Vaccination therapy of Canine Parvovirus (CPV) infected on dogs

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Abstract. Canine Parvovirus (CPV) is highly contagious virus, it has become the most remarkable factor for causing death among pet dogs since it was discovered and recorded in the decades. The variant CPV-2 attacks rapid dividing cells after entering blood flow, leading to inflammation in heart, for puppies, and small intestines, for adults, both of the disorders are extremely fatal. Currently, there are no effective treatments to fully treat myocarditis and enteritis caused by CPV-2, the best way to resist the diseases for patients to receive conservative treatment, including analgesia, antiemesis, antidiarrhea, intravenous nutrition. New therapies like Ozone therapy and fecal microbiota transplantation (FMT), have a good therapeutic effect, reduce mortality to some extent, which are quite prospecting. As a result, the best choice is to take prevention by injecting vaccines. Contemporary vaccines can be divided into attenuated vaccines and inactivated vaccines, which are relatively easy to be synthesised and are used in a wide range, and virus-like particles (VLP), all of them can produce antibodies against CPV-2.

Keywords: CPV, vaccination therapy.

1. Introduction

Canine parvovirus (CPV) is a common virus for dogs, with highly infectiousness, pathogenicity and lethality. Non-encapsulated icosahedral viruses can cause canine parvovirus infection. CPV was first discovered in the late 1970s. CPV contains 2 types, CPV-1 and CPV-2, and some theories suggested that CPV-2 is an entirely different variant mutated from CPV-1 [1]. CPV-2 mostly infects rapidly dividing cells in bone marrow, small intestines and heart muscle [1], and this may lead to canine parvovirus enteritis (PVE) and canine myocarditis. Without treatments, the diseases caused by CPV-2 are fatal, and this is the main reason of dogs' death worldwide. The virus can infect dogs with all ages, among them, enteritis is observed in adults, myocarditis is common in juveniles, in addition, no intestine inflammation is reported in young puppies' cases [2].

CPV is mostly transmitted through feces and vomit [3]. When dogs get in touched with these secretions, there is an extremely highly risk for the virus to get into animals. After CPV-2 enters the dogs' body, the virus multiplies in the oropharyngeal lymphoid tissue before moving into the circulation causing a plasma viraemia, and attacking rapidly dividing cells all over the body, especially in the myeloid lymphogenic tissue [2,4]. Blood that carries virus flows systematically, and spreads to intestine crypts, about 3 days later, inflammation takes place in heart muscles for puppies and small intestines for adults [5]. Myocarditis will lead to permanent heart damage and disorders, which is a fatal disease, most puppies die of these. Myocarditis is identified by non-specific clinical symptoms such as sudden weakness, fainting, inability to exercise, breathing difficulties, and swelling in the abdomen. Potentially life-threatening consequences of myocarditis include abnormal cardiac rhythms or congestive heart failure on either the left or right side, and then lead to myocardial necrosis [4,6]. The virus invades the rapidly proliferating epithelial cells located in the crypts of the intestinal villi in the ileum and jejunum [2]. Consequently, there is a disturbance in the protective lining of the intestines, coupled with the deterioration of the finger-like projections called villi and the inability to absorb nutrients properly [3,7]. This leads to a significant decrease in white blood cells, particularly

neutrophils and lymphocytes, resulting in excessive diarrhoea and vomiting. Additionally, there is a severe loss of fluids and a decrease in blood volume, leading to dehydration and low blood volume [3,5]. Non-encapsulated icosahedral viruses can cause canine parvovirus infection. CPV was first discovered in the late 1970s. After infection with CPV, the virus infects the gastrointestinal tract, causing necrosis of the villi and epithelium in the intestine. This causes the mucous membrane to be exposed and can cause hemorrhagic gastroenteritis. More bacteria entering the bloodstream through the wound could further trigger sepsis and other infections [8].

Clinical signs and laboratory tests are considered for the diagnosis of CPV includes. For PVE caused by CPV-2, it is the most common to be observed in 6~20 weeks old puppies [4]. Usual symptoms appear in 3~7 days after infection, include fever, depression, emesis, and hemorrhagic diarrhoea [4]. Their feces are often described as rotten tomato smell. Clinical diagnose should be confirmed through laboratory tests, including Immunochromatography Test (ICT) which is a quick and easy diagnostic technique is employed in clinical settings due to its straightforward test protocol [4]. Three virus variations may be identified by this test (CPV2a, CPV2b, and CPV2c) [4]. And also enzyme-Linked Immunosorbent Assay (ELISA). Which is a simple and convenient diagnostic method that has been designed to determine the concentration of IgG antibodies in the serum of vaccinated dogs and puppies.

The current mainstream treatment methods are fluid therapy, ozone therapy, antibiotic treatment and fecal microbiota transplantation (FMT).The cost of conventional treatment for CPV infection and related complications is generally high, and some people choose to forgo treatment or euthanasia. Fluid therapyapy is crucial in the treatment of PVE. It can maintain hydration and tumor support, as well as reduce acid-base and electrolyte interference. Ozone treatment kills bacteria and fights viruses, which can reduce inflammation and infection [7,8]. Antibiotic treatment is mainly used in dogs with severe infections. Antibiotics can treat sepsis and cell adhesion disorders caused by CPV. But antibiotic therapy is not a treatment for CPV [7]. There are no targeting treatments today, the supporting treatment is the most commonly used, like fluid therapy, by injecting water, nutrients and ions. In addition, Fecal microbiota transplantation (FMT) and ozone therapy are discussed in the article, and ozone therapy, as well as a new sort of treatment, is effective and economical, which is quite prospecting [9].

Currently, many vaccines against CPV are being developed and tested. Examples include traditional attenuated vaccines, inactivated vaccines and emerging genetically engineered vaccines. CPV viruses are divided into many subtypes, three of which are major. The two main antibodies are CPV-2a and CPV-2b. Compared with existing conventional treatment methods, the vaccine's price and treatment effectiveness have significant advantages. But the number of successful cases so far is small, and there are many problems that need to be solved to better achieve the effectiveness of immunization. So, many improvements are still needed for the CPV vaccine to develop into a mature mainstream treatment [10, 11].

This article will discuss the principles, advantages and disadvantages of existing treatments for CPV, and summarize the advantages and disadvantages of CPV vaccination.

2. Current Treatments: Fluid therapy, Ozone therapy, Fecal microbiota transplantation (FMT) and Antibiotic treatment

There are no treatments targeting on completely cured PVE. Today, PVE is mostly treated with supportive and symptomatic care. Treatment consists of fluid therapy, antibiotics, antiemetic medication, nutritional assistance, pain management and antiviral therapies [7].

For dogs with PVE, their small intestines are damaged significantly, it is almost impossible for them to absorb nutrients through small intestine epithelium, and they get dehydrated. The patients should be treated with intravenous use of water, glucose, ions (K+, Na+, Cl-), amino acids if hypoalbuminemia, whole blood or packed red blood cells if severe anemia. Fluid therapy may be difficult to perform if an IV line cannot be placed effectively. In addition, inserting a catheter in the

jugular vein increases the risk of thrombosis. This treatment is relatively expensive and carries a risk of cancer [3,7].

Ozone therapy is an efficient and economical treatment, as it is easy and inexpensive for preparation and storage, and has been proven to be used in many domains, either human or animals. To compete with CPV-2, Ozone therapy possesses antiviral, bactericidal, and fungal properties that increase the amount of oxygen available to the tissues, encouraging tissue to get repaired and regenerated, decreasing platelet aggregation, and serving as an analgesic and anti-inflammatory. Experimental data showed that ozone-treated puppies still had a large number of problems with vomiting and diarrhea. The therapeutic effect of ozone therapy is not very satisfactory [8].

Antibiotic treatment is mainly used in individuals with severe infections. Due to the damage of the gastrointestinal epidermis and villi, bacteria can enter the blood and cause sepsis and endotoxemia. Antibiotics can be effective in the treatment of these complications [3].

Standard treatment (STD) as a supportive care and main method to cope with PVE, often takes long to fully recover and has a high probability of dying [9]. FMT, being an adjunctive treatment, is very effective. Dogs have a large population of bacteria, known as the microbiota, in their gastrointestinal system. The intestinal microbiota provides several advantages to the host, like promoting movement in the gastrointestinal tract. Alterations in the intestinal microbiota have been associated with various diseases in numerous species, including acute and chronic gastrointestinal diseases in dogs [9]. PVE influences the microbiota in dogs' intestines, so recover or improve the initial microbiota is a successful way, and patients who received STD+FMT more quickly got rid of diarrhoea. This type of treatment has a higher treatment rate, lower cost and shorter hospital stay. Fecal transplant treatment can reduce the incidence of complications. In addition, there is new evidence that surface fecal transplantation can also play a role in helping gut microbiota rebuild [9].

To sum up, there are still some problems with the existing conventional treatment. The cost and length of treatment is a concern for many guardians. The high cost and time investment makes people more likely to forgo treatment. In addition, there is no complete treatment for canine parvovirus and some existing treatments are not effective [7,9].

2.1. Efficiency

2.1.1. Diarrhea and vomiting

In experimental groups, the diarrhea symptom stop in 48 hours after ozone therapy, and their feces were forming shape during this period [8]. No vomiting was observed in the experimental group.

In control groups, control group 1 died before 24h treatment, with severe diarrhea and emesis [8]. Another group control group 2 had no symptoms after 48h treatment, or less frequently and more consistently [8].

2.1.2. Abdominal pain score

The scores for experimental groups were 5 and 7, which reduced to 0 and 3 after 48h ozone therapy [8].

The score for control group 1, the pain was significant, with score 18, and needed analgesics, however, the animal died later [8]. For control group 2, the score is 3, which reduced to 0 after 48h, got rid of analgesics [8].

2.1.3. Blood glucose

Experimental groups and control group 2 revealed a normal content of blood glucose during the treatment, while control group 1 presented hypoglycaemia (32mg/dl), and then died [8].

2.2. Hospitalisation and mortality

No emesis is witnessed in animals from experimental groups after 48h treatment, so they kept on receiving supportive treatment, until experimental group 1 clinical discharged after 4.5 days and experimental group 2 discharged after 5.5 days [8]. For control groups which were still alive still occurred diarrhea, and the animals discharged after 6.5 days [8].

3. Vaccination

3.1. Traditional treatment

Traditional treatment methods mainly include antibiotics and antiviral treatment, usually using antiviral serum or antibiotics, interferon. Severe infections may include vomiting, blood in the stool, and fasting and hydration to prevent dehydration and malnutrition. For this reason, severe infections are usually treated with antiviral serum or monoclonal antibodies, antibiotics (cefotifor or cefquinolme), interferon, antiemetics (antioxidants or bropivacaine), hemostatic agents (hemostatin or snake venom thrombin), and energy rehydration (ATP).

3.2. Antibody and development of vaccines

Currently, vaccines are the most effective way to treat CPV. Attenuated vaccines and inactivated vaccines are the two most common types. These two vaccines are more traditional, relatively simple to make and widely used. In addition, virus-like particle vaccines are also an option. Traditional vaccines require adjuvants and multiple injections to work, and cross-infection is frequent due to allergies, virulent atavism, and viral contamination of the environment. So genetically engineered vaccines are also a good option [11]. The vaccine has the same shape and size as the virus, but lacks the genetic material to actually infect cells. It can induce an immune response in the body. In addition, virus-like particle vaccines, which have the same shape and size as viruses, are a very effective approach. But it lacks the genetic material to actually infect cells [10].

Cpv-2a and CPV-2B are two antibodies to CPV. In current vaccines, CPV-2b dominates. In recent years, CPV-2c has also been detected, but the amount is not very large [11]. Beside, peptide NVVLKTVSESATQPPTK, residues 147 ~ 163 in VP2, can induce CPV antibody production and identify CPV T cell epitopes. Studies have shown that amino acid 3-19 (DGAVQPDGQPAVRNER) linear peptide epitope (3L17) can induce antibodies when binding to keyhole hemocyanin (KLH) [12].

VP2 is the viral protein coat of CPV, so it can be a good platform for CPV vaccine. VP2 has only limited amino acid variations, and it can characterize changes in three subtypes [10]. VP2 has suitable solubility and low hydrophilicity, and can be combined with viral proteins to make vaccines [12].

The vaccine has significant advantages over existing conventional treatments. The relatively low price of the vaccine solves the problem of time and expense. In addition, vaccines can provide a durable immune response that works once and for all. So the development of a CPV vaccine is very important [8,11]. However, many improvements are needed to develop the CPV vaccine into a full-fledged mainstream treatment.

The failure rate of CPV vaccine immunization is more than half, and there are many reasons for this. For example, the mutation of CPV virus, the influence of dog breed, breeding methods, etc. Maternal antibody interference is a crucial factor, too low maternal antibody will affect the vaccination effect. In order for the vaccine to have the desired immune effect, the maternal antibody against. In addition, lower costs are also an important consideration [11].

4. Conclusion

Canine Parvovirus (CPV) is an extremely contagious virus that has emerged as the leading cause of death among domestic dogs since its discovery and documentation in recent decades. The variant CPV-2 attacks rapid dividing cells after entering blood flow, leading to inflammation in heart, for puppies, and small intestines, for adults, both of the disorders are extremely fatal. Currently, there are no effective treatments to fully treat myocarditis and enteritis caused by CPV-2, the best way to resist the diseases for patients to receive conservative treatment, including analgesia, antiemesis, antidiarrhea, intravenous nutrition. New therapies like Ozone therapy and fecal microbiota transplantation (FMT), have a good therapeutic effect, reduce mortality to some extent, which are quite prospecting. As a result, the best choice is to take prevention by injecting vaccines. Contemporary vaccines can be categorised as attenuated vaccines and inactivated vaccines, both of

which are extremely simple to create and have a broad range of applications. Additionally, there are virus-like particles (VLP) that also have the ability to generate antibodies against CPV-2.

Authors Contribution

Each of the authors made an equal contribution, and their names were arranged in alphabetical order.

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