ENDOCRINE CHANGES AND CIRCULATING INSULIN-LIKE GROWTH FACTORS IN NEWBORN CALVES FED COLOSTRUM, MILK OR MILK REPLACER

C.-Y. Lee[1], H. H. Head, C. R. Feinstein, J. Hayen and F. A. Simmen[2]

Department of Dairy and Poultry Sciences, University of Florida,
P.O. Box 110920, Gainesville, Florida 32611-0920, USA

Summary

To examine whether colostral growth factors are transferred to the general circulation, concentrations of plasma cortisol, insulin, prolactin, growth hormone, insulin-like growth factors (IGFs) - Ⅰ and - Ⅱ, IGF-binding proteins (IGFBPs) and total protein were measured in newborn calves fed colostrum, milk or milk replacer before and after feeding at 12 h intervals during the first two days after birth. Plasma protein concentrations increased with time after birth, but this was apparent only in colostrum-fed calves. The mean protein concentration was greater in colostrum-fed than in milk- or milk replacer-fed calves. Plasma cortisol levels transiently declined after each feeding regardless of the type of diet, while insulin levels tended to increase. Mean concentrations of these hormones did not differ between dietary groups, nor did they change with time after birth. Plasma concentrations of prolactin and growth hormone did not differ between dietary groups and also did not change with time after birth or after feeding. Concentrations of IGF-Ⅰ and IGF-Ⅱ transiently increased at the second feeding period, but these, as well as plasma IGFBP profiles, were not different between groups or before and after feeding. Results did not indicate significant transfer of colostral growth factors across the newborn ruminant small intestine.

(**Key Words** : Colostrum, Insulin-like Growth Factors, Hormones, Calf, Gastrointestinal Tract)

Introduction

Mammary gland secretions are complex biological fluids which provide nutrients, immunoglobulins, water, minerals, and possibly other factors for the developing neonate. Work of the past decade has documented the presence in colostrum and milk of a large number of hormones and other trophic factors (Brown and Blakeley, 1984; Shing and Klagsbrun, 1984; Francis et al., 1986; Cera et al., 1987; Simmen et al., 1988; Donovan et al., 1991). Hormones and growth factors secreted by the mammary gland are potential mediators of growth and development of the neonate (Peaker and Neville, 1991; Grosvenor et al., 1992). For instance, ruminant colostrum stimulates proliferation of a variety of cell types (Brown and Blakeley, 1984; Francis et al., 1986; Simmen and McClure, 1987). Furthermore, the mitogenic activity of ruminant mammary secretions declines during the transition from colostrum to mature milk (Simmen and McClure, 1987; Corps and Brown, 1987) which is coincident with decreasing concentrations of growth factors and hormones in the secretion (Malven et al., 1987; Shing and Klagsbrun, 1987; Simmen et al., 1988). Only limited information is available, however, regarding the transfer of hormones and growth factors from mammary secretions to the neonatal circulation and any subsequent biological actions elicited by the maternally-derived factor (Grosvenor et al., 1992). To initially address this question, circulating concentrations of a number of hormones and growth factors were measured in newborn calves fed colostrum, milk or milk replacer.

Materials and Methods

Animals

Newborn Holstein male calves were fed 1.9 liters of colostrum (pool obtained from the first and second

[1]National Institute of Diabetes, and Digestive and Kidney Diseases, Bethesda, MD 20892, USA.

[2]Address reprint requests to Dr. F. A. Simmen, Department of Dairy and Poultry Sciences, University of Florida, P.O. Box 110920, Gainesville, FL 32611-0920, USA.

Received January 22, 1994
Accepted September 26, 1994

milkings of multiparous cows) (three calves), cow's milk (five calves) or milk replacer (four calves) (Land-O Lakes, Land O'Lakes, Inc., Minneapolis, MN, USA) four times at approximately 12 h intervals, beginning within 2 h after birth. A blood sample from each calf was obtained from the jugular vein into a Vacutainer tube (Becton Dickinson VACUTAINER System, Rutherford, NJ, USA) containing heparin, within a 1 h period before and 2 h period after each feeding. The last blood sample was obtained approximately 12 h after the fourth feeding.

Radioimmunoassays

Concentrations of growth hormone (GH) and insulin in plasma were measured by RIAs as previously described and validated for use with bovine serum (Badinga et al., 1991). Recombinant bGH (standard and radioiodination; Monsanto Co., St. Louis, MO, USA) and rabbit antiserum to oGH (distributed by the National Hormone and Pituitary Program, USA) were used in the GH RIA. Used in the insulin RIA were bovine insulin (standard and radioiodination; Sigma Chemical Co., St. Louis, MO, USA) and guinea pig antiserum to ovine insulin (Miles Laboratories, Elkhart, IN, USA). Cortisol was measured by use of a RIA kit (Ventrex Laboratories, Portland, ME, USA) as previously described (Elvinger et al., 1992). The assay for prolactin was also previously described (Malven et al., 1987).

Prior to IGF RIAs, IGF-binding proteins (IGFBPs) were removed from plasma by acidification and C_{18} Sep-Pak Plus (Waters, Milford, MA, USA) chromatography as previously described for porcine serum (Lee et al., 1991). In brief, 0.2 ml of plasma was mixed with 1.3 ml of 1% aqueous trifluoroacetic acid (TFA) and incubated for 10 min at room temperature. The acidified sample was loaded on a Sep-Pak cartridge which had been conditioned by sequential washes of 100% acetonitrile, water and 0.1% aqueous TFA. After washing the cartridge with three 1 ml volumes of 0.1% aqueous TFA, the retentate was eluted in 2 ml of acetonitrile/0.1% TFA, evaporated to dryness and solubilized in RIA buffer (30 mM sodium phosphate, pH 7.5, 0.02% protamine sulfate, 10 mM EDTA, 0.05% Tween-20, 0.02% sodium azide). Recombinant hIGF-Ⅰ and hIGF-Ⅱ (standards; Amgen, Thousand Oaks, CA, USA) were iodinated to specific activities of ~300 μCi/μg using chloramine-T (Lee and Henricks, 1990). The recoveries of these preparations and monoiodinated IGFs (Amersham Corp., Arlington Heights, IL, USA) in the acetonitrile eluate which were added to plasma prior to acidification were 81.8 ± 1.5% (n = 3) and 66.1 ± 0.8% (n = 4) for [^{125}I]IGF-Ⅰ and 72.6 ± 1.5% (n = 3) and 74.2 ± 0.2% (n = 4) for [^{125}I]IGF-Ⅱ, respectively. IGF-Ⅰ and IGF-Ⅱ RIAs (Lee et al., 1991) were performed using rabbit antiserum to hIGF-Ⅰ (distributed by the National Hormone and Pituitary Program, USA) and mouse monoclonal antibody to rat IGF-Ⅱ, respectively (Lee et al., 1991). Crossreactivity in the IGF-Ⅱ RIA of hIGF-Ⅰ, which is identical to bIGF-Ⅰ (Honegger and Humbel, 1986), was 10% (Lee et al., 1991); therefore, IGF-Ⅱ values were corrected accordingly. The hIGF-Ⅱ had negligible cross-reactivity in the IGF-Ⅰ RIA (Lee et al., 1991). Recoveries of unlabeled IGF-Ⅰ and IGF-Ⅱ measured by RIA which were added to plasma prior to Sep-Pak chromatography at low, medium and high doses were 71.1 ± 5.4% and 71.3 ± 7.8%, respectively. Final RIA values were adjusted for the recovery of unlabeled IGF (71%). In each RIA, all plasma samples were analyzed at one time to avoid inter-assay variation.

Other procedures

Total plasma protein was determined by use of a clinical refractometer (Schuco Model 5711-2020). Hematocrit was determined by a microcapillary procedure (Lane and Campbell et al., 1969). IGFBPs contained in the diets and plasma before and after Sep-Pak chromatography or N-glycanase treatment were analyzed by charcoal assay and/or Western ligand blot procedure (Hossenlopp et al., 1986) as described previously (Lee et al., 1991).

Statistical analysis

The General Linear Models Procedures of SAS (SAS, 1986) were used for the analysis of variance of blood measurements. The statistical model included dietary treatment (TRT), calf nested within TRT [calf (TRT)], feeding, and period (time after birth associated with feeding). Also included in the model were two-way interactions for TRT × feeding, calf (TRT) × feeding, period × TRT, calf (TRT) × period, feeding × period and a three-way interaction, TRT × period × feeding. The main effects for TRT, feeding and period were tested using calf (TRT), calf (TRT) × feeding and calf (TRT) × period, respectively, as the error terms.

Results

Plasma protein concentrations increased with time after birth ($p < 0.01$); however, this was apparent only in the colostrum-fed calves (figure 1). Mean protein concentration was greater in colostrum-fed than in milk or milk replacer-fed calves ($p < 0.05$). Although the effect of feeding on mean protein concentration was not significant ($p = 0.69$), a tendency of increased protein concentration

after feeding colostrum, but not milk or milk replacer, was apparent which reflected by the nearly significant interaction ($p = 0.06$) between the diet and feeding.

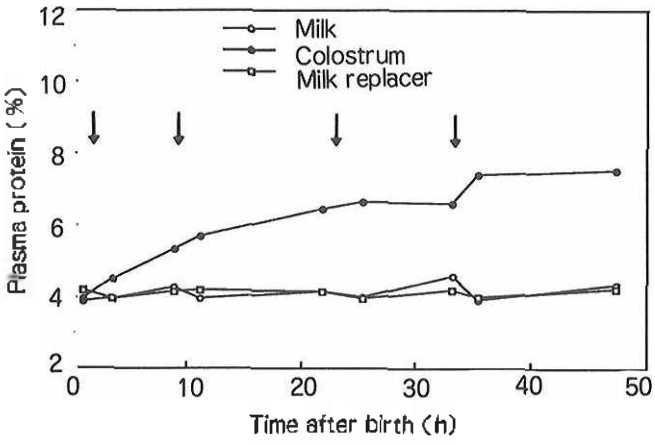

Figure 1. Plasma protein concentrations of newborn calves fed colostrum, milk, or milk replacer. Each point represents a mean of 3-5 observations. Vertical arrows indicate the times of feeding. Effects of the diet and period associated with each feeding were significant at the 5% and 1% levels, respectively. Effect of feeding was not significant ($p = 0.69$).

Mean hematocrit and plasma prolactin and GH concentrations did not differ between dietary treatment groups, nor did these change with time after birth or in response to feeding (table 1). Plasma cortisol concentrations were relatively high during the experimental period. Mean cortisol concentrations did not differ between dietary treatment groups or individual feeding periods. However, after each feeding, a transient decline in cortisol concentration was observed ($p < 0.05$) independent of type of diet, whereas plasma insulin concentrations tended to increase after each feeding ($p = 0.12$) (figure 2).

TABLE 1. MEAN HEMATOCRIT AND PLASMA CONCENTRATIONS OF PROLACTIN AND GROWTH HORMONE OF NEWBORN CALVES[1]

	Hematocrit (%)	Prolactin (ng /ml)	GH (ng /ml)
Mean ± SE	31.8 ± 0.6	15.1 ± 1.6	23.8 ± 1.7

[1]Results are overall means ± standard errors of means. Effect of diet, feeding, or period associated with each feeding was not significant for any of the above parameters.

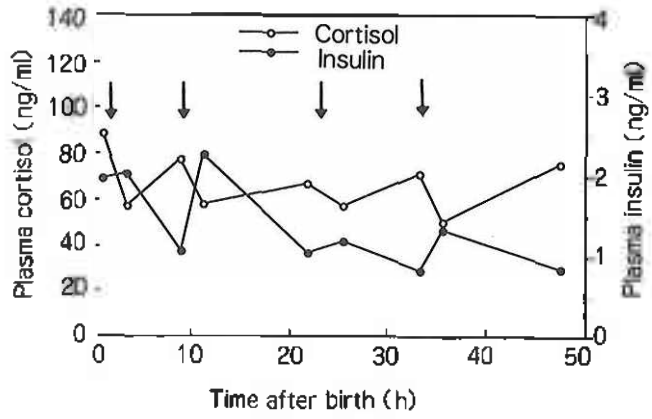

Figure 2. Plasma cortisol and insulin concentrations of newborn calves. Each point is a mean of 12 observations. Vertical arrows indicate the times of feeding. Effect of feeding on plasma cortisol concentrations was significant ($p < 0.05$).

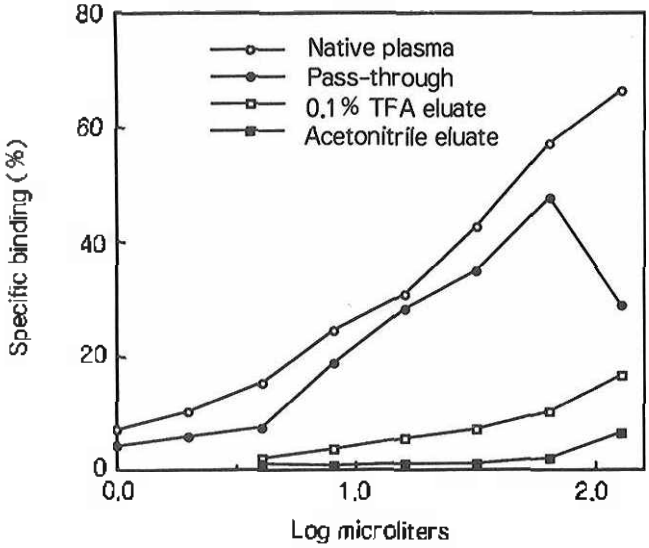

Figure 3. Removal of IGF binding proteins from calf plasma using a Sep-Pak Plus C_{18} cartridge. An aliquot (0.8 ml) of a composite plasma sample from several calves was subjected to chromatography on four Sep-Pak cartridges (Materials and Methods). The fraction obtained after each of the indicated steps was evaporated to dryness, reconstituted in 0.8 ml of RIA buffer and graded doses were incubated with [^{125}I]IGF-II (30,000 cpm) for 3 h at room temperature followed by charcoal separation of bound radioligand from the unbound.

Concentrations in plasma of IGF-Ⅰ and IGF-Ⅱ were measured by RIA after the removal of IGFBPs. To confirm that IGFBPs were removed from plasma during the separation procedure, eluted fractions were monitored for ability to bind [^{125}I] IGF-Ⅱ in solution (figure 3). The acetonitrile eluate was nearly devoid of IGFBP activity, whereas the bulk of IGFBP activity resided in the pass-through and TFA wash fractions (figure 3). Further, the reconstituted acetonitrile eluate paralleled the IGF standards in dose-response inhibition of binding of [^{125}I] IGF-Ⅰ and [^{125}I] IGF-Ⅱ to their corresponding antibodies in RIAs (figure 4).

The IGF concentrations in colostrum, milk and milk replacer were determined using Sep-Pak columns as well as by the acid-ethanol extraction method (Daughaday et al., 1980). The RIA values for colostrum were ~60% greater after acid-ethanol extraction as compared to Sep-Pak chromatography (table 2). The basis for this difference was not pursued further since IGF RIA results are inherently different for different extraction methods (Lee and Henricks, 1990) and this was found to not significantly affect the conclusions. As expected, colostrum had IGF concentrations comparable to or higher than those for calf plasma, whereas milk and milk replacer had much lower amounts of IGFs compared to colostrum (see figure 5).

TABLE 2. IGF CONCENTRATIONS IN BOVINE COLOSTRUM, MILK AND MILK REPLACER

	Sep-Pak chromatography		Acid-ethanol extraction	
	IGF-Ⅰ (ng /ml)	IGF-Ⅱ (ng /ml)	IGF-Ⅰ (ng /ml)	IGF-Ⅱ (ng /ml)
Colostrum[1]	192	113	312	187
Milk	< 5	25	< 5	32
Milk replacer	< 5	18	< 5	40

[1]Values were adjusted for the recoveries of radiolabeled IGFs which were 75.4 ± 0.8%, 76.4 ± 0.9%, 98.8 ± 4.7% and 73.1 ± 2.2% with n = 4 for columns 1 to 4, respectively.

Plasma IGF-Ⅰ concentrations increased transiently during the second feeding period ($p < 0.01$) and remained relatively stable thereafter (figure 5, upper panel). Although IGF-Ⅰ levels appeared to be lower in milk replacer-fed than in colostrum- or milk-fed calves, neither effect of diet nor feeding was significant due to relatively large variation among animals. IGF-Ⅰ, but not IGF-Ⅱ concentrations for plasma obtained at birth were positively correlated with calf birth weights ($r = 0.64$ and -0.004, $p = 0.03$ and 0.88 for IGF-Ⅰ and IGF-Ⅱ, respectively). Plasma IGF-Ⅱ concentrations, which were ~ two-fold

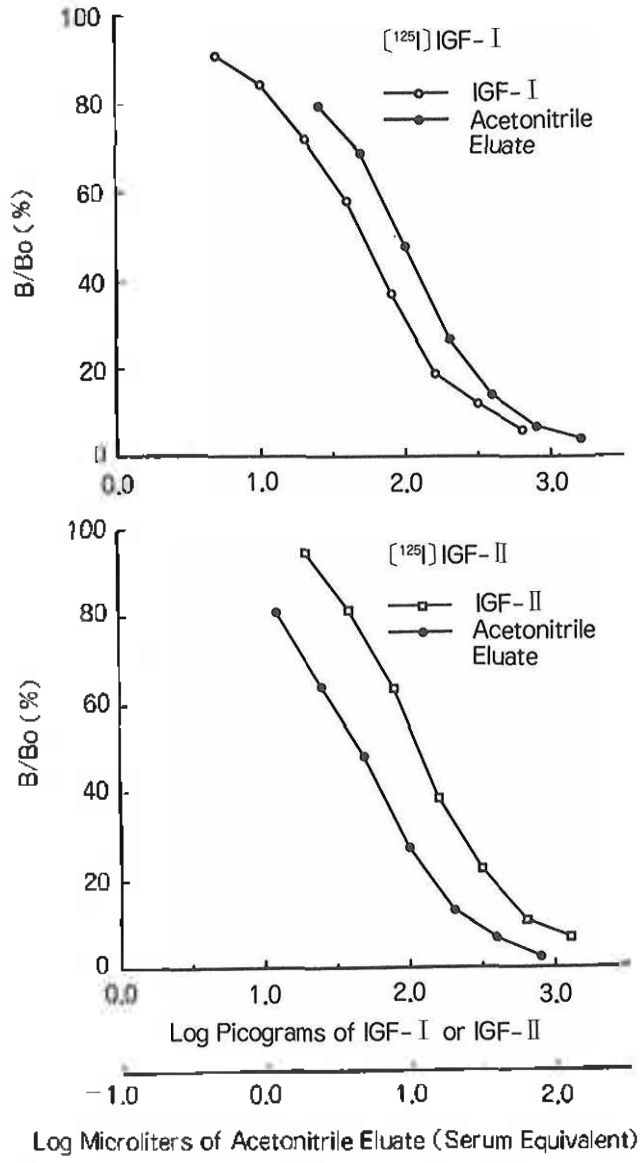

Figure 4. Inhibition of binding of [^{125}I] IGF-Ⅰ and [^{125}I] IGF-Ⅱ by reconstituted acetonitrile eluate of calf plasma. A composite plasma sample was acidified, subjected to the Sep-Pak procedure and the reconstituted acetonitrile eluate used in IGF-Ⅰ and IGF-Ⅱ RIAs (Materials and Methods). Dose-dependent inhibition by the acetonitrile eluate is compared with that exhibited by the assay standards. B /Bo is the ratio of the counts at each dose (B) divided by the counts at zero dose (Bo) after subtraction of the nonspecific counts.

greater than IGF-Ⅰ concentrations, declined within 24 h postnatal ($p < 0.01$) (figure 5, lower panel). Mean plasma IGF-Ⅱ concentrations did not differ between dietary treatment groups, nor did these change in response to feeding.

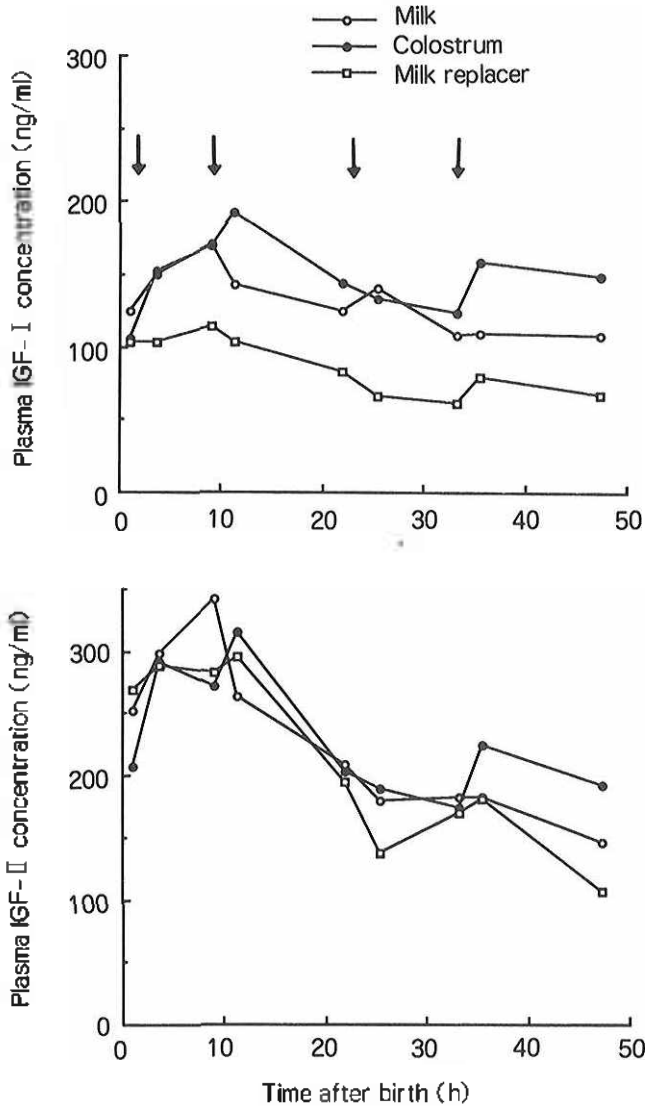

Figure 5. Plasma IGF-Ⅰ (upper) and IGF-Ⅱ (lower) concentrations of newborn calves fed colostrum, milk, or milk replacer. Each point represents a mean of 3-5 observations. Vertical arrows indicate the times of feeding. Effects of the period associated with each feeding on plasma IGF-Ⅰ and IGF-Ⅱ concentrations were significant ($p < 0.01$). Effects of the diet ($p = 0.61$ for IGF-Ⅰ; $p = 0.99$ for IGF-Ⅱ) or feeding ($p = 0.72$ for IGF-Ⅰ; $p = 0.88$ for IGF-Ⅱ) were nonsignificant.

IGFBPs in the liquid diets and calf plasma were identified by the Western ligand blot procedure. Milk and milk replacer were nearly devoid of any detectable IGFBPs (figure 6, left panel). Colostrum exhibited IGFBPs at molecular mass of 43, 40, 37, 34, 30 and 26 kDa with the ~40 kDa multimer being predominant. The 37 kDa IGFBP appears to be a deglycosylated form of the

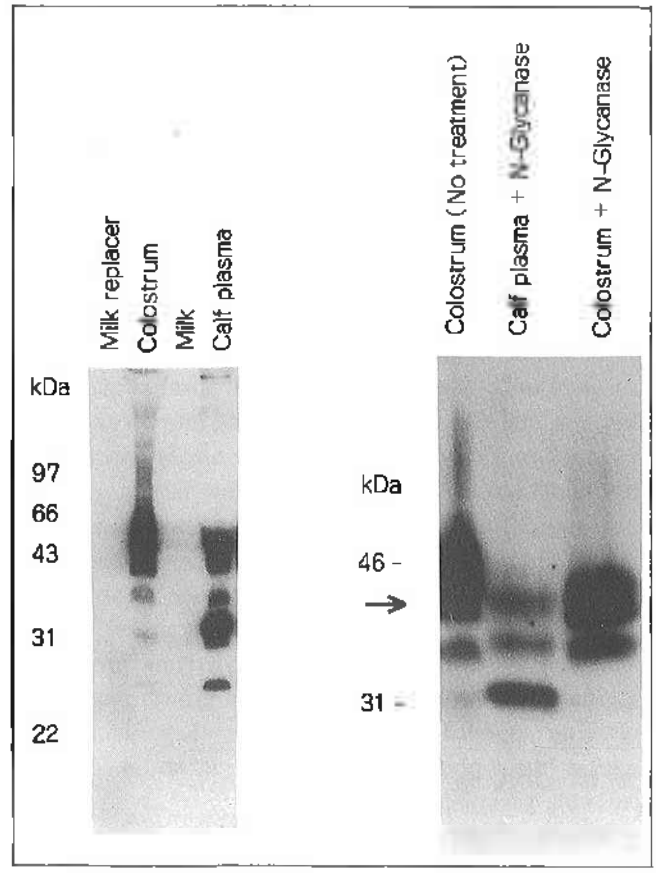

Figure 6. Western ligand blotting of IGFBPs in calf plasma and bovine colostrum, milk and milk replacer. Left, 5 μl of milk replacer, 2 μl of colostrum, 5 μl of milk or 3 μl of a pooled plasma sample was subjected to SDS-PAGE under non-reducing conditions and separated proteins were electrotransferred to a nitrocellulose membrane which was subsequently incubated with [^{125}I]hIGF-Ⅱ, washed and exposed to Kodak X-Omat RP film at −80 ℃ using an intensifier screen. Right, 1 μl of each sample was subjected to ligand blotting as for *Left* before or after N-glycanase treatment. A 37 kDa deglycosylated form of IGFBP is indicated by the arrow.

~40 kDa IGFBP as indicated by the increased intensity of this band after N-glycanase treatment of colostrum (figure 6, right panel). Calf plasma also exhibited a major IGFBP band at ~40 kDa (doublet), but unlike colostrum, it had another major IGF-binding activity at ~30 kDa and did not exhibit the 37 kDa band. The total IGF-binding activity in colostrum, as judged from the intensity of individual IGFBP bands, was comparable to or greater than that for calf plasma. However, no consistent differences in plasma IGFBP profiles between animals of the different feeding groups or periods were apparent (data not shown).

Discussion

It is well documented that concentrations of prolactin, insulin, IGF-Ⅰ and IGF-Ⅱ in bovine precolostrum and colostrum are significantly higher than for maternal serum and that these decline during the transition from colostrum to mature milk (Malven et al., 1987; Simmen et al., 1988). This temporal variation likely represents the accumulation of hormones and growth factors in the highly concentrated prepartum secretions but a relatively low rate of secretion postpartum. The high concentrations of these proteins in the colostrum, as well as their known growth-promoting actions (Philipps et al., 1988), prompted the present study to examine their possible intestinal transfer to the circulation of newborn calves. The underlying premise of this study was that the total amounts of growth factors and hormones ingested via colostrum are large enough to increase their plasma concentrations if absorbed intact across the gastrointestinal tract.

Results of the present study indicated that although plasma protein concentration was increased significantly after feeding colostrum, probably reflecting the absorption of some proteins (e.g., immunoglobulins), the IGFs and IGFBPs are not transferred to the neonatal circulation to any significant extent. Theoretically, if the total amount of IGF-Ⅰ contained in one ration of colostrum (1,900 ml × ≃ 250 ng/ml) is transferred via the intestine to 2,500 ml of calf plasma (36 kg body weight × 10%) body weight for total blood (Phillis, 1976) × 68.2% plasma ratio (31.8 % hematocrit), this would have raised the plasma IGF-Ⅰ concentration by ≃ 200 ng/ml which would then be reduced to ≃ 140 ng/ml 2 h after absorption assuming a 4 h plasma half-life for this peptide (Zapf et al., 1986). The lack of an observed elevation of plasma IGF concentrations in response to ingestion of colostrum did not have any relation to the blood sampling interval between feedings, because additional studies with more frequent blood sampling revealed no change in plasma IGF concentrations during the first 12 h after birth and initial feeding (data not shown). Similarly, Baumrucker and Blum (1994) reported that feeding colostrum or milk replacer supplemented with IGF-Ⅰ and globulins to newborn calves did not result in elevated blood IGF-Ⅰ concentrations during the first two days after birth. It has been documented, however, that orally administered free IGF-Ⅰ in a buffer solution increased blood IGF-Ⅰ concentrations in newborn calves (Baumrucker et al., 1992). It thus seems plausible that whereas free IGF-Ⅰ is readily absorbed at the gastrointestinal tract of newborn calves, absorption of IGFs bound to IGFBPs or added to a protein-rich diet is blocked or delayed (Baumrucker and Blum, 1994).

Although we found no evidence for gastrointestinal transfer of colostral IGFs in newborn calves, this does not eliminate the possibility that such growth factors are sequestered in the small intestine (Schober et al., 1990; Young et al., 1990). Indeed, there is some evidence supporting a role for colostrum in growth of the ruminant gastrointestinal tract. Mirand et al. (1990) reported that colostrum and, to a lesser extent, milk stimulated gastrointestinal protein synthesis. Similarly, human and ruminant mammary secretions are mitogenic for intestinal epithelial cells *in vitro* (Corps and Brown, 1987) and orally administered IGFs can stimulate the activity of intestinal enzymes in newborn rats (Young et al., 1990).

Plasma IGF-Ⅰ concentrations were highly correlated with birth weights and were relatively stable during the early postnatal period. In contrast, IGF-Ⅱ concentrations were not correlated with birth weights and rapidly declined during this same period. These results, which are consistent with previous studies of ruminants (Coxam et al., 1987; Breier et al., 1988), suggest that IGF-Ⅰ, rather than IGF-Ⅱ, may be an important endocrine growth factor for the bovine fetus and neonate, as previously suggested for human fetuses (Chard, 1989).

As expected, plasma cortisol levels decreased and insulin increased after feeding, which are consistent with previous reports for newborn primates (Lewis and Jackson, 1990) and cattle (Trenkle, 1970; Baumrucker and Blum, 1994), respectively. Furthermore, these changes occurred regardless of the type of diet fed. We interpret these results as indicating that these glucoregulatory endocrine systems respond passively to the nutrient flux and that this is not influenced by regulatory substances such as IGFs, potent inhibitors of insulin secretion (Leahy and Vandekerkhove, 1990), contained in the diet. In other words, cortisol and insulin as well as other regulatory substances such as IGFs contained in colostrum are not absorbed to any significant extent by the newborn calf

intestine to alter the circulating levels of the hormones.

In summary, the present study provided no evidence for intestinal transfer of any of the hormones and growth factors examined here. However, the possibility that hormones and growth factors in colostrum mediate neonatal gastrointestinal growth and/or functional differentiation cannot be ruled out.

Acknowledgements

This is Journal Series No. R-03476 from the University of Florida Agricultural Experiment Station. This paper is published in memory of Ms. Cheryl R. Feinstein, deceased March 2, 1992. The authors thank Rosalia C. M. Simmen for many helpful discussions and for critically reading the manuscript, Mary Ellen Hissem for expert secretarial assistance, Dale Hissem and Yong Ko for help with animals, Lokenga Badinga for assistance with the GH RIA and Charles J. Wilcox for consultation regrading the statistical analysis. The National Hormone and Pituitary Program is acknowledged for provision of IGF-Ⅰ, GH and prolactin antisera. This work was supported by grants from the Florida Dairy Check-Off Program (H.H.H., F.A.S.) and by USDA Grants 89-37265-4545 and 91-37203-6485 (F.A.S).

Literature Cited

Badinga, L., R. J. Collier, W. W. Thatcher, C. J. Wilcox, H. H. Head and F. W. Bazer. 1991. Ontogeny of hepatic growth hormone receptors in cattle. J. Anim. Sci. 69:1925-1934.

Baumrucker, C. R. and J. W. Blum. 1994. Effects of dietary recombinant human insulin-like growth factor-Ⅰ on concentrations of hormones and growth factors in the blood of newborn calves. J. Endocrinol. 140:15-21.

Baumrucker, C. R., D. L. Hadsell, T. C. Skaar, P. G. Campbell and J. W. Blum. 1992. Insulin-like growth factors (IGFs) and IGF binding proteins in mammary secretions: origins and implications in neonatal physiology. In: M. F. Picciano and B. Lonnerdal (Eds). Contemporary Issues in Clinical Nutrition, vol. 15. Mechanisms Regulating Lactation and Infant Nutrient Utilization, pp 285-308, John Wiley & Sons, Inc., New York, USA.

Breier, B. H., P. D. Gluckman and J. J. Bass. 1988. Plasma concentrations of insulin-like growth factor-Ⅰ and insulin in the infant calf: ontogeny and influence of altered nutrition. J. Endocrinol. 119:43-50.

Brown, K. D. and D. M. Blakeley. 1984. Partial purification and characterization of a growth factor present in goat's colostrum. Similarities with platelet-derived growth factor. Biochem. J. 219:609-617.

Cera, K., D. C. Mahan and F. A. Simmen. 1987. In vitro growth-promoting activity of porcine mammary secretions: initial characterization and relationship to known peptide growth factors. J. Anim. Sci. 65:1149-1159.

Chard, T. 1989. Hormonal control of growth in the human fetus. J. Endocrinol. 123:3-9.

Corps, A. N. and K. D. Brown. 1987. Stimulation of intestinal epithelial cell proliferation in culture by growth factors in human and ruminant mammary secretions. J. Endocrinol. 113:285-290.

Coxam, V., M. -J. Davicco, J. Robelin and J. -P. Barlet. 1987. Growth hormone secretory pattern and somatomedin-C plasma concentrations in newborn calves. J. Dev. Physiol. 9:113-121.

Daughaday, W. H., I. K. Mariz and S. L. Blethen. 1980. Inhibition of access of bound somatomedin to membrane receptor and immunobinding sites: a comparison of radioreceptor and radioimmunoassay of somatomedin in native and acid-ethanol-extracted serum. J. Clin. Endocrinol. Metab. 51:781-788.

Donovan, S. M., R. L. Hintz, D. M. Wilson and R. G. Rosenfeld. 1991. Insulin-like growth factors Ⅰ and Ⅱ and their binding proteins in rat milk. Pediatr. Res. 29:50-55.

Elvinger, F., R. P. Natzke and P. J. Hansen. 1992. Interactions of heat stress and bovine somatotropin affecting physiology and immunology of lactating cows. J. Dairy Sci. 75:449-462.

Francis, G. L., L. C. Read, F. J. Ballard, C. J. Bagley, F. M. Upton, P. M. Gravestock and J. C. Wallace. 1986. Purification and partial sequence analysis of insulin-like growth factor-Ⅰ from bovine colostrum. Biochem. J. 233:207-213.

Grosvenor, C. E., M. F. Picciano and C. R. Baumrucker. 1992. Hormones and growth factors in milk. Endocr. Rev. 14:710-728.

Honegger, A. and R. E. Humbel. 1986. Insulin-like growth factors Ⅰ and Ⅱ in fetal and adult bovine serum. Identification, primary structures, and immunological cross-reactivities. J. Biol. Chem. 261:569-575.

Hossenlopp, P., D. Seurin, B. Segovia-Quinson, S. Hardouin and M. Binoux. 1986. Analysis of serum insulin-like growth factor binding proteins using Western blotting: use of the method for titration of the binding proteins and competitive binding studies. Anal. Biochem. 154:138-143.

Lane, A. G. and J. R. Campbell. 1969. Relationship of hematocrit values to selected physiological conditions in dairy cattle. J. Anim. Sci. 28:508-511.

Leahy, J. L. and K. M. Vandekerkhove. 1990. Insulin-like growth factor-Ⅰ at physiological concentrations is a potent inhibitor of insulin secretion. Endocrinology 126:1593-1598.

Lee, C. Y., F. W. Bazer, T. D. Etherton and F. A. Simmen. 1991. Ontogeny of insulin-like growth factors (IGF-Ⅰ and IGF-Ⅱ) and IGF-binding proteins in porcine serum during fetal and postnatal development. Endocrinology 128:2336-2344.

Lee, C. Y. and D. M. Henricks. 1990. Comparisons of various acidic treatments of bovine serum on insulin-like growth factor-Ⅰ immunoreactivity and binding activity. J. Endocrinol. 127:139-148.

Lewis, D. S. and E. M. Jackson. 1990. Feeding influences plasma cortisol levels during preweaning life in baboons. Am. J. Physiol. 259:R157-R162.

Malven, P. V., H. H. Head and R. J. Collier. 1987. Secretion and mammary uptake of prolactin in dariy cows during lactogenesis. J. Dairy Sci. 70:2241-2253.

Malven, P. V., H. H. Head, R. J. Collier and F. C. Buonomo. 1987. Periparturient changes in secretion and mammary uptake of insulin and in concentrations of insulin and insulin-like growth factors in milk of dairy cows. J. Dairy Sci. 70:2254-2265.

Mirand, P. P., L. Mosoni, D. Levieux, D. Attaix, G. Bayle and Y. Bonnet. 1990. Effect of colostrum feeding on protein metabolism in the small intestine of newborn lambs. Biol. Neonate 57:30-36.

Peaker, M. and M. C. Neville. 1991. Hormones in milk: chemical signals to the offspring? J. Endocrinol. 131:1-3.

Philipps, A. F., B. Persson, K. Hall, M. Lake, A. Skottner, T. Sanengen and V. R. Sara. 1988. The effects of biosynthetic insulin-like growth factor-Ⅰ supplementation on somatic growth, maturation, and erythropoiesis on the neonatal rat. Pediatr. Res. 23:298-305.

Phillis, J. W. 1976. Veterinary Physiology. W. B. Saunders Company, Philadelphia, PA, USA.

SAS User's Guide: Statistics. 1986. SAS Inst., Inc., Cary, North Carolina, USA.

Schober, D. A., F. A. Simmen, D. L. Hadsell and C. R. Baumrucker. 1990. Perinatal expression of type I IGF receptors in porcine small intestine. Endocrinology 126:1125-1132.

Shing, Y. W. and M. Klagsbrun. 1984. Human and bovine milk contain different sets of growth factors. Endocrinology 115:273-282.

Shing, Y. W. and M. Klagsbrun. 1987. Purification and characterization of a bovine colostrum-derived growth factor. Mol. Endocrinol. 1:335-338.

Simmen, F. A. and K. E. McClure. 1987. Differential expression in ovine colostrum and milk of a mitogenic factor for embryonic (AKR-2B) fibroblasts. J. Anim. Sci. 65 (Suppl 1):241 (abstract).

Simmen, F. A., R. C. M. Simmen and G. Reinhart. 1988. Maternal and neonatal somatomedin C/insulin-like growth factor-Ⅰ (IGF-Ⅰ) and IGF binding proteins during early lactation in the pig. Dev. Biol. 130: 16-27.

Smith, V. R. 1959. Physiology of Lactation. Iowa State University Press, Ames, IA, USA.

Trenkle, A. 1970. Plasma levels of growth hormone, insulin and plasma protein-bound iodine in finishing cattle. J. Anim. Sci. 31:389-393.

Young, G. P., T. M. Taranto, H. A. Jonas, A. J. Cox, A. Hogg and G. A. Werther. 1990. Insulin-like growth factors and the developing and mature rat small intestine: receptors and biological actions. Digestion 46: (Suppl 2), 240-252.

Zapf, Z., C. Hauri, M. Waldvogel and E. R. Froesch. 1986. Acute metabolic effects and half-lives of intravenously administered insulin-like growth factors Ⅰ and Ⅱ in normal and hypophysectomized rats. J. Clin. Invest. 77:1768-1775.