Effect of high arterial carbon dioxide tension on efficiency of immunoglobulin G absorb in calves

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Objectives—To determine whether high Paco₂ reduced apparent efficiency of IgG absorption (AEA) in calves and whether assisted ventilation of calves with high Paco₂ increased AEA.

Animals—48 Holstein calves.

Procedures—Articular and venous blood samples were collected 1, 13, and 25 hours after birth; an additional venous sample was collected at 37 hours after birth. Articular samples were analyzed for Paco₂, PaO₂, pH, and bicarbonate and base excess concentrations; venous samples were analyzed for plasma IgG concentrations. On the basis of 1-hour Paco₂, calves were assigned to nonrespiratory acidosis (Paco₂ < 50 mm Hg; n = 19) or respiratory acidosis (Paco₂ ≥ 50 mm Hg; 29) groups. Calves in the respiratory acidosis group were assigned randomly to receive no further treatment (n = 17) or to be given 6 minutes of assisted ventilation (12). All calves received between 1.8 and 2.0 L of colostrum 2, 14, 20, and 38 hours after birth. Plasma volume and AEA were determined 25 hours after birth.

Results—1-hour Paco₂ had no effect on AEA or on plasma IgG concentrations determined 13, 25, or 37 hours after birth. Artificial ventilation had no effect on plasma IgG concentration or AEA.

Conclusions and Clinical Relevance—Lack of effect of 1-hour Paco₂ on AEA and IgG concentration indicated that calves compensated for moderate acid-base imbalances associated with birth. Calves born with high Paco₂ achieved adequate plasma IgG concentrations if fed an adequate amount of high-quality colostrum early in life. The effect of artificial ventilation on Paco₂ was temporary and did not increase AEA. (Am J Vet Res 1996;60:600-614)

Calves are born hypogammaglobulinemic and require acquisition of passive immunity through absorption of colostral immunoglobulins. Research has indicated a large percentage of calves die if they fail to achieve adequate serum immunoglobulin concentrations. Transfer of immunoglobulins to calves is influenced by a number of factors, including age at first feeding, volume and immunoglobulin concentration of colostrum fed, birth weight, method of feeding, seasonal influences, stress, disease, use of colostral supplements, presence of the dam, and individual variation in absorption efficiency. Additionally, during the early postpartum period, time of exposure to the absorptive environment may be crucial. Furthermore, the metabolism of metabolic acidosis is not well understood.

A 52% decrease in colostrum in 35% decrease in serum IgG concentration of acidotic calves (venous blood pH < 7.4) in this study may have resulted from a reduction in the availability of IgG absorbed from the gut. The results of this study demonstrated that reduced absorption of IgG in newborn calves is associated with hypercapnia in newborn calves. Simultaneous blood collection for serum IgG and IgA concentrations indicated that decreased IgG absorption was associated with respiratory acid-base disorder. Blood samples from newborn calves were collected within 24 hours of birth. This study also demonstrated that the time of exposure to the absorptive environment is crucial. Despite adequate intestinal absorption of IgG, absorbed fetuses did not demonstrate improved immune competence.
following groups on the basis of PaCO₂ measured 1 hour after birth: nonrespiratory acidosis (NA), PaCO₂ < 50 mm Hg (n = 19); and respiratory acidosis, PaCO₂ ≥ 50 mm Hg (29). Calves in the respiratory acidosis group were randomly assigned to receive no further treatment (acidosis/not ventilated [ANV]; n = 17) or 5 minutes of assisted ventilation (acidosis/ventilated [AV]; 12). Beginning immediately after assignment of a calf to the AV group, and using a self-inflating resuscitation bag, a breath was stimulated every 5 seconds for 5 minutes. Arterial blood gas analysis after ventilation indicated that treatment was effective in reducing PaCO₂.

Calf management and sample collection—Pregnant cows were housed on a drylot and fed a diet of mixed-grass hay and commercial nonlactating cow concentrate. Estimated dietary cation-to-anion difference was approximately +65 mEq/100 g of concentrate. At birth, calving ease scores were assigned on the basis of a scale of 1 to 4. A score of 1 indicated a normal (unassisted) birth, 2 indicated an easy assisted birth, 3 indicated a difficult assisted birth, and 4 indicated a cesarean section. Calves were separated from their dams at birth and were not allowed to suckle. Arterial blood samples were collected 1, 3, and 25 hours after birth. Arterial blood was collected from the brachial artery into heparinized (1,000 IU/ml) syringes. Analyses were performed within 30 minutes of sample collection to determine arterial pH (pH), PaCO₂, PaO₂, and HCO₃⁻ and base excess (BE). Concentration equations were used to calculate pHi, PaCO₂ and PaO₂ at rectal temperatures other than 37°C. Venous blood samples were collected 1, 3, 23, and 37 hours after birth for analysis of plasma IgG and lactate concentrations. Plasma volume was measured at 25 hours, using the Evans’ blue dye technique.

Feeding management—Calves were fed between 1.8 and 2.0 L of independent pools of colostrum from a nipple bottle 2 hours (±5 minutes) after birth. If calves did not drink the entire amount, remaining colostrum was fed via an esophageal tube. Calves also were fed pooled colostrum 14, 26, and 38 hours after birth. Colossal IgG concentration was measured by use of one radial immunodiffusion and the method of Fahey and McKeever.

Apparent efficiency of IgG absorption was calculated at 25 hours by the method of Husband et al., using the formula:

\[ \text{AEA} = \frac{\text{plasma IgG (g/L)} \times \text{plasma volume (L)}}{\text{colostal IgG (g/L)} \times \text{colostal intake (L)}} \]

Data analysis—Blood gas tensions (PaCO₂ and PaO₂) and plasma lactate concentration 1 hour after birth were analysed, using the model:

\[ Y = \mu + T_i + e_i \]

where \( Y \) = PaCO₂, PaO₂, or lactate concentration; \( \mu \) = overall mean; \( T_i \) = effect of ith treatment group; \( e_i \) = random error associated with the ith treatment group and the jth calf (i = 1, 2, 3; j = 1, 2, ..., n).

Plasma IgG concentrations 13 and 25 hours after birth and AEA at 25 hours, with IgG intake as a covariate, using the model:

\[ Y = \mu + T_i + (X_j - \bar{X}) + e_i \]

where \( Y \) = plasma IgG concentrations or AEA; \( \mu \) = overall mean; \( T_i \) = effect of ith treatment group; \( X_j - \bar{X} \) = adjustment for the effect of the covariate; \( e_i \) = random error associated with the ith treatment group and the jth calf (i = 1, 2, 3; j = 1, 2, ..., n).

General linear model procedures were used in ANOVA and to generate least squares means and SEM for blood gas tensions, plasma IgG concentration, and AEA. Regression analysis was used to determine relationships among blood gas tensions, plasma IgG concentrations, and AEA.

Results

Body weight of calves ranged from 22.3 to 50.0 kg with a mean ± SEM of 39.8 ± 0.70 kg (Table 1). Mean calving ease score was 1.79 ± 0.12, and ranged from 1 to 3, indicating that cesarean sections were not performed. Eleven of 48 births were considered difficult and assisted; all dams in this group were primiparous. Parity of dams ranged from 1 to 5, with a mean parity of 2.08 ± 0.21.

Mean plasma IgG concentration for all calves 13 hours after birth was 8.31 ± 0.50 g/L, and ranged from 3.66 to 16.51 g/L (Table 1). Mean IgG concentrations increased to 11.73 ± 0.66 g/L at 25 hours and 12.90 ± 0.74 g/L at 37 hours. Plasma IgG concentrations 13, 25, and 37 hours after birth were unaffected by treatment group (Table 2; Fig 1 and 2) and increased in all 3 groups throughout the first 37 hours of life.

Mean AEA determined 25 hours after birth for 43/48 calves was 26.0 ± 1.5% (Table 1). Apparent efficiencies of IgG absorption were unaffected by treatment group (Table 2; Fig 3) and were similar to values reported by others.

Mean IgG concentration in colostrum was 42.37 ± 1.93 g/L; colostrum was considered of moderate quality. Concentrations of IgG in colostrum ranged from 12.10 to 65.95 g/L and did not differ among treatment groups. Grams of IgG intake were calculated as the product of IgG concentration in colostrum (g/L) and the amount of colostrum (L) consumed by calves. Intake of IgG from the first 2 feedings determined for 48 calves ranged from 65.7 to 247.4 g and did not differ among treatment groups (Tables 1 and 2). Mean IgG intake for all calves was 165.0 ± 8.2 g.

Table 1—Descriptive statistics for data collected from 48 Holstein calves beginning 1 hour after birth. Calves did not suckle from dams but received between 1.8 and 2 L of colostrum 1, 2, 3, and 38 hours after birth.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SEM</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>33.60 ± 0.70</td>
<td>22.30–50.00</td>
</tr>
<tr>
<td>Ease of birth</td>
<td>1.79 ± 0.12</td>
<td>1.00–3.00</td>
</tr>
<tr>
<td>Parity of dam</td>
<td>2.03 ± 0.21</td>
<td>1.03–5.00</td>
</tr>
<tr>
<td>Colostral IgG concentration (g/L)</td>
<td>42.37 ± 1.93</td>
<td>12.10–65.95</td>
</tr>
<tr>
<td>IgG intake at 25 h (g/L)</td>
<td>165.00 ± 8.20</td>
<td>65.70–247.40</td>
</tr>
<tr>
<td>Plasma IgG concentration (g/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 h after birth</td>
<td>1.40 ± 0.03</td>
<td>1.19–2.65</td>
</tr>
<tr>
<td>12 h after birth</td>
<td>8.31 ± 0.15</td>
<td>3.86–16.51</td>
</tr>
<tr>
<td>25 h after birth</td>
<td>11.73 ± 0.86</td>
<td>3.82–22.00</td>
</tr>
<tr>
<td>37 h after birth</td>
<td>12.90 ± 0.74</td>
<td>3.81–22.62</td>
</tr>
<tr>
<td>Total IgG in plasma at 25 h (g/L)</td>
<td>41.55 ± 1.80</td>
<td>12.22–96.80</td>
</tr>
<tr>
<td>AEA at 25 h (%)</td>
<td>26.00 ± 1.50</td>
<td>9.95–47.60</td>
</tr>
<tr>
<td>Plasma lactate concentration (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 h after birth</td>
<td>4.03 ± 0.36</td>
<td>1.42–12.32</td>
</tr>
<tr>
<td>12 h after birth</td>
<td>3.95 ± 0.19</td>
<td>0.85–7.56</td>
</tr>
<tr>
<td>25 h after birth</td>
<td>2.57 ± 0.16</td>
<td>1.03–4.76</td>
</tr>
</tbody>
</table>

1 = unassisted birth; 2 = easy assisted birth; 3 = difficult assisted birth.
4 = cesarean section. 1 Determined from values for colostrum used at 1 and 16 h. Intravenous injection or colostrum used at 16 h. Draz and 24 h after birth and colostral IgG concentration. Product of plasma volume (determined by use of Evans’ blue dye technique) and plasma IgG concentration. Apparent efficiency of G absorption (AEA) determined for 43 calves using the equation (total IgG in plasma / IgG intake) × 100.
Table 2—Least squares means of variables measured by analysis of arterial blood samples 1 hour after birth, and of plasma IgG and lactate concentrations, and apparent efficiencies of IgG absorption (AEA) for 48 Holstein calves assigned to 2 groups on the basis of 1-hour PaCO₂. Calves in the nonrespiratory acidosis (NA) group (PaCO₂ < 50 mm Hg) received no treatment. Calves with PaCO₂ ≥ 50 mm Hg were assigned randomly to respiratory acidosis/not ventilated (ANV) or respiratory acidosis/ventilated (AV) groups; the AV group received assisted ventilation for 5 minutes 1 hour after birth. Calves did not suckle from dams but received between 1.8 and 2 L of colostrum 14, 26, and 36 hours after birth.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment groups (n)</th>
<th>Comparison*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NA (15)</td>
<td>ANV (17)</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>45.52</td>
<td>53.64</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>76.11</td>
<td>66.96</td>
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<td>pHi</td>
<td>7.008</td>
<td>7.062</td>
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<tr>
<td>Base excess (mEq/L)</td>
<td>2.23</td>
<td>-0.75</td>
</tr>
<tr>
<td>1-h plasma lactate (mmol/L)</td>
<td>5.673</td>
<td>4.318</td>
</tr>
<tr>
<td>Igg plasma (g/l)</td>
<td>174.5</td>
<td>185.6</td>
</tr>
<tr>
<td>Plasma Igg (g/L)</td>
<td>7.92</td>
<td>5.71</td>
</tr>
<tr>
<td>15 h after birth</td>
<td>10.87</td>
<td>12.58</td>
</tr>
<tr>
<td>37 h after birth</td>
<td>11.74</td>
<td>13.58</td>
</tr>
<tr>
<td>AFA at 75% (mg/dL)</td>
<td>0.74</td>
<td>0.81</td>
</tr>
</tbody>
</table>

*Significant differences not detected between ANV and AV groups. Amount of IgG in volume or colostrum fed at 2 and 14 h. If total IgG in plasma (Igg plasma intake) × 100.

NS = not significant (P > 0.05).

Mean plasma lactate concentration for all calves 1 hour after birth was 4.93 ± 0.39 mmol/L and decreased to 2.67 ± 0.16 mmol/L at 25 hours. However, 1-hour plasma lactate concentration was significantly (P < 0.05) higher for calves of the NA group (5.673 mmol/L), compared with concentrations for calves of the ANV and AV groups (4.318 and 4.057 mmol/L, respectively; Table 2). Mean lactate concentration in calves of all treatment groups decreased during the first 25 hours of life, although concentrations at all times measured remained above the recommended range (0.56 to 2.22 mmol/L).

Mean PaCO₂ for all calves 1 hour after birth was 50.80 ± 0.67 mm Hg and decreased to 45.74 ± 0.44 and 45.44 ± 0.46 mm Hg at 13 and 25 hours, respectively.

![Figure 1](image1.png)

Figure 1—Scatterplot of 1-hour PaCO₂ versus 13-hour plasma IgG concentrations (g/L) for 48 Holstein calves that did not suckle from dams but received between 1.8 and 2 L of colostrum 2 hours after birth. The line determined by the depicted regression equation is superimposed.

![Figure 2](image2.png)

Figure 2—Scatterplot of 1-hour PaCO₂ versus 25-hour plasma IgG concentrations (g/L) for 48 Holstein calves that did not suckle from dams but received between 1.8 and 2 L of colostrum 2 and 14 hours after birth. The line determined by the depicted regression equation is superimposed.

![Figure 3](image3.png)

Figure 3—Scatterplot of 1-hour PaCO₂ versus apparent efficiency of IgG absorption (AEA; total IgG in plasma 25 hours after birth/Igg plasma intake) for 48 Holstein calves that did not nurse from dams but received between 1.8 and 2 L of colostrum 2 and 14 hours after birth. The line determined by the depicted regression equation is superimposed.

Mean pHi for all calves 1 hour after birth was 7.303 and ranged from 7.113 to 7.400 (Table 3). By 13 hours, mean pHi had increased to 7.386 ± 0.004 and by 25 hours was 7.425 ± 0.005, slightly greater than the optimal pH of 7.4; pHi at any time measured did not differ among groups (Table 2). Mean pHa for all treatment groups indicated that calves were born slightly acidic and had partially compensated by 25 hours of age.32,23,24 Similar pHa values determined at or shortly after birth have been reported.33,34 A steady compensation in pHa also was observed in those studies, with mean pHa of 7.4 measured 24 hours after birth.

Mean PaO₂ for all calves 1 hour after birth was 69.1 ± 2.8 mm Hg and increased to 80.6 ± 2.7 mm Hg at 13 hours (Table 3). A wide range of PaO₂ values was observed at all 3 sample collection times. At 25 hours, mean PaO₂ decreased to 72.2 ± 2.8 mm Hg, with a range of 39.0 to 118.0 mm Hg. Calves of the NA group
tended to have higher 1-hour PaO₂ than did calves of the ANV and AV groups, but the difference was not significant (Table 2).

Mean HCO₃⁻ concentration 1 hour after birth was 24.72 ± 0.45 mmol/L, and increased to 27.30 ± 0.32 mmol/L by 13 hours. At 25 hours, mean HCO₃⁻ concentration had increased to 29.66 ± 0.35 mmol/L, ranging from 23.20 to 33.40 mmol/L. One-hour HCO₃⁻ concentrations differed significantly (P < 0.001) among groups (Table 2); calves of the ANV and AV groups had significantly higher HCO₃⁻ concentrations, compared with calves of the NA group.

Base excess concentration for all calves 1 hour after birth ranged from -13.90 to 4.40 mEq/L with a mean of -0.98 ± 0.52 mEq/L. Base excess concentration at 1 hour differed significantly among groups (Table 2); calves of the NA group had significantly (P < 0.05) lower BE concentration, compared with calves of the ANV and AV groups. Mean BE concentration for all calves increased to 2.85 ± 0.33 mmol/L at 13 hours and 5.74 ± 0.36 mmol/L at 25 hours.

Discussion

Mean plasma IgG concentration of 11.73 g/L 25 hours after birth indicated that calves in our study achieved adequate transfer of colostral IgG after the first 2 feedings. Failure of passive transfer is indicated by plasma IgG concentration < 10 g/L.² Four weeks after birth, plasma IgG concentrations at 13 and 25 hours, and AEA determined at 25 hours, were unaffected by treatment. Regression analysis of plasma IgG concentrations at 13 and 25 hours and AEA at 25 hours on PaCO₂ also indicated that a relationship did not exist between these variables (Fig 1–3). Our results indicated that calves with high PaCO₂ 1 hour after birth were able to compensate for increased CO₂ and absorb adequate amounts of colostral IgG and are in agreement with results of other studies.³⁷,³⁸ Partial compensation of acidosis also was indicated by a decrease of mean Paco₂ to 45.74 and 43.44 mm Hg at 13 and 25 hours, respectively. Lack of effect of 1-hour PaCO₂ on plasma IgG concentrations at 25 hours is likely attributable to compensatory mechanisms enabling neonates to reduce PaCO₂ prior to the onset of closure of intestinal absorptive capacity.²,³⁴ Walser and Maurer-Schweizer²³ stated that unassisted deliveries often are followed by prepathologic acidosis in neonates. However, recovery to expected values for acid-base balance is completed by 24 hours, allowing for adequate absorption of colostral immunoglobulins.

Lack of a significant effect of treatment on plasma IgG concentrations and AEA determined 25 hours after birth among groups in this study contradicts results of other studies regarding association of immunoglobulin absorption and respiratory acidosis.¹³ Discrepancies may be attributable to differences in sample collection techniques (arterial vs venous blood, sample collection site), experimental design, sample collection time, sample handling, and degree and type of acidosis. Values for Paco₂ in neonatal calves of this study are in agreement with values obtained from brachial artery blood samples in other studies.¹³,¹⁴ Compensation of high PaCO₂ observed in those studies occurred within 24 hours without medical intervention.¹³

Differences between PvaCO₂ and Paco₂ are an important consideration in interpreting data from these types of studies. Neonatal lungs have decreased ability to expire CO₂, compared with adult lungs and, therefore, arterial blood would contain high concentrations of CO₂. Tissue metabolism would contribute further to increased CO₂ concentration in venous blood, thereby making analysis of venous blood a poor indicator of respiratory function or tissue CO₂ concentration. Furthermore, in our study, blood gas analysis was performed within 30 minutes of sample collection, compared with storage times as long as 24 hours in other studies. Prolonged storage of blood (> 6 hours) will lead to overestimation of PvaCO₂ by 2 to 3 mm Hg.¹³,¹⁴ Our ability to rapidly determine blood gas tensions could have contributed further to observed differences in results. Finally, calves of our study appeared clinically normal. Differences in results among our study and others may have been a function of differences in calves’ metabolic state, degree of acidosis, or both.

Experimental design dictated that calves were assigned to groups on the basis of 1-hour PaCO₂ which, therefore, differed significantly among groups. Significant differences in 1-hour PaCO₂ were not detected among groups, but PaO₂ was related inversely to PaCO₂. However, pha at any time measured did not differ among groups, indicating that factors other than PaCO₂ and PaO₂ at 1 hour were contributing to the decrease in pha that occurred during the study. Furthermore, mean pha (7.303) for all calves suggested that, as a group, calves were born slightly acidic, and was in agreement with results of other studies.¹³,¹⁴ Data from studies utilizing venous samples indicated a mean pH of 7.22 in calves born of a normal delivery, compared with a mean pH of 7.06 in calves considered at high risk for acidosis.⁹ In our study, mean calving ease score of 1.79 ± 0.12 indicated that few calves were predisposed to risk factors associated with severe
acidosis at birth. Although calves were slightly acidotic 1 hour after birth, they appeared clinically normal. Therefore, metabolic contributions of HCO₃⁻ and BE concentrations to pHa should be considered as possible influencing factors.

One-hour HCO₃⁻ and BE concentrations were significantly lower in the NA group, compared with the ANV and AV groups. Higher HCO₃⁻ concentrations observed in calves of the ANV and AV groups may have resulted from increased PaCO₂ through the equilibrium of carbonic acid. Increased HCO₃⁻ concentrations in these calves suggest either a partial metabolic alkalosis or compensation for acidosis of respiratory origin. Significantly lower HCO₃⁻ and BE concentrations in calves of the NA group suggest that the metabolic portion of the acid-base system contributed more to the acid-base balance in these calves, whereas the respiratory portion, or PaCO₂, contributed more to acid-base balance in calves of the ANV and AV groups.

Plasma lactate concentrations at 1 hour were significantly higher in the NA group, compared with the ANV and AV groups. Lactate concentrations in calves of this study were above recommended ranges for mature cattle (0.56 to 2.22 mmol/L). However, Kasari²⁰ reported that concentrations of 4.4 mmol/L in newborn calves indicated lactic acidemia. Randall²¹ also reported that high lactic acid concentrations caused by low glycogen stores resulting in anaerobic glycolysis during parurition are common in neonates. As respiration reaches homeostasis and glucose is provided by colostrum, anaerobic glycolysis ceases, and lactate concentrations decrease. Tyler and Ramsey²² observed lactate concentrations > 6 mmol/L in hypoxic calves. Those authors concluded that high lactate concentrations were attributable to anaerobic metabolism exceeding the capacity of neonates to utilize lactate as an energy source. Similarly, high lactate concentrations in our calves represent lactate production in excess of the ability of calves to utilize lactate. High concentrations contribute to progressive metabolic acidosis,²³ which is common in calves < 8 days old.²⁴ Values for lactate concentrations for calves of the NA group suggested acidosis of metabolic origin.

The combination of increased lactate concentration and decreased HCO₃⁻ and BE concentrations in calves of the NA group, compared with calves in the other groups, indicated that tissue metabolism had not reached a balance by 1 hour after birth, and calves of the NA group were in a state of acid-base compromise similar to calves of the ANV and AV groups. All 3 groups appeared to be physiologically but not clinically challenged at the time of birth. However, lack of effect of treatment on plasma IgG concentrations and AEA among groups indicated that calves were able to compensate for acid-base disturbances during the first 24 hours after birth and achieved adequate immunity through absorption of colostral IgG.

Assisted ventilation had no effect on any of the variables measured in this study. Blood gas analysis after ventilation indicated that this intervention was successful at decreasing PaCO₂ and increasing pHa. However, the effect appeared temporary and did not influence absorption of immunoglobulins or plasma concentrations of selected metabolites. Correction of high PaCO₂ did not require clinical intervention. However, further research is warranted to evaluate the duration and degree of compensation required by calves to correct high PaCO₂ associated with birth.

References

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