Plasma Levels of Cortisol, Free Fatty Acids, Glucose and Calcium in Cows with Milk Fever

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(Received for publication March 26, 1979)

Abstract. Various biochemical aspects of milk fever in cows were investigated. Affected cows had significantly increased plasma levels of cortisol, free fatty acids (FFA), glucose and Mg, and significantly lowered plasma levels of Ca and K, as compared with normal postpartum cows. There were significant positive correlations between cortisol-FFA and cortisol-glucose and significant negative correlations between Ca-cortisol, Ca-glucose and Ca-FFA in cows with milk fever. None of these correlations were significant in control cows.

Milk fever is a metabolic disorder characterized by hypocalcemia which occurs around parturition. The actual mechanism of its occurrence, however, is still obscure. Recently, in the Hokkaido region of Japan, the incidence of milk fever was noted to have increased gradually. Statistics from the Hokkaido local government showed that the incidence of milk fever was 1.22% of the total dairy cow population in 1966, 2.14% in 1970, and 3.11% in 1975. The actual numbers of cows affected with milk fever were 3,544 in 1966, 9,588 in 1970, and 18,427 in 1975.

Several authors have observed that lipolysis is associated with the uptake of calcium (Ca) in adipose tissue. Akugüm and Rudman [2] reported that there was a 260–680% increase of free fatty acids (FFA) concentration and a 27% reduction of Ca concentration in rabbit serum after administration with 50U of ACTH. Luthman et al. [19] and Luthman and Holtenius [17] found that norepinephrine caused hypocalcemia in sheep. They suggested that the fall in serum Ca might be correlated to the increase in FFA. Luthman and Jonson [18] reported that FFA increased in hypocalcemic cows, and that there was a significant negative correlation between FFA and serum Ca. They advanced the hypothesis that the movement of calcium into the adipose tissue might contribute to parturient hypocalcemia. Neither Luthman and Persson [20] nor Horst et al. [14] lend support to this hypothesis in their studies. In his early studies, Hayden [12] observed hyperglycemia in cows with milk fever. Littledike et al. [16] reported that hypocalcemia was associated with the inability of insulin secretion. Smith et al. [25], Hoffman et al. [13] and Hudson et al. [15] noticed an increase of serum corticoids during parturition.

The purpose of this investigation is to study relationships among plasma cortisol, FFA, glucose and Ca in cows with milk fever.

Materials and Methods

Blood samples were collected from 50 cows with
Table 1. Plasma cortisol, FFA, glucose, Ca, P, Mg, K, GOT and GPT in cows with milk fever

<table>
<thead>
<tr>
<th></th>
<th>Control cows [13]</th>
<th>Cows with milk fever [50]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (ng/ml)</td>
<td>4.8 ± 2.2</td>
<td>11.3 ± 8.7*</td>
</tr>
<tr>
<td>FFA (mg/dl)</td>
<td>10.7 ± 4.1</td>
<td>17.3 ± 5.0**</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>60.3 ± 14.8</td>
<td>84.3 ± 20.5**</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>7.2 ± 1.0</td>
<td>4.2 ± 0.9**</td>
</tr>
<tr>
<td>P (mg/dl)</td>
<td>5.4 ± 1.7</td>
<td>4.3 ± 1.8</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>1.6 ± 0.3</td>
<td>1.9 ± 0.4**</td>
</tr>
<tr>
<td>K (mg/dl)</td>
<td>17.0 ± 2.6</td>
<td>16.3 ± 2.8**</td>
</tr>
<tr>
<td>GOT (U/ml)</td>
<td>93.2 ± 33.9</td>
<td>165.3 ± 67.3</td>
</tr>
<tr>
<td>GPT (U/ml)</td>
<td>19.8 ± 7.4</td>
<td>19.4 ± 4.6</td>
</tr>
</tbody>
</table>

Remarks.
Mean ± S.D. * P<0.05. ** P<0.01.

Table 2. Plasma cortisol, FFA, glucose, Ca, P, Mg, K, GOT and GPT in cows a week after treatment with milk fever

<table>
<thead>
<tr>
<th></th>
<th>Control cows [13]</th>
<th>Cows with milk fever [29]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (ng/ml)</td>
<td>3.7 ± 1.9</td>
<td>3.1 ± 1.8</td>
</tr>
<tr>
<td>FFA (mg/dl)</td>
<td>7.6 ± 2.4</td>
<td>10.0 ± 3.7*</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>62.4 ± 11.1</td>
<td>55.5 ± 12.6</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>8.5 ± 1.7</td>
<td>7.7 ± 1.0</td>
</tr>
<tr>
<td>P (mg/dl)</td>
<td>6.1 ± 1.0</td>
<td>7.7 ± 1.6**</td>
</tr>
<tr>
<td>Mg (mg/dl)</td>
<td>1.7 ± 0.4</td>
<td>1.7 ± 0.4</td>
</tr>
<tr>
<td>K (mg/dl)</td>
<td>16.6 ± 2.2</td>
<td>15.8 ± 1.8</td>
</tr>
<tr>
<td>GOT (U/ml)</td>
<td>91.7 ± 42.3</td>
<td>122.6 ± 64.3</td>
</tr>
<tr>
<td>GPT (U/ml)</td>
<td>18.5 ± 7.2</td>
<td>19.1 ± 7.0</td>
</tr>
</tbody>
</table>

Remarks.
Mean ± S.D. * P<0.05. ** P<0.01.

In this study the Ca level was 7.2 ± 1.0 mg/dl in the control cows. It was from this result that cows were considered to be affected with milk fever when their plasma Ca level was below 6.0 mg/dl.

Results

The mean values of the plasma constituents in cows with milk fever are shown in Table 1. The plasma cortisol level was 11.3 ± 8.7 ng/ml in those cows and 4.8 ± 2.2 ng/ml in the control cows. In the affected cows the cortisol level was significantly higher than in the control cows (P<0.05). The mean values of plasma FFA and glucose levels were 17.3 ± 5.0 mg/dl and 84.3 ± 20.5 mg/dl, respectively in the affected cows. They were significantly higher in the affected cows than in the control cows (P<0.01). Plasma Ca and K levels were 4.2 ± 0.9 mg/dl and 13.6 ± 2.8 mg/dl, respectively, in the former cows. They were significantly lower in these cows than in the control cows (P<0.01).

Table 2 shows the plasma constituents in cows one week after the beginning of treatment of milk fever. No significant differences were seen in plasma cortisol or glucose between treated and untreated control cows. Plasma FFA level was 10.0 ± 3.7 mg/dl in the treated cows and 7.6 ± 2.4 mg/dl in the control cows.
Table 3 shows the correlations among plasma cortisol, FFA, glucose, Ca, P, Mg and K in the affected and control cows. A significant positive correlation was observed between cortisol and FFA, and between cortisol and glucose and a negative correlation between Ca and cortisol, between Ca and glucose, and between Ca and FFA in the affected cows. No significant correlation was observed between any two substances except Ca and P in the control cows.

Discussion
From the results of their recent experiments, Sherwood et al. [24] and Blum et al. [3] they lent no support to the parathyroid insufficiency theory of Dryerre and Greig [8]. An increase in thyrocalcitonin secretion was suggested to be a contributory cause of milk fever by Capen and Young [5] and Care et al. [6]. Garel and Barlet [11] reported that both plasma thyrocalcitonin and parathyroid hormone increased in cows with milk fever, but gave no explanation on the cause of this sudden release. Philippo et al. [22] showed that catecholamines caused the release of thyrocalcitonin. Littledike et al. [16] found the plasma hydrocortison level to be 3.2±1.4 µg/dl in cows with milk fever and 1.2±0.9 µg/dl in normal postpartum cows. Smith et al. [25] reported that serum glucocorticoid levels averaged 16.7 ng/ml at parturition and 5.1 ng/ml 12 hours after parturition.

As seen in Table 1, the plasma cortisol level was 11.3±8.7 ng/ml in the affected cows and 4.8±2.2 ng/ml in the control cows. It was significantly higher in those cows than in these cows (P<0.05). It was 19.9±6.2 hours after parturition that blood samples were collected from the cows with milk fever. Blood samples were collected from the control cows almost at the same time as this. The mean cortisol level obtained from the control cows was almost identical with that reported by Smith et al. [25].

Table 3 shows significant correlations between the plasma levels of cortisol and FFA and between those of cortisol and glucose. It is therefore considered that the increase in plasma cortisol level is accompanied with an increase in plasma FFA and glucose levels in the cows with milk fever. The plasma FFA and glucose levels in these cows were significantly higher in the control cows (P<0.01). Adler et al. [1] reported that in normal cows the level of blood glucose decreased as plasma FFA levels increased. Littledike et al. [16] and Blum et al. [4] found an inability of cows with milk fever to release insulin because of low Ca levels. Thus, cow with milk fever are in a diabetes-like condition. This may be the reason for the increase in blood levels of both FFA and glucose. There were negative correlations between Ca and glucose and between Ca and FFA (Table 3). These causal relations may have appeared, since low Ca levels reduced insulin secretion and subsequently increased the blood levels of FFA and glucose. It is also shown that high plasma cortisol levels helped the blood levels of FFA and glucose to be high.

A significant negative correlation existed between plasma Ca and cortisol levels in the cows with milk fever (Table 3). From Table 1, the high plasma levels of cortisol, FFA and glucose in these cows suggest a stimulation of the sympathetic nervous system. Moseley and Axford [21] reported that a variety of minor interference and adrenalin administration caused consistent reduction in the plasma Ca concentration of ewes. Luthman et al. [19] pointed out a 30% reduction of serum Ca by norepinephrine administration in sheep. It is obvious that such a factor as stimulating the sympathetic nervous system reduces Ca levels in blood.
Ca reduces the tension of muscle and nerve. By contrast, K increases tension. If the Ca level is low and the K level normal in blood, tetany will be induced in muscle. If both Ca and K levels are low in blood, no tetany will occur. In the cows with milk fever the blood Ca and K levels were significantly lower than in the control cows (P<0.01). This may be the reason why those cows showed no tetany normally. These characteristically low blood Ca and K levels do not appear in the normal physiological body function.

Tokachi Young Veterinarians’ Association [26] reported that 72.5% of cows with milk fever showed a high NO₂-N concentration in serum. Dishington [7] mentioned that cows given a basal diet supplemented with Na₂CO₃ and NaHCO₃ were frequently attacked by milk fever. Froslie [10] observed that when pH increased in the rumen, undissociated ammonia increased and was absorbed into the blood. Ammonia acts as a cellular poison even at a relatively low concentration and may induce disturbances in cellular energy metabolism. Ammonia has a local effect on the rumen and a general effect on the body after absorption. The authors propose a hypothesis that ammonia or N-metabolite in the rumen and other parts of the alimentary tract may induce an imbalance in the autonomic nervous system. Especially, the sympathetic nervous system is stimulated at the time of parturition thus, cows with milk fever show high cortisol levels in blood. Then the secretion of thyrocalcitonin may increase, causing a fall in blood Ca level simultaneously. With this hypothesis, it is easy to explain the increase in blood level of both glucose and FFA, and the decrease in blood level of both Ca and K in the present studies and the increase in blood level of both thyrocalcitonin and parathyroid hormones in cows with milk fever reported by Gerel and Barlet [11].

Acknowledgments: The authors wish to thank veterinarians in Obihiro, Otofuke and Sarabetsu Veterinary Hospitals who generously supplied the samples used in the present studies.

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要 約

乳熱牛の血漿コルチゾール、遊離脂肪酸、グルコースならびにカルシウム値について：林 優克・小野 斉・佐藤邦浩・三宅 勝（帯広畜産大学家畜臨床繁殖学教室）——乳熱牛の発病機序解明のため、帯広市およびその近郊の乳熱牛50頭を対象に治療前と治療後1週間後に採血し、
対照牛として帯広畜産大学附属農場ならびに帯広市A酪農家の正常分離牛18頭を用い、分離1日後と1
週間後に採血した。これらの牛の血中コルチゾール、遊離脂肪酸（FFA）、グルコース、Ca, P, Mg, K,
GOT, GPT 値を測定し、次の結果を得た。
1) 乳熱牛の血漿コルチゾール、FFA、グルコースならびに Mg 値は、対照牛に比べて有意に高かった。
2) 乳熱牛の血漿 Ca, K 値は対照牛に比べて有意に低かった。
3) 治療1週間後の乳熱牛の血漿 FFA, P 値は、対照牛に比べて有意に高かった。
4) 乳熱牛のコルチゾールと FFA、コルチゾールとグルコースの相関は正の相関が、また Ca とコ
ルチゾール、Ca とグルコースおよび Ca と FFA の間には負の相関関係が有意に認められたが、対照
牛にあってはこれらの有意な相関関係を認めなかった。