



Efficiency of Forvet in Treating Feline Coronavirus Infection: Clinical Cases

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Abstract

Feline coronavirus (FCoV) is the ubiquitous virus of domestic and wild cats. Coronaviruses infect animals and humans, causing a wide range of diseases. One common type of enteric infection is coronavirus - FECV, which causes feline enteritis. The fatal disease caused by highly virulent coronavirus is feline peritonitis (FIP). In this article, we will consider the efficiency of the Forvet polysaccharide complex in specific clinical cases of feline coronavirus enteritis (FECV) and infectious feline peritonitis (FIPV). Based on the presented clinical cases, we can draw the following conclusions:

- **Clinical case No. 1 (coronavirus peritonitis):** with the use of Forvet, the feline infectious peritonitis changes from an acute stage to complete remission and, based on the results of laboratory tests, coronavirus passes into the "grey zone";
- **Clinical case No. 2 (coronavirus enteritis):** with the use of Forvet, clinical signs of coronavirus enteritis have rapidly disappeared and results of analysis for the presence of viral RNA in the animal body were negative; therefore, a mutation of coronavirus enteritis into feline infectious peritonitis is prevented;
- **Clinical case No. 3 (coronavirus enteritis):** after prescribing Forvet, titravirus has reduced rapidly within a short period of time (by prescribing 1 course of the medicine, the doctor has reduced the viral load 10 times within 14 days).

Keywords: Coronavirus; Coronavirus Peritonitis; Coronavirus Enteritis; Coronavirus Gastroenteritis; Cats; Forvet

Abbreviations: Feline Fcov-Coronavirus; FECV-Coronavirus Enteritis, FIP (FIPV): Coronavirus Peritonitis; OT-PCR: Reverse Transcriptase Polymerase Chain Reaction

Introduction

Feline coronavirus (FCoV) is an ubiquitous virus of domestic and wild cats. Coronaviruses infect animals and humans, causing a wide range of diseases [1]. Coronaviruses have a single-stranded genome with positive RNA and are divided into four genes of alpha-, beta-, gamma- and delta-coronaviruses [2]. The variety of coronaviruses in many mammal species is caused by relatively high rates of mutation and recombination during the replication. [3,4]. This dynamic nature of coronaviruses can facilitate cross-species transmission and shifts in tissue or cellular tropism of the host, leading to significant changes in virulence. One of the most common types of enteric infection is coronavirus, FECV, which causes feline enteritis. Fatal disease, caused by highly virulent coronavirus, is infectious feline peritonitis (FIP). A seemingly harmless coronavirus infection can also become fatal after changing its tropism, as exemplified by the mutation of feline enteric coronavirus (FECV) into the feline infectious peritonitis virus (FIPV) [5,6]. Feline infectious peritonitis can be caused by mutation of FECV into the FIP virus (FIPV) [1]. Most often, cats become infected orally, after the contact with coronavirus (FCoV) in the faeces. Since the virus is rarely found in the saliva of healthy cats, close contact or shared use of feed pans are not the main routes of infection. Transplacental transmission is extremely rare.

No FCoV transmission through blood transfusions has been reported. After natural infection, the cats begin secreting the virus after a week and continue secreting it for weeks, months and sometimes even for a life time (virus carriage) [7]. The growing risks of highly virulent coronavirus infections in humans or animals require effective antiviral drugs [1]. It is assumed that effective therapeutic intervention in cases of coronavirus infections with immunopathological component, such as SARS, MERS, and FIP implies reasonable use of immunomodulatory agents to increase the protective immunity of the host and reduce the pathological

immune responses, as well as antiviral drugs to directly suppress the virus replication. In 2015, Rakhmanina N.A. conducted a research on the impact of Forvet on antibody counts of cats with coronavirus peritonitis and concluded that the administration of Forvet to coronavirus-infected cats reduced the antibody titer and did not have a negative impact on animal clinical status [8]. In this article, we will discuss the efficiency of the Forvet polysaccharide complex in specific clinical cases of feline coronavirus enteritis (FECV) and feline infectious peritonitis (FIPV).

Etiology and Pathogenesis

Feline coronavirus (FCoV), RNA virus, is a large spherical viral particle with an envelope that is classified in the order of Nidovirales; Coronaviridae family; Alphacoronavirus genus; Alphacoronavirus 1 species, which also includes canine coronavirus (CCoV), transmissible gastroenteritis virus (TGEV) and porcine respiratory coronavirus (PRCoV) [7]. Feline coronaviruses (FCoV) include two biotypes: feline enteric coronaviruses (FECV) and feline peritonitis viruses (FIPV). FECV is associated with asymptomatic permanent enteric infections, while FIPV causes feline infectious peritonitis (FIP), usually a fatal systemic disease of domestic cats and some wild cats. FIPV is caused by a mutation of FECV [9]. Two theories of FIP infection have been proposed: the hypothesis of “internal mutation” and the hypothesis of “different circulating avirulent and virulent strains”. The first model assumes that FIPV arises *in vivo* from FECV mutations in infected animals. Indeed, the mutations in S protein probably contribute to tropism of FCoV monocytes/macrophages and allow it to spread systematically beyond the intestinal tract, promoting FIP. The second model suggests that high frequency of viral mutations in FCoV leads to the generation of viral quasi-dispersed species that include more virulent mutants [10].

In vitro FECV and FIPV may replicate in isolated peritoneal macrophages of cats, BMDM (bone marrow macrophages), and monocytes, but only FIPV undergoes consistent replication and spread the infection in cell culture. Host factors also play a role, as cats show individual differences in the resistance and sensitivity of their monocytes to the infection. It is the activation of monocytes and macrophages that directly leads to pathological features of FIP, including vasculitis, exudate in body cavities, and fibrinous and granulomatous inflammatory lesions [11]. Also, FIP pathogenesis is closely associated with immune responses and involves the depletion of T cells.

Most studies have shown that plant polysaccharides regulate macrophage production by recognizing and binding to specific receptors on macrophage surface, which initiates an immune response and has an immunomodulatory effect. These macrophage receptors are called pattern recognition molecules. Macrophages can bind to plant-derived polysaccharides and/or glycoproteins using a Toll-like receptor [12]. Toll-like receptors (TLRs), as a family of pattern recognition receptor (PRR), are highly expressed in dendritic cells (DC) and T cells. Activation of TLRs leads to the maturation of DC and the secretion of pro-inflammatory cytokines, which may induce an immune response of the T cells [12] and, consequently, promote their increase. Plant-derived polysaccharides can simultaneously regulate the expression of pro- and anti-inflammatory cytokines (IL-12 acts as a negative feedback factor, preventing excessive activation of macrophages in the inflammatory response) [12], which reduces monocyte production and, according to one theory of transition of viral enteritis to infectious peritonitis, prevents this transformation.

Clinical Signs

FECV coronavirus enteritis infection is most commonly associated with the mild course of the disease. Coronavirus enteritis (FECV) does not appear clinically or is characterized by mild self-limiting gastroenteritis, but vomiting and diarrhoea can sometimes be acute and severe, or become chronic [13]. The clinical pattern of coronavirus peritonitis (FIP) varies considerably. Vasculopathy can lead to (“wet”) exudate, while the formation of granuloma leads to (“dry”) mass lesions. Non-specific clinical signs can occur in both forms of coronavirus with or without exudate and include lethargy (fatigue), anorexia and weight loss (or inability to gain weight / slow growth of kittens), although sometimes some cats remain seemingly healthy and maintain a good body condition. There is usually a fever which can be fluctuated or moderate and is usually below 40°C [11].

Diagnostics

The virus can be found in the faeces of infected animals by electron and microscopic examination or by reverse transcriptase polymerase chain reaction (RT-PCR). However, many clinically healthy cats and kittens will also secrete FCoV in the faeces. Thus, in addition to identifying a carrier or demonstrating the presence of feline coronavirus infection (FCoV), such studies are of limited value [14,15]. Many authors agree that only serological data are of limited diagnostic value. PCR tests can directly detect the FCoV genome. Although PCR seems more sensitive for detection of feline coronavirus infection, the results should be interpreted in combination with other clinical data and cannot be used as the only criterion for FIP diagnosis. Final FIP diagnosis should be confirmed by histopathology or detection of the intracellular FCoV antigen by immunofluorescence or immunohistochemical staining [16].

Clinical Cases of the use of Forvet Polysaccharide Complex in the Treatment of Feline Coronavirus Infection

Clinical Case No. 1

Leningrad region, Kudrovo, Leningradskaya street, 7, MiMi Veterinary Clinic, veterinarian Gladkikh Alexei Vladimirovich. Anamnesis: female cat, 7 years old, 4.6 kg, desexed, nutrition: dry food Hills. 21.09.2019, the owners addressed to the clinic with complains about cat's weakness, lack of appetite, weight loss, elevated body temperature of 39.8 °C, occasional gastrointestinal

upset and coordination disturbance. The examination at the clinic revealed enlarged mesenteric lymph nodes and liver at palpation. The doctor made a preliminary diagnosis of feline coronavirus infection and prescribed additional laboratory tests: enzyme immunoassay (IFA) for the presence of antibodies to coronavirus, general blood test and biochemical blood test [17,18].

The analysis for antibodies to coronavirus showed the result of 0.517; in the general blood test changes were found only in the percentage of lymphocytes - 60% (normal range - 25% -5%); biochemical blood test showed a slight decrease in AST - 18.87U/l (20-55 U/l) and calcium - 2.04 mmol/l (2.23-2.8 mmol/l).

Based on the test results, the diagnosis of feline coronavirus infection was confirmed, and the following treatment was prescribed:

1. Sinulox, 0.3 ml 1 time per day, s/d, 10 days
2. Forvet, 1 ml once a day, s/d, 14 days. Re-examination of the animal is appointed in 14 days.

At the second visit (5.10.2019), the doctor found a noticeable improvement of the animal's condition, normal appetite; the animal began gaining weight; absence of subfebrile body temperature and less pronounced increase of lymph nodes. The doctor decided to perform an additional enzyme immunoassay of feline infectious peritonitis for coronavirus infection differentiation.

The result of the assay confirmed the diagnosis of infectious peritonitis (titer 1:3200, diagnostic titer). Based on the obtained result, the doctor prolonged the course of treatment with Forvet medicine. 4 courses of Forvet for 14 days with a break of 14 days, in the dosage of 1 ml, s/d and body temperature control were prescribed. After the taken treatment courses, at the follow-up visit (04.02.2020), the tests for the control of antibodies titer for coronavirus were taken. The result was 0,301. As can be seen from the result of the last assay, the coronavirus infection has moved into the grey zone. The animal showed no signs of coronavirus infection during the treatment. Further monitoring of the cat's condition, scheduled examinations once in 2 months, and preventive injections of Forvet during 14 days in the previous dosage 3 times a year were recommended. 8 months after the treatment, the animal had no clinical signs of coronavirus infection.

Clinical Case No. 2

St. Petersburg, Revoluytsii highway, 31, Vetuniversal Veterinary Clinic, veterinarian Pronyaev Pavel Sergeevich.

Anamnesis: female cat, 5 months, 1,8 kg, not desexed, nutrition: dry food.15.06.2019, the owners addressed to the clinic with complaints about poor appetite and loose stool with mucus of the cat. During the examination, the doctor revealed the following clinical signs: elevated body temperature 39.5 °C, swollen abdomen and painful abdomen on palpation, increased mesenteric lymph nodes. The doctor suggested taking PCR analysis to make an accurate diagnosis for the following diseases: panleukopenia, coronavirus enteritis, toxoplasmosis, giardiasis, cytoisporosis.

On the basis of the obtained test results, the diagnosis of coronavirus gastroenteritis was confirmed (other infections were not found). The doctor prescribed the following treatment:

- Forvet, 1 ml one time a day, i/m, 10 days.
- Omez ½ tab. 1 time a day, 15 days.

At the repeated visit on 10.07.2019, the cat had no clinical signs that had been reported earlier (appetite was normal, stool has normalized, body temperature was 38.3 °C). The doctor decided to prescribe the second PCR test. Based on the result of the repeated test, titer 1/3, the doctor prescribed to continue the previous treatment with Forvet in courses of 10 days, 1 time per month, for 2 months in a row. The appointment was scheduled for 1.09.2019 to control the PCR test. Having performed the control PCR test, the result of which was negative, the doctor decided to stop treatment of the cat and concluded its clinical recovery. 7 months after the treatment, the animal stays healthy, including according to PCR analysis results.

Clinical Case No. 3

St. Petersburg, Korablestroiteley street, 30 k 9, Ryzhyi Pes Veterinary Clinic , veterinarian Nosova Yulia Mikhailovna.

Anamnesis: male cat, 4 months, 1,6 kg, nutrition: dry food. 9.03.2020, the owners addressed to the clinic with the following complaints: a month ago, the kitten was bought in the breeding cattery and already at that time it had eye discharge. About a few days after purchase, the kitten suffered from loose stool with blood inclusions and clots of mucus, which did not stop until the moment of visiting the doctor. During the examination, the doctor revealed the following clinical signs: body temperature of 39.3 °C, increased abdomen volume, pain in abdomen on palpation.

The doctor suggested taking PCR test to make an accurate diagnosis for the following diseases: mycoplasmosis, chlamydia, coronavirus gastroenteritis, giardiasis, Helicobacter. Coronavirus gastroenteritis (titer 300/1) was confirmed based on the results of the tests; the other diseases were not found.

The doctor prescribed the following treatment:

- Forvet, 0,5 ml one time a day, i/m, 5 days.
- Enterofuryl, orally, 1 ml 2 times a day, 5 days. At the repeated visit on 22.03.2020, the cat had no previously described clinical signs (stool has normalized, painfulness and swelling of the abdomen were not observed, body temperature was 38.6 °C). The doctor decided to repeat the PCR test.

Based on the results of the analysis, titer 30/1, the doctor prescribed a repeated treatment course with Forvet, 0.5 ml, i/m, one time a day, for 5 days, 14 days after the first course of injections. The repeated visit was scheduled for 10.04.2020. On 10.04.2020, the animal did not have any clinical signs of coronavirus enteritis, and the owners decided not to repeat the tests.

Conclusion

Based on the above clinical cases, the following conclusions can be drawn:

- Clinical case No. 1 (coronavirus peritonitis):** with the use of Forvet, the feline infectious peritonitis changes from an acute stage to complete remission and, based on the results of laboratory tests, coronavirus passes into the “grey zone”;
- Clinical case No. 2 (coronavirus enteritis):** with the use of Forvet, clinical signs of coronavirus enteritis have rapidly disappeared and results of analysis for the presence of viral RNA in the animal body were negative; therefore, a mutation of coronavirus enteritis into feline infectious peritonitis is prevented;
- Clinical case No. 3 (coronavirus enteritis):** after prescribing Forvet, titravirus has reduced rapidly within a short period of time (by prescribing 1 course of the medicine, the doctor has reduced the viral load 10 times within 14 days).

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