PATHOBIOLGY OF ROTAVIRAL DIARRHOEA IN CALVES: A POTENT ZOONOTIC THREAT: A REVIEW

CHOUDHARY, M., 1 CHOUDHARY, B. K., 1 GHOSH, R. C., 2 GIRI, D. K. 2 AND NETTY, S. 2

ICAR-National Institute of Biotic Stress Management, Raipur 493 002 (Chhattigarh); 2 Chhattisgarh Kamdhenu Vishwavidyalaya, Durg 491 001. E-mail: chiyamum@gmail.com Cell: 09644095446

Received: July 12, 2017; Accepted: July 28, 2017

Abstract: Bovine rotaviruses (BRVs) are the major etiological agents of neonatal calf diarrhoea worldwide. They cause economic losses to the cattle industry because of calf mortality, retarded physical growth, and treatment costs. The majority of group A rotaviruses (GARs) are differentiated based on the origin of host species (human rotavirus, bovine rotavirus and equine rotavirus) although natural GAR cross-species infection and disease have been identified [1]. Recently, Gulati et al., 2007 reported very high prevalence of G10,P8[11] strains in diarrheic calves which accounted for 80 to 85% of the bovine isolates in some farms in different regions of India. Age old traditions, the extensive use of cattle waste as manure and firewood, and the close proximity of the majority of the Indian population with cattle appear to have played a facilitating role in the evolution and persistence of genotype G10,P[11] and G9,P[11] reassortant asymptomatic/symptomatic strains in newborn children in India. Strains that are reassortants between animal-human or animal-animal strains have also been reported for both humans and cattle in India. Transmission of animal rotaviruses to humans is believed to be rare and probably does not lead to clinical illness.

Key words: Rotaviral diarrhoea, Calves

INTRODUCTION

Neonatal diarrhoea is one of the major disease syndromes affecting calves in different countries and a cause of important economic losses [2]. However, the etiology of such infections is multifactorial, and calf diarrhoea can be attributed to infection with a single agent or multiple agents. Bovine rotaviruses (BRVs) are the major etiological agents of neonatal calf diarrhoea worldwide. They cause economic losses to the cattle industry because of calf mortality, retarded physical growth, and treatment costs. They have been shown to infect the young ones of other mammals and birds. In experimental infections in calves, rotavirus-associated diarrhoea is restricted to the first week of life, but under field conditions, rotaviruses are often isolated from diarrhoeic calves up to 8 weeks old [3]. Large numbers of rotavirus particles are excreted in faeces of diarrhoeic calves and are highly resistant to inactivation [4]. Thus, the main source of rotavirus in an outbreak is environmental contamination and the spread of infection can temporarily be broken by thorough cleaning and disinfection of the premises [5]. However, subclinically infected older calves and adult cows may play a role in the spread of infection to young calves as well as in the perpetuation of infection within a herd [6]. These rotaviruses are a potential reservoir for genetic exchange with human rotaviruses. There is evidence that animal rotaviruses can infect humans, either by direct transmission of the virus or by contributing one or several RNA
segments to reassortants with human strains. Strains that are reassortants between animal-human or animal-animal strains have also been reported for both humans and cattle in India. Age old traditions, the extensive use of cattle waste as manure and firewood and the close proximity of the majority of the Indian population with cattle appear to have played a facilitating role in the evolution and persistence of genotype of bovine origin reassortant asymptomatic/symptomatic strains in newborn children in India [5]. Rotavirus is a pathogen of livestock and cause economic loss to farmers because of costs of treatment associated with high morbidity and mortality rates.

Rotavirus is one of the main viral pathogens involved in calf scours, along with coronavirus. Rotavirus is particularly challenging, because antibiotics won’t help fight this viral infection. Once those management practices are in place, however, attaining high levels of antibody in the colostrums through the use of potent vaccines has proven effective in protecting newborn calves during the critical first weeks of life. Colostral antibody works within the intestine to block infection by bacteria and other viruses that cause neonatal scours.

**Etiology:** The Rotavirus comprises viruses that infect only vertebrates (birds and mammals). The rotavirus particles are non-enveloped and possess an icosahedral symmetry. Rotavirus a member of family Reoviridae, consists of 11 segments of double stranded RNA (dsRNA) and a triple layered protein shell comprising six structural proteins (VP1, VP2, VP3, VP4, VP6 and VP7). The rotaviruses have a common antigen – the protein VP6, which is present in the middle capsid called group antigen. The group antigenic determinants conferred by VP6 enable classifying the rotavirus into five species, also called rotavirus groups, namely: Group A rotavirus (RVA), Group B rotavirus (RVB), Group C rotavirus (RCV), Group D rotavirus (RVD) and Group E rotavirus E (RVE). There are three additional attempts of species: Group F rotavirus (RVF), Group G rotavirus (RVG) and Group H rotavirus (RVH). Recently, a new Group I rotavirus (RVI) was described in dogs. Based on antigenic differences in outer capsid proteins, group A rotaviruses have been classified into at least 20 different P (VP4) types and 14 G (VP7) types [8]. The most common G serotypes of group A rotaviruses affecting calves are G6 and G10. Three P serotypes have been identified in calves with diarrhea: P6 [1], P7 [5] and P8 [11]. Very high prevalence of G10, P8[11] strains in diarrheic calves accounted for 80 to 85% of the bovine isolates in some farms in different regions of India [9].

**Genetic recombination:** Mixed infections may also be due to genetic exchange. Eleven distinct gene segments can be exchanged when animals are infected by more than one rotavirus strain. This genetic reassortment results in progeny viruses, which can evade the host immune response and persist in a susceptible population. One problem with rotavirus genetic recombination is that the new strain may be particularly hard on a calf. In addition, it’s unlikely that a vaccine containing only one rotavirus isolate will offer effective protection against new strains. These rotaviruses are a potential reservoir for genetic exchange with human rotaviruses. There is evidence that animal rotaviruses can infect humans, either by direct transmission of the virus or by contributing one or several RNA segments to reassortants with human strains [10,11]. Due to its segmented genome, genetic reassortment may occur when at least two different RV-A strains infect a single cell, resulting in (i) new strains, (ii) characterization of more than one G or P-type in one sample, (iii) introduction of animal rotavirus genes in human rotaviruses (HuRV) populations and vice-versa. BoRV-A have been classified as G6, G8 or G10 genotypes, associated with either P[1], P[5] and/or P[11] and genotypes G6P[5], G6P[1] and G10P[11] are considered the most common ones. However, genotypes G1, G3, G5, G7, G11, G15 and P[7], P[14], P[17] and P[21] have also been described for BoRV-A samples, but with less frequently.

**Pathogenesis:** Calves become infected via the faecal-oral route. Virus is excreted into the environment after an incubation period that varies from 15 hours to five days. The virus invades the mature enterocytes of the villus tip of the small intestine. Replication outside the small intestine and systemic spread of the virus (viremia) are believed to be uncommon. Affected host cells are mature enterocytes lining the middle and upper end of the intestinal villi. Loss of the epithelial cells results in shortened villi, which become covered by immature cells arising from the villous crypts. The immature cells and the loss of surface area dramatically reduce the absorptive capacity of the gut and the secretion of normal digestive enzymes. Infections may result in decreased intestinal absorption of sodium, glucose and water; and decreased levels of intestinal lactase,
alkaline phosphatase and sucrase activity, that may lead to isotonic diarrhea. The NSP4 protein plays a crucial role in the development of diarrhea by demonstrating functions of enterotoxin [12]. Accumulation of carbohydrates in the intestinal lumen as well as malabsorption of nutrients and a concomitant inhibition of water absorption can lead to a malabsorptive component of diarrhea. The subsequent diarrhoea causes dehydration, acidosis and hypoglycaemia. In severe cases death may occur. Large amounts of viral particles are shed in diarrheal stools. Recent discoveries suggest that rotavirus infection can disseminate throughout the host body, leading to a systemic infection [13]. Neurological manifestations associated to rotavirus infection have been reported and occur in approximately 2 to 5% of cases, ranging from benign seizures to lethal encephalitis. Nonetheless, it is still not clear if the rotavirus remains active and replicating in extraintestinal sites, or if the virus is just passively transferred through the bloodstream.[14]. Together, these data suggest pathogenesis of rotaviruses can be more complex than currently thought.

Clinical Signs: Typical early signs include a reluctance to stand and suck, mild depression and salivation. Calves are often quite depressed, lose their appetite and there is an acute onset of diarrhoea. There is the passage of very watery diarrhea initially but later it becomes pasty and pale yellow to yellow/green faeces with infection spreading rapidly among young calves in the group. The calf rapidly becomes dehydrated and recumbent. The eyes are sunken and the skin becomes tight and inelastic. The abomasum and intestines are often distended with fluid and gas. Clinical signs range from mild to severe diarrhea which results in dehydration, depression, and sometimes death. The severity of the disease is often worse in calves co-infected with other enteropathogens. A high incidence of rotaviruses has been detected in scouring calves on both beef and dairy farms and ranches.

Pathology: The abomasum and intestines are often distended with fluid and gas. The eyes are sunken and the skin becomes tight and inelastic. Diarrhea can occur in the absence of histological changes in the intestine and, conversely, the histological changes can be asymptomatic. Histopathology of infected intestines shows villous atrophy and blunting due to death of the mature enterocytes and infiltration of lamina propria with mononuclear cells. Additionally, there is formation of sycytia or multinucleated cells by fusion of enterocytes on the surface of villi. Cell dysfunction and death results in a net secretion of intestinal fluid, hence the watery diarrhea. Subsequently there is repopulation of the villous tips with immature secretory cells (crypt hyperplasia). In surviving animals, villi return to normal in 3 to 4 weeks [15].

Diagnosis: Rapid and accurate detection of rotaviruses is important to prevent the spread of infection. Rotavirus is excreted in large numbers in the faeces and thus can be easily identified on electron microscopy of stool samples which is one of the most specific tests for diagnosis [16]. Direct EM examination of stools for rotavirus has a sensitivity of 80-90 per cent. Other methods like immunoelectroosmosphoresis and modified complement fixation test were developed, but they lacked sensitivity. Following this, many rapid and economical assays like latex agglutination (LA), reverse passive haemagglutination assay (RPHA), solid phase agglutination of coated erythrocytes (SPACE), enzyme immuno assay (EIA) and polyacrylamide gel electrophoresis (PAGE) were used for diagnosis. Of these, the most widely used methods currently are LA, ELISA and PAGE. ELISA using polyclonal sera may give false positive results and requires validation by confirmatory or blocking ELISA. However, specific ELISA assays based on monoclonal antibodies have been developed. ELISA is the most widely used method for the diagnosis of rotavirus infection in stool specimens [7]. The detection of rotavirus by polyacrylamide gel electrophoresis followed by silver staining (RNA-PAGE) though a highly specific technique but require more efforts and expertise than ELISA. New methods like dot blot hybridization using radio labeled cDNA probes and reverse transcriptase – polymerase chain reaction (RT-PCR) are now being used as confirmatory methods for detecting rotavirus in stool samples [8]. RT-PCR has been found to be a highly sensitive and specific method for diagnosis of rotavirus in stool sample from patients with acute diarrhea.

Treatment: Oral and/or parenteral rehydration therapy is the main treatment for rotavirus diarrhoea in calves. Antibiotics are not indicated in viral infections, but are often used in severely affected animals that are suspected of having a secondary bacterial infection in addition to the viral disease. The
addition of antibiotics to the rehydration solution does not improve recovery. The use of oral antibiotics should be carefully considered in the case of undiagnosed outbreaks of calf scours to avoid further disruption of gut flora. If the calf is incapable of drinking the rehydration solution, parenteral rehydration needs to be provided. Withholding of milk for 24 hours is beneficial but not necessary. Suckled calves should be left with the dams. Non-suckled animals should be isolated immediately from other calves to avoid spread of infection.

**Control:** As the pathogens are ubiquitous, it is virtually impossible to prevent exposure to them. Spread of infection occurs most rapidly in housed calves. As the viruses are often isolated from both healthy and diseased calves, it is assumed that other risk factors play a more important role. Prevention of infection during the first five days of life (by adequate colostrum ingestion) and avoidance of stress (cold stress, travel stress, other exposure) are seen as the best practices to protect calves from getting diarrhea.

Vaccines are available for giving to the dam about a month before they calve to increase the amount of rotavirus specific immunoglobulins in the colostrum. The levels of antibodies in the colostrum of vaccinated cows are high enough to result in a protection period of at least seven days if given within 12 hours of birth. Early immunity in new-born farm animals depends almost entirely on their obtaining antibodies via colostrum. The transfer of colostral antibodies is the single most important form of protection of the new-born calf.

**REFERENCES**