Veterinary Microbiology 140 (2010) 204–212

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Review

Zoonotic aspects of infections with noroviruses and sapoviruses

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ARTICLE INFO

Article history:
Received 3 July 2009
Received in revised form 3 July 2009
Accepted 21 August 2009

Keywords:
Noroviruses
Sapoviruses
Caliciviruses
Zoonoses

ABSTRACT

The close genetic relationship of noroviruses and sapoviruses found in animals and humans has raised the question whether these viruses have a zoonotic potential. Transmission from animals to humans and vice versa would have far-reaching consequences for epidemiology and food safety. So far animal noro- and sapoviruses have not been found in humans. However detection of human noroviruses in animals as well as simultaneous presence of animal and human viruses in bivalve molluscs suggest a risk of transmission. Furthermore, antibodies against animal noroviruses were detected in humans as well as antibodies against human noroviruses in swine. Experimental infection of gnotobiotic calves and pigs with human noroviruses demonstrated that virus replication and seroconversion can occur. Accordingly the possible role of noro- and sapoviruses as zoonotic agents needs to be further investigated.

Contents

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doi:10.1016/j.vetmic.2009.08.021

1. Introduction

Noro- and sapoviruses belong to the virus family *Caliciviridae* and constitute their own genera *Norovirus* and *Sapovirus* within this family. Noroviruses as the most important causative agents of non-bacterial epidemic human gastroenteritis are important for public health. Sapoviruses play a minor role as causative agents of gastroenteritis mainly in young children. The detection of noroviruses and sapoviruses in the faeces of healthy as well as diseased farm animals increased public interest in a possible zoonotic transmission of these viruses (Saif et al., 1980; van der Poel et al., 2000; Sugieda et al., 1998; Dastjerdi et al., 1999; Liu et al., 1999).

Virus isolates from animals and humans belong to the same two genera. This raises the questions whether transmission of these viruses between animals and man and vice versa occurs and whether animals represent a reservoir for enteric disease in man (Guo et al., 2001a). The aim of this review is to summarize the respective literature and to evaluate the zoonotic aspects.

2. History

2.1. Noroviruses

Symptoms of norovirus infections in humans have already been described in 1929 as "winter vomiting disease". This term refers to the typical seasonality of the infection as well as the high percentage of patients suffering from projectile vomiting. At that time the disease could not be related to any known bacterial or parasitic agent. Later experimental infection of volunteers with stool filtrates showed that viruses are responsible for the disease, but the causative agent remained unknown. It took 29 years until Kapikian and co-workers were able to demonstrate viral particles with a size of 27–32 nm in a 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). Noroviruses do not exhibit the typical calicivirus morphology with cup-shaped surface depressions and were thus first called "small round structured viruses" (SRSV). Examination of the Norwalk virus proteins showed their similarity to caliciviruses. Cloning of the viral genome and its characterization finally proved that noroviruses belong to the caliciviruses. Since then they form their own genus within the family *Caliciviridae* initially called "*Norwalk-like viruses*" and later "*Norovirus*" (Green et al., 2000; Koopmans et al., 2005).

Noroviruses have also been identified in animals. Bovine noroviruses were already found in 1976 (Newbury agent-1) and 1980 (Jena virus) in faeces of cattle suffering from diarrhoea (Woode and Bridger, 1978; Günther and Otto, 1987). Both samples contained viral particles exhibiting a feathery appearance in electron microscopy (Bridger et al., 1984; Günther and Otto, 1987). It took again several years until molecular studies demonstrated that these viruses belong to the family *Caliciviridae* (Dastjerdi et al., 1999; 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). The causative agent called murine norovirus 1 (MNV-1) led to a lethal disease with encephalitis, vasculitis, meningitis, hepatitis and pneumonia. In the meantime three additional murine noroviruses (MNV-2, -3 and -4) were identified which cause persistent infection and prolonged faecal shedding (Hsu et al., 2006).

Recently, noroviruses with tropism for the intestinal tract have also been described in a captive lion cub and a canine pup; in both cases the animals showed enteritis (Martella et al., 2007, 2008b).

2.2. Sapoviruses

Morphologically typical caliciviruses in humans have been depicted for the first time in Great Britain in 1975. The prototype strain Sapporo virus was detected in 1977 during an outbreak of acute gastroenteritis in an infant home in Sapporo/Japan (Chiba et al., 1979). Two years later faecal samples which originated from an outbreak at a school in London were examined by immune electron microscopy and a morphological similarity with caliciviruses was demonstrated. Due to this observation the viruses were designated as "typical human caliciviruses" (Pringle, 1998). The name was changed first into "*Sapporo-like viruses*" (Green et al., 2000) and later into "*Sapovirus*" (Koopmans et al., 2005).

Animal sapoviruses comprise the porcine enteric sapovirus as well as the mink enteric sapovirus. The porcine enteric sapovirus strain Cowden was isolated from faeces of a 27-day-old piglet (Saif et al., 1980). Until now the Cowden strain is the only member within the genus which can be propagated in cell culture. Initially called porcine enteric calicivirus the resulting abbreviation "PEC" is still commonly used.

The mink enteric sapovirus, first called mink enteric calicivirus (MEC), was detected in connection with an outbreak of diarrhoea at a mink farm in the USA. Typical caliciviral particles were found using immune electron microscopy of faecal samples with anti-PEC hyperimmune sera. Phylogenetic analyses grouped the agent into the genus *Sapovirus* (Guo et al., 2001a).