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Research Article
Successful Treatment of Canine Parvovirus Infection in Naturally Infected Puppies

[1]Romane Adieb Awad, [2,3]Brit Martens and [2,3]Safwat Ali Hassan

[1]Department of Parasitology and Animal Diseases, Veterinary Division, National Research Center, 33 Bohouth St., 12622 Dokki, Giza, Egypt
[2]Department of Internal Medicine and Intensive Care, Small Animals Referral Hospital, Merkurring 50, 22143 Hamburg, Rahlstedt, Germany
[3]Department of Small Animal Surgery and Neurosurgery, Head of Small Animals Referral Hospital, Merkurring 50, 22143 Hamburg, Rahlstedt, Germany

Abstract

Background and Objective: Canine Parvovirus infection (CPV) causes high moralities among infected puppies, low survival and recovery rate in most of treated cases. So, the aim of this study was to develop a successful method for treatment of CPV infection in dogs with high recovery rate and to evaluate different types of treatment used to treat CPV infection. **Materials and Methods:** In this study, 360 puppies showing signs suggestive for CPV infection were subjected to clinical examination; Rapid Immunochromatography assay (IC) on fecal samples to detect viral antigen. Treatment of disease was applied using supportive classical treatment for all of the infected puppies while 2 groups (each of 120 puppies) received also Feliserin Plus and Zylexis as trail for treatment using antibodies specific against Feline panleukopenia virus (FPV) as a source for interferon to control viral infection. **Results:** Clinical examination of diseased puppies revealed the presence of depression, pyrexia, anorexia, thirst, vomiting, diarrhea and dehydration. The IC on fecal samples was positive for CPV in all the 360 examined puppies. Recovery rate in the form of clinical improvement and survival of diseased animals were significantly higher in the group treated by Feliserin Plus (81.7%), followed by the group treated by Zylexis (16.6%). **Conclusion:** The results of this study exhibited that the use of Feline specific neutralizing antibodies against FPV showed promising results against CPV infection in comparison to the old classical treatment and could be applied for CPV infection in diseased dogs.

Key words: Canine Parvovirus, treatment, puppies, clinical signs, IC, specific antibodies, feliserin plus, IFN

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Corresponding Author: Romane Adieb Awad, Department of Parasitology and Animal Diseases, Veterinary Division, National Research Center, 33 Bohouth St., 12622 Dokki, Giza, Egypt Tel: 00201223578982

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Canine parvo-viral enteritis is an acute, sub-acute infectious disease caused by highly contagious agent, canine parvovirus type 2 (CPV-2)[1], while CPV-1 recorded as a symptomatic[2], CPV-2 within the last three decades mutated to three highly pathogenic variants CPV-2 a, CPV-2b,CPV-2c which distributed all over whole world now[3,4] CPV-2 belong to parvoviridae family, autonomous group, antigenically similar to Feline panleukopenia (FPV) but there is minute difference in gene sequence responsible for major capsid protein (VP2) related to some limited number of amino acids[5].

Infections occur via the fecal-oral route mostly affect puppies and dogs between age of weaning and 12 month old[3].

The CPV-2 is stable in the environment and remains infectious for more than 6 months. So, infected dogs shed billions of virus particles in faeces during acute phase of the disease for 2 weeks or more[6,7].

The severity of clinical signs varies with animal age, maternal immunity, status of immune response, virulence of viral strain. Further certain dog breeds are more susceptible for CPV-2 enteritis than other breeds e.g., Rottweiler and Doberman. In addition, some predisposing factors include environmental factors e.g., overcrowding, poor sanitation and colony environment are associated with CPV-enteritis[3,8].

Infected dogs suffered from acute form which characterized clinically by depression, anorexia, fever, vomiting, dehydration and diarrhea. This acute form rapidly developed to sever sub-acute form with increase of vomiting times and profuse diarrhea which mostly being bloody, end by severe dehydration, subclinical body temperature, collapse and death of the infected dogs. Mortality rate may reach to 100% among infected dogs if not treated[1,4].

Infection of dogs with CPV still causes high moralities among infected puppies, low survival and recovery rate in most of treated cases. Thus, many trials for treatment were achieved to overcome the clinical symptoms including dehydration, electrolytes imbalance and secondary bacterial infection, septicemia by many of researchers all over the world but with poor and limited success[3,8]. Therefore, the main objective in this study was to create a successful treatment regimen for canine parvovirus infection with high recovery and survival rate in comparison to other modern and old classical treatment trials.

MATERIALS AND METHODS

Duration of the study: This study had been conducted during the period between December, 2013 and August, 2018.

Table 1: The examined puppies in this study

		Sex	
Groups	Race	Male	Female
Small sized breed	Bull dog	6	3
	Chihuahua	3	3
	Chinese crusted	3	3
Large sized breed	Saint bernard breed	10	8
	Caucasian dog	6	3
	German shepherd	33	33
	Rottweiler	36	36
	Pitbull	18	18
	Golden retriever	18	18
	Labrador retriever	15	15
	Siberian husky	21	15
	Doberman	18	18

Ethical approval and informed consent: The owners of dogs were informed and permission was received from them. The puppies were included in this study for taking samples. Samples were collected as per standard sample collection procedure without any harm to animals. The proposal of this study had approval from National Research Center committee No: 21/11/2013.

Examined animals: About 360 puppies (45-90 days old) of different breeds and sex were investigated in this study. They were received and treated at German vet clinic at 6th October, in Giza, Egypt. These dogs were suffering from clinical signs suggestive for canine parvovirus (CPV) infection and were classified into different age groups and sex (Table 1).

Clinical examination: The received diseased dogs were subjected to clinical examination according to the method described by Gaskell *et al.*[1] and Hall *et al.*[8]:

- Fecal samples were collected from all of 360 diseased dogs and were examined by Rapid Immuno-chromatography assay (IC). Rapid antigen test using kits obtained from (Bionote Inc. Korea) for qualitative detection of CPV viral antigen in faeces[9-11]
- Clinical determination of dehydration type and rate were done according to Brown and Otto[12] and DiBartola and Bateman[13]
- **Treatment trail:** All of the diseased dogs (n = 360) received the following treatment:
  - **Fluid therapy:** Each individual diseased puppy of the 360 examined dogs checked clinically and received the estimated amount of fluids therapy

mixture according to the degree and type of the dehydration with daily re-adjustment for first 5 successive days of treatment[12-14]

- **Supportive therapy:** According to severity of anorexia and body weight of each diseased puppy the amount of balanced formula of amino acids, electrolytes and water soluble vitamins calculated, then administered intravenously with fluid therapy for the first 4 successive days[14-16]
- **Stomach protection agents:** Against hyperacidity like H_2 antagonist or proton pump inhibitors, dose according to body weight of each individual puppy and administered once daily intravenously with fluid therapy for 4 successive 4 days[17,18]
- **Vitamin K:** Injection form (10 mg/vial) once daily intravenously with fluid therapy for first 3 successive days of treatment for each diseased puppy[19]
- **Anti emetic:** Metoclopramide hydrochloride in form of injection 10 mg/2 mL vials i.v. or sub/cut by rate of 0.2 mL kg^{-1} b.wt., for 5 days[3,20]
- **Antibacterial drug:** Ampicillin 10% solution and enrofloxacin 5% solution injections, subcutaneously with dose as recommended (1 mL/10 kg b.wt.) by producing companies for 7 days[3,15,16]

A group of 120 dogs from the above mentioned dogs received purified specific antibodies (neutralizing antibodies) against FPV (Feliserin PLUS®) for injection intramuscularly or subcutaneously at a rate recommended by producing company (4-8 mL) according to breed and size of the dogs and severity of CPV infection (acute and sub-acute) daily repeat until recovery for at least 3 successive days was obtained from IDT, Biologika GmbH, Am Pharmapark, D-O6861 Dessau-Roβlau, Germany, according to Gerlach *et al.*[21].

Another group of 120 dogs received lyophilized inactivated Parapox ovis virus strain D1701, reconstituted with its supplied diluents, 1 mL dose for 1 puppy, administered subcutaneously at day 0, 2 and 4 of acute occurrence of canine Parvovirus enteritis as a source for generation of 230 IFN units as indicated by producing company obtained from Zoetis Belgium SA, Rue Laid Burniat 1, 1348 Louvain-la-Neuve-Belgium under commercial product name zylexis®, according to[22-24].

Statistical analysis: The statistical methods were applied on the data of results to detect if there is any difference between male and female in each treated group and in group 1, 2 and 3 by using Chi-square test. T-distribution test was used to study the effect of breed of dogs on the response to different treatment methods in the 3 treated groups according to Smith[25].

RESULTS

Clinical examination: Clinical changes in the form of depression, fever (pyrexia), anorexia, thirst, vomiting, diarrhea and dehydration were recorded in different rates and severity among the diseased puppies. Table 2 showed the distribution, rate and severity of these clinical changes in different breeds and sex groups in the three treated groups.

Rapid Immunochromatography (IC): All of the examined diseased (n = 360) puppies were positive to IC.

Clinical improvement:

- **Group 1 (treated with Feliserin plus):** The improvement began in the 2nd day and increased significantly ($p<0.05$) till the 4th day post isolation and treatment, 98 dogs survived while 22 died (Fig. 1, 2)
- **Group 2 (treated with Zylexis):** The improvement began in the 3rd day and increased significantly ($p<0.05$) till day 5th post isolation and treatment, 20 dogs survived and 100 dogs died (Fig. 1, 2)
- **Group 3 (that received fluids therapy, anti emetic and antibacterial agents only):** The improvement began in the 4th day and increased significantly ($p<0.05$) till 6th day post isolation and treatment, only 10 dogs survived (Fig. 1, 2)

Improvement parameters:

- Improvement was manifested in different groups by significant decrease ($p<0.05$) in body temperature at day 2nd post treatment in group 1 (treated with Feliserin) and day 3rd in group 2 (treated with Zylexis)
- Vomiting times began to decrease significantly ($p<0.05$) on day 2 and stopped on day 4 in group 1 (treated with Feliserin), while the vomiting began to decrease ($p<0.05$) on day 3 and stopped on day 5 in case of group 2 (treated with Zylexis) and stopped on day 6th in group 3 (received fluids therapy, anti-emetic and antibacterial agent)

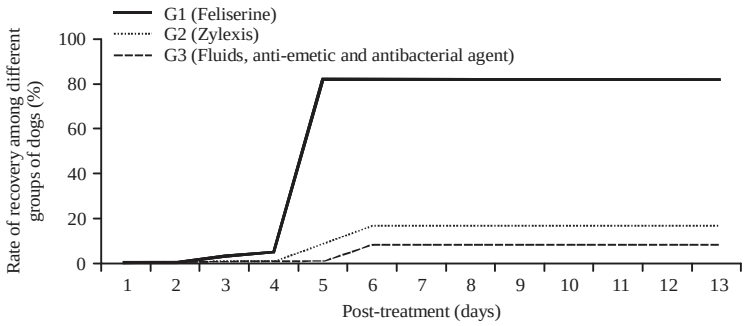

Fig. 1: Starting days of improvement and recovery (%) in different treated groups of dogs

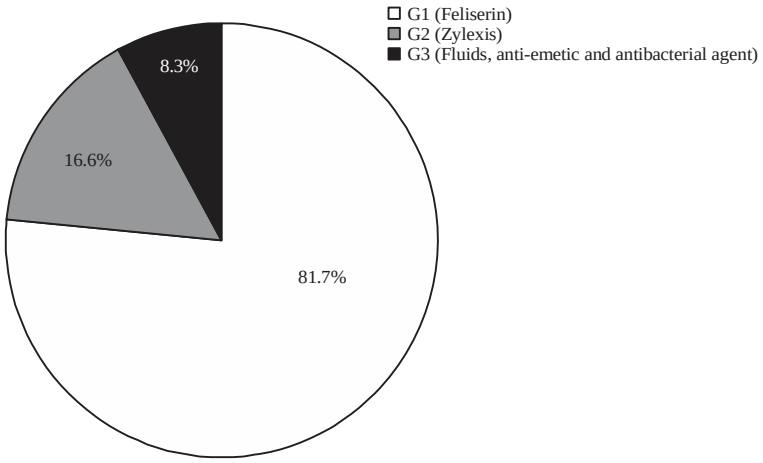

Fig. 2: Survival (%) among different treated groups of dogs

Table 2: Clinical signs recorded in diseased dogs (n = 360)

		Sex								
Total No.	Breeds	Male	Female	*Depression	Pyrexia	**Anorexia	#Thirst	##Vomiting	Dehydration (%)	ᵠDiarrhea
9	Bull dog	6	3	++	40°C	+++	++	++	6-8	++
6	Chihuahua	3	3	+++	40°C	+++	++	++	8	++
6	Chinese crusted	3	3	++	39.5-40°C	+++	++	++	6-8	++
18	Saint bernard breed	10	8	+++	39.5-40.5°C	+++	++	+++	8	++
9	Caucasian dog	6	3	+++	39.5-40.5°C	+++	++	+++	8	++
66	German shepherd	33	33	+++	Above 40°C	+++	+++	++	6-8	++
72	Rottweiler	36	36	+++	Above 40°C	+++	+++	++	6-8	+++
36	Pitbull	18	18	++	39.5- 40°C	++	++	++	6-8	+
36	Golden retriever	18	18	++	Above 40°C	+++	++	+++	8	++
30	Labrador retriever	15	15	++	Above 40°C	+++	+++	++	8	++
36	Siberian husky	21	15	+++	Above 40°C	+++	+++	+++	Above 8	+++
36	Doberman	18	18	+++	Above 40°C	+++	+++	+++	8	+++

*Depression: Normal (-), mild(+), moderate(++), sever (+++), **Anorexia: Normal appetite (-), mild (+), moderate(++), sever(+++) (no appetite), #Thirst: Normal (-), mild(+), moderate(++), sever (+++), ##Vomiting: Mild(+) (once per 12 h), moderate(++) (2-5 times per 12 h), sever (+++) (>6 times per 12 h), ᵠDiarrhea: Normal faeces(-), mild (soft or pasty) (+), moderate (watery diarrhea) (++), sever (watery and bloody) (+++)

- Diarrhea began to decrease significantly ($p<0.05$) on the 2nd day and stopped at the 4th day in group 1 (treated with Feliserin), while it began to decrease ($p<0.05$) in 3rd day and stopped on 6th in group 2 treated with Zylexis and in group 3 received fluids therapy, anti-emetic and antibacterial agent diarrhea stopped on 7th day

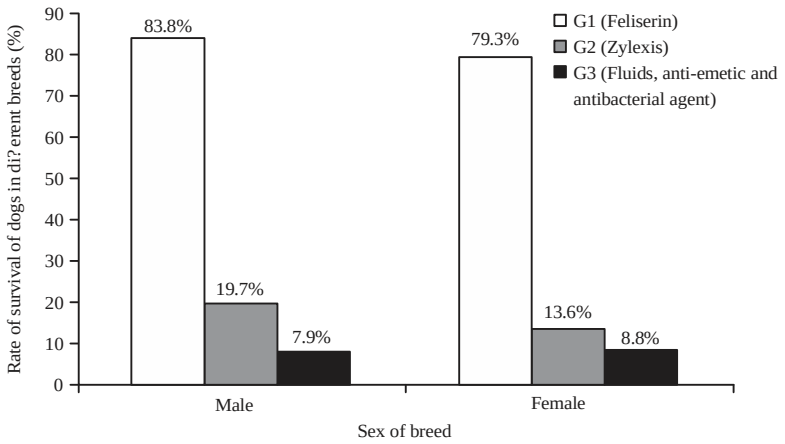

Fig. 3: Comparison between survival rate (%) of males and females in different treated groups

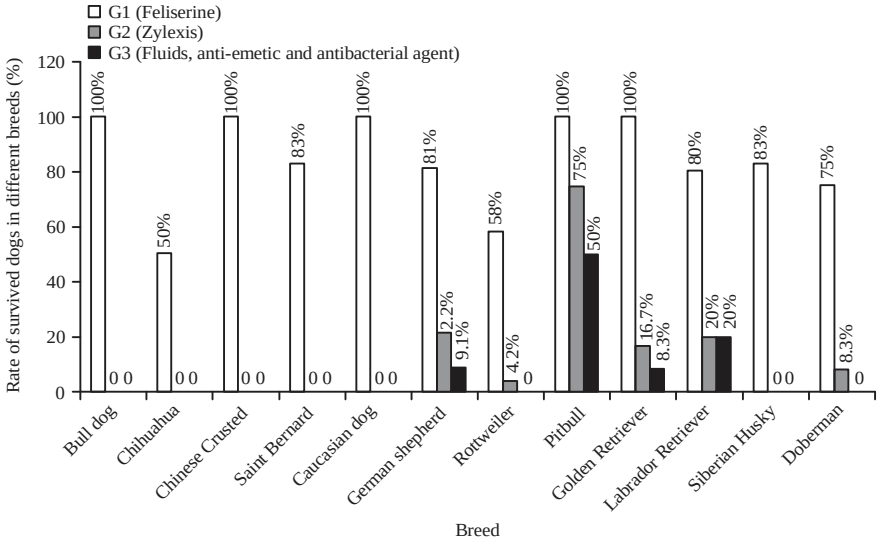

Fig. 4: Survival rate (%) in relation to dog breeds in different treated groups

Results of statistical analysis:

- There was no significant difference ($p>0.05$) in recovery rate and survival between males in group 1 and males in group 2 and 3
- There was no significant difference ($p>0.05$) in recovery rate and survival between females in group 1 and females in group 2 and 3
- There was no significant difference ($p>0.05$) in recovery rate and survival between males and females of small breed in group 1
- There was no significant difference ($p>0.05$) in recovery rate and survival between males and females of large breed in group 1
- There was no significant difference ($p>0.05$) in response to treatment between small and large breeds in group 1, 2 and 3

This study resulted that both males and females in group 1 treated with Feliserin revealed significant difference in recovery rate ($p<0.05$) more than group treated with Zylexis and group received fluid therapy, anti-emetic and anti-bacterial agent. While there was no significant difference in recovery rate ($p<0.05$) between group treated with Zylexis and fluid therapy, antiemetic and antibacterial agents (Fig. 3). The current study concluded that there was no significant effect of sex in response to treatment within each treated group and also no significant effect for breed in response to treatment within each treated group (Fig. 3, 4).

DISCUSSION

This study was attempted to establish a new strategy for CPV therapy in diseased puppies. The results of this study

exhibited that the use of Feline specific neutralizing anti-bodies showed promising results against CPV infection in comparison to the old classical treatment and could be applied for CPV infection in diseased dogs.

It is knowing that Canine parvo enteritis resulted in about 90% mortality among infected dogs of different ages, sex and breeds if not treated[1,3]. In majority of cases, death occurs due to dehydration, electrolytes imbalance, septicemia, severe colitis and damage of colon which is a vital organ for fluid and food absorption[1,3].

Long time ago many trials for treatment of CPV enteritis were tried but of limited successes, low recovery and survival rates[3].

This work aimed to develop successful method for CPV infection treatment with high recovery and survival rate when compared to other modern and classical treatment trials.

The use of IFN[8,22-24] and the use of IgG antibodies[26] have not been conducted in dogs either experimentally or therapeutically in a large scale[27], to the best of authors knowledge.

The use of zylexis® was tried in present treatment plan to study its impact as a treatment for diseased dogs.

In the first group, the use of specific neutralizing antibodies (consisting of IgM (+), IgG (++), IgA (+)) against FPV was applied in this study according to Tizard[28]. Current study showed that, a good prognosis and recovery was present in form of 81.7% survival rate among 120 treated dogs and detected clinically by stopping vomiting, subsiding of fever, decrease diarrhea and reduce anemia[4].

The effective role of neutralizing anti-bodies against CPV virions in viraemic stage was excellent in diminishing viraemia rapidly, then reduce destructive effect of CP viral replication in lymphoid tissue, bone marrow, circulating WB cells[4,27,29-31]. This role was achieved by different mechanisms via antibody mediated immunity. Neutralizing antibodies prevent cell invasion by blocking the adsorption of virons to target cells and stimulating phagocytosis of viruses. Neutralizing antibodies kill infected cells by complement mediated cytolysis or by antibody dependent cell mediated cytotoxicity.

The use of neutralizing anti-bodies proved to be more efficient through anti-body mediated destruction of infected cells. This was reported by Stuetzer and Hartmann[27], Tizard[28] and Paltrinieri *et al.*[32].

In this group 18.3% of 120 treated cases died, majority of them were Rottweiler, Labrador retriever, Doberman and German shepherd, this referred to breed susceptibility and the main cause for these mortalities was myocarditis as reported by Goddard and Leisewitz[3] and Sime *et al.*[33].

In the 2nd group, use of recommended dose of lyophilized Parapox Ovis virus strain D1701 as a precursor for generation of 230 IFN units[27,28] was tried.

Survival rate in CPV infected dogs of this group (group 2) was 16.6%, similar results were reported by Stuetzer and Hartmann[27] and Klotz *et al.*[34].

The IFN includes three fractions as IFN-α, IFN-β, IFN-γ and IFN-ω binding to receptors of target cells creating resistance to virus infection within few minutes to 5 h, also IFN-γ induce production of certain synthase enzyme result in preventing virus growth in interferon activated macrophages. The IFNα, β play important role on activation of certain enzymatic reaction lead to inhibition of viral growth and IFN-γ established that play effective role in treatment of CPV infection as concluded by Ishiwata *et al.*[22], Martin *et al.*[23], De Mari *et al.*[24], Tizard[28], Paltrinieri *et al.*[32] and Klotz *et al.*[34].

In the 3rd group that received supportive treatment, the survival rate was 8.3% and recovered dogs were of breeds (Pit Bull, German shepherd, Golden Retriever and Labrador Retriever) known to hold good natural resistance against CPV[3,8]. Stuetzer and Hartmann[27] stated that CPV is one of the main causes of immune suppression in dogs that is the reason for using antibiotic therapy to prevent development of septicemia and endotoxemia in diseased dogs[3,27]. The use of antibiotics Enrofloxacin and Ampicillin to control secondary bacterial infection in immune-suppressed animals, help to decrease percentage of mortality from septicemia[3,27]. While, anti-emetic included in supportive therapy to control continous vomiting was helpful to obtain clinical recovery. Oral caloric food intake and water prohibited while anti-emetic was recommended[3,27].

The CPV infection causes anorexia, vomiting and diarrhea which resulting in abnormalities in the serum chemistry of infected dogs but these abnormalities are non-specific. So, this study not included in the current examination profile as recommended by Goddard and Leisewitz[3].

However, statistical analysis were conducted using Chi square revealed that both males and females in group 1 treated with Feliserin revealed significant recovery rate ($p<0.05$) more than group treated with Zylexis and group received fluid therapy, anti-emetic and anti-bacterial agent. While, there were no significant differences in recovery rate ($p<0.05$) between group treated with Zylexis and fluid therapy, anti-emetic and anti-bacterial agents. The results of this study concluded that there was no effect of sex in response to treatment within each treated group and also by using T-Distribution test proved that no effect for breed in response to treatment within each treated group.

CONCLUSION

The use of feline specific neutralizing anti-bodies against FPV was proven to be more efficient in treatment of Canine Parvovirus infection in dogs with survival rate of 81.7% in comparison to the use of lyophilized inactivated Parapox Ovis virus strain D1701 as a source for production of IFN with survival rate of 16.6%. While the use of fluid therapy and supportive treatment in the third group gave a recovery rate of 8.3% in diseased dogs.

SIGNIFICANCE STATEMENT

This study creates the successful treatment for Canine Parvovirus infection that can be effective for treating infected dogs and reducing case fatality among diseased dogs significantly. This study will help the researchers to uncover the critical areas of failure of treatment trials that many researchers were not able to explore. Thus, a new CPV effective treatment regimen may be arrived at. These results recommend the use of specific neutralizing anti-bodies against FPV than the use of inactivated parapox ovis strain D1701 in treatment of Canine Parvovirus infection in dogs.

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