RESEARCH ARTICLE

Therapeutic Efficacy of Heterogenous Immunoglobulin in Canine Parvovirus Infected Dogs

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Abstract

The present study was conducted to assess the efficacy of heterogeneous immunoglobulin @ 0.4 mL/kg body weight per day intravenously along with supportive conventional therapy in CPV infected 10 puppies till recovery. One additional group of 10 normal healthy dogs was kept as a control group. CPV infection was diagnosed on the basis of clinical signs, rapid CPV antigen test kit and PCR assay. The clinical, haemato-biochemical parameters were investigated before and 7th day after treatment. The clinical study showed significant rise in rectal temperature, heart rate, respiratory rate and CRT in CPV infected dogs. The haemato-biochemical investigation showed significant decrease in Hb, TEC and increase in PCV and absolute neutrophil count together with significant decrease in serum total protein, albumin, globulin, creatinine, sodium and potassium, whereas, increase in BUN in parvovirus infected dogs. The study concluded that the treatment with injection heterogeneous immunoglobulins i/v with supportive conventional treatment found effective in inducing complete clinical recovery within 7 day of treatment along with improvement in altered haemato-biochemical parameters without any mortality in parvovirus infected puppies.

Key words: Canine parvovirus, Dogs, Immunoglobulins, Haemato-biochemical profile.

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Introduction

Canine parvovirus infection (CPV) is one of the highly contagious viral diseases of dogs causing gastroenteritis or haemorrhagic gastroenteritis. It occurs in all age groups of dogs, however, puppies between 6 weeks and 6 months are more susceptible to the CPV infection as the maternal antibody titres start declining. Out of various types, CPV-2 is highly pathogenic and causes severe form of disease in dogs (Singh *et al*., 2022). The disease is mainly presenting the clinical signs such as anorexia, lethargy, depression, dehydration, fever, frequent vomiting, abdominal pain and diarrhoea, which is often haemorrhagic (Crawford and Sellon, 2010; Goddard and Leisewitz, 2010). The mortality rate is higher in puppies and they die within two days after infection, if not attended immediately.

Therefore, treatment in the early stage of infection is essential and includes symptomatic and supportive care to reduce the risk of death in CPV infected dogs. Even though, the survival rate in CPV infected puppies with conventional therapy is questionable and would not guarantee a favorable prognosis, many researchers have tried purified hyperimmune immunoglobulins for treatment in CPV infected dogs due to their high antigen neutralizing capacity along with supportive therapy and reported effective and quick clinical recovery in CPV-infected dogs without any mortality (Naveenkumar *et al.,* 2019; Rishikesavan *et al.,* 2021; Zope, 2023). In view of the aforementioned fact, the current investigation was undertaken to evaluate the efficacy of heterogeneous immunoglobulin in conjunction with standard conventional therapy in CPV-infected puppies.

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Materials and Methods

In the present study, 10 puppies irrespective of sex and breed positive for CPV infection based on rapid CPV antigen test kit (ACCUVET Vet Cetera Animal Health) and PCR assay in the faeces were selected for the study. DNA extraction was done with the help of (Himedia HiGenoMB) DNA Extraction Kit with standard procedure given with the kit and tested by a VP2 gene of CPV PCR assay as per the method developed by Pereira *et al.* (2000).

A group of 10 puppies positive for CPV infection was treated with injection heterogeneous immunoglobulins anti-parvovirus canis (1 ml contains: Canine Parvovirus immunoglobulins / antibodies NLT 1024 HIU) @ 0.4 mL/kg

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body weight per day intravenously along with conventional therapy that includes antiemetic, antacids, haematinics, fluid therapy, antibiotics and multivitamins etc. as per standard doses based on the clinical signs and severity of the case till recovery. Another group of 10 normal healthy puppies irrespective of sex and breed was kept as a normal control for comparison.

The clinical parameters such as rectal temperature, heart rate, respiratory rate and CRT were studied on '0' day and daily after treatment till recovery. Haematological parameters, *viz*. haemoglobin (Hb), packed cell volume (PCV), total leukocyte count (TLC), total erythrocyte count (TEC), absolute neutrophil count (AbNC), absolute lymphocyte count (AbLC)), absolute monocyte count (AbMC), absolute eosinophil count (AbEC), absolute basophil count (AbBC) were estimated on '0' day and on 7th day after treatment by using automated haematology analyzer (ABAXIS VetScan HM5). Serum bichemical parameters, *viz.,* total protein, albumin, globulin, ALT, AST, BUN, creatinine, sodium, potassium, and chloride were estimated on '0' day and 7th day after treatment by using fully automated biochemical analyzer (ABAXIS VetScan VS2). The effectiveness of treatment regimen was evaluated on the basis of improvement in altered clinical and haemato-biochemical parameters and recovery period, through analysing the data by one-way ANOVA and t-test.

Results and Discussion

In the present work, the CPV infected dogs showed signs of dullness, vomition, fever, anorexia, diarrhoea, dehydration, lethargy and weakness. Many cases showed offensive bloody diarrhoea. Most of the infected dogs showed high fever initially and later on it became subnormal. Several workers reported similar clinical signs in CPV infected dogs (Bhalekar, 2020; Saravanan *et al.,* 2020; Abdullaziz *et al.,* 2022; Zope, 2023). In CPV infected dogs there is destruction of enterocyte due to parvovirus, which causes disruption of intestinal mucosal barrier resulting into erosive inflammatory damage of the intestinal mucosa that causes profuse haemorrhagic diarrhoea (Streck *et al*., 2009; Van den Berg, *et al*., 2018).

In CPV infected dogs (Group II), the mean rectal temperature, heart rate, respiratory rate and capillary refill time (CRT) were significantly ($p<0.01$) increased on '0' day as compared to normal healthy group I (Control, Table 1). Similar findings were also recorded by Baruah *et al.* (2007), Abdullaziz *et al*. (2022) and Zope (2023) in CPV infected dogs. The mean values of these clinical parameters were significantly improved during different post-treatment intervals as compared to pre-treatment values ('0' day). The conjunctival mucous membranes of normal healthy dogs were pink colour (group I). In parvovirus infected group (II), 3 dogs (30%) had congested to slightly congested mucous membrane, 4 dogs (40%) had pale to somewhat pale mucous membrane, whereas 3 dogs (30%) had pink colour mucous membrane.

Haematological study revealed significant ($p<0.01$) decrease in Hb and TEC and increase in PCV in CPV infected dogs (Group II) on '0' day as compared to healthy group I (Control, Table 2). The decrease in Hb and TEC in CPV infected dogs was also recorded by Bhargavi *et al.* (2017), Arora *et al.* (2018), Bhalekar (2020), Khare *et al.* (2020), Harizan *et al.* (2021), Tambe (2022) and Zope (2023). The decrease in Hb and TEC in CPV infected dogs might be because of mucosal barrier disruption and damage of vascular epithelium of the intestine induced by the virus causing massive slugging of intestinal epithelial cells that leads to capillary damage of the intestinal villi resulting in severe haemorrhages and blood loss through the faeces and vomitus in the disease process (Baruah *et al.,* 2007; Bhargavi *et al.,* 2017; Bhalekar, 2020; Harizan *et al.,* 2021). Some researchers opined that the suppression of erythropoiesis due to direct inhibitory effect of CPV on the bone marrow could be one of the reasons for low Hb and TEC (Elsayed *et al*., 2020). According to Macintire and Smith-Carr (1997) the CPV causes cytotoxic effect on haematopoitic cells leading to myeloid and erythroid hypoplasia in bone marrow during acute stages of the disease.

Table. 1: Mean ±SE clinical parameters in group I and II dogs on '0' day (before treatment) and daily up to 7th day after treatment

Groups	Intervals (days)	Rectal temperature (˚F)	Heart rate (beat/ min)	Respiratory rate (breaths/ min)	Capillary refill time (CRT, Sec)
Group I (Control)	'0' day	101.46^{b} ±0.04	122.4^{d} ±2.68	30.80^{b} ±1.79	2.0^{cd} ±0.00
Group II (Treatment)	'0' day	102.11^{a} ±0.21	150.4^{a} ±8.78	47.40^{a} ±8.44	2.60^{ab} ±0.22
	1st day	101.82^{ab} ±0.17	145.8^{ab} ±7.90	48.10^{a} ±7.87	2.70^{a} ±0.21
	2nd day	101.48^{b} ±0.20	142.5^{abc} ±6.20	40.90^{ab} ±5.9	2.60^{ab} ±0.16
	3rd day	101.39^{bc} ±0.25	136.9^{abcd} ±7.97	35.70^{ab} ±4.88	2.40^{abc} ±0.16
	4th day	100.93^{c} ±0.26	130.1^{bcd} ±6.52	32.50^{b} ±3.56	2.20^{bcd} ±0.13
	5th day	101.42^{bc} ±0.10	125.6^{bcd} ±5.07	30.20^{b} ±2.37	1.90^{d} ±0.18
	6th day	101.40^{bc} ±0.10	126.2^{cd} ±5.07	31.0^{b} ±2.22	1.90^{d} ±0.10
	7th day	101.33^{bc} ±0.05	128^{bcd} ±5.16	31.10^{b} ±2.31	1.90^{d} ±0.10

Means bearing the same superscript in different parameters within the column do not differ significantly.

Table. 2: The mean ± SE haematological parameters in group I and II dogs on '0' day (before treatment) and 7th day after treatment

Parameters	Normal Control Group I	Treatment Group II	
		'0' day	7th Day
Hb (g/dL)	12.31^{a} ±0.25	9.61^{c} ±0.29	11.19^{b} ±0.26
PCV (%)	35.74^{b} ±0.49	43.59^{a} ±1.57	32.92^{c} ±0.25
TEC (x 10^6/µL)	6.26^{a} ±0.16	4.37^{b} ±0.32	5.6^{a} ±0.02
TLC (x 10^3/ µL)	12.48 ±0.55	15.72 ±1.73	13.15 ±0.31
AbNC (x 10^3/µL)	8.14^{b} ±0.96	12.55^{a} ±1.97	8.95^{ab} ±0.51
AbLC(x 10^3/µL)	3.25 ±0.50	2.08 ±0.11	2.96 ±0.03
AbMC(x 10^3/µL)	0.62 ±0.03	0.53 ±0.23	0.69 ±0.01
AbEC(x 10^3/µL)	0.43 ±0.10	0.50 ±0.06	0.57 ±0.08
AbBC(x 10^3/µL)	0.05 ±0.00	0.06 ±0.03	0.02 ±0.00

Means bearing the same superscript within the row do not differ significantly (p>0.05).

The present study showed increase in PCV in CPV infected dogs that might be due to haemoconcentration as a result of dehydration (Bhargavi *et al.,* 2017; Kataria *et al*., 2020). Many workers demonstrated decline in PCV in parvovirus infected dogs that might be due to severe haemorrhagic diarrhoea leading to blood loss (Bhargavi *et al.,* 2017; Arora *et al.,* 2018; Khare *et al.,* 2020; Saravanan *et al.,* 2020; Harizan *et al.,* 2021). The mean Hb and TEC were significantly (p<0.01) increased and PCV was significantly (p<0.05) reduced on 7th day post-treatment over the pre-treatment values ('0' day) that indicated improvement in these parameters after treatment. The mean TLC did not show any significant variation between control group (I) and treatment group (II).

The mean absolute neutrophil count (AbNC) showed significant (p<0.05) increase in CPV infected dogs (Group II) on '0' day as compared to group I (Normal Control). There was no significant change in eosinophil, monocyte and basophil count (Table 2). Kataria *et al.* (2020), Saravanan *et al.* (2020), Patel *et al.*(2022), Tambe (2022) and Zope (2023) also recorded increase in AbNC in CPV infected dogs. The concomitant bacterial infections and parvoviral enteritis may be the cause of the elevated AbNC (Biswas *et al.,* 2005). Saravanan *et al.* (2020) speculated that the increase in neutrophils could be due to reactive leuckocytosis causing myeloid hyperplasia and bacterial infection in the damaged intestinal tract. The AbNC was significantly (p<0.05) reduced on 7th day post-treatment over the pre-treatment values ('0' day) and restored to normalcy that indicated improvement in AbNC after treatment.

The mean serum total protein, albumin and globulin levels were significantly (p<0.01) decreased in CPV infected dogs (Group II) on '0' day as compared to normal Control group I (Table 3). The findings were in accordance with the reports of Saravanan *et al.* (2020), Harizan *et al*. (2021), Patel *et al.* (2022) and Zope (2023). The decrease in total serum protein, albumin and globulin levels could be due to changed gastrointestinal mucosal barrier with protein losing-enteropathy and reduced absorption of proteins through the injured villi of the intestines (Grigonis *et al.,* 2002; Biswas *et al.,* 2005; Kumar *et al.,* 2020). The mean serum total protein and serum globulin levels were significantly (p<0.01) improved on 7th day post-treatment over the pre-treatment values ('0' day), whereas, serum albumin level before treatment ('0' day) and on 7th day post-treatment did not differ significantly (Table 3).

Table. 3: Mean ±SE biochemical parameters in group I and II dogs on '0' day (before treatment) and 7th day after treatment

Parameters	Normal Control Group I	Treatment Group II	
		'0' day	7th Day
Total protein (g/dL)	6.16^{a} ±0.24	3.87^{c} ±0.08	5.15^{b} ±0.36
Albumin (g/dL)	3.39^{a} ±0.34	2.36^{b} ±0.17	2.67^{b} ±0.04
Globulin (g/dL)	2.77^{a} ±0.34	1.56^{b} ±0.09	2.49^{a} ±0.4
ALT (IU/L)	47.26^{a} ±2.64	52.97^{a} ±1.33	25.01^{b} ±2.5
AST (IU/L)	42.9^{a} ±0.89	40.95^{a} ±6.62	18.46^{b} ±1.70
BUN (mg/dL)	17.96^{b} ±1.23	35.95^{a} ±3.18	18.72^{b} ±2.55
Creatinine (mg/dL)	1.03^{a} ±0.03	0.72^{b} ±0.01	0.44^{c} ±0.04
Serum Na (mmol/L)	141.4^{b} ±1.12	137.0^{b} ±1.48	147.5^{a} ±2.54
Serum K (mmol/L)	4.81^{a} ±0.18	3.90^{b} ±0.23	4.71^{a} ±0.16
Serum Cl (mmol/L)	108.1^{b} ±2.46	106.9^{b} ±2.96	120.86^{a}±3.89

Means bearing the same superscript in different parameters does not differ significantly (p>0.05).

The mean ALT and AST levels were apparently increased in CPV infected dogs (Group II) on '0' day as compared to group I (Normal Control), however, did not show any significant variation between groups (Table 3). Similar observations were also reported by Khare *et al.* (2020), Saravanan *et al.* (2020), Harizan *et al.* (2021) and Zope (2023).

The mean serum urea nitrogen level was significantly (p<0.01) increased in CPV infected dogs (Group II) on '0' day as compared to group I (Table 3). Similar observations were also reported by Bhargavi *et al.* (2017), Saravanan *et al.* (2020), Abdullaziz *et al.* (2022), Ogbu *et al.* (2022), Patel *et al.* (2022) and Zope (2023). Prerenal azotemia, which is caused by decreased renal blood flow (reduced glomerular filtration rate) as a result of vomiting and diarrhoea-related dehydration and hypovolemia, might be the cause of the elevated BUN levels (Kataria *et al*., 2020; Zope 2023). The mean BUN level was significantly (p<0.01) reduced on 7th day post-treatment over the pre-treatment values ('0' day) and restored to normalcy.

The statistical analysis revealed significant (p<0.01) decrease in serum creatinine level in CPV infected dogs (group II) on '0' day as compared to normal Control group I, however, the level was within the normal range. Many experimenters observed non-significant alteration in creatinine level in CPV infected dogs as compared to healthy dogs (Kataria *et al.,* 2020; Harizan *et al.,* 2021; Patel *et al*., 2022). In the contradiction, some authors reported higher level of serum creatinine in parvovirus infected dogs as compared to healthy dogs (Saravanan *et al.,* 2020; Abdullaziz *et al.,* 2022; Ogbu *et al.,* 2022).

The electrolyte profile study revealed significant ($p<0.01$) decrease in serum potassium level and non-significant decrease in serum sodium and serum chloride levels in CPV infected dogs (group II) on '0' day as compared to group I (Table 3). Similar observations were also reported by Saravanan *et al.* (2020), Abdullaziz *et al.* (2022) and Zope (2023). The falling off of serum sodium, potassium and chloride levels in CPV infected dogs could be attributed to losses of sodium through vomition and diarrhoea due to villous atrophy of the intestine (Rewerts and Cohn, 2000; Kataria *et al.,* 2020). The mean levels of these three elements were significantly ($p<0.01$) increased on 7th day post-treatment over the pre-treatment values ('0' day). These findings indicated improvement in serum electrolytes profile after treatment that showed effectiveness of the treatment.

Out of 10 dogs treated in group II, 2 (20%) dogs recovered completely on 4th day post-treatment. Subsequently, 6 dogs (60%) by 5th day, 9 dogs (90%) by 6th day and all dogs (100%) by 7th day post-treatment recovered completely. These findings suggested that the use of hyper-immune heterogeneous purified immunoglobulin in conjunction with conventional therapy can shorten the duration of recovery, which has been shown to be beneficial and hasten complete clinical recovery. The group treated with hyper-immune heterogeneous purified immunoglobulin along with conventional therapy showed complete clinical recovery within 7 day post-treatment along with improvement in altered clinical and haemato-biochemical parameters without any mortality.

Similar observations were also reported by Goddard and Leisewitz, (2010), Naveenkumar *et al*. (2019), Rishikesavan *et al.* (2021) and Zope (2023), who also noted quick recovery in CPV infected dogs those received hyper-immune heterogeneous purified immunoglobulin in addition to conventional therapy. Anti-CPV immunoglobulins (IgY) are of heterologous origin and are therefore believed to be incapable of inducing complement activation and binding to the mammalian Fc receptor (Narat, 2003). Thus, anti-CPV immunoglobulins (IgY) therapy effectively neutralized the viral load and also reduced the damage and other serious complications in CPV infected dogs. They are also safer, more effective and do not cause any unintentional inflammatory and adverse reactions (Kovacs-Nolan and Mine, 2004). Because immunoglobulins (IgY) have a relatively short half-life, IgY is cleared right away, preventing potential harmful responses and immune recognition. Therefore, intravenous administration of IgY is a safe and efficient therapy regimen for dogs infected with canine parvovirus (CPV). The dogs in group II infected with a parvovirus and received hyper-immune heterogeneous purified immunoglobulin along with conventional medication, proved to be successful in accelerating the clinical recovery.

Conclusion

The findings of this study concluded that the therapy with injection purified immunoglobulins anti-parvovirus canis @ 0.4 mL/kg body weight intravenously with supportive conventional treatment proved effective in inducing complete clinical recovery along with improvement in altered haemato-biochemical parameters without any mortality in parvovirus infected dogs.

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