Research Article

Evolution of The Effect of Canine Parvovirus (CPV) Ab Value on Recovery Time and Survival Rate in Dogs Infected with CPV

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Doi : 10.5281/zenodo.18147163

Acknowledgement
This study is produced from Ahmet Yurtseven's master's thesis, a student at the Institute of Health Sciences, Kırıkkale University.

Abstract

Parvoviral enteritis is a viral disease that commonly presents with clinical symptoms such as vomiting, hemorrhagic enteritis, and lethargy. Many studies have been conducted on the prevention and treatment of the disease. Prevention methods are more prominent than treatment methods, and vaccination is of utmost importance. If vaccination is not performed at a sufficient level or with appropriate procedures, the desired level of immunity is not achieved, and full protection cannot be provided. In our study, stool samples taken from patients with sterile swabs were immersed in dilution solution and waited, then dropped into the test kit with the help of a vacuum pipette, and individuals with double lines were considered parvoviral enteritis was accepted as positive. Blood was taken from patients with positive test results into a gel yellow capped blood collection tube and sera were obtained by centrifugation. 100 microliters of the mixture were taken and dropped into the relevant section of the CPV Ab test kit and evaluated with the V - check V200 automatic veterinary hormone analysis and immunity test device after 10 minutes. Serum parvovirus Ab levels of 40 patients (22 female, 18 male) who were vaccinated in various numbers were examined with the V-check V200 automatic veterinary hormone analysis and immunity test device. Data were obtained showing that 80% of patients with high and medium level protection survived and 52.5% of all patients survived. It was observed that factors such as gender and number of vaccinations had no effect on survival. The possibility of 2 doses of vaccination with a large sample size was considered.

Keywords: Canine Parvovirus (CPV), diarrhea, antibody, hemorrhagic enteritis, V-check, antigen, prognosis, CPV Ab

Introduction

Canine Parvovirus (CPV) is one of the viral pathogens with enterohemorrhage, which is common among all dogs globally regardless of breed and causes high morbidity and mortality. The course of the virus leads to acute gastroenteritis (Neeraj et al. 2020, Eregowda et al. 2020). The virus is a species of Canine Protoparvovirus in the genus Protoparvovirus of the Parvovirinae, a subfamily of the family Parvoviridae, and is in the order Piccovirales. In 1978, a second new virus was detected that causes disease in domestic and wild dogs. The course and symptoms of the disease include vomiting, high fever, bloody diarrhea and myocarditis, especially in younger individuals, and it has been observed that it causes serious clinical infections (Decaro and Buonavoglia 2012). Canine Parvovirus Type 2 was named by taking these into account while defining the virus, and it was distinguished from Canine Parvovirus type 1 (CPV-1), also known as the "dog minute virus" (Kwan et al, 2021). The disease can be easily transmitted to susceptible individuals by inhalation, consumption of feces-contaminated foods, direct contact or contaminated bedding, toys, living space, etc. The CPV-2a, 2b, 2c variant has been reported to be more pathogenic than the CPV strain (Sykes, 2014; Mylonakis et al. 2016). After ingestion of the CPV-2 virus, it multiplies in the thymus, mesenteric and oropharyngial lymph nodes and becomes viremic in an average of 1 to 5 days (Goddard and Leisewitz, 2010). Virus shedding also occurs during the incubation period (4 to 14 days) or before clinical symptoms take effect (Smith Carr et al. 1997; McCAW and Hoskins, 2006). The virus, which affects many organs and systems, is considered the cause of death of many patients as a result of myocarditis before the start of vaccine applications. Although there are many clinical manifestations, the disease commonly includes vomiting, diarrhea, lethargy and loss of appetite. Diarrhea can be yellow, brown depending on the course and severity of the disease, and bloody and watery depending on the intensity of hemorrhage. The density of the destroyed intestinal villi determines the severity of hemorrhage. A high amount of fluid loss can lead to dehydration and hypovolemic shock. Various seizures may occur with malabsorption, hypotension with systemic infection, organ failure and septic shock. The developing clinical picture may vary due to age, vaccination, serum antibody level and many other reasons. The diagnosis of physical examination is only accurate to a certain percentage. Slowing down in capillary filling, bad smell in the stool, fever, hypothermia and abdominal pain will give an idea about the disease. In particular, invagination of the small intestine can be detected on palpation by hand (Rallis et al. 2000; Faz et al. 2019). (Sime et al. 2015; Strom et al. 2015; Ford et al. 2017). Although many parameters affecting survival in parvoviral enteritis have been studied, ways of preventing the disease are of greater importance. Undoubtedly, vaccination is one of them. The aim of the study is to emphasize the necessity of vaccination of dogs against CPV at the right time, with the appropriate vaccination program and the right vaccines, and then to show the importance of determining serum antibody levels against CPV and its effects on survival. Although this study includes some parameters that affect the process, the aim of the study is to measure the serum antibody (CPV-Ab) levels formed against parvovirus with vaccination and the relationship between survival and its correlation with other parameters.

Materials and methods

This study was approved by Kırıkkale University Animal Experiments Local Ethics Committee (Approval No: E.334147). The study group consisted of 40 dogs, 22 females and 18 males of different breeds and genders, aged 2-8 months, who were brought to Kırıkkale University Faculty of Veterinary Medicine Animal Hospital and Gölbaşı VSM Veterinary Clinic with parvovirus findings, and who were positive for the Parvoviral enteritis rapid diagnostic test kit (Vetfor CPV Ag rapid diagnostic test kit). CPV Ab was measured with V-check V200 automatic veterinary hormone analysis and immunity testing device of the dogs constituting the study.

Stool samples were taken rectally with sterile swap swabs from the patients constituting the study, the stool sample was immersed in the dilution solution and waited for a while. Then, with the help of a vacuum pipette, 3 drops were dripped into the relevant part of the test kit. It was waited for 10 minutes for the result and evaluated according to the line formed in the test kit. Tests with a single line, that is, only a control line, were considered negative, and tests with double lines were evaluated as a positive group and included in the study.

Blood was taken from the patients with a positive test result into gel yellow capped serum tubes, the blood samples were kept at room temperature for 20 minutes and then centrifuged at 3000 cycles for 10 minutes to obtain serum. 100 microliters of serum and CPV Ab solution were mixed and pipetted 5-6 times, 100 microliters of the mixture were taken and dripped into the relevant part of the CPV Ab test kit. After 10 minutes, the V check was evaluated with the V200 automatic veterinary hormone analysis and immunity testing device. Sex, vaccination status, CPV Ab scale and survival of the animals were included in the evaluation. Dogs with a serum antibody titer of less than 1:10 were evaluated as having no protection level, those with a serum antibody titer between 1:20 and 1:40 were considered to have a low level of protection, those with a serum antibody titer of 1:80 to :1:120 were considered to have a moderate level of protection, and those with a serum antibody titer above 1:160 were evaluated as having high protection.

Metronidazole was administered 12.5 mg/kg dose 2 times 12 hours apart, antiemetic Maropitant at 0.1 ml/kg dose 24 hours apart, Duphalyte® for vitamin-mineral supplement was administered at a dose of 5ml/kg at 12 hours intervals to the participants included in the study. In addition, all patients were treated with fluids (Lactated ringer's solution, 5% Dextrose solution, 0.09% NaCl solution) according to the degree of dehydration and blood pH.

Statistical Analysis

Two types of statistical analysis were done in this study. In the first part, descriptive statistics of the study were given, and in the second part, the results of logistic regression analysis of parameters affecting survival for a group of 40 dogs were presented. In statistical analyses, $p<0.05$ value was considered significant (Fox and Weisberg, 2023, Jamovi, 2024; R Core Team, 2024).

Results

The participants of this study, 40 dogs, 25% had Ab levels of high, 25% moderate, 25% low, and 25% with no level of protection. The gender distribution is balanced, with 55% of dogs being female and 45% being male. The survival rate was in favor of the survivors with 52.5%, and 47.5% of the dogs died. When the vaccination status was examined, it was seen that 32.5% of the dogs had received 1 dose, 35% had received 2 doses and 32.5% had received 3 doses or more of mixed vaccines, and the distribution of vaccine doses was homogeneous (Table 1).

The relationship between CPV antibody levels and survival was evaluated by both Chi-square test and logistic regression analysis; The two types of analysis have been interpreted together. In Table 2, the survival rates, odds ratios and statistical significance levels of the groups are presented together.

Table 1: Distribution of the number of vaccines administered in dogs

Variable	*Category*	*Frequencies (n)*	*Percentage (%)*
Ab level	High	10	25%
	Middle	10	25%
	Low	10	25%
	No protection	10	25%
Gender	Female	22	55%
	Male	18	45%
Living situation	Right	21	52.5%
	Dead	19	47.5%
Vaccination status	1 dose	13	32.5%
	2 doses	14	35%
	3 doses or more	13	32.5%

Table 2: Relationship between CPV Ab Level and Survival and Regression Summary

CPV Ab Level	*Living (n)*	*Deceased (n)*	*Total (n)*	*Life Rate(%)*	*Odds Ratio*	*p-value*
High	9	1	10	90%	0.005	0.012
Medium	7	3	10	70%	0.039	0.045
Low	3	7	10	30%	0.613	0.658
No protection	2	8	10	20%	Reference	Reference

When the Ab level and survival and mortality rates were examined, it was seen that the mortality rate increased significantly as the Ab level decreased (p=0.004). 90% of individuals with high antibody levels lived, while only 10% died. In the unprotected group, this ratio was reversed; 80% of individuals died, only 20% lived. This suggests that antibody level has a strong and decisive effect on survival (Table 2).

The relationship between Ab level and survival status was examined by Chi-Square test, and a statistically significant relationship was found between Ab level and life/death status ($\chi^2(3) = 13.133$, $p = 0.004$). It was observed that the survival rate was significantly increased in individuals with high and moderate levels of protection (Table 3). Cramer's V value (0.573), which indicates a medium-high effect size, showed that the difference in Ab level had a very strong effect on survival (Table 4).

In this study, pairwise logistic regression analysis was applied to evaluate the effect of CPV Ab level, vaccination status, and gender variables on survival (life/death) status in dogs. Survival status (0 = survival, 1 = death) were used as dependent variables, CPV Ab level (1 = high protection, 2 = moderate, 3 = low, 4 = no protection), vaccination status (1 = 1 dose, 2 = 2 doses, 3 = 3 doses and above), and gender (1 = female, 2 = male) were used as independent variables.

The risk of death was statistically significantly reduced in individuals with high levels of CPV antibodies (OR = 0.005, p=0.012). The risk of death was also significantly reduced in individuals with moderate protection (OR = 0.039, p = 0.045). In individuals with low levels of protection, this relationship is not statistically significant. The group without protection was evaluated as a reference category. As a result, CPV Ab level stands out as a strong variable determining survival in terms of both categorical relationship and risk modeling (Table 2).

Vaccination status, gender and Ab levels regression

When the results of the analysis are evaluated, it is seen that as the Ab level increases (i.e. the immunity level increases), the risk of death decreases significantly, and the strongest protection is provided by high-titer antibodies. Although the risk of death tended to decrease in individuals who received more doses of vaccine, statistical significance was found to be borderline in 2 doses and not significant in 1 dose (Table 5). With a larger sample, 2 doses of vaccine will likely make sense. Gender was found to have no significant effect on mortality. No difference in mortality risk was observed between males and females (Table 5).

CPV Ab level stands out as the strongest factor in determining the survival status of dogs. In particular, the presence of high and moderate levels of CPV Ab significantly reduced the probability of death ($p < 0.05$). A negative correlation was observed between vaccination status and death, and 2-dose vaccine administration was found to be marginal. Gender did not have a significant effect on survival.

Table 3: Chi-Square Test Results

Test Type	*Chi-Square (χ^2)*	*sd*	*Significance (p)*
Person Chi-Square	13.133	3	0.004
Likelihood Ratio	14.407	3	0.002
Linear-by-Linear Assoc.	12.218	1	0.000

Table 4: Effect Size – Cramer's V and Phi

Measurement	*Value*	*Significance (p)*
Non	0.573	0.004
Cramer's V	0.573	0.004

Table 5: Vaccination status, gender and Ab levels, Regression analysis results

Variable	*Coefficient (B)*	*Standard Error*	*Wald Test Value*	*Degree of freedom*	*Significance Level (p)*	*Probability Ratio (Exp(B)) or Odds Ratio*
Ab			7,127	3,000	,068	
Ab (High)	-5,379	2,130	6,380	1,000	,012	,005
Ab (Medium)	-3,237	1,618	4,003	1,000	,045	,039
Ab (Low)	-,490	1,107	,196	1,000	,658	,613
Vaccination status			3,421	2,000	,181	
Vaccine (1 dose)	-2,777	1,974	1,979	1,000	,160	,062
Vaccine (2 doses)	-2,805	1,518	3,413	1,000	,065	,061
Gender (Female)	,206	,908	,051	1,000	,821	1,228
Fixed Term	4,028	1,930	4,357	1,000	,037	56,122

Discussion

Symptoms of parvoviral enteritis include vomiting, high fever, bloody diarrhea and myocarditis, especially in younger individuals, and it has been observed that it leads to serious clinical infections (Decaro and Buonavoglia 2012). Diarrhea can be yellow, brown depending on the course and severity of the disease, and bloody and watery depending on the intensity of hemorrhage. Similar symptoms of varying severity were also detected in dogs with parvoviral enteritis that constituted our study. It has been observed that the symptoms are milder and respond more positively to treatment in patients with high antibody titers.

It has been reported that animals vaccinated with modified live virus vaccines may give antigen positive results for 10 days and may be misleading and vomiting and diarrhea should be considered as true infection in cases where this positivity is accompanied (Decaro et al. 2007). Modified live vaccine formulations mainly use the CPV-2 strain and its variant, CPV-2b. These strains used can lead to viremia and multiply in the intestines, spreading through feces for 3-4 weeks, even at lower antigen titers than field strains (Decaro et al. 2014; Freisl et al. 2017). The vaccines used in the vaccinated patients in this study were attenuated live vaccines and no similar situation was encountered.

Although there is no definitive treatment for patients with parvoviral enteritis, the main lines are shaped by stopping vomiting and diarrhea and fluid treatment in general. The aim of supportive treatment is symptomatic support of the infected patient until the disease process is completed. Treatment costs in parvovirus cases are challenging for patient owners, and the number of cases is high in socioeconomically low regions (Brady et al. 2012, Kelman et al. 2019). In our study, it was seen that the treatment process and costs of individuals with high protection obtained by vaccination were reduced by 60%. Since the severity of symptoms is milder, especially in patients with high and medium protection, supportive treatment, antibiotics and fluid therapy were minimally needed.

One of the major reasons why dogs undergoing the CPV vaccination program do not develop an adequate level of protection is the presence of maternal antibodies. Antibody transmission during pregnancy is around 5-10% due to low placental permeability. Maternal antibodies are largely taken up by colostrum.With colostrum, maternal antibodies are taken up by the offspring orally for about 38 days, thus providing protection to the offspring from lactogenic immunity (Decaro et al. 2004). In the course of the disease, low or high maternal antibodies (serum antibody level)

have a different role in shaping the disease. The presence of antibodies neutralizes antigens and greatly reduces virus replication (Bragg et al. 2012). Since inactivated vaccines are weak against this effect of maternal antibodies, it has been reported that the desired antibody level is not formed, and immunity is not formed in puppies under 12 weeks of age (Altman et al. 2017). It has been reported in some studies that the incidence of severe clinical symptoms and hypovolemic shock due to fluid loss decreases, and survival increases after the use of antibody-rich hyperimmune plasma as an alternative therapy (Meunier et al. 1985). In our study, it was observed that survival increased in patients whose serum antibody level was increased by accurate and effective vaccination. The occurrence of different levels of antibody titer in dogs vaccinated with the same dose suggested that the maternal antibody level may have neutralized the first vaccine at the time of vaccination in these dogs.

While vaccinating, some factors that need to be evaluated individually, such as the region-specific incidence of the disease and the age of the dog, are also important. This situation takes the standards in vaccination protocols out of a certain pattern. In general, the protocol for modified live vaccines starts at 6-8 weeks of age, while there are some vaccines that can be administered to puppies at 4 weeks of age (Day et al. 2016; Ford et al. 2017). It was observed that 30% of the dogs in our study started their vaccination program with vaccines that could be administered at 4 weeks of age, and 70% of the vaccination program started with vaccines that could be administered to dogs aged 6-8 weeks and older.

There are some studies that show vaccination failures in the world and their causes. There is an epidemiological study in Australia in which it was stated that 3.3% of dogs infected with CPV were adult dogs that had been vaccinated with their primary vaccination (Ling et al. 2012). The dogs in our study covered the age range of 2-8 months and the number and periods of vaccines administered varied. A study conducted in Australia in 2017 found that half of dog owners infected with CPV did not comply with the vaccination schedule (Kelman et al. 2020). In our study, similar problems were encountered, and it was observed that the vaccination of some of the sick dogs was not carried out in accordance with the procedures.

For dogs that start a vaccination program at 6-8 weeks, an intermittent revaccination program of 2-4 weeks is recommended until they reach 16 weeks of age and older. In some puppies, there are some studies that vaccination should not be done until they are 16 weeks old and that a single dose of vaccination will be sufficient after 20 weeks of age. A single dose of vaccination is considered sufficient because there should be no maternal antibodies in the blood serum after 16 weeks (Day et al. 2016; Ford et al. 2017). The vaccination schedules of the dogs in our study started at 4 weeks and 6-8 weeks. For this reason, no data have been obtained on whether a single dose of vaccination after the 16-week period can create an adequate level of antibodies. Statistically, obtaining such data can be difficult, and often impossible, for dog owners and veterinarians, as it requires dogs to be in a disease-free, isolated environment until they reach the 16-week period. The reason for this is that the agent can be carried in many ways and it is very easy to be transmitted.

As an alternative to revaccination, laboratory or in-clinic tests can be applied to dogs whose initial vaccination process has been completed. One of these pathways is hemagglutination inhibition (HI) with fresh porcine erythrocytes. The titer of HI antibodies, which still inhibits the known amount of virus, is the counterpart of high serum dilution (Decaro et al. 2005). The other alternative and more reliable way is virus neutralization (VN). It is the counterpart of a high serum antibody concentration that completely inhibits viruses (Cavalli et al. 2008). There are point-ELISA tests to detect the level of intraclinical antibodies. These tests identify serum antibody levels by the color intensity of the dots. The results obtained are scored with a certain scale with reference positive points (Killey et al, 2018). In our study, V-check V200 hormone analyzer, which is a fully quantitative automatic analyzer of serum antibody levels, working with the working principle of immune fluorescent antibody tests, was used.

Survival may vary for many reasons such as vaccination status, type of treatment, when treatment was started, mother's vaccination status, gender, secondary infection or presence of parasitic infestation. It has been reported that the percentage of survival varies between 60% and 90% according to the patient's response to treatment (Prittie 2004, Kalli et al. 2010, Miranda et al. 2015). It is stated that mortality can reach 90% if treatment is not

started (Prittie 2004). In our study, it was determined that the vaccination factor gained significance in patients with high and medium protection whose serum Ab level was measured, and the survival rate was 52.5%. As can be seen in Table 2, the survival rate was found to be 90% and 70% in patients with high and medium Ab levels, respectively.

Conclusion

The results obtained in our study show that serum antibody level has a great effect on survival. However, for various reasons; It was thought that the formation of sufficient antibodies was prevented due to reasons such as the cold chain of vaccine application, insufficient number of vaccines, wrong selection of the vaccination period or failure to carry out the vaccination program in accordance with the guideline, maternal antibodies neutralizing the first or first few vaccines, and the desired vaccine protection could not be achieved despite the same or high number of vaccines. Although the importance of vaccination is emphasized in the studies, it is possible that the desired immunity does not occur for various reasons. For this reason, it is of great importance to check the serum parvovirus Ab levels of individuals at the end of the vaccination program, individuals with no protection, low protection or moderate protection should be re-vaccinated and serum antibody levels should be measured again for parvovirus. As in the study, the survival rate will increase in individuals with high protection, and the fight against the disease will be a right step.

Conflict of Interest

The authors declare that there is no conflict of interest for this study.

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