Adrenal Response of the Newborn Calf to Acute Inanition and Colostral Feeding

G. T. NIGHTENGALE and G. H. STOTT
Department of Animal Sciences
University of Arizona
Tucson 85721

ABSTRACT

This is a study of hyperadrenalemia from inanition in neonatal calves and the influence of elevated postpartum concentrations of cortisol in serum in intestinal absorption of colostral immunoglobulins. Feeding of newborn Holstein-Friesian calves was delayed up to 24 h after parturition. Concentrations of cortisol in serum were measured at 0, 12, 24, and 40 h following birth. Delaying colostrum intake 8 h or more elevated cortisol concentrations in serum at 24 h postpartum. Adrenal response as indicated by concentrations of cortisol in serum followed a positive linear trend with delay in feeding.

Concentrations of cortisol also were increased acutely by ingestion of colostrum following inanition. As time elapsed after the feeding, concentration of cortisol in serum decreased.

Partial correlations were negative between concentrations of cortisol and maximum Immunoglobulin G but not Immunoglobulin M or Immunoglobulin A.

INTRODUCTION

The calf, born devoid of immunoglobulin (Ig) in serum, relies on antibodies absorbed from colostrum for immune protection during early life. As hypogammaglobulinemia is associated with high mortality and morbidity (5, 21), substantial research has investigated mechanisms of intestinal absorption of Ig.

It is assumed that stress during the neonatal period decreases the capacity of Ig absorption in calves (13, 20). Presumably efficiency of absorption is reduced by premature termination of macromolecular transport (closure) caused by elevated concentrations of circulating adrenal corticoids (15, 20). From other species (11, 12, 23), it is reasonable that elevated endogenous adrenal steroids could produce a change in permeability of the neonatal bovine intestine reducing absorption of colostral Ig. Our experiment investigated hyperadrenalemia due to inanition and the influence of postpartum concentrations of cortisol in serum on absorption of colostral Ig by neonatal calves. It is part of a larger experiment to determine how age of calf at first colostral feeding, amount of colostrum fed, and concentration of Ig in the colostrum interact to affect the permeable period of calf intestine to Ig transfer, rate of colostral Ig absorption, and maximum concentration of Ig in serum after absorption is complete.

METHODS

Newborn Holstein-Friesian calves were separated from their dams at birth to prevent suckling and were housed in individual pens during the experimental period. Calves were collected in blocks of 42 animals to account for environmental effects and differences in colostral Ig. Colostrum of first milking was pooled for each of the five blocks and refrigerated. Blood samples were drawn from the jugular vein of each calf at birth and at 4-h intervals up to 40 h postpartum to monitor Ig absorption. Collection of calves and experimentation were completed within 4 to 6 days from the start of each block (28).

The experiment was under a randomized complete block, split plot design with the cells of the $3 \times 7$ factorial design of each block as main plots. Treatments consisted of three volumes of pooled colostrum per feeding (.5, 1, and 2 liters) initiated at seven intervals after parturition (0, 4, 8, 12, 16, 20, 24 h). Calves received additional colostrum equal in

Received March 20, 1980.
1 Department of Animal Sciences.
2 Arizona Agricultural Experiment Station Paper 3208.

volume to the first feeding, at 12-h intervals following initial feeding. Each of the 21 treatments was replicated twice per block.

Serum IgG, IgM, and IgA were measured by radial immunodiffusion (RID) gel procedures. Methods for assaying serum Ig in our laboratory are outlined in (28).

Blood samples at 0, 12, 24, and 40 h after parturition were analyzed for total cortisol concentration by a radioimmunoassay adapted from that of Abraham et al. (1). Serum proteins were precipitated with ethanol (100%) and removed by centrifuging. Recovery of known amounts of cortisol by this method was greater than 95%. Within assay variability was 3.3% for duplicate determinations. Between assays variability was 7.0%. When analysis of variance indicated significant differences between treatments, means were compared by the least significant difference test (27).

RESULTS

Effects of Delayed Feeding on Concentration of Serum Cortisol

Mean concentrations of serum cortisol of the seven treatment groups are summarized in Table 1. Effect on concentration of serum cortisol of volume of colostrum fed was not significant. Therefore, data were combined for the three volumes of feeding under each of the seven feeding periods. Each mean and standard error in Table 1 represent 30 experimental animals.

Calves fed before 12 h of age (0, 4, and 8-h feedings) exhibited a rapid decline in concentration of cortisol in serum from birth to 12 h postpartum and a gradual decline thereafter. In calves subjected to delays in feeding of 12 h or more, cortisol decreased during the first 12 h after birth and increased again between 12 and 24 h postpartum. The increase in cortisol concentration between 12 and 24 h postpartum in calves deprived of colostrum enlarged with longer deprivation.

Of the seven treatments, only those calves fed at 8 h of age had a mean cortisol concentration at 12 h postpartum (69±5) (Table 1), which differed (P<.05) from that of calves fed at birth (54±4). When measured at 24 h after calving, mean cortisol concentrations in serum in all treatments in which feeding was initiated 8 h or more postpartum were greater (P<.05) than in calves fed at birth. In general, cortisol concentration at 24 h postpartum increased with longer deprivation. The most pronounced adrenal response was in calves deprived of food for 20 h following birth (89±5), exceeding that of calves fed at parturition (49±4) by 185% at the 24-h bleeding.

By 40 h postpartum, cortisol concentrations in all treatments were similar to what might be expected if cortisol in serum had continued to decrease throughout the experimental period (Table 1). Differences in cortisol in serum between some treatments at final sampling did not follow any trend and appeared unrelated to time of feeding.

Ingestion of Colostrum Affecting Serum Cortisol Concentration

Concentrations of cortisol in serum (Table 1) related to time of first feeding were increased acutely following ingestion of colostrum. As time elapsed after feeding, cortisol concentrations decreased, suggesting an inverse relationship between concentration of cortisol and time from first feeding to blood sampling. Treatment

<table>
<thead>
<tr>
<th>Hours postpartum</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>112</td>
<td>110</td>
<td>97</td>
<td>109</td>
<td>110</td>
<td>108</td>
<td>92</td>
</tr>
<tr>
<td>SE</td>
<td>7</td>
<td>8</td>
<td>5</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>X</td>
<td>54</td>
<td>61</td>
<td>69</td>
<td>60</td>
<td>59</td>
<td>55</td>
<td>47</td>
</tr>
<tr>
<td>SE</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>X</td>
<td>49</td>
<td>51</td>
<td>64</td>
<td>66</td>
<td>71</td>
<td>89</td>
<td>62</td>
</tr>
<tr>
<td>SE</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>X</td>
<td>55</td>
<td>52</td>
<td>41</td>
<td>45</td>
<td>42</td>
<td>44</td>
<td>38</td>
</tr>
<tr>
<td>SE</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

*aLeast significant difference = 11.0 (P<.05).
groups receiving their first feeding of colostrum prior to the blood sampling at 12 h exhibited increasing cortisol in serum at 12 h (Table 1) associated with decreasing time from feeding to sampling. Cortisol concentrations were 54±4 in the 0-h feeding group, 61±7 in the 4-h group, and 69±5 in the 8-h feeding group. Corresponding times from feeding to blood sampling were 12, 8, and 4 h. Only the 8-h postpartum feeding group differed significantly from the 0-h feeding group. Treatment groups not fed prior to sampling at 12 h showed cortisol concentrations that did not differ from calves fed at birth.

When feeding was initiated at 12, 16, and 20 h after birth, cortisol concentrations were 66±5, 71±7, and 89±5 ng/ml at the 24-h sampling (Table 1). Times elapsed from feeding to bleeding were 12, 8, and 4 h. Mean cortisol concentration in the 24-h feeding group (62±5), which was the only group not fed prior to sampling was less (P<.05) than either the 16 or 20-h feeding groups. Similar increases in cortisol concentration were not observed following the second colostrum feeding.

**Immunoglobulin Absorption Related to Cortisol Concentration**

Partial correlation coefficients related concentrations of the three Ig classes (IgA, IgM, and IgG) with cortisol concentration at sampling periods 0, 12, 24, and 40 h postpartum. Coefficients in Table 2 are adjusted for effects of amount of colostrum fed, age at initial feeding, and Ig content of the colostrum fed, all of which can influence final serum concentration of Ig in calves (17).

Partial correlations (P<.05) were significant between maximum serum IgG and serum cortisol at 24 h and 40 h postpartum. Serum IgA was not correlated significantly with cortisol concentration at any of the times examined.

**DISCUSSION**

The discovery by Halliday (12) that glucocorticoids induce precocious closure of the intestine of nursing rats to macromolecular absorption has stimulated interest in hormonal regulation of intestinal maturation in other mammalian neonates (24). Assumptions have been that this could apply to the calf, shortening the period of permeability and the resulting amount of colostral Ig absorbed. If effective, it necessarily would have to occur before closure occurs spontaneously near 24 h postpartum (7, 10, 28).

Food deprivation in many mammals elevates circulating adrenal corticoids (2, 3, 4). Adrenal cortical response in the calf to this kind of stimulus has not been reported. Feed deprivation in the calf beyond 8 h postpartum resulted in a gradual, consistent increase in cortisol concentration of serum at 24 h postpartum but seemingly had no effect at 12 h postpartum. The response to inanition was confounded by an apparent second response following the ingestion of colostrum, making interpretation of these observations difficult.

In most instances, immunoglobulin absorption was complete in experimental calves by 24 h postpartum (28). For this reason, cortisol effects on Ig absorption are discussed within this time. Partial correlation coefficients between concentrations of cortisol and Ig in the experimental calves for each bleeding period (0, 12, 24 h postpartum) (Table 2) indicate a significant negative relationship at 24 h for only IgG. The coefficient (−.15) could indicate that elevated concentrations of cortisol in serum depressed colostral IgG absorption in the calf near the end of the absorption period. The evidence is weak, however, since the coefficient is small and neither IgM nor IgA shows evidence of cortisol influence.

The increase in concentration of cortisol in serum following colostral feeding was unexpected; otherwise expression of the adrenal response to feeding could have been better by blood samples taken at appropriate intervals nearer to the time of feeding. Samples taken at

| TABLE 2. Partial correlation coefficients of cortisol concentration in serum at four sampling times with maximum serum concentrations of Ig. |
|------------------|----------|----------|----------|----------|
|                  | 0        | 12       | 24       | 40       |
| IgG              | -.043    | -.042    | -.147*   | .156*    |
| IgM              | .005     | .043     | -.080    | .220*    |
| IgA              | -.096    | -.023    | -.106    | .059     |

*P<.05.
4 h after feeding had higher concentrations than those taken at 8 or 12 h following feeding, indicating a consistency of adrenal response with the highest concentrations of cortisol in serum being nearer the time of stimulus followed by a graduated decline from 4 to 8 to 12 h following colostral ingestion.

To attach some biological significance to the adrenal response to colostral ingestion is only speculative. There is, however, evidence that the adrenal response by induced feeding may be related to early closure of the neonate intestine to macromolecular absorption. There are several characteristics of intestinal development in rodents, including closure, that can be accelerated by pharmacological doses of exogenous corticosteroids (12, 22). Adrenalectomy in the rat, up to 18 days of age, delays the onset of closure by 4 to 5 days (9). The eventual cessation of intestinal macromolecular absorption following adrenalectomy indicates the involvement of the adrenal gland is not the final mediator of closure in the rat intestine.

Research with nonrodent animals has not been as extensive. In calves, administration of corticosteroids, ACTH, or corticosteroid depressors (metyrapone) did not alter colostral Ig absorption or absorptive period significantly (10, 16). When pregnant cows were injected with slowly-released corticosteroid during the last 2 mo of gestation, calves from the treated cows had significantly lower serum immunoglobulin than calves from the untreated cows (14). It was not known whether the corticosteroid treatments produced a precocious closure or if they reduced the efficiency of protein absorption. It did suggest that corticosteroids can have an effect on intestinal absorption of colostral Ig if administered early enough in fetal development of the calf. In contrast, high endogenous concentrations of serum corticoids in calves at birth, related to weather and dystocia, did not influence colostral Ig absorption (29).

Attempts to delay closure in large animals by adrenocortical suppression have met with little success. Gillette and Filkins (11) used metyrapone on newborn puppies but found it had no effect on ability to absorb antibodies. Patt and Eberhart (25) found that postpartum injections of metyrapone severely reduced cortisol in plasma of piglets but had no effect on duration of intestinal absorption of immunoglobulins. They reported, however, that metyrapone-treated pigs had lower Ig than controls prior to closure. They suggested that absorption of antibodies is not maximal unless cortisol in plasma is adequate. Patt (24) further raised the possibility that the high perinatal cortisol in farm animals has a net benefit on postnatal absorption of antibodies regardless of any possible effect they might have on closure.

In relationship to the adrenal response to feeding in this experiment and in lambs (19), piglets (18, 26), and calves (28), feeding colostrum or other specific organic substances can shorten the period of intestinal absorption of macromolecules whereas feed deprivation can prolong the period. Though there is a lack of information on adrenal response to colostral ingestion in other species, it well could be a phenomena as indicated in this experiment. This leads to the question of whether hyperadrenalemia in response to feeding in the neonate is involved in initiating closure.

It is probably important in the calf that closure (termination of cellular uptake) does occur as soon as possible after colostral ingestion to prevent transmigration of proliferating microorganisms into systemic circulation (8). Broughton and Lecce (6), using the electron microscope to study intestinal cells of piglets following colostrum or glucose feeding, found the solutions stimulated intense pinocytotic activity, the mechanism for macromolecular absorption. They found that there was almost no pinocytosis in the intestinal cells in starved pigs or in those not subjected to closure-inducing conditions. Lecce (18) proposed that closure occurs once the plasmalemma of the intestinal epithelial cell makes contact with the ingested nutrients and digestive fluids. This contact would stimulate the cells to discharge their finite amount of pinocytotic activity. With exhaustion of pinocytotic activity macromolecular absorption would cease. Stimulation of pinocytosis, resulting in rapid macromolecular uptake and initiation of closure, seems in harmony with the adrenal response to colostral ingestion in the present experiment with regard to the findings and view of Patt (24), that maximal absorption of antibodies does not take place unless cortisol in plasma is adequate. The mechanisms of corticosteroid action is not clear, but from (24), the role of the adrenal gland responding to colostral ingestion in the

neonate could be both to mediate absorption and to initiate closure.

ACKNOWLEDGMENTS

The authors are grateful to Shamrock Dairies, Inc. and Arizona Feeds, Tucson, AZ for the animals and facilities that were supplied generously for this project. The financial assistance of the United Dairymen of Arizona also is acknowledged gratefully.

REFERENCES