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NEONATAL FOALS AND HYPERIMMUNIZED EGG PROTEIN - A VIABLE THERAPY ?

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Viewpoint

Foals are immunocompetent at birth, but they are immunologically "naive" and rely on colostrum and non-specific defence mechanisms for their first two months of life. Foaling itself causes a decrease in immune function because the fetal glucocorticoids, produced at the time of parturition, depress immune function. Foals do not receive a maternal transfer of antibodies; colostrum is the only way that foals obtain immunoglobulins. Colostral protein is not broken down in the gastrointestinal tract because colostrum contains a trypsin inhibitor and, there is very little proteolysis in the gastrointestinal tract of the newborn. Colostral proteins are absorbed intact by specialized enterocytes through the process of pinocytosis. The absorption of entire immunoglobulins in foals decreases after the first six hours of life and essentially stopps by 24 to 36 hours after birth.

Failure of passive transfer (FPT) is the term used when foals do not receive adequate immunoglobulins from colostrum. In the newborn, the prevalence of FPT is anywhere from 3-25% depending upon the farm management system used.[1] FPT is common in immature, premature and dysmature foals (less than 320 d gestation) and it is usually assessed within 18-24 hours after birth. This is about the time that enterocytes change their pattern of absorption. FPT is assessed by measuring IgG levels and if this is less than 800 mg/dL at 18 hours or 200 mg/dl at 8-12 hours the foal is considered to have FPT.[1]

The normal healthy foal suckles seven times per hour and consumes 155mL/kg/day of milk or 20-25% of its body weight. Even when suckling in an apparently normal manner, they can still have FPT or be hypogammaglobulinemic.[2] The amount and quality of colostrum a newborn foal ingests is really not known. It is often inadequate and difficult to assess within a time frame (12 hours) that permits adequate supplementation, either by IV or oral hyperimmune plasma, with frozen colostrum or bovine colostral supplements.

FPT is an important component of neonatal foal mortality and morbidity. It renders the newborn animal vulnerable to a multitude of respiratory and enteric infections. The most important bacterial and viral agents involved in foal mortality/morbidity are: *E. coli, Actinobacillus, Pasteurella, Klebsiella, Pseudomonas, Streptococcus, Salmonella, Staphylococcus, Bordetella*, Equine herpes virus, Influenza, *Rotavirus, Coronavirus, Clostridia, Campylobacter*, and *Rhodococcus*.[3,4]

The treatment, often in an intensive care unit, for neonatal foal infections includes oral and intravenous fluids, immunoglobulins, antibiotics, intestinal protectants, and NSAIDS. These treatments can be extremely expensive. As with most diseases, it is much better for the health of the foal, future performance and for economic reasons, to practice prevention rather than having to treat the disease.

In one study in a mare herd in Western Canada (1994), the incidence of neonatal foal mortality was 22%, of 334 foals born, 74 died before they reached 10 days of age, 74% of these deaths were within 48 hours of birth, 26% were due to septicemia, and 27% were due to starvation and/or exposure.[5] In another study in Texas, of 2,468 foals born, 116 deaths occurred. These deaths were primarily due to pneumonia and/or septicemia; the highest risk period was within the first seven days of life. The practice of assessing passive immunity was significantly associated with decreased morbidity from septicemia and pneumonia.[6]

In 1998 The American National Health Monitoring System received statistics from 28 States regarding the mortality and morbidity of foals. There were 7,320 foals born on the farms that were a part of the study, and 120 died within the first two days of life. The management practices that seemed to increase the mortality rate within the first two days of life were: a lack of testing for the failure of passive transfer of immunity and the introduction of new residents on, or about the time of foaling (new disease introduction).[7] From these studies it is apparent that neonatal foals need to receive an adequate quantity of high quality immunoglobulins, and that testing for FPT and the immediate treatment of FPT is essential. The oral administration of hyperimmunized egg protein is a relatively novel approach for the prevention of enteric and respiratory infections in neonatal animals.

Hyperimmune Egg Process and Efficacy

Immunizing hens with inactivated multivalent vaccines results in the production of eggs that contain antibodies against the antigens for which they are vaccinated, along with physiologically active, small molecular weight "cofactors" that are reported to have some immunoregulatory function.[8-18] The specific antibodies produced appear approximately 20 days after vaccination of the hen, reach a plateau at around 30 days, and remain high until at least 81 days after vaccination.[19,20] The hens passively transfer protection to their young by secreting antibodies and immune co-factors into their eggs. The transfer of avian antibodies, from the hen's serum to the egg, and from the egg to the chick, is analogous to crossplacental transfer of IgG from the mammalian mother to its offspring. Both eggs and milk contain naturally occurring antibodies. However, the concentration of antibodies in avian eggs is significantly higher than those in serum or milk.[21-24] This is because birds have only one opportunity to transfer all of the components necessary for the survival of their offspring. Therefore the egg serves as a concentrated source of immune products.

Hens are highly efficient producers of polyclonal antibodies, producing 20g of yolk antibodies (IgY) per year.[25] Due to evolutionary differences, chicken IgY will react with more epitopes on a mammalian antigen which will produce an amplification of the signal.[26] The antibodies have biochemical properties which make them attractive for oral immunotherapy: they do not activate mammalian complement, they do not interact with mammalian Fc receptors which could mediate an inflammatory response and they do not interfere with maternal antibodies.[27] Chicken antibodies appear to be acid and heat resistant.[25] It has been found that antibodies in a rich lipoprotein solution such as egg yolk, are more resistant to degradation than normal globulin fractions or normal antibodies.[28] In neonatal pigs, IgY is absorbed intact as efficiently as colostral antibodies.[29] Therefore the oral administration of IgY antibodies is an attractive approach for the prevention of enteric and respiratory infections in neonatal animals.

There are many challenge studies published that used hyperimmunized egg yolk antibodies in the treatment of *E. coli* diarrhea and that demonstrated a decrease in the shedding of *E.coli* in piglets, calves and mice.[30-37] There are also a number of studies in which egg-derived antibodies were successfully used for the treatment of salmonella, bovine rotavirus and coronavirus infections in calves and mice.[38-41] In all of the studies in which weight gain was measured, the treated groups demonstrated a higher weight gain than the control groups. Most of the controls used non-hyperimmunized whole egg products. In a recent study at a Kentucky horse farm, where hyperimmunized whole egg was used, the authors attributed the virtual elimination of neonatal foal diarrhea problems to the use of hyperimmunized egg protein.[42]

Conclusion

Neonatal foals are most susceptible to disease during the first two days of life. It is imperative that they receive adequate amounts of high quality immunoglobulins either from colostrum or by other means. The administration of hyperimmunized whole egg protein (IgY) appears to be a convenient and relatively successful insurance against the problems that the failure of passive transfer may confer upon the neonate.

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