Response of Holstein Cows with Milk Fever to First Treatment using Two Calcium Regimens: A Retrospective Clinical Study

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ABSTRACT. The responses of 64 Holstein cows with milk fever to first treatment with 500 ml of either of 2 intravenous calcium (Ca) solutions, one containing Ca alone (group A, n = 32) or 1 containing Ca, phosphate and magnesium (group B, n = 32), were evaluated by selected clinical signs and serum biochemical data. Based on the cow’s ability to stand, treatment response was categorized into “immediate response” (stood after single treatment), “delayed response” (stood after repeated treatments) and “non-response” (slaughtered despite repeated treatments). No significant differences among the response categories were found between the two groups, suggesting that the solution containing Ca borogluconate alone was sufficient for the first treatment of milk fever.

KEYWORDS: calcium solution, parturient paresis, response to first treatment, retrospective clinical study.


Milk fever (MF) is an afebrile disease of adult dairy cows that occurs most commonly during or after parturition [11]. Affected cows show characteristic clinical signs such as progressive neuromuscular dysfunction with flaccid paralysis, recumbency, circulatory collapse, cold extremities and depressed consciousness [7, 8, 10–12]. Because acute calcium (Ca) deficiency after parturition is the major cause of this paralytic recumbent disease, affected cows are treated with parenteral Ca solution [7, 8, 10–12]. For many years, conventional treatment of MF has comprised intravenous infusion of a 500-ml solution of Ca borogluconate, which supplies 8–12 g of Ca [6, 11, 12]. Alternatively, infusion of a solution containing a combination of Ca, phosphate (P) and magnesium (Mg) sources [6–8, 12] and increasing Ca dose [3, 7] is often applied clinically, although the efficacy of these alternative methods has been controversial [3–5]. In Japan, 2 major types of commercial veterinary formulations of Ca solution (500 ml) are widely used for the treatment of MF; one contains Ca borogluconate alone, and the other contains sources of Ca, P and Mg. It is therefore suggested that veterinary clinicians in Japan should decide which of these solutions to administer during the first treatment of MF. However, to our knowledge, there is little scientific information regarding the efficacy of treatment using different types of Ca solutions in Japan. In the present study, clinical data of cows with MF were retrospectively collected from clinical records of one veterinary clinic situated in a dairy region in Iwate prefecture. The aim of the study was to evaluate the response of cows with MF to the first treatment with the Ca solutions most commonly used in Japan.

Clinical records from Iwate Veterinary Hospital from 2007 to 2010 were reviewed. A total of 187 Holstein dairy cows from 43 farms were examined and treated using Ca solution, because of anorexia, dysstasia and/or recumbency within 1 week postpartum. In each case, the cause of the abnormal condition was investigated before each treatment. A tentative clinical diagnosis of MF was made based on the clinical history and presence of clinical signs characteristic of MF. Before treatment initiation, each animal was checked for the presence of any of eight characteristic clinical signs of MF described by early studies: astasia, anorexia, cold extremities, flaccid tail, tachycardia (>80 beats/min), tachypnea (>36 breaths/min), decreased rectal temperature (<38.0°C) and coma [7, 8, 11, 12]. Other problems were identified by the owners’ information, careful physical examination, and serum biochemical data during the clinical course. Complicated MF cases (n = 81) were excluded, namely cows showing clinical signs of mastitis, puerperal metritis, ketosis, abomasal displacement and traumatic conditions after parturition and during the clinical course, cows with nutritional and locomotor ailments prior to calving, cows that had been recumbent in for>12 hr prior to the first treatment, and those that were not given proper and timely care by the owners. Next, cows that showed normocalcemia or slight hypocalcemia (≥ 7.0 mg/dl of serum Ca concentration in the blood samples obtained before the first treatment) [10] (n = 42) were also excluded. Finally, the clinical data of 64 cows suffering from uncomplicated, severe-to-moderate hypocalcemic MF within 4 days postpartum in 33 farms were used.
These 64 cases were divided into 2 groups according to the type of Ca solution used in the first treatment. Group A (n = 32) received a single-dose intravenous infusion of a 500-mL solution that contained 250 mg/mL of Ca borogluconate alone (Guruka-20%; Kyoritsu-seiyaku, Tokyo, Japan) to provide 10.5 g of Ca. Group B (n = 32) was treated with a single-dose intravenous infusion of a 500-mL solution that contained 250 mg/mL of Ca borogluconate, 20 mg/mL of Ca glycerophosphate and 20 mg/mL of Mg chloride (Nyuguron Plus; Kyoritsu-seiyaku), providing 12.4 g of Ca, 1.5 g of P and 2.6 g of Mg. All of these first treatments were provided by 1 of 2 veterinarians (the second and third authors). Calcium solution was selected at the discretion of the veterinarian. The solutions were administered at the rate of ≤ 50 mL/min.

The response of the cows to the first treatment was assessed and divided into 3 categories on the basis of the cow’s ability to stand thereafter. The first category was an immediate response in which the cow could stand within 1 day after a single Ca treatment. The second category was a delayed response in which the cow stood after repeated treatments over 1 day. The third was a non-response in which the cow remained recumbent despite repeated treatments; these cows were sent for slaughter.

Variables for statistical analyses were age, days of onset of MF after parturition, total number of clinical signs recorded among the eight characteristic clinical signs at the first visit, serum levels of Ca, inorganic phosphorus (iP), Mg and aspartate aminotransferase (AST). Blood samples to measure the serum levels of Ca, iP, Mg and AST were obtained just before the first Ca treatment. Numerical data of the variables were expressed as means ± standard deviations (SD). The Kruskal–Wallis test, followed by Dunn’s multiple comparison test, was performed to detect significant differences in the variables among the groups, the categories of the response to the first treatment within each group (intragroup difference) and the same response category among the groups (intergroup difference). A chi-square test was used to compare the 3 response categories (immediate response, delayed response and no response) after treatment according to the number of cows in groups A and B. Significance was set at P<0.05. Analyses were performed using the Sigmaplot software, version 12.0 (Systat Software Inc., San Jose, CA, U.S.A.).

Of the 64 cases, 6 cases showed only hypocalcemia, and 58 cases showed hypocalcemia and hypophosphatemia, with serum Ca and iP concentrations of <7.0 mg/dL and <4.0 mg/dL, respectively [2]. However, there were no cases showing hypomagnesemia. Table 1 shows the intra- and inter-group variations in age, postpartum days of onset and total number of clinical signs among the three response categories after the first treatment. There were no significant intra- or inter-group differences in these variables among the three response categories. Likewise, the intra- and inter-group differences in serum levels of Ca (4.1 ± 1.3 to 5.2 ± 1.5 mg/dL), iP (1.7 ± 0.9 to 3.0 ± 2.1 mg/dL), Mg (2.1 ± 0.5 to 2.5 ± 0.4 mg/dL) and AST (61.7 ± 23.1 to 83.4 ± 50.3 U/L) at the first treatment among the three response categories were not significant (Fig. 1). Table 2 shows the comparison among the treatment responses in the 2 groups. There were no significant differences among the 3 response categories according to the number of cows in the 2 groups.

In clinical bovine medicine, veterinary clinicians must evaluate the clinical condition of a diseased cow by only physical examination and immediately determine a potential diagnosis and treatment without reference to blood laboratory test results. Therefore, the clinical signs of the cow at the first visit are the sole, but immensely valuable, key information for assessment of the severity of its physical condition to make a tentative diagnosis and initiate proper treatment. Marr et al. [9] reported a high correlation between the severity of clinical signs and the extent of serum Ca level depression in cows affected with MF. In the present study, eight clinical signs used for the field diagnosis of MF were evaluated to assess the severity of the clinical condition because uniform evaluation was possible even when cases were diagnosed by different veterinarians. The total number of clinical signs between the 2 groups was not statistically different, suggesting that cows in both groups displayed a similar clinical severity at the first treatment. In fact, the degree of hypocalcemia between the 2 groups was similar in the present study.

Several investigations have aimed to identify the optimum first-treatment intravenous Ca dose for cows suffering from MF. A therapeutic trial in the Nordic countries reported no significant difference in response to 6, 9 or 12 g of Ca given intravenously [1]. A similar trial in Australia reported an

<table>
<thead>
<tr>
<th>Variables</th>
<th>Immediate response (n=9)</th>
<th>Delayed response (n=15)</th>
<th>Non-response (n=8)</th>
<th>Immediate response (n=10)</th>
<th>Delayed response (n=14)</th>
<th>Non-response (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6.2 ± 1.7</td>
<td>7.1 ± 1.6</td>
<td>6.9 ± 1.8</td>
<td>6.8 ± 1.7</td>
<td>6.6 ± 1.6</td>
<td>6.6 ± 1.4</td>
</tr>
<tr>
<td>Postpartum days of onset (days)</td>
<td>1.2 ± 1.4</td>
<td>0.6 ± 1.1</td>
<td>0.4 ± 0.5</td>
<td>0.7 ± 1.2</td>
<td>0.4 ± 0.5</td>
<td>0.4 ± 0.7</td>
</tr>
<tr>
<td>Total number of clinical sings*</td>
<td>3.0 ± 0.9</td>
<td>3.6 ± 1.1</td>
<td>3.8 ± 1.3</td>
<td>3.3 ± 1.0</td>
<td>3.3 ± 1.0</td>
<td>4.3 ± 1.0</td>
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</table>

*: Before initiation of the first treatment, number of clinical signs out of the total 8 clinical signs; astasia, anorexia, cold extremities, flaccid tail, tachycardia (>80 beats/min), tachypnea (>36 breaths/min), decreased rectal temperature (<38.0°C) and coma, were recorded. Group A: cows received a single-dose intravenous infusion of a 500 mL solution containing 250 mg/mL Ca borogluconate. Group B: cows received a single-dose intravenous infusion of a 500 mL solution containing 250 mg/mL Ca borogluconate, 20 mg/mL Ca glycerophosphate and 20 mg/mL Mg chloride.
optimal dose of 7.25–9.5 g [4, 5]. Another study in the USA reported no need to increase the Ca dose from 7.4–12.3 g for treatment of naturally occurring MF [5]. A textbook for large animal internal medicine noted that the most effective Ca dose is 2 g/100 kg body weight [6], which suggests that the recommended Ca dose for a 700-kg cow is 14 g. In the present study, the first treatment doses of Ca in groups A and B were 10.5 and 12.4 g, respectively, which seemed to be sufficient compared with those used in previous studies.

Depression of the calcium level in tissue fluids is the basic biochemical factor in MF. In addition, cows with MF usually show hypophosphatemia [6, 7, 11, 12]. Magnesium deficiency reduces the ability of cows to maintain calcium homeostasis, and thus hypocalcemia may occur [7]. Therefore, the combination of P and Mg sources together with Ca sources in intravenously administered infusions is often recommended for the first treatment of MF. However, the comparative trials that have been conducted so far are insufficient. A therapeutic trial in Switzerland [2] reported no significant difference in the response of the cows between 500 ml of a 40% Ca borogluconate solution and this solution plus 200–500 ml of a 10% sodium hydrogen P (SHP) solution (containing 4–10-g P). However, serum iP concentrations in cows given SHP were initially increased above the normal range. A solution containing 1.5–4 g of Mg chloride is often recommended to correct concurrent hypomagnesemia [6–8, 12] and antagonize the cardioexcitatory effects of Ca administration [8]. In the present study, hypophosphatemia in response to the first Ca treatment was detected equally in both groups; however, serum Mg levels were almost within the normal range. The dose of P administered to group-B animals was 1.5 g, which was lower than that in the Swiss

Fig. 1. Intra- and inter-group variations of serum levels of calcium (Ca), inorganic phosphorus (iP), magnesium (Mg) and aspartate aminotransferase (AST) among the responses (immediate, delayed or non-response) after treatment of cows suffering from parturient paresis with two types of Ca regimen.

Table 2. Comparison among three responses categories (immediate, delayed or non-response) after treatment of cows suffering from parturient paresis with two types of Ca regimen

<table>
<thead>
<tr>
<th>Groups*</th>
<th>n</th>
<th>Responses</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Immediate</td>
</tr>
<tr>
<td>A</td>
<td>32</td>
<td>9 (28.1%)</td>
</tr>
<tr>
<td>B</td>
<td>32</td>
<td>10 (31.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
<td>19 (29.7%)</td>
</tr>
</tbody>
</table>

*Group A cows received a single-dose intravenous infusion of a 500 ml solution containing 250 mg/ml Ca borogluconate, and group B cows received a single-dose intravenous infusion of a 500 ml solution containing 250 mg/ml Ca borogluconate, 20 mg/ml Ca glycerophosphate and 20 mg/ml Mg chloride.
study. The Mg dose given to group-B cows was 2.6 g, which was within the recommended range.

Each parameter in the present study did not distinguish the different response to treatments. Since this was a retrospective study based on the past clinical records, the parameters that could be analyzed in the present study were limited. Future studies are virtually impossible, but if attempted they should include production records, management systems and biochemical evaluation of nutritional and muscle damage status.

In conclusion, our results demonstrate that the treatments administered to groups A and B were equally efficacious in terms of the responses of cows with MF, regardless of the addition of P and Mg. In other words, the data suggest that the solution containing Ca borogluconate alone was sufficient as a first treatment of cows tentatively diagnosed with MF. However, further studies should re-examine the efficacy of treatment with different types of Ca solutions by analyzing the clinical data of veterinary clinics in multiple dairy regions in Japan. The clinical picture of MF and its response to Ca treatment seem to vary between regions and countries [1]. It is also necessary to elucidate the factors—other than the Ca regimen—that affect the response to treatment and the prognosis of cows with MF in Japan.

REFERENCES