.82 (24)	6.17 (24)	7.77 (25)
+ 24 hours	5.83 (22)	7.42 (24)	6.55 (21)	6.88 (24)
+ 48 hours	8.39 (16)	7.91 (23)	9.47 (15)	7.80 (23)

The numbers are the average levels for that treatment group at that time.
The numbers in parentheses are the number of animals whose data produced the mean.
The lines under the number indicate the pairs of means which were compared.
An asterisk indicates a difference between these means significant at $p \leq 0.05$.
Tested using Analysis of Variance.
[a]CADEX 1 – Ca, P, Mg, dextrose preparation, 500 ml IV
CAGLU 1 – Ca borogluconate, 500 ml IV
CADEX 2 – Ca, P, Mg, dextrose preparation, 500 ml IV and 500 ml SC
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subcutaneously with hot water twice a day for two days.

Blood samples were taken from each cow on the trial for serum calcium and inorganic phosphorous determinations. Samplings were made prior to treatment, then 12, 24, and 48 hours after treatment. The biochemical analyses were performed in one laboratory. Serum calcium was measured by atomic absorption, using a Techtron AA5.[3] Serum inorganic phosphorous was measured by the colorimetric method of Goldenberg and Fernandez (1). When a cow relapsed she was taken from the trial and treated with CADEX 2. Blood samples were not taken when a cow relapsed.

The results were analyzed using standard statistical methods (4).

Results

Five cows were rejected from the trial because they did not stand up following the initial treatment. Therefore, 105 cows were treated in order to obtain the 100 cows for the trial. None of the cows treated subcutaneously developed abscesses or any other serious reaction.

On this trial, the average age of the 100 cows with parturient paresis was 7.4 years (range 4-14 years). The mean, estimated weight was 750 kg (range 550-850kg). Initial treatment was usually 16 hours after calving with a range of from 18 hours before calving until 48 hours after calving.

Details of the physical examination of clinical cases before the initial treatment were recorded. Most of the clinical findings were those described as typical for parturient hypocalcaemia. For example, 30 cows had a history of previous milk fever, pupils were dilated in 44 cows, 90 cows showed complete rumen stasis and 46 cows retained their foetal membranes (20 cows passed their membranes with initial calcium therapy).

The interval from initial treatment until relapse was 25 hours (range 12-36 hours). A total of 22 cows relapsed and were retreated.

The difference in proportion of relapses by treatment group is recorded in Table I.

The serum calcium and inorganic phosphorous levels related to type of treatment at 12, 24, and 48 hours after treatment are recorded in Tables II and III respectively.

Discussion

Relapse occurs in 22% of the cows treated on this trial. The minimal relapse rate (4%) is seen in cows in treatment group CADEX 2 while it peaks at 40% in cows in treatment group CAGLU 1. This is slightly higher than an overall relapse rate of 16% reported in a treatment trial conducted in

TABLE III

INORGANIC PHOSPHOROUS LEVELS (mg %) BY TYPE OF TREATMENT FOR PARTURIENT PARESIS AND TIME POSTTREATMENT IN HOLSTEIN COWS

Time	Treatment[a] CADEX 1	CADEX 2	CAGLU 1	CAGLU 2
Initial	1.83 (25)	1.78 (25)	1.47 (23)	1.50 (25)
+ 12 hours	2.99 (25)	4.60 (24)	3.30 (24)	4.32 (25)
+ 24 hours	3.81 (22)	5.45 (24)	4.71 (21)	4.84 (24)
+ 48 hours	5.69 (16)	6.03 (24)	6.62 (15)	5.53 (23)

The numbers are the average levels for that treatment group at that time.
The numbers in parentheses are the number of animals whose data produced the mean.
The lines under the number indicate the pairs of means which were compared.
The asterisk indicates a difference between these means significant at $p \leq 0.05$.
Tested using Analysis of Variance.
[a]CADEX 1 – Ca, P, Mg, dextrose preparation, 500 ml IV
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Denmark (8), but lower than the 25.3% overall relapse reported from England (6).

No significant difference in relapse rate is noted in cows which received both intravenous and subcutaneous administration of calcium, regardless of the type of calcium preparation used. A significantly greater number of relapses is seen in cows which received calcium by the intravenous route only, regardless of the calcium preparations used.

It had been suggested that a supplementary subcutaneous injection given as a depot therapy may mask a natural relapse and delay recovery. Such delays may provide time for complications to occur (3). There is no evidence of any such delays in the trial. The fact that significantly fewer cows relapsed when given the calcium preparations subcutaneously has obvious advantages; it reduces the cost of a second visit for treatment and avoids the possible complications of a cow becoming recumbent for the second time.

In Sweden a therapeutic trial reports no significant difference in response to six, nine or twelve grams of calcium given intravenously (2). In Holland, when milk fever is treated with one of the usual intravenous solutions, containing approximately seven grams of calcium, the relapse rate did not show any improvement when additional calcium was administered subcutaneously. It was suggested that additional calcium given subcutaneously is unnecessary and economically undesirable (9). The results of this study do not support this advice. The reasons for the conflicting results in different countries are not clear. It is possible that the cows in this trial were of significantly greater body weight and that a depot of calcium may be beneficial in these larger cows by maintaining higher levels of serum calcium during the period when they are likely to relapse.

There was no significant difference in the serum levels of calcium and inorganic phosphorous in the four groups before treatment. Cows which received the treatments intravenously and subcutaneously have significantly increased levels of serum calcium and inorganic phosphorous at 12 hours after treatment compared to the intravenous treatments alone. This is also the case at 24 hours posttreatment with CADEX 2 compared to CADEX 1. By 48 hours posttreatment, the serum levels of calcium and inorganic phosphorous are significantly higher in CAGLU 1, than in CAGLU 2. The reasons for this finding are not clear but may be related to the fact that smaller amounts of calcium might not have as great an inhibitory effect on parathyroid secretory rate (5).

There is no evidence in this trial that the addition of phosphorous to a treatment increased serum levels of inorganic phosphorous or was beneficial in the prevention of relapses.

Summary

A therapeutic trial was conducted using 100 Holstein cows which were recumbent with parturient hypocalcaemia (milk fever). The trial was designed to determine if the type of calcium preparation used and the amount and method of its administration influenced relapse rate and serum levels of calcium and inorganic phosphorous.

The overall relapse rate in this trial was 22%. Significantly more cows relapsed (36% and 40%) in the two groups which received only intravenous therapy. Only a few cows relapsed (4% and 8%) in the two groups which received therapy both intravenously and subcutaneously. There was no significant difference in relapse rate between cows which received calcium borogluconate and those receiving a preparation containing calcium, phosphorous, magnesium and dextrose.

There was no significant difference in the serum levels of calcium and inorganic phosphorous in the four groups before treatment. Cows which received the treatments subcutaneously and intravenously had significantly increased levels of serum calcium and inorganic phosphorous at 12 hours after treatment compared to the intravenous treatments alone.

Resumé

Les auteurs ont traité de faξon expérimentale 100 vaches Holstein qui étaient en décubitus parce qu'elles souffraient de l'hypocalcémie de parturition (fiévre du lait). Leur expérience visait á déterminer si le type de préparation calcique, sa quantité, ainsi que la faξon de l'administrer, influenceraient le taux de rechute et la teneur sérique en calcium et en phosphore inorganique.

Le taux global de rechute atteignit 22%, au cours de cette expérience. Un nombre sensiblement plus élevé des vaches des deux groupes qui ne recurent qu'un traitement intra-veineux manifestérent une rechute, soit 36% et 40%. Seulement quelques-unes des deux goupes qui reξurent un traitement intra-veineux et sous-cutané manifestérent une rechute, soit 4% et 8%. On ne releva pas de différence appréciable dans le taux de rechute entre les vaches qui reξurent du borogluconate de calcium et celles auxquelles on injecta une préparation contenant du calcium, du phosphore, du magnésium et du dextrose.

Avant le traitement, on ne nota pas de différence appréciable dans la teneur du sérum en calcium et en phosphore inorganique, chez les vaches des quatres groupes expérimentaux. Celles qui reξurent á la fois un traitement intraveineux et sous-cutané possédaient, au bout de 12 heures, une teneur sérique en calcium et en phosphore inorganique plus élevée que celles auxquelles on n'avait donné qu'un traitement intra-veineux.

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