Failure of Passive Transfer in Calves

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INTRODUCTION

Roughly 35% of dairy calves suffer from failure of passive transfer (FPT), causing a major economic impact for livestock producers.[9] FPT is also detected in beef calves but less so when compared to dairy calves.[9] In a national survey, results of heifer management practices showed mortality rates for calves with low antibody levels (less than 10 grams per liter) were more than twice of calves with higher levels.[9]

The cow has a syndesmochorial placenta which creates a syncytium among the fetal trophectoderm and the maternal endometrium.[9] This particular type of placenta divides the maternal and fetal blood supplies and inhibits the transmission of immunoglobulins (Ig) from the dam to the fetus in utero.[9] Consequently, the dam provides all of the protection needed before birth so calves are essentially born agammaglobulinemic.[6,2,9] Hence why absorption and ingestion of sufficient amounts of colostral immunoglobulins are essential for instituting passive immunity to maintain health and prevent infection.[6] Therefore, it is extremely critical to achieve the adequate amount of immunoglobulins by passive transfer via colostrum.[6] The transfer of immunoglobulins from the dam to the calf via colostrum is termed passive immunity.[6] Colostrum, the first milk produced by the dam, ideally should be ingested within the first few hours of birth.[6] If calves do not absorb sufficient immunoglobulins either through delayed or inadequate colostrum intake or poor quality colostrum intake, we designate that "Failure of Passive Transfer".[1,6]

Through the first twenty-four hours of life, calves can absorb whole antibodies via their small intestinal wall.[8] These antibodies are then distributed in the calves' bloodstream to aid in fighting off infections during the first weeks of life.[7,10] However, it is crucial that calves ingest and absorb a satisfactory amount of colostrum soon thereafter birth.[1] Ideally, calves need to be fed colostrum within the first hour of birth.[7,10] The neonates' ability to absorb IgG starts to diminish dramatically after four to six hours.[7,10] It is recommended that a volume of 3 to 4 L of colostrum should be fed within two hours and ideally no later than six hours after birth.[7,10] The colostrum should contain at least 50 g/L of immunoglobulins.[7,10] The greatest level of Ig absorbed is dependent on how quickly the calf is fed or suckles after birth since the intestinal tract only briefly allows absorption of immunoglobulins.[7,10] If a calf does not ingest a suitable amount of colostrum (Ig levels should be 1000 mg/dl), the calf will be at a higher risk of acquiring an infection and subsequent poor performance will ensue.[1]

To ensure the appropriate amount of immune protection in calves has been met, blood samples from calves at 24 to 48 hours of age can be acquired and serum total protein can be measured to quickly assess IgG levels in calves.[1] More than 10g/L of Ig have been established for immunoglobulin levels needed for successful passive transfer.[10] Total protein in blood is exceedingly correlated with immunoglobulin levels, thus it is directly related to effective absorption of colostrum.[1] If calves have received plentiful high quality colostrum, serum total protein will be measured at 5.5 grams per deciliter (g/dl) or greater.[1] If total protein is measured between 5.0 and 5.5 g/dl, there is a minimal risk for morbidity and mortality.[1] When total serum protein levels are measured less than 5.0 g/dl, the calf is considered to be at a much greater risk for subsequent infections and health problems.[1] Identifying herd problems of defective colostral absorption may help facilitate to improve future management efforts.[1]

HISTORY AND PRESENTATION

D053, an approximately 12-hour old Angus and Hereford cross heifer calf, presented to MSU-CVM Food Animal Department for non-ambulation and laterally recumbent. D053 was born on the early morning of March 11, 2016 at the MAFES Prairie Branch in Prairie, Mississippi. No dystocia or birthing complications were observed. The owner stated that the heifer calf was lethargic and unable to stand at 7:30 am. A suckle response was present, and the calf was fed frozen bovine colostrum. At 1:30 pm, she was depressed, laterally recumbent and referred to MSU-CVM for further assessment. Prior to presentation she received 1 cc of B vitamin complex intramuscular in the rump and approximately 1.5 Liters of colostrum total orally.

On presentation, D053 was severely depressed, laterally recumbent, and non-ambulatory. Her capillary refill time was prolonged with a CRT of 3 seconds and her mucous membranes were slightly tachy and light pink. She was estimated to be 5% dehydrated. Her vital parameters were as following: Temperature of 97.8 degrees Fahrenheit, pulse was 140 beats per minute, and respiratory rate of 60 breaths per minute. She weighed 27.3 kilograms and had a poor body condition score of 4 out of 9. Auscultation of her heart and lungs were within normal limits. She was unable to ambulate on her own due to her contracted tendons present on both forelimbs. Injected sclera bilaterally, a severe under bite, and a dome forehead were also all present upon presentation. A dried umbilicus was also present on physical examination, supporting an age older than 12 hours as reported by owner. All other physical exam findings were unremarkable.

Diagnostics performed upon presentation were the following: glucose of 42 mg/dl; total protein of 4.9 g/dl, and packed cell volume of 31%. Her jugular vein was aseptically prepped and a jugular catheter was placed. One Liter of LRS/2.5% Dextrose intravenously was given to correct dehydration and hypoglycemia. To correct the hypothermia, a Bair Hugger was used until she reached a temperature of 101 degrees Fahrenheit. A diagnosis of failure of passive transfer was made based on physical exam parameters suggesting the calf was at least 24 hours old and an inadequate total protein measurement.

Due to the degree of dehydration and concurring signs of septicemia, a 20ml/kg dose of Bovine Plasma was given intravenously after stabilization. Medications administered included 1.5 mL of Excenel subcutaneously every 24 hours (3/11/16- 3/15/16) and 0.75 ml of Banamine IV every 12 hours (3/11/16-3/12/16 to treat signs of septicemia. Milk was offered every 4 hours. D053 was administered 2 pints of milk via esophageal feeder on 3/12/16 due to prolonged anorexia and absent suckle reflex. Thereafter, she was offered milk every 4 hours until consumption of 12-25% was obtained. Splints were also placed on both forelimbs to treat limb contracture.

PATHOPHYSIOLOGY

Failure of passive transfer is not a disease, but instead a condition that can dispose the calf to infectious agents.[9] IgG1, which is derived from maternal serum IgG1, is the primary immunoglobulin in bovine colostrum.[9] Several weeks before parturition, immunoglobulins transport from the serum to the mammary where it reaches its peak approximately one to three days before parturition.[9] Facilitating concentration of IgG1 in the colostrum are receptors on the mammary alveolar epithelial cells.[9] At the beginning of lactation, the glandular epithelial cells terminate the expression of these receptors.[9] Soluble mediators, such as lactoferrin, and immunologically active cells are also transferred in addition to immunoglobulins via the colostrum.[9] In the past, it has been proven that decreased neutrophil function is present in calves that failed to absorb colostral lactoferrin.[9] This is suggestive that soluble mediators enhance the immunologic capabilities of the neonate when absorbed through the colostrum.[9] Many factors have alluded to having an effect on passive transfer in the calf.[9] Some of these factors include the age of the dam, the timing of colostrum ingestion, the immunoglobulin concentration of the colostrum ingested, and the method and volume of colostrum administration.[9] The presence and breed of the dam, practice of colostrum pooling, and the presence of respiratory acidosis in the calf also may influence passive transfer.[9]

During the initial 24-36 hours of life, the enterocyte's of the neonate have the exclusive ability to absorb protein macromolecules.[7,9] The enterocytes of the small intestine will non-selectively absorb a diversity of macromolecules, immunoglobulins included.[7,9] This is done by pinocytosis, which moves proteins into the epithelium.[7,9] Immunoglobulins are then transported across the cell into the lymphatics by another process known as exocytosis.[7,9] This is done through the thoracic duct, when immunoglobulins gain access to the circulatory system.[7,9] The non-selectivity of this path is confirmed with the increase of additional protein macromolecule concentrations and enzyme activities such as glutamyltransferase (GGT) after the consumption of colostrum.[7,9]

The termination of macromolecule absorption has been dubbed closure, and occurs at different times depending on the species.[7,9] For example, closure occurs at approximately 24 hours post-partum in calves, and may be extended to 36 hours if feeding is hindered.[7,9] Most likely a combination of exhaustion of pinocytotic capability and enterocyte replacement by a more mature population of gut epithelial cells is the root of what drives closure.[9] In addition to the maturation of intestinal cells, digestive enzymes being secreted may also contribute to lower immunoglobulin absorption by degrading immunoglobulin prior to absorption.[9] For a limited time during birth, and shortly thereafter, the secretion of digestive enzymes remains restricted to allow macromolecules to escape digestion.[9] Approximately 12 hours after birth, further enzyme secretion is apparent and thereby reduces the ability of IgG to reach the peripheral circulation without first being degraded.[9] Due to ongoing transport of immunoglobulins across the enterocytes, peak serum immunoglobulin concentrations are not seen until 32 hours postpartum.[9] Immunoglobulin transfer across the gut epithelium is optimal in the first 4 hours postpartum despite the length of time it takes for gut closure.[9] Immunoglobulin transfer begins to promptly wane after 12 hours postpartum.[9] Calves that have been fed earlier will have noticeably elevated serum IgG concentrations than those fed at a later time, even though similar volumes and concentrations and of colostrum were ingested.[9]

Although the method of colostrum administration is imperative, the colostral immunoglobulin volume and concentration of colostrum consumed by the calf is even more crucial.[9] It is recommended that at least three to four liters of colostrum should be ingested as soon as possible and at the very least before six hours of birth for adequate passive transfer.[10] Maternal colostrum should contain at least a minimum of 50 g/L of immunoglobulins to be deemed adequate.[10] If colostrum contains <22 mg/ml of IgG it is ranked poor, colostrum is considered moderate if it is between 22 and 50 mg/ml, and then ranked excellent if the level is >50 mg/ml of IgG.[10]

Essential influences on neonatal survival include ensuring the delivery of good-quality colostrum by the dam, along with sufficient colostrum intake by the neonate.[9] Influences that might compromise colostrum volume, quality, and delivery to the neonate should be acknowledged.[2] These influences include maternal factors such as premature lactation, disease during gestation, or maiden dam.[2] Delivery factors such as abnormal parturition or placental abnormalities could also influence colostrum.[2] Neonatal factors such as dymaturity, prematurity, multiple birth, maternal rejection, or any other condition limiting neonatal strength and mobility also serve as negative influences.[2]

Effective Ig intake and absorption in beef cattle in conventional production environments is easily succeeded.[4] Within two hours of giving birth, calves should be up and nursing.[4] In Calf D053 case, she was failure of passive transfer due to both of her front legs being contracted leading to her inability to walk and consume colostrum like she should. If there are any concerns a calf is not adequately ingesting colostrum, it is instructed to observe the pair to make sure that the calf knows how or can nurse.[4] In the instance that the calf needs assistance being fed, it must have two quarts of colostrum by six hours of age, and an additional two quarts by twelve hours of age.[4] Beef calves are left to nurse the dam whereas in dairy calves natural suckling by the calves does not take place or is essentially ineffective.[4] To make sure that the newborn does indeed absorb adequate antibodies, numerous producers remove the dairy calf from the cow at birth, and force feed the calf immediately. [4]

DIAGNOSTIC APPROACH AND CONSIDERATION

Diagnosis of FPT can be suspected based on the patient's signalment and history, clinical presentation and signs, and ante mortem tests.[9] Numerous number of blood tests have been established to assess passive transfer status in calves. [5,9]

Currently, the only tests that measure serum IgG concentration are the radial immunodiffusion, and enzyme-linked immunosorbent assay (ELISA).[5,9] All other tests, such as serum total solids by refractometry, the sodium sulfite turbidity test, the zinc sulfate turbidity test, the serum GGT activity, and the whole-blood glutaraldehyde gelation, estimate serum IgG concentration based on concentration of total globulins or alternative proteins whose passive transfer is mathematically comparable to that of IgG. [5,9]

An excellent test for herd monitoring, also commonly used by practitioners, is serum protein measurement by refractometer.[5] It provides a reasonably accurate assessment of passive transfer status in calves with a test endpoint of greater than 5.5 g/dL.[5] A serum total protein of less than 5.2 g/dL correlates with FPT.[5] A serum total protein between 5.2-5.5 g/dL is considered marginal passive transfer. It is important to remember that total protein measured by refractometer should only be measured up to seven days of age due to interference of endogenous IgG and that a dehydrated calf can cause a false positive.[5]

The gold standard to determine Ig levels, is radial immunodiffusion (RID).[5] RID directly measures the Ig concentration in the serum, but is time consuming (at least 24 hours) and expensvie.[5] Due to the tests drawbacks, it is not used for routine testing in diagnostic laboratories and instead is used most commonly in research settings.[5] A result of 1,000 mg/dl or higher is deemed normal.[5]

Originally introduced as a way to detect hypergammaglobulinemia in adult cattle, a modified version of the whole-blood glutaraldehyde coagulation test used serum as opposed to whole blood, eradicating the potential interaction of fibrinogen.[5] After five minutes, a clot formation is demonstrative of adequate passive transfer.[5] A previous study that looked at the test performance of 242 calves was deemed inadequate for routine use.[5]

There have been several tests constructed to measure Ig levels indirectly, one of which involves the precipitation of Ig using solutions of metal salts.[5] In turn, this causes turbidity, which will be assessed either visually or by colorimeter, and giving a result in units of turbidity.[5] Tests using sodium sulphite and zinc sulphate are examples of such tests.[5]

When looking for a substitute for direct and indirect measurements of Ig levels, gamma-glutamyltransferase (GGT) is present in colostrum and its concentration in neonatal serum rises dramatically in line with the absorption of colostrum constituents.[5] Studies in the past have described how elevated blood GGT levels in the first few days post-partum are indicators of absorption from colostrum.[5] A test of this nature could be used less than eight days of age in beef calves and up to ten days of age in dairy calves.[5] Although GGT levels correlate moderately with serum IgG concentrations, it does not directly measure IgG therefore it should not be used as a sole indicator of passive transfer.[5]

Additional tests which have been suggested to evaluate Ig concentrations include a gluteraldehyde coagulation test and a commercially accessible latex agglutination test. [4] Serum electrophoresis can be also be used.[4]

TREATMENT AND MANAGEMENT

The decision to treat a calf with FPT should be determined on multiple factors including age, clinical condition, surrounding environment, value to the owner, and the ability to collect and administer plasma or whole blood.[9] Preferably all calves should be evaluated for FPT within the first 12 to 24 hours after birth and then at least one more time within the first days of life.[5] A colostrometer, which measures the specific gravity of colostrum, can be used to gauge the immunoglobulins levels in colostrum.[5] False positives can occur, but a specific gravity of 1.050 is correlated with high quality colostrum.[5] Therefore, use of the Brix refractometer is recommended due to the absence of confounders such as temperature, fat, and other solids. Reading of 22% on the Brix refractometer correlates with IgG of 50 g/L. Good colostrum management is a key factor in success of healthy calves.[8] Good colostrum comes from a cow that is healthy, vaccinated, proper udder prep, and milked within four hours of calving.[8] Guidelines to follow for colostrum management include high quality colostrum indicated by having more than 50 g/L of IgG, less than 100,000 colony forming units/ml, and approximately 4 quarts or 10% of the calf's body weight given orally in less than six hours after birth. [8]

Natural suckling is a common route of colostrum ingestion in beef breeds.[5] Beef calves that have failed to rise and nurse within 2 hours should be targeted for assessment and colostrum administration. The calf should also be assessed and inspected for congenital problems that could potentially inhibit the ability of the calf to stand or nurse effectively.[2] For example, signs of prematurity, musculoskeletal abnormalities, and a cleft palate.[2] Bottle feeding, which is more common in dairy breeds, should be given a minimum of 2 Liters by 6 hours of age and then another subsequent 2 L by 12 hours after birth.[5] Esophageal feeder, also common in dairy breeds, which administer 3 to 4 L per 45 kg weight habitually result in the least number of FPT calves.[5]

Ideally the best and most cost effective treatment for FPT should be constituted within the first 12 hours of life with high quality colostrum from a cow (2-4 liters) given orally.[5] Since several cases are discovered after gut closure, treatment with commercially available plasma (20 ml/kg IV) is recommended for treatment.[5] A whole blood transfusion (1-3 liters) from the dam can also be done on very valued calf.[5] Due to the substantial number of blood types present in cattle, whole blood transfusion reactions are deemed rare and cross-matching is not needed for most cases.[5] While not commonly practiced, plasma or whole blood can be administered via intraperitoneal (IP) route in the left paralumbar fossa.[5] Colostrum replacers can also be utilized.[5] Colostrum replacers are bovine serum based products that comprise at minimum 150g of IgG per liter plus protein, vitamins, fat, and minerals.[5] Colostrum replacers are considered better than using poor quality colostrum and are also labeled for the use when colostrum is not obtainable.[5] Colostrum supplements can also be used to supplement low quality colostrum but should not be considered as a replacement for colostrum since it cannot raise the IgG levels above 10 mg/ml.[5] Colostrum supplements can be used when closure has occurred to provide some protection at the level of the gut lumen.[9]

Reducing potential bacterial exposure in known failure of passive transfer calves should be a minimum in management practice.[8] Housing pens, feeding equipment, and feed should be cleaned and disinfected to reduce the pathogen load.[8] Prophylactic antibiotics can be given to at high risk calves but it is imperative to remember that antimicrobials will not nullify the effects of a high pathogen burden.[9]

Calves with FPT do have an increased susceptibility of acquiring septicemia and infections.[9] It is important to keep in mind though that not every untreated FPT will become unwell.[9] Although calves suffering FPT are at a much greater risk to succumbing to infections, they can survive if they are in housed in a clean environment which in turn reduces their exposure to potentially infectious pathogens.[1,8]

EXPECTED OUTCOME AND PROGNOSIS

A neonate's immunoglobulin concentrations are based on statistical analysis of substantial populations.[9] There are several components that interact with the correlation amount of passively acquired immunoglobulin to determine that a disease has developed.[9] Components include, but are not limited to management, environment hygiene, infection pressure, virulence of infectious organisms, and antibody specificity.[9] In colostrum-deprived calves, the "clinical threshold dose" (level of exposure that results in disease) is much lower when compared to colostrum-fed calves.[8] Calves who have received enough high quality colostrum will showcase serum total protein at 5.5 grams per deciliter (g/dl) or greater.[8,9] If the total protein measures between 5.2 and 5.5 g/dl, there is a minimal risk for morbidity and mortality.[8,9] Altogether, serum protein levels that are less than 5.2 g/dl put the calf at an elevated risk for health problems.[8,9] Low serum immunoglobulin concentrations do not guarantee disease if the neonate lives in a clean environment and is not open to virulent organisms.[9] Furthermore, neonates with sufficient passive transfer can suffer from disease if placed in an unclean environment that exposes them to virulent organisms.[9] Examples of some of the complications that occur in result of passive transfer include scours, respiratory disease, and growth rate.[6]

CASE OUTCOME

During her hospitalization, Calf D053 was consuming 15% body weight daily of her dam's milk for the first four days. After the dam refusal, she was substituted with calf replacer orally every eight hours thereafter. She continued to improve while she was hospitalized with increased ambulation, and resolution of signs of septicemia and tendon contracture. On March 14, 2016 her total protein was measured at 6.1 mg/dl and a pack cell volume of 25%. Due to her severe under bite and dome forehead, Bovine Viral Diarrhea (BVD) was suspected. A BVD ear notch was taken and the result was negative. The splints placed on both forelimbs were removed on March 16, 2016 and slightly contracted tendons were still observed. Toe extensions were applied to facilitate her to ambulate on her own. Calf D053 was discharged on March 17, 2016 and it was instructed to continue to feed her calf replacer orally every 8 hours and house her in a clean environment to decrease pathogen exposure.

Calf D053 presented to MSU-CVM Food Animal Department on March 28, 2016 laterally recumbent with stargazing. An umbilical abscess and three swollen joints (carpus bilateral and left hock) were noted on physical exam. Due to poor prognosis, she was then humanely euthanized for suspected septicemia, septic arthritis, and bacterial meningitis. Necropsy was then performed and revealed a septic arthritis of carpus, locally extensive cranioventral bronchopneumonia, and a mild suppurative meningitis. Despite appropriate treatment of FPT in this case, environmental load and/or potential residual infection from the initial insult resulted in the demise of this calf.

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