Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.59.009344

Canine Parvovirosis: Diagnosis and Recommendations Regarding Its Treatment

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ARTICLE INFO

Received: November 18, 2024

Published: December 02, 2024

Citation: Bueno S and Navarro C. Canine Parvovirosis: Diagnosis and Recommendations Regarding Its Treatment. Biomed J Sci & Tech Res 59(4)-2024. BJSTR. MS.ID.009344.

SUMMARY

Canine parvovirus is an infectious contagious disease that first appeared in North America, specifically in the United States (US) in 1977. Later in 1978, a severe outbreak was detected in the south of this country, which spread to Canada and later to the rest of the world. At the national level, viral hemorrhagic gastroenteritis is a very common disease in puppies under 1 year of age, especially if they have not been vaccinated or because the vaccination schedule received was not adequate. Although there are different etiological agents that cause enteritis in dogs, such as: poisoning, acute pancreatitis, canine distemper virus (CDV), canine parvovirus (CVP), bacterial and parasitic infections, and even acute kidney and liver disease, this thesis will focus on the disease caused by CVP, a gastrointestinal disease that occurs as an acute condition with symptoms mainly of hemorrhagic diarrhea and vomiting, causing high mortality rates - mainly in puppies - which is why it is considered an interesting disease to study. In clinical practice, patients who arrive with hemorrhagic gastroenteritis should be treated in a timely and appropriate manner, mainly treating the signs and symptoms of the condition by administering various medications such as antiemetics, antacids, gastric protectors, antibiotics, vitamins, among others. Considering that there is no definitive laboratory diagnostic method, this work proposes to generate an updated document with information regarding this gastrointestinal pathology suffered by puppies, describing its characteristics, prevention and the diagnostic methods used for confirmation, as well as establishing a definitive treatment and diagnosis of Canine Parvovirus, which allows taking all preventive treatment measures for the patient as well as for the environment in which he lives.

Abbreviations: CPV: Canine Parvovirus Type; DNA: Deoxyribonucleic Acid; BUN: Blood Urea Nitrogen; HA: Hemagglutination Test; IC: Immunochromatography; FMT: Fecal Microbiota Transplant

Background

Canine Parvovirus

Dogs have recently been incorporated as another member of the family, therefore, their care becomes another concern of the family unit. In this context, the health of dogs is directly related to an emotional component for both pet owners and veterinarians (1). Two types of parvoviruses are described in dogs, 1 and 2. Canine parvovirus type 1 (CPV-1), was isolated for the first time in the United States in 1968 and produces infections without clinical signs. Canine parvovirus type 2 (CPV-2) was first detected in puppies with diarrhea in Texas in 1977, which produces myocarditis and fatal enteritis, mainly in puppies (2). There is a close relationship from the antigen point of view with the Feline Panleukopenia virus and multiple studies maintain that it was generated from a mutation of the deoxyribonucleic acid (DNA) of the Feline Panleukopenia virus (3). The etiological agent of the disease is a virus of the Parvoviridae family, Parvovirus genus. The virion has an icosahedral capsid without a lipid envelope, which gives it resistance to the environment, lipid solvents such as ether and chloroform, proteolytic enzymes and it is stable at pH intervals between 3.0 and 9.0, making it very difficult to eliminate from a contaminated environment (4,5).

Pathogenesis of the Disease

Primary infection occurs when an animal is infected with the virus via the oronasal route, either directly from the feces of infected animals or from contaminated surfaces. Viral replication then occurs in the lymphatic tissue of the oropharynx and mesenteric lymph nodes, with a general incubation period of 4 to 10 days (6). After the virus enters, primary viremia occurs, spreading throughout the body,

reaching the crypts of the small intestine, invading and destroying intestinal cells, thus causing the loss of the epithelium and shortening of the intestinal villi. Consequently, the typical signs of parvovirus hemorrhagic enteritis are generated, which are vomiting, hemorrhagic diarrhea and intense dehydration (6). This virus can destroy precursors of mitotic activity of lymphocytes and myeloproliferative cells, generating severe infections, lymphopenia and panleukopenia (4).

Associated Clinical Alterations

The most common clinical signs are vomiting and diarrhea, generally of a grayish appearance which frequently becomes hemorrhagic. At first, the disease presents with depression or weakness, anorexia and fever, diarrhea appears 6 to 24 hours after the first signs. Vomiting may occur simultaneously with diarrhea, both generating a picture of severe dehydration, which leads to bacterial translocation due to damage to the intestinal mucosa, generating a picture of sepsis (7).

Associated Hematological and Biochemical Alterations

The hematological results in patients with the disease show leukopenia (decrease in lymphocytes), neutropenia (decrease in neutrophils) due to the loss of neutrophils at the intestinal level and interruption of their production in the bone marrow. In 88.9% of animals infected with CPV, hypoproteinemia is present, due to the loss of proteins through the intestinal wall towards the lumen, and an increase in blood urea nitrogen (BUN) due to dehydration (6).

Diagnostic Tests

The diagnosis of this disease is based on the anamnesis, signs and physical examination. The general examination includes color of the mucous membranes, capillary refill time, skin fold, pulse, auscultation and heart rate, respiratory rate and rectal temperature. Through this examination, the presence of dehydration, signs of hypoperfusion derived from dehydration (pale mucous membranes and prolonged capillary refill time), abdominal pain, hypothermia, etc. can be detected. The signs that can be observed in case of hypovolemic shock are depression, tachycardia, hypotension, cold extremities and hypothermia. For confirmation of the etiology of enteric disease, complementary tests are performed, such as: blood counts, coproparasitic tests, biochemical profile and abdominal ultrasounds (8). In clinical practice, the diagnosis is mainly based on the signs and anamnestic history, with rapid ELISA tests (9) and laboratory tests for viral isolation. The main types of diagnostic detection are the following:

- **Viral Isolation:** using stool samples from patients suspected of having the disease, basophilic intranuclear inclusion bodies are sought, or specific viral antigens are detected by immunofluorescence (6).
- **Serological Tests:** hemagglutination inhibition test that shows the presence of antibodies that inhibit hemagglutination of porcine erythrocytes by CPV (6).
- **Clinical Laboratory:** complete blood count or white blood cell count to identify leucopenia, and red blood cell count to identify the degree of anemia due to intense bleeding in diarrhea (6).
- **Post-Mortem Pathology:** watery, hemorrhagic and dark intestinal content, severe vascular congestion, enlarged mesenteric lymph nodes, acute necrosis of the intestinal epithelium is observed at the microscopic level (6).
- There are some molecular diagnostic methods such as the PCR technique (10-13), however, it has not yet been fully implemented in Chile.
- Elisa: Rapid commercial enzyme-linked immunosorbent assay for diagnosing parvovirus in the stool of young canines affected by hemorrhagic gastroenteritis. It uses monoclonal antibodies to detect canine parvovirus antigens in feces (9).

Prevention

Prevention of canine parvovirus is through an adequate vaccination protocol. The use of vaccines prepared with modified live virus has managed to reduce the number of susceptible animals and mortality, since these effectively induce a cellular and humoral immune response (mediated by antibodies). The guidelines for the vaccination of dogs and cats propose a vaccination plan for puppies which contemplates starting the basic vaccination at 6 to 8 weeks of age with vaccines containing CPV and VDC, with revaccinations every 2 to 4 weeks, until 16 weeks of age. It should be considered that puppies have maternal antibodies that decrease at 8 to 12 weeks of age, which can interfere with the immune response of the vaccines, causing them to be ineffective, so a booster of the vaccine is recommended at 12 months of age or 12 months after the last vaccination (14).

Treatment

The treatment of canine parvovirus is symptomatic. Its main objective is to restore hydro electrolytic balance and prevent secondary bacterial infections. Hospitalization, together with intensive fluid therapy, is essential to increase the chances of survival from the disease. Patients who come to the clinic without severe dehydration or hemorrhagic diarrhea can be treated without being hospitalized. On the contrary, patients who present dehydration and diarrhea should be hospitalized and managed as soon as possible with fluid therapy, using intravenous fluids, since it is the route that presents greater and faster absorption (15). Antibiotics are recommended given the severe destruction of the intestinal epithelium, through which bacteria penetrate the blood, increasing the risk of sepsis. Antibiotics reduce fluid loss and facilitate the absorption of nutrients (15). In this document was generated with information regarding this gastrointestinal pathology suffered by puppies, describing its characteristics, prevention and the diagnostic methods used for confirmatory purposes, as well as establishing an appropriate treatment for patients suffering from the condition.

Materials and Methods

This study was carried out at the Faculty of Veterinary and Animal Sciences of the University of Chile, located in the commune of La Pintana, Metropolitan Region. The process of collecting bibliographic information was carried out during the second semester of 2023 and the process of analyzing the information during the first semester of 2024.

Materials and Sources of Information

The information necessary to carry out this study was obtained from the use of various bibliographic sources and the following keywords were mainly used for its search: Canine Parvovirus, Canine parvovirus, canine hemorrhagic gastroenteritis, hemorrhagic gastroenteritis in dogs, acute canine hemorrhagic enteropathy, acute hemorrhagic enteropathy in dogs, canine parvovirus treatment. The databases used were PubMed and ScienceDirect, scientific electronic journals, the Digital Library of the University of Chile, ICTV, Scielo, Genbank® and others. The search operators (boolean operators) used were((CPV) OR Canine Parvovirus)) AND (Dog) AND (dogs) AND (Canine) AND (canines) and (canine parvovirus) OR (CPV) AND (diagnosis) OR (treatment) OR (therapy). This search for articles was carried out with a maximum age of 15 years, excepting some citations due to lack of information and/or that have fundamental concepts that have not been modified currently. The information was obtained from books and journals related to the study topic, obtained from existing electronic and university libraries, theses and dissertations of undergraduate and graduate degrees from different universities, both national and international. In relation to the study of CPV, articles from scientific journals and web platforms duly recognized in the scientific field such as Pubmed, Science Direct, ICTV, Scielo, Genbank® and others were used.

Methodology

The methodology used contemplated as a search criterion for information, the last 15 years in the sources mentioned and others outside the date range, which are relevant to Canine Parvovirus, emphasizing the diagnosis and detection of CPV and related to the appropriate treatments for patients with hemorrhagic gastroenteritis due to CPV.

Determining the Types of CPV Diagnosis

The diagnosis of CPV infection is based on the detection of the virus by electron microscopy, serological tests and by molecular techniques. The tentative diagnosis can be made based on clinical symptoms and patient history, but for confirmatory diagnoses the clinical samples of choice are feces and pieces of tonsil, spleen and lymph nodes (16). The virus in feces can be detected by hemagglutination test (HA) with pig erythrocytes and ELISA test. Isolation of the virus from feces and other tissues can be done during the acute stage of the disease. The virus particles can also be demonstrated under electron microscopy. The ELISA test is useful to detect the viral antigen in feces and clinical samples (16).

Virus Isolation

Virus isolation and identification has been a consistent and most appropriate method. CPV was successfully isolated and identified using cell cultures and cell lines such as in MDCK and CFRK for which cells were used for its isolation and characterization (16).

Electron Microscopy

Negative stain electron microscopy has been used to detect CPV particles. Electron microscopy was found to have a sensitivity of 90% and a specificity of 40% in detecting CPV in fecal samples. Although electron microscopy is very specific and sensitive, it is often too time consuming and expensive for routine use in a clinical setting (16).

Serological Tests

The simplest and most reliable procedure for laboratory diagnosis of canine parvovirus infection is the detection of CPV antigen in fecal extracts by hemagglutination test using pig or rhesus monkey red blood cells. The specificity of the hemagglutination test is determined by assessing the fecal sample in parallel on the response of normal and immune canine serum. The authors suggest that the HA test can be easily and successfully used for the detection of parvovirus in fecal samples from dogs shedding the virus, in 1983 the diagnosis of canine parvovirus enteritis was made by the combined use of hemagglutination and hemagglutination inhibition tests in fecal samples from suspected cases of canine parvovirus. Other serological tests used include ELISA and slide coagglutination tests for the detection of CPV antigen in fecal samples and reported that ELISA was more sensitive while HA and coagglutination have almost similar sensitivity. The authors advocated that the coagglutination test should be specific and easy to perform while the HA test should be good for screening field samples but not a confirmatory test (16). Serological tests are used to check for the presence of antibodies or specific levels of antibodies in the blood. Antibodies are proteins that the immune system produces to fight a pathogen by detecting antigens. Antibodies against canine parvovirus type 2 are quantified in the laboratory using a diagnostic test known as hemagglutination.

Direct or semi-quantitative methods are those that detect the presence of the virus or any of its components in clinical samples, the presence of the infectious agent is investigated by viral isolation (17), the detection of viral antigens by immunostaining technique with enzyme-linked immunosorbent assays, is a test known as ELISA which detects viral antigens in fecal matter, being the most commonly used in different veterinary clinics for rapid diagnoses of the disease, according to different authors this test can, in many cases, give false negatives, due to the excretion of viral antigens is decreased, which

could be due to the binding of neutralizing antibodies to viral antigens, in the intestinal lumen of the patient, by dilution due to diarrhea and can also give false positives in animals that have been vaccinated with live CPV-2 vaccine (18). The specificity (ability to detect subjects who do not have the condition or do not suffer from the disease) and sensitivity (ability to obtain a positive value in the presence of those being sought) are mentioned below (19), of some rapid tests that are commercially available, which is determined by each laboratory.

- **Speed Parvo:** 97% sensitivity and 100% specificity.
- **Zoetis VetScan test:** 96.6% sensitivity and 96.7% specificity.
- **Bionote Antigen Rapid CPV Ag:** 100% sensitivity and 98.8% specificity

Viral antigen tests are the only ones available today at field level, that is, in veterinary clinics, the main disadvantage being their low level of sensitivity compared to other molecular methods. A study revealed that immunochromatography (IC) presented sensitivities lower than 50% with respect to methods based on nucleic acids, but presenting specificities of 100%, since it requires large amounts of viral antigen to produce a reliable result. Low sensitivity (actually detecting positives) may be associated with a low amount of virus in the feces in early stages of the disease or with a high number of antibodies that neutralize the viral antigen load (17). Another study revealed that the IC test had less than 50% sensitivity and 100% specificity compared to molecular methods (5). Regarding the hemagglutination and viral isolation tests, which are only performed in specialized laboratories, it is important to highlight that CPV is capable of agglutinating pig red blood cells and for the inhibition of hemagglutination fresh erythrocytes are needed, which is the problem of maintaining donor pigs in the facilities. Hemagglutination also requires good quality erythrocytes, since the test is affected by the globular sedimentation that occurs in cases of stress or disease in the donor pig. On the other hand, viral isolation requires cell cultures that are only used in laboratories with trained personnel and requires a long time to obtain results, being 5 to 10 days of incubation and additional tests by immunofluorescence, both tests have in some cases low sensitivity due to the low amount of antigens in the intestinal lumen and can give false negatives, which is ideally verified by PCR that is capable of detecting the amounts of viral DNA in the sample (17).

CPV-2 strains have also been reported that lack hemagglutinating activity, so it would not be effective to perform the hemagglutination inhibition test with these fecal samples, and false negatives may also be obtained (5). Among the diagnostic tests, IC is fast and simple but requires large amounts of viral antigen to produce a reliable result (20). The ELISA test is also an effective and rapid method, it allows to detect specific IgM antibodies for CPV 2 which appear in the early stages of infection and disappear in 2 to 3 weeks after the disease, because the virus has a binding to the sialic acid of the HA test and inhibition of hemagglutination, it can be used as a diagnostic method by detecting the virus in fecal matter, being effective in the acute phase of the infection usually in the first 5 days, when antibody titers have not yet risen (20). The humoral immune response is mainly composed of two types of immunoglobulins or antibodies, IgG and IgM. In the first days after vaccination, large amounts of IgM are produced, later the levels of IgM decrease and those of IgG begin to increase, therefore in dogs that can mount an immune response, elevated levels of IgM indicate a recent infection. The absence of IgM antibodies with high IgG titers suggests that exposure occurred earlier and the dog is immune. High levels of IgG are found in dogs that survived the acute phase of infection (20).

Molecular Methods

The PCR (Polymerase Chain Reaction) technique is a highly sensitive test since it requires few DNA molecules in the sample to be analyzed for amplification, fecal material or serum samples are used. However, the cost of the necessary equipment and reagents is high, so many laboratories do not have this technique (20) PCR has gained wide acceptance for the laboratory diagnosis of viral infections due to its high sensitivity and specificity. It is recommended that PCR be used later in the evolution of the disease, when fewer viruses are eliminated in the feces, which may not be detectable by ELISA (5). Molecular detection methods are not affected by the host response, PCR assays present greater sensitivity and specificity compared to traditional methods, but they require more time and experience of the staff, which must be specialized. Among the types of PCR currently available is real-time PCR, which has greater advantages than conventional PCR: a greater number of samples can be processed, obtaining a higher yield, automated steps and the detection of low CPV titers in stool. This type of PCR has the capacity to determine a minimum of 10 copies of viral DNA, improving the results in those patients who have low release of viral particles, either due to the phase of the disease in which the sample is taken or due to sequestration in the lumen. Additionally, it provides the possibility of defining the viral types of CPV 2a and CPV 2b in a single analysis (5). According to (21), when comparing 3 different diagnostic tests (viral antigen test, conventional PCR and quantitative PCR), fecal samples were taken from 17 vaccinated dogs and 41 unvaccinated dogs, with signs consistent with CPV, obtaining the following results:

- The antigen test positivity was 41.2% of vaccinated dogs and 73.2% of unvaccinated dogs.
- PCR and qPCR (real-time PCR) were positive in 82.4% of vaccinated dogs and 92.7% of unvaccinated dogs.
- The 21 fecal samples from apparently healthy dogs were negative in all three tests.

The viral antigen test turned out to be the most nonspecific, since it detects only a part of the total sample of positives, which can be associated with a low amount of viral antigens, either due to low elimination of viral particles according to the stage of the disease,

due to sequestration at the level of the intestinal lumen or due to the patient's antibodies produced by the vaccine, so the negative results of the CPV fecal antigen should be observed with caution, until confirmed by molecular methods. This study did not consider patients from 9 to 16 weeks of age so that there was no interference from maternal antibodies for detection.

Another study carried out in Bangladesh (22) that sought to determine the presence of CPV in 96 unvaccinated dogs, resulted in 17.7% positivity in the IC test. Subsequently, when the VP2 gene was detected by a conventional PCR assay, 15.62% tested positive, and demonstrated that IC had 100% sensitivity since it detected the real patients, however, it was concluded that IC is not specific, since two samples gave false positives. It should be noted that the study was carried out with a small sample. According to a study carried out by (13) that compared the effectiveness of two diagnostic methods (IC and conventional PCR), 12 samples positive by PCR were subjected to IC and it was determined that the positivity was only 41.7% compared to conventional PCR (100%). These results coincide with various studies that have determined that traditional methods such as IC have lower sensitivity than molecular methods such as conventional PCR. Although real-time PCR is more efficient than conventional PCR, the former requires greater investment in equipment, specialized reagents such as the probe that allows quantification of the amplified product, and more trained personnel Another study (23) evaluated the accuracy of a combined IC test kit and the detection of canine coronavirus (CCoV)/CPV fecal antigens. Random multicenter fecal samples from 115 dogs with gastroenteritis were analyzed for the presence of CPV antigens using the Sens PERT IC combination test kit and the result was compared with a reference PCR.

Parvovirus was detected in 105 (91.3%) and 108 (93.9%) fecal samples by the point-of-care test kit and PCR, respectively. The point-of-care IC test kit showed a relative sensitivity of 95.4% and a specificity of 71.4%. Among the main therapeutic goals when establishing a treatment protocol for patients with CPV is to maintain the hydro electrolytic balance, prevent secondary bacterial infections, and manage symptoms such as vomiting, diarrhea, and pain. In different countries, studies and comparisons have been carried out on different therapeutic protocols used in different veterinary clinics, as well as the use of new treatments and drugs that improve the prognosis and hospitalization time of patients affected by the gastrointestinal condition caused by CPV. An example of this is a retrospective study that was carried out in the USA (24) regarding the treatment used in 5,127 dogs infected with CPV in a private shelter between 2008 and 2019, indicated that during the study period there was a survival rate of 86.6% (4,438/5,127) and it was concluded that the first 5 days of treatment are the most critical with 80% mortality and then it decreases to 13.7%, which reflects the need to act quickly when implementing a treatment for a patient with CPV. The success rate of therapeutic treatments is also affected by the time elapsed since the pet begins to show clinical signs and receives medical attention, since there are owners who wait for the clinical signs to progress to take their pets to veterinary centers, when the patient presents progressive signs of bloody diarrhea, lethargy, severe vomiting, so the probability of a treatment being successful decreases.

This study describes the type of treatment each patient receives according to the clinical signs they present. The protocol used is shown in Annex 2. Regarding the management of patients in shock, which are those who show rapid deterioration, such as sticky, pale or white gums, cold extremities, seizures, vocalizations, inability to swallow, low body temperature, coma/extreme lethargy, the following protocol was followed:

- Wrap the patient in a blanket, apply a 50% oral dextrose solution, include an intravenous catheter and an intravenous bolus of Ringer lactate at 22 ml/kg, perform rectal temperature, blood glucose, cell volume and total protein tests, apply forced feeding and an intravenous infusion pump.

- Another study carried out at the Activet veterinary clinic in Bolivia (20) sought to determine the effectiveness of an outpatient therapeutic protocol in patients with canine parvovirus. For this, positive patients were identified through rapid antigen detection tests in feces, based on immunochromatography, allowing a diagnosis in a few minutes.

In this case, the following support therapy was used:

- **Restitution Of Fluids and Electrolytes:** Prolonged vomiting leads to a loss of fluid, Hydrochloric acid (HCl), Chlorine (Cl) and Potassium (K), producing dehydration and metabolic alkalosis. If it leads to excessive dehydration, it leads to metabolic acidosis.

- **Diarrhea:** In addition to being a route of water loss, sodium (Na) and bicarbonate are lost → also triggering metabolic acidosis.

- If there is vomiting without diarrhea, intravenous physiological serum or lactated Ringer is administered, in addition to potassium if laboratory tests indicate it.

- If there is diarrhea and vomiting, isotonic glucose-salt fluid should be administered subcutaneously, and lactated Ringer's should be administered intravenously.

- If there is only diarrhea, Ringer lactate should be used for hydration (20)

The treatment of digestive signs followed the following protocol:

- Metoclopramide

- Maropitan → Cerenia (use with caution because it causes intussusception if there is severe diarrhea) or Ondansetron

- Gastric protectors → Ranitidine or Sucralfate

In relation to antibiotic therapy, the following was used:

- Ideal treatment combines broad-spectrum beta-lactams such as Penicillin (Amoxicillin with Clavulanic Acid, Sulbactam) or cephalosporins (Cephalexin, Cefazolin, Cefadroxil) with Gram-covering aminoglycosides such as Amikacin or Gentamicin (which should not be used in patients with a high % of dehydration, since it causes acute renal failure)
- For anaerobic microorganisms add Metronidazole to therapy.

Finally, aspects related to Nutrition were considered

- It should be progressive, first parenteral when there is vomiting, a soft diet of high digestibility with low amounts of fat and protein, using commercial gastrointestinal diets, they should be frequent intakes in small amounts.

In this study (Bellot, et al. [20]) the total number of suspected patients was 25, of which 10 were diagnosed with a rapid test, all were treated, there were no records of deaths and all treated patients were under 8 months old. The main bacterial agents that invade the digestive system are Clostridium perfringens, Escherichia coli and other enteric bacteria. There is evidence that the combined use of penicillin and aminoglycosides has been very effective in patients without risk of dehydration. If we decide to use aminoglycosides (for example, gentamicin, neomycin, amikacin), it must be considered that the patient must be well hydrated and renal function must be carefully monitored. Regarding the use of antiemetics, metoclopramide reduces fluid loss and facilitates the absorption of nutrients, being especially useful if vomiting is prolonged. Puppies with simple infections survive the first 3 to 5 days after the onset of the condition, whereas the most affected dogs, especially those with sepsis, often require prolonged hospitalization. This study evaluated the therapeutic protocol for CPV in 7 different clinics in 3 municipalities of Bolivia (15) A more recent study (25) has evaluated the use and efficacy of Xylazine administration within the therapeutic protocol of patients with CPV, which has been shown to reduce recovery time and mortality rate in puppies. Xylazine is a drug with sedative action and antispasmodic capacity at the digestive level, which greatly reduces the pain associated with this syndrome, since it inhibits gastrointestinal motor and secretory function, the xylazine use protocol is used at doses of 4 mg / kg.

Xylazine belongs to the group of alpha 2 adrenergic, which binds to presynaptic and postsynaptic adrenergic receptors or alpha 2 adrenoreceptors in the central nervous system and induces hyperpolarization, inhibiting the release of norepinephrine and dopamine, it also has a certain effect on alpha 1 receptors, through central stimulation of alpha 2 adrenergic receptors, xylazine also has analgesic activity. Muscle relaxation occurs by inhibition of intraneuronal impulses at the central level of the central nervous system. It is applied intravenously, subcutaneously or intramuscularly and has a binding to plasma proteins. In this study (25) a total of 30 patients participated. The success rate with the typical treatment was 63.64% in 5.2 days on average, and 90% success with the xylazine treatment in 3.7 days on average.

The 30 puppies were clinically diagnosed and the therapeutic protocol for xylazine applied was the following:

- Intravenous isotonic crystalloids
- Central and peripheral action antiemetics: ondansetron
- Gastric protector: Ranitidine
- Visceral analgesia (drug under study): xylazine
- Antibiotic: ampicillin (beta-lactam) and metronidazole.

The results were the following: when applying the conventional treatment in 8 patients, 7 died and the patient who survived did so on the eighth day. In contrast, of 12 patients treated with conventional treatment and xylazine, 3 died, those who survived did so in an average of four days. Another promising therapeutic approach that has been used in both human and veterinary medicine is intestinal microbiota transplantation (26). This study evaluated 66 puppies with parvovirus infection in 2 veterinary hospitals. They were randomly divided into 2 groups of 33 puppies, some received conventional fluid treatment plus antimicrobials and the rest received conventional treatment plus fecal microbiota transplant (FMT). FMT consisted of 10 g of feces from a healthy dog diluted in 10 ml of saline solution, which was deposited rectally between 6 and 12 hours after being hospitalized. Patients who received FMT had a faster resolution of diarrhea and shorter hospitalization time with a median of 3 days, while those receiving conventional treatment had a median of 6 days, we know that CPV affects the crypts of the intestinal villi, decreasing absorption and increasing intestinal permeability, currently the mechanism of how FMT resolves the clinical sign in dogs with viral-mediated diarrhea is uncertain, it can be assumed that diarrhea is associated with bacterial dysbiosis caused by inflammation, hypersecretion and hypermotility, although scientific evidence of FMT is scarce, it is likely that the response to the procedure is related to the reconstitution of the intestinal microbiota and its corresponding metabolites,

we know that mortality in puppies due to CPV can reach 39% in treated animals and up to 91% in untreated animals, being in this study almost double the mortality in animals treated with the standard treatment versus those with the addition of FMT, which indicates a potential in recovery by adopting this treatment, which is easy, inexpensive and practical. In the future, further tests will be necessary to determine its true effectiveness and mechanism of action.

Treatment Proposal for a Patient with CPV

PCR is the ideal method to diagnose canine parvovirus as the causative agent of a patient with gastrointestinal symptoms, whether conventional or in real time, since it has 100% sensitivity and spec-

ificity according to different studies and can be detected at different stages of the disease and regardless of the amount of viral antigen in the sample. It is necessary to have a comprehensive therapeutic protocol for patients diagnosed as positive.

Based on the information collected, the following therapeutic protocol is generated

- **Antibiotic Therapy:** It has been shown that the highest survival rates occur in patients in whom the combination of different antibiotics is used, such as beta-lactams (penicillins, amoxicillins with clavulanic acid) or cephalosporins (cefadroxil) together with aminoglycosides that attack Gram-positive bacteria, for example, gentamicin or amikacin. In the presence of severe diarrhea, supplementation with metronidazole should be considered, which attacks anaerobic infectious agents.
- **Pain and Vomiting Management:** Persistent vomiting can cause dehydration problems, electrolyte disturbances and acid-base imbalances, so the use of antiemetic drugs is necessary (27). The articles collected mainly use metoclopramide or maropitant (with antiemetic and visceral analgesic effects), which can be replaced by ondansetron. Famotidine is widely used in veterinary medicine, it is an antagonist of histamine receptors, has a longer duration of action and is administered once a day (27). If a drug with a low analgesic effect such as metoclopramide is used, it can be supplemented with the use of metamizole, which also has an antipyretic effect.
- **Fluid Therapy:** The replacement of fluids of choice is the use of Ringer Lactate, which provides water and the three most important cations for the body (sodium, potassium and calcium). In patients with vomiting, it can be supplemented with subcutaneous glucosaline solution.
- **Nutrition:** Ideally, patients with vomiting should be fed through a nasogastric tube until they receive oral feeding voluntarily.
- **Others:** It has been seen in clinical practice that the use of vitamins such as B complex, pro and prebiotics increases the survival rate of patients.

New Management

Intestinal microbiota transplantation has improved the recovery rate of patients, decreasing the time of hospitalization and the time they are with diarrhea, being an easy and economic management to apply in clinical practice, this study is mainly based on the successful response in human use but further studies are still needed in veterinary use. Also, the use of Xylazine as an analgesic has been shown to decrease the severity of the condition, which is a good management to perform in in-hospital patients in continuous infusions.

Discussion

The main objectives of this work were to determine the different diagnostic methods used today to detect CPV in puppies with clinical signs consistent with the condition, determining that the main diagnostic method is through IC at the field level, and regarding the therapeutic management currently used. A systematic search for information based on the Prisma method was carried out, where, in the first instance, when searching for studies dealing with canine parvovirus, we obtained a total of 783 articles. Then, the documents were filtered based on their age or titles not relevant to either the diagnostic methods or treatments, where only 14 articles were included that met the search criteria, including the year of publication, the publication site and its impact, among others. The systematic search for information yielded studies with empirical and scientific evidence of the various diagnostic methods comparing their efficacy where it is described that the one with the highest sensitivity and specificity is PCR, a method that is not routinely applied in veterinary clinics today, it is not the method of choice due to its cost, since it is more affordable for the owner to afford a rapid IC test than to confirm the sample by PCR, knowing that due to different factors the IC tests can give false negatives, directly affecting the management of these patients, whether in-hospital or at home, which agrees with what has been described by other authors (26,25).

Regarding therapeutic management, none was found carried out in Chile, that is, there would be no collection of information on the protocols used in veterinary clinics in our country, which should be an aspect of future study, along with the diagnostic methods they use, which would be important to carry out by PCR and be able to identify the strains circulating today in Chile. The above would allow determining if the vaccines used are being effective, since the current commercial vaccines only present CPV variants of type 2a and 2b, not the 2c variant, which has been found circulating in other countries, according to what was mentioned in this study (21). Considering that the first 5 days after the onset of clinical signs are the most critical (4), it is vitally important to educate owners that, when faced with signs such as vomiting or diarrhea, they should not wait for the spontaneous resolution of the signs, but should take their pets to a veterinary care service, since early care reduces the mortality rates of puppies with CPV [28-35].

Conclusion

- Although there are various protocols and diagnostic methods for the management of patients with CPV, the most widely used diagnostic method in veterinary clinics is IC, although in some cases it is not entirely accurate.
- There are some professionals who, when faced with a test with a doubtful result, suggest performing a PCR, however, the cost is still an obstacle for tutors.
- The guidelines regarding an appropriate treatment proto-

col include a wide variety of medications, covering pain management, fluid therapy, secondary infections and electrolyte loss.

- A treatment protocol as complete as possible is suggested, which helps in clinics with regard to both the guidelines to follow and the level of education, considering those assistants who are still studying Veterinary Medicine, in order to obtain high rates of success and survival.

- It is necessary to evaluate the effectiveness of the vaccines currently used, since new strains of CPV have emerged, such as type 2c, against which it is not clear whether there is protection with the vaccines currently applied, and because the presentation of the condition in adult patients has increased.

Acknowledgments

The authors thank Dr. Aron Mosnaim of Wolf Found, Illinois, USA, for his constant support in the development of science in countries like ours.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.59.009344

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