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Original Research Paper

Veterinary Science

FOODBORNE VIRUSES PAPER I – NOROVIRUS

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ABSTRACT Noroviruses are chief viral etiologies of severe gastroenteritis. Noroviruses are the primary cause of nonbacterial diarrheal outbreaks in humans. Although the enteric virus substantially impact human health and economies, there are no approved drugs against noroviruses. The most advanced norovirus vaccine has recently completed phase-I and II trials. Here we review the important aspects of norovirus infections in humans and animals and their prevention and control.

KEYWORDS : Norovirus, animals, humans, prevention.

Introduction

Noroviruses are a group of genetically diverse single-stranded RNA viruses. There are six known genogroups (G), two of which (I and II) commonly cause human disease, and further can be subdivided into nine and 22 genotypes, respectively (Green, 2013). Norovirus, a member of the genus *Norovirus* and the family *Caliciviridae*, is one of the leading causes of viral gastroenteritis in people of all ages and settings, accounting for approximately 18% of all cases of diarrhea worldwide (Lopman *et al*., 2016). Norovirus is known as the most common cause of non-bacterial diarrheal occurrences in children as well as adults in developed countries (de Graaf *et al*., 2015). In developing countries, though rotaviruses are recognized as the main cause of infantile diarrhea, noroviruses are nowadays rapidly emerging as the most predominant causal agent of severe gastroenteritis in children in countries where rotavirus vaccines are implemented in their immunization programs. Over 2,00,000 childhood deaths have been attributed to norovirus in a recent review from developing countries (Patel *et al*., 2009).

The isolation of norovirus from the faeces of both healthy and diseased farm animals elevated public interest in a probable zoonotic transmission of this virus (van der Poel *et al*., 2000). Virus isolates from humans and animals belong to the same two genera. This raised the question whether transmission of these viruses between animals and man and vice versa occurs and whether animals act as a reservoir for enteric disease in man (Guo *et al*., 2001a). (Animal noroviruses)

History

Symptoms of norovirus infections in humans were first described in 1929 as 'winter vomiting disease.' This term refers to the characteristic seasonality of the infection as well as the high proportion of patients suffering from projectile vomiting. At that time the illness could not be related to any recognized bacterial or parasitic agent. Later experimental infection of volunteers with stool filtrates revealed that viruses are responsible for the disease, but the causative agent remained unidentified. After 29 years, Kapikian and co-workers were able to determine viral particles of 27–32 nm size in the stool sample collected during an outbreak of acute gastroenteritis at a school in Norwalk/Ohio/USA by immune electron microscopy using convalescent sera taken 4 years earlier (Kapikian *et al*., 1972). Under electron microscopy noroviruses exhibited typical calicivirus morphology with cup shaped surface depression and thus were first named 'small rounded structured viruses' (SRSV). Further investigation of the Norwalk virus proteins showed their resemblance to caliciviruses. Finally, cloning of the viral genome and its characterization finally proved that noroviruses belong to caliciviruses. From then noroviruses were initially included in separate genus 'Norwalk-like viruses' and later 'Norovirus' within the family *Caliciviridae* (Koopmans *et al*., 2005)..

Noroviruses have also been isolated from animals. Bovine noroviruses were found in 1976 (Newbury agent-1) and 1980 (Jena virus) in faeces of cattle suffering from diarrhoea (Gunther and Otto, 1987). Both samples contained viral particles displaying a feathery appearance in electron microscopy (Gunther and Otto, 1987). It took several years until molecular studies confirmed that these viruses belong to the family Caliciviridae (Liu *et al*., 1999). Porcine noroviruses were detected in the Netherlands (van der Poel *et al*., 2000) and in faecal samples from clinically healthy swine in Japan (Sugieda *et al*., 1998). Additional representatives of the genus Norovirus in animals are the murine noroviruses isolated during an infection of immunocompromised laboratory mice (Karst *et al*., 2003). Noroviruses with tropism for the intestinal tract have also been described in a captive lion cub and a canine pup; the animals showed enteritis in both cases (Martella *et al*., 2007, 2008).

Mode of Transmission

Although noroviruses have been identified from bovines, porcine, canines and mice these virus strains appear to be highly species-specific, and zoonotic transmission does not appear to be common. In humans, the virus typically spreads directly through person-to-person transmission (faecal–oral and vomit–oral) or indirectly via foodborne, waterborne and environmental transmission. Direct person-to-person transmission is reported in >90% of the norovirus outbreaks in healthcare facilities (Lopman *et al*., 2003). The majority of foodborne norovirus illness is a result of contamination by infected food-handlers during preparation. Ready-to-eat foods (such as leafy greens) and foods handled after cooking are the most frequently identified products associated with outbreaks (Hall *et al*., 2012).

The contributing factors to the ability of noroviruses to utilize different routes of transmission are, the high levels of virus shedding in feces and vomit (Atmar *et al*., 2008), the low infectious dose (Teunis *et al*., 2008) and the environmental stability of the virus (Lopman *et al*., 2012). Furthermore, transmission has been described to occur before the beginning of symptoms (Ozawa *et al*., 2007), in the post-symptomatic period, and throughout subclinical infections (Sukhrie *et al*., 2012). Moreover, certain genotypes are associated with different modes of transmission and, perhaps, severity of disease outcomes. Genogroup I viruses are more often associated with food and waterborne outbreaks. For example, the recently emerged GI.6 virus is more often associated with foodborne disease (Leshem *et al*., 2013). Conversely, GII.4 viruses are strongly associated with person-to-person transmission and healthcare settings.

Disease in man and animals

Elderly people, children and immunocompromised individuals are most susceptible for the norovirus infection. An acute, self-limiting diarrhoea develops after incubation time of 15–36 h. Distinguishing symptom of a norovirus infection is the projectile vomiting that occurs chiefly during the first day of disease and was described by 'Kaplan criteria' (Kaplan *et al*., 1982). These criteria are still valid today and include a mean incubation time of 24–48 h, a mean duration of disease of 12–60 h, no detection of bacterial or parasitic agents in stool samples as well as vomitus in more than 50% of the patients. Additional symptoms compromise fever, nausea, abdominal pain and cramps (Rockx *et al*., 2002). Virus shedding can last for up to 3 weeks. The route of transmission is faecal–oral but vomit is also infectious which can lead to aerogen infection as well as infection via contaminated surfaces. Immunocompromised individuals such as individuals with organ transplantation, may stay chronically infected. In Japan, a case of norovirus-associated encephalitis was reported in a 23-month-old child.

Noroviruses in bovines are associated with diarrhea mainly in calves. The Jena strain could be passaged 11 times in cattle fostered without colostrum and resulted into diarrhoea at each passage (Liu *et al*., 1999). The second prototype strain, Newbury agent-2, caused anorexia, diarrhoea and xylose malabsorption after an incubation time of 12–24 h (Woode and Bridger, 1978).

Porcine noroviruses have been exclusively isolated from faecal samples of adult swine without any clinical signs (Scipioni *et al*., 2008). Noroviruses have also been detected in the intestinal content of a captive lion cub euthanized because of severe haemorrhagic enteritis. However, the pathogenic potential and origin of this virus still have to be explained (Martella *et al*., 2007).

The canine norovirus was detected together with canine parvovirus (CPV) in the faeces of a pup suffering from vomiting and diarrhoea. The isolated norovirus could be detected for 22 days indicating viral replication in the pup (Martella *et al*., 2008b)..

Norovirus in India

Reports of norovirus infection in India have been published in recent years. Chhabra *et al.* (2008) carried out a study to determine the norovirus prevalence in sporadic cases of acute gastroenteritis in western India. The study demonstrated the predominance of GIII/4 (Genogroup II/genotype 4) along with co-circulation of GII/1, GII/2, GII/3 and GIIb revealing the possibility of norovirus as the second most cause of non-bacterial acute gastroenteritis after rotavirus in western India. This study documented the first time occurrence of norovirus GIIb infections in India. Rachkonda *et al.* (2008) detected 34 GGII and 2 GGI norovirus strains from children with acute sporadic gastroenteritis in New Delhi, india.

Similarly, Chhabra *et al.* (2009) conducted the study to investigate the molecular epidemiology of norovirus from western India. The study revealed that norovirus positivity varied between 6.3% and 12.6% in different cities with the predominance of GII (96.6%). NoV infections were very common in the patients ≤2 years of age. Recently, Menon *et al*. (2016) revealed that out of 1856 diarrheal episodes in south India, 207 were associated with Norovirus. Out of 49(2.6%) were norovirus GI, 150(8.1%) norovirus GII, and 8 (0.4%) were mixed infections with both norovirus GI and GII.

Prevention and Control

Prevention and control of norovirus infections include diverse set of recommendations, given the different transmission modes of norovirus spread. In general, hand hygiene should be actively encouraged among the health personnel, patients and visitors in patient-care areas affected by norovirus gastroenteritis.

Improved cleaning and disinfection protocols may control the spread of norovirus. This consists of increasing the frequency of cleaning and paying closer attention to regularly touched surfaces such as door handles and telephones. A bleach solution at a minimum concentration of 1000 p.p.m. sodium hypochlorite prepared fresh daily is recommended for disinfection (CDC, 2011).

Food such as leafy vegetables, fruits which are commonly consumed raw can be the major source of infection. Such foods should be thoroughly washed before eating. Two important infection control measures specific to food-service settings include eliminating bare-handed contact with ready-to-eat foods and the presence of certified kitchen managers with food safety training [USFDA, 2013].

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