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ORIGINAL RESEARCH

Therapeutic efficacy of acyclovir in the treatment of canine parvo virus infection

S.A.Mehta[1]*, S.V. Mavadiya[1], J.A.Vala[2], S.M. Parmar[2], A.A. Vagh[1] and R.M.Patel[3]

[1]Department of Veterinary Medicine, [2]Department of Veterinary Clinical Complex, Veterinary College, N.A.U., Navsari, Gujarat, India
[3]Department of Veterinary Clinical Complex, SDAU, Sardar Krushi Nagar, Gujarat, India

**Corresponding author : drsudhiram7@gmail.com*

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ABSTRACT

A total of 145 faecal samples were collected from the dogs suspected for canine parvovirus (CPV) infection over a period of one year. The faecal samples screened by Scan Vet Parvo kit and PCR. Out of 145 dog faecal samples, 63 samples were positive with an overall prevalence of 43.44 %. Out of 63 positive dogs, 28 dogs were randomly divided in four different treatment groups (n=7) for determining the efficacy of treatments. The groups I, II, III and IV dogs were treated with antimicrobial agent Inj.Cefotaxim, Metronidazole, acyclovir and Inj. Cefotaxim + Acyclovir, respectively with similar supportive drugs in all the groups for five days. The case fatality rate was recorded 0% in group I and IV whereas it was 57.14% and 42.85% in groups III and II. It found that the treatment with acyclovir alone was not efficient however; the combined use of cefotaxim + Acyclovir could accelerate rapid recovery from the CPV infection.

Keywords: Parvo Virus, Acyclovir, Cefotaxim, Dogs

INTRODUCTION

Canine parvo virus is an important pathogen of domestic and wild canines and has spread worldwide since its emergence in 1977. There are two different parvo viruses known to infect dogs – the pathogenic CPV-2 and CPV-1 or the Canine Minute Virus (CnMV). Season-wise incidence showed that cases were almost exclusively occurred in winter followed by monsoon (Pandya *et al*., 2017). Host associated risk factors like age, sex,breed, vaccination and seasons also

responsible for occurrence of canine parvo virus infection. The disease is clinically represent in two prominent forms, enteritis with vomition and diarrhea in dogs of all ages and myocarditis and subsequent heart failure in pups of less than 3 months of age with high morbidity and frequent mortality 10% in adult dogs and 91% in pups (Nandi and Manojkumar, 2010). The virus kills one of two ways, diarrhea and vomiting lead to extreme fluid loss and dehydration until shock and resulted in death and loss of the intestinal barrier allows bacterial invasion of potentially the entire body. The survival rate of CPV infection is as low as 9.1% in the absence of treatment and 64% or higher with treatment because of no agent-specific treatment exists for CPV enteritis, management of clinical signs remains supportive care (Otto, 2010). Till now, none of the clinical research was conducted using any anti-viral agent in the treatment of parvo virus infection. Therefore, the said study was planned with use of acyclovir (an antiviral agent effective against DNA herpes virus) in the treatment of canine parvo virus infection.

MATERIALS AND METHODS

The study was carried out on dogs presented at the Teaching Veterinary Clinical Complex, College of Veterinary Science, NAU, Navsari during April 01, 2016 to March 31, 2017. The dogs showing probable clinical signs like diarrhea with/without blood, vomition, anorexia, anemic and dehydrated due to vomition/diarrhea were selected and screened through Scan Vet Parvo (rapid faecal parvo Ag detection kit). The test results were read within 5-10 minutes. One red-purple band appears in the control line with no apparent band in the test line (T) considered as negative sample (Fig. 1) and two red-purple bands appear one in the control line (C) and other in the test line (T) noted as positive sample (Fig. 1). A total of 63 dogs found positive through ScanVetParvo and among them 28 dogs were randomly divided in four treatment groups (n=7). The detailed history, clinical scores, hematological parameters, treatment administered was recorded of each dog of all the groups. The group wise treatments adopted for aforesaid dogs were mentioned in table I.

The clinical score of CPV affected dogs were determined on basis of various attributes given in Table II (Mohr *et al.,* 2003). The Score of each category was assigned to each dog twice daily to encompass the previous 12 hours period and score was decided on the basis of majority in three clinical attributes.

PCR assay:

The genomic DNA of CPV from the faecal samples was extracted by phenol-chloroform method (Manojkumar *et al*., 2011). Two sets of primer pairs, P*ab* which detects CPV types 2*ab* and 2*b* designed for this study (Pereira *et al.,* 2000). Primer pair P*ab* sense (5′-AAGAGTGGTTGTAAATAATA-3′) and P*ab* anti-sense (5′-CCTATATCACCAAAGTTAGTAG-3′) located, respectively, at 3025-3045 and 3685-3706 of the CPV genome, yields a 681 base pair (bp) product, while P*b* sense (5′-CTTTAACCTTCCTGTAACAG-3′) and P*b* anti-sense (5′-CATAGTTAAATTGGTT ATCTAC- 3′) located, respectively, at 4043-4062 and 4449-4470 yields a 427 bp product (Fig.2).

RESULTS AND DISCUSSION

The groups were continually monitored from day 1 to day 5 and clinical scoring recorded in clinical attributes of each patient: attitude, appetite, vomiting, temperature and feces. A score of

0 represented a clinically normal parameter, with increasing severity of signs as the score increased up to a maximum of 3 for each variable.

The clinical score of day 2 were remain constant in group I, II and III as on day 1 but the score decreased from 2.43 ± 0.20 to 1.57 ± 0.20 in group IV indicated improvement in clinical condition due to effectiveness of treatment received in that particular group. The clinical score reached to 0 of group IV (0.86 ± 0.26) on day 3 onwards, group I on day 4 onwards and group II and III on day 5th. The case fatality rate was 57.14 % and 42.85% in group III and II. The clinical efficacy in group I, II, III and IV were 100.00% (7/7), 57.14% (4/7), 42.85% (3/7) and 100.00% (7/7) in terms of survivability from CPV affected animals. The clinical score 0 suggestive of either of three presents; normal attitude, appetite, no vomition, well formed feces and temperature in normal reference range of particular group's dog. While comparing the clinical score of day 1 to day 5 of individual groups, it was found that treatment administered in the group I to IV were highly significant. Different variations in the clinical signs in different dogs might be due to individual host resistance, virulence of the viral agent and nutritional status of the individual dog (Banja *et al.,* 2002). Diarrhea might be due to destruction and collapse of the germinal epithelium of the intestinal crypts by CPV and resulted as villous atrophy (Bastan *et al.,* 2013).

Leucopenia can be associated with infection of viral origin that destroys actively dividing blast cells of bone marrow. After viral infections, decreased production and cell destruction result in leucopenia. (Brar *et al.,* 2014). The TLC of all the groups on day 0 could be considered as leucopenia which may be due to the Canine Parvo Virus infection. After five days of continuous treatment, the mean TLC of group I, II and group IV showed non significant variation compared to healthy control groups. It was suggestive of improvement in immune status of particular groups due to antibiotic treatment administered in particular groups which contributed to enhance the ability to combat against infection. However, total leukocyte count of group III (3785.71 ± 647.13) on day 5 was significantly lower ($P < 0.01$) than that of healthy control and suggestive of marked leucopenia. The leucopenia at day 5 was seen in group III could be due to use of acyclovir alone and none of the antibiotic was included in therapy.

Moreover, it was observed that the Immuno+ was very effective in delivering immunomodulator agent as it was available in spray from, hence, easy to administer on tongue in puppies compare to other commercially available products.

The antiviral agent Acyclovir converted into Acyclo-GTP (acyclo-guanosine triphosphate) by cellular kinase has approximately 100 times greater affinity for viral than cellular polymerase. As a substrate, acyclo-GTP is incorporated into viral DNA, resulting in chain termination. It has also been shown that viral enzymes cannot remove acyclo-GTP from the chain, which results in inhibition of further activity of DNA polymerase and thereby multiplication could be inhibited. Similar results were obtained by Elion (1983) and Albaz *et al.* (2015) who tested the antiviral effect of Acyclovir against herpes virus type-1 (which is a DNA virus as CPV) and experimental induced Canine Parvo Virus infection, respectively. Thus, the significant recovery in group IV might be due to combined use of antiviral agent Acyclovir and antibiotic agent Cefotaxim worked synergistically and resulted in early restoration of physiological and pathological changes to normal.

CONCLUSION

It could be concluded that all the treatments administered were efficient against CPV infections as clinical score came to 0 at end of fifth day but clinical recovery and returning to normal physiological signs was earlier in group IV followed by group I in comparison with other treatment groups. Nevertheless, 100 percentages survivability score and clinical score was return to normal at the end of fifth day in groups I and IV only. Therefore, it can be stated that treatment with acyclovir alone is not effective but in combination of any sensitive antibiotic i.e. group IV will show early recovery from clinical conditions.

CONFLICT OF INTEREST: Any authors of said article have no any conflict for publication of article.

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Table 1: Details of drug administered.

Class	Group I	Group II	Group III	Group IV
	Treatments were given for five days			
Antimicrobials	Cefotaxim @ 25mg/kg BW/ Day IV	Metronidazole @ 20mg/kg BW/ Day. IV in two divide doses	Acyclovir @ 20mg/kg BW/ at every eight hours. IV	Cefotaxim @ 25mg/kg BW/ Day. IV +Acyclovir @ 20mg/kg BW/ at every eight hours IV
Gastrointestinal protectants	Pentoprazole @ 1 mg/kg BW/ Day IV OD			
Antiemetics	Ondansetron @ 0.5 mg/kg BW IV TID			
Fluid therapy Crystalloid	Replacement fluid /24 hrs as per % of Dehydration[a]			
Endotoxemic agent	Flunixin @ 1 mg/kg BW IV once only			
Supportive and Immune modulator	Immuno + < 5 kg : 1 serving TID, 5-10 kg: 2 serving TID			
Haemostatic	Ethamcylate @250-500 mg (Total dose) IV BID in dogs where bloody diarrhea or melena was clinically present.			

% of Dehydration[a] X BW in kg = Liter of fluid required. Ringer lactate (RL) followed by Dextrose Normal saline (DNS), Immuno + is a multivitamin commercially available product in spray form by Venttura Bioceuticals Private Limited, Mumbai, Maharashtra, India. The ScanVet Parvo was obtained from M/S INTAS Pharmaceuticals Limited Matoda-382210, Ahmedabad, Gujarat, India

Table 2: Pattern of clinical score.

Score*	Attitude	Appetite	Vomiting	Feces	Temperature(°F)
0	Normal	Normal	Absent	Well formed or absent	Normal (100.4)
1	Mild to Moderate depression	Voluntarily eats small amounts	Mild; once per 12 hrs	Soft or pasty feces	Mild increase (103.1)
2	Severe depression	No interest in Food	Moderate; 2-5 times per 12 hrs	Watery dirrrhea, non bloody	Increase (104.0)
3	Collapsed or Moribund	Not offered	Severe; 6 times per 12 hrs	Watery bloody dirrrhea	Severe increase (105.8)

Table III: Clinical score of CPV affected dogs.

Groups	Day 1	Day 2	Day 3	Day 4	Day 5	P Value
Group I	2.29 ± 0.29	2.14 ± 0.26	1.57 ± 0.20	0.86 ± 0.26	0.29 ± 0.18	< 0.01*
Group II	2.37 ± 0.19	2.18 ± 0.34	1.71 ± 0.18	1.0 ± 0.31	0.50 ± 0.22	< 0.01*
Group III	2.57 ± 0.20	2. 43± 0.30	1.86 ± 0.34	1.57 ± 0.37	0.33 ± 0.22	< 0.01*
Group IV	2.43 ± 0.20	1.57 ± 0.20	0.86 ± 0.26	0.29 ± 0.18	0.0 ± 0.0	< 0.01*

P < 0.05*****: Significant

Table IV: Group wise TLC and DLC of CPV affected dogs.

Groups	Treatment	TLC(/µl)		Neutrophils (%)		Lymphocyte (%)		Eosinophils (%)		Monocytes (%)	
		Mean ± SE	Control	Mean ± SE	Control	Mean ± SE	Control	Mean ± SE	Control	Mean ± SE	Control
Group I	Day 0	3614.29 ^{b} ±748.47**	9185.71 ^{a} ±311.24	69.47 ^{a} ±4.33	58.57 ^{ab} ±2.93	24.60 ^{a} ±4.01	29 ^{a}.00 ±1.31	2.86 ^{a} ±0.51**	1.29 ^{b} ±0.18	2.57 ^{a} ±0.30**	1.14 ^{b} ±0.26
	Day 5	8180.00 ^{a} ±460.04		54.27 ^{b} ±4.53		25.19 ^{a} ±2.68		1.57 ^{b} ±0.20		1.43 ^{b} ±0.30	
Group II	Day 0	5200.00 ^{b} ±1414.89*	9185.71 ^{a} ±311.24	66.71 ^{a} ±5.33	58.57 ^{a} ±2.93	24.43 ^{a} ±4.44	29.00 ^{a} ±1.31	1.23 ^{a} ±0.18	1.29 ^{a} ±0.18	1.43 ^{a} ±0.20	1.14 ^{a} ±0.26
	Day 5	6042.86 ^{a} ±1708.36		57.14 ^{a} ±5.85		21.71 ^{b} ±1.95**		1.14 ^{a} ±0.14		1.29 ^{a} ±0.18	
Group III	Day 0	5271.43 ^{b} ±980.212**	9185.71 ^{a} ±311.24	73.06 ^{a} ±5.45*	58.57 ^{b} ±2.93	22.23 ^{ab} ±5.83	29.00 ^{a} ±1.31	2.71 ^{a} ±0.28**	1.29 ^{b} ±0.18	1.71 ^{a} ±0.42	1.14 ^{a} ±0.26
	Day 5	3785.71 ^{c} ± 647.13**		72.74 ^{a} ±3.30*		18.71 ^{b} ±2.68**		2.57 ^{a} ±0.30**		1.43 ^{a} ±0.20	
Group IV	Day 0	4642.86 ^{b} ± 443.93**	9185.71 ^{a} ±311.24	75.69 ^{a} ±3.48**	58.57 ^{b} ±2.93	22.46 ^{a} ±5.70	29.00 ^{a} ±1.31	3.43 ^{a} ±0.37**	1.29 ^{b} ±0.18	2.43 ^{a} ±0.37*	1.14 ^{b} ±0.26
	Day 5	8171.43 ^{a} ± 351.67		59.76 ^{b} ±1.87		26.56 ^{a} ±2.23		2.43 ^{a} ±0.43**		1.57 ^{b} ±0.20	

P < 0.05*: Significant, P < 0.01**: Highly Significant and P > 0.05: Non Significant

Note: Same alphabet showing no significant difference and different alphabet were significantly differed from each other.

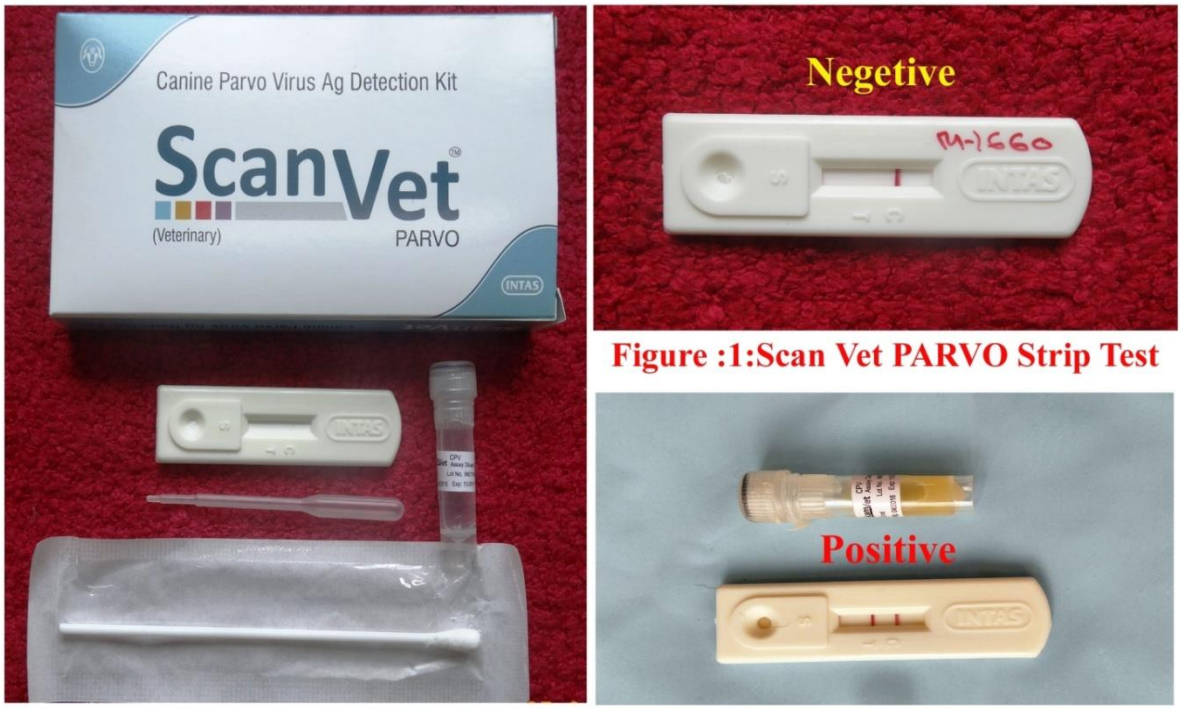

Figure 1. Rapid test kit with result demonstration.

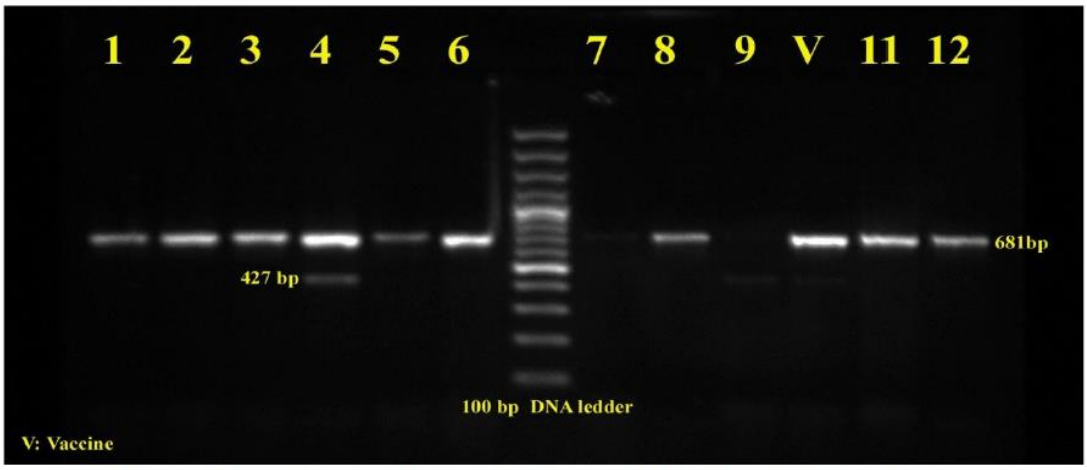

Figure 2. Amplified products at 681 bp and 427 bp through PCR