Effect of Withholding Macromolecules on the Duration of Intestinal Permeability to Colostral IgG in Foals

Sharanne L. Raidal, BVSc, PhD; Claudia McTaggart, BSc; John V. Yovich, BVMS, PhD, DipACVS; and John Penhale, BVSc, PhD

Delayed ingestion of macromolecules for 12 hours had no effect on the subsequent absorption of colostral IgG in neonatal foals, suggesting that macromolecular uptake does not mediate gut closure in this species. Factors present in colostrum may accelerate closure. Authors’ Address: Division of Veterinary and Biomedical Sciences, Murdoch University, South Street, Murdoch, Western Australia, 6150. © 2000 AAEP.

Introduction

The failure of passive immune transfer from mare to foal is the most commonly recognized immune deficiency in horses and may predispose affected foals to septic disease in the neonatal period. Colostrum is the best source of passive immunity for the neonatal foal because it contains a high concentration of immunoglobulins (IgG), as well as substances which exert a local protective effect on the intestine and factors other than immunoglobulins which may enhance systemic immunity. Proteins and macromolecules, such as immunoglobulins, are absorbed from colostrum nonselectively and without significant digestion during a finite period after birth. Maximum absorption occurs soon after birth and progressively declines during the first hours of life until, by 24 hr, absorption no longer occurs. It has been widely recommended that colostrum should be consumed by foals within 12 hr of birth. As absorption may be dramatically reduced by 6 hr, it has further been suggested that colostrum feeding should begin within 2 hr of birth for optimal uptake. However, good quality colostrum is not always available for administration within this time.

In some species, the opportunity for intestinal absorption of immunoglobulins can be prolonged if the ingestion of large molecules can be delayed. Absorptive capacity was retained for up to 106 hr after birth in piglets not fed milk products, although the efficiency of absorption decreased with time. The administration of a 5% glucose and electrolyte solution to neonatal piglets resulted in retention of the ability to absorb macromolecules at 24–36 hr. The ability to absorb colostral proteins has also been preserved for 48–54 hr in starved lambs. Conversely, in calves, the period of permeability cannot be prolonged by withholding large molecules.

The effect of the ingestion of large molecules on intestinal closure to immune protein absorption has not been investigated in the horse. If the absorption of macromolecules intrinsically mediates clo-
sure when the finite ability of intestinal cells for uptake has been exceeded, closure could be delayed by withholding such molecules. This then would prolong the period during which colostral immunoglobulins could be absorbed and reduce the incidence of failure of passive transfer of immunity.

However, colostrum may exert a controlling influence on the type of bacteria that establish in the digestive tract of the neonatal foal.9 Delayed ingestion of colostrum may render the foal more susceptible to infection if such treatment permitted the establishment of pathogenic bacteria within the neonatal intestine or if the non-selective absorptive process permitted passage of bacteria across the intestinal epithelium.9 Rather than enhancing the development of septic disease.

Increased understanding of the mechanism of intestinal closure to the absorption of immunoglobulins is, therefore, important for decisions on management of neonatal foals. The current study aimed to determine whether macromolecular absorption intrinsically mediates closure of intestinal cells to immunoglobulin uptake in foals. We evaluated the hypothesis that immunoglobulin absorption would be better in foals administered a glucose-electrolyte solution for 12 hr after birth than would be evident in foals administered a milk substitute.

Materials and Methods

Experimental Animals

Eight foals of mixed breeding were available for inclusion in the current study. Parturition was attended for all foals. Mares and foals were allowed to bond in the immediate postpartum period and foals were observed for normal neonatal behaviour. Foals were randomly assigned into two treatment groups, each of four foals. Group 1 (electrolyte fed, EF) foals were prevented from suckling the mare and were maintained on commercial glucose and electrolyte replacer (Lectadea) for 12 hours after birth. Group 2 (milk fed, MF) foals were prevented from suckling the mare as for Group 1 (EF) foals, but were maintained on commercial milk replacer (Di-Vetelact). Glucose-electrolyte solution or milk replacer, according to the group assigned, was offered to each foal from within 30 to 60 min after birth and thereafter on an ad lib basis until 12 hr postpartum.

Mares were milked for colostrum every 30 to 60 min during the first 18 hr postpartum. After 12 hr, foals were offered stored colostrum by bottle on an ad lib basis. Foals were stomach tubed if they failed to voluntarily suckle colostrum, to ensure an appropriate volume (approximately 3 l) of colostrum was consumed by 18 hr postpartum. Colostrum from the foal’s dam was fed to each foal, that collected first (and therefore having the highest IgG concentration) was fed first. When greater than 3.5 l of colostrum was collected from any mare, additional colostrum was stored frozen to supplement the volume of colostrum available to foals from mares producing less than 3 l of colostrum. The volume of colostrum ingested by each foal was recorded. Aliquots of colostrum were stored frozen at −20°C for determination of IgG concentration by single radial immunodiffusion (SRID).

Foals were monitored by physical examination and observation. None experienced disease complications in the experimental period. Venous blood samples were collected at 0, 12, 24, and 36 hr postpartum for hematology and IgG determination.

IgG Quantitation

 Serum samples collected at 0 and 12 hr (prior to the ingestion of colostrum) and 36 hr postpartum (18 hr after ingestion of colostrum) were stored at −20°C for determination of IgG status by SRID at the completion of the experiment. Stored colostrum samples were diluted, to permit accurate determination of their greater IgG concentration, and similarly assayed. SRID was performed according to a previously published technique.10

Efficiency of IgG Absorption

The expected IgG concentration was calculated for each foal by determining the amount of IgG ingested and dividing by plasma volume (calculated as 95 mL/kg).11 This value was then corrected to allow for equilibration between the intra- and extracellular spaces.12 The measured IgG concentration was compared to the expected IgG concentration to determine the efficiency of absorption (measured IgG concentration:expected IgG concentration), expressed as a percentage.

Statistics

The effect of withholding colostrum on the efficiency of IgG absorption was determined by comparing results from Group 1 (EF) foals with those of Group 2 (MF) foals by unpaired t-test. Results were considered significant for p < 0.05. The possible effect of foal body weight, plasma volume, volume of colostrum ingested and the amount of IgG ingested on the efficiency of absorption were evaluated by simple linear regression analysis.

Results

All foals remained well during the experimental period. One foal (Group 1) developed acute septic arthritis of the tarsocural joint at 40 hr postpartum, but responded well to plasma transfusion, systemic antibiotics, and lavage of the affected joint.

Group 1 foals consumed, on average, 4.3 l of glucose-electrolyte solution during the first 12 hr postpartum. Group 2 foals consumed a smaller volume of milk replacer (average 3.3 l). There was no significant difference in the volume of colostrum consumed by each group (Group 1, 2.9 l; Group 2, 2.9 l, p = 0.83). This volume was consumed within 7 hr of being offered (i.e., 12–19 hr postpartum). No foal...
consumed this entire volume voluntarily—all received some colostrum by stomach tube. Repeat stomach tubing or indwelling nasogastric tubing was well tolerated.

Despite the relatively uniform volume of colostrum ingested, colostral quality and hence IgG content varied dramatically, resulting in a very variable dose of maternal IgG received by each foal. Despite this individual variation, there was no significant difference between groups in the amount of IgG ingested (p = 0.91).

Mean efficiency of absorption for both groups was 56.9% of administered colostral IgG. Hence most foals absorbed approximately 30% of ingested IgG into the intravascular fluid compartment, although again there was considerable individual variation. There was no significant difference between the two groups (p = 0.92).

There was no correlation between the efficiency of absorption and body weight (r^2 = 4.0%), plasma volume (r^2 = 4.1%), volume of colostrum ingested (r^2 = 1.9%) or amount of IgG ingested (r^2 = 11%).

Discussion

The current study demonstrated the mean efficiency of absorption of colostral IgG to be approximately 57%. Previous studies, based on the absorption of PVP.60, a macromolecule of similar size to IgG, reported a mean efficiency of absorption of approximately 22% at 3 hr postpartum in colostrum fed foals. This earlier study did not allow for equilibration with the extravascular space; hence the calculated absorption of PVP.60 from the small intestine was approximately 44%. The efficiency of absorption of immunoglobulins or other macromolecules by equine neonates has not been further assessed, however, similar findings have been reported in calves (46% for IgG1 and 49% for IgG2).13

The dose of IgG administered to each foal in the current study was consumed over a 7-hr period between 12 and 19 hr after birth. The results generated hence represent a mean value for this period, although again there was considerable individual variation. The value obtained in the current study was much higher than the value of 20% (corrected for equilibration between intravascular and extravascular spaces) obtained previously at 12 hours postpartum. This suggests that closure was delayed in colostrum deprived foals in the current study and supports the contention that factors present in colostrum may mediate closure.

There was no difference in the efficiency of IgG absorption evident between the two treatment groups in the current study, suggesting that the administration of macromolecules (contained in milk replacer, but not in glucose-electrolyte solutions) did not influence the closure process. This finding is consistent with similar observations in calves, but contrasts the situation in lambs and piglets. In the foal, therefore, it would appear that closure is not mediated intrinsically due to a finite capacity for macromolecular absorption by small intestinal epithelial cells.

The individual variation in efficiency of absorption, and in colostral IgG concentration, observed in the current study is consistent with clinical observations of erratic colostral transfer of immunoglobulins to foals and supports routine testing of 24-hr serum IgG levels to document satisfactory passive immune status. The amount and concentration of IgG administered and the volume of colostrum consumed did not influence the efficiency of IgG absorption.

One foal in the current study (foal number 1, Group 1) developed septic arthritis shortly after the completion of the experimental protocol. *Actinobacillus equuli* was isolated from the affected tarsocrural joint. *A. equuli* is a common pathogen in equine neonatal septic disease and may be acquired in utero or soon after birth. Because these organisms cannot survive in the environment for long periods, the mare is the usual source of infection. The possible contribution of delayed intestinal closure to the development of neonatal septic disease, as has been suggested, cannot be commented on in this instance or for other foals in the present study. As factors present in colostrum appear to facilitate closure, the administration of colostrum in the immediate postpartum period may reduce susceptibility to sepsis by preventing bacterial translocation across the intestine. As diarrhea has been identified as the most common localizing sign in septicemic foals in a number of studies, further evaluation of the effect of colostral ingestion on bacterial colonisation of and/or invasion across the neonatal intestine is warranted.

Withholding the administration of macromolecules did not delay closure of the equine neonatal small intestine to immunoglobulin absorption. The choice of fluid administered to foals when colostrum is not immediately available is therefore unlikely to influence subsequent passive immune status, as measured by serum IgG concentration. The measured IgG concentration obtained by foals in both groups in the present study was “inadequate” (less than 8 g/l) for 3 foals in each group. This suggests that there is no opportunity for prolongation of the time when colostrum can be supplied to neonatal foals and that colostrum should ideally be provided to foals within 12 hr postpartum. However, if colostrum administration is delayed for 12–18 hr, the results of the current study suggest that approximately half the administered IgG would be absorbed. In the current study, delayed administration of colostrum resulted in serum IgG concentrations between 4–8 g/l (mean for both groups was 6.7 g/l), which may be adequate for healthy foals in well managed environments.

Funding for these studies was provided by the Rural Industries Research and Development Corpo-
ration. Dr Raidal is supported by the National Australia Bank.

References

*Beecham Veterinary Products, Dandenong, Victoria.
*Sharpe Laboratories, Artarmon, New South Wales.