

# Treatment of Severe Canine Parvoviral Enteritis Associated with Coccidia

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**Abstract** | Parvovirus enteritis is one of the most dangerous viral infections in dogs, but today the issues of microbiocenosis, features of the epizootic process, pathogenesis, and treatment of dogs with parvovirus enteritis complicated by associations of coccidia remain poorly understood. The aim of this work was to develop and evaluate the effectiveness of a method for treating dogs with parvovirus enteritis, complicated by associations of coccidia, with a severe course of the disease. The study was carried on in Veterinary Medicine Hospital of Al-Muthanna Province, south of Iraq. Puppies with Diarrhea, oocysts of *Cystoisospora canis* were identified. The suspected cases were diagnosed by using a rapid test for parvovirus. The effectiveness of the method of therapy for dogs with parvovirus enteritis complicated by associations of coccidia in a severe form of the course of the disease was evaluated in two stages. The first stage was carried out at the time of the appointment of treatment, and the second stage after 14 days. Globcan-5 wa, Suprastin, Fosprenil, Gamavit-forte, Levofloxacin, Gordox, Okrestatin, Lactobifadol, Polyoxidonium, Ringer's solution, rheosorbilact and stabilizol were used as therapy. Firstly, the general clinical, biochemical, and immunological parameters of the blood of sick animals were examined at the time of treatment. The results of A comparative analysis of the recorded was carried out. In the process of treating sick dogs, positive changes occur, which are characterized by an improvement in the general clinical condition, a decrease in body temperature, elimination of vomiting, diarrhea, gastrointestinal bleeding, intoxication, and dehydration syndromes, normalization of the concentration of hemoglobin in the blood, total protein, albumin, urea, creatinine, total bilirubin, circulating immune complexes, the activity of alanine and aspartic aminotransferases,  $\alpha$ -amylase in blood serum, erythrocytes, leukocytes, T- and B-lymphocytes, O-cells, and T-helpers. From this study concluded the treating sick dogs, positive changes occurred, which are characterized by an improvement in the general clinical condition, normalization of the concentration of hemoglobin in the blood, total protein, albumin, urea, creatinine, total bilirubin, circulating immune complexes, the activity of alanine, aspartic aminotransferases,  $\alpha$ -amylase in blood serum, the number of erythrocytes, leukocytes, T- and B-lymphocytes, O-cells, and T-helpers in the blood.

**Keywords** | Parvovirus, Canine enteritis, *Cystoisospora*, blood counts, Coccidia, Immunological parameters, Protozoa, Contagious, Biochemical indices

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Canine parvovirus enteritis is a highly contagious viral disease of dogs, which is accompanied by a significant variability of clinical symptoms, acute hemorrhagic enteritis, myocarditis, leukopenia, rapid dehydration, and high mortality (Nandi and Kumar, 2010; Sykes, 2014). Diarrhea accopain with enteritis characteristic by extreme pain and loss of appetite, feces yellow in colore, watery and may contains blood in severe cases. Vomiting and diarrhea lead to rapid dehydration which cause death (Khatri et al., 2017). The parvoviruses are a series of tiny, DNA involving viruses that infect eukaryotic cells. These viruses have been detected from a varied of hosts but their features are strikingly similar. The independent, non-defective parvoviruses are characterized by a small helical protein capsid 18 to 28 nanometer in diameter that involve a single-stranded DNA genome of molecular weight  $1.35 \times 10^6$  to  $1.7 \times 10^6$ . The protein content of the viruses composed of the more avialable that can be proteolytically cleaved to VP2 in the mature virus, and the less abundant (but larger) VP1 (Paradiso et al., 1982). The oocyst wall is composed from the component of two specific specialized subunit, wall developing bodies Type 1 (WFB1) and 2 (WFB2), present specially in the sexual, macro-gamete stage of coccidian parasites. In the first stages of macrogamete biogenesis, the macrogametocyte involve a central nucleus and many sphere-shaped accumulate of electron dense substanses within distended regions of the (rough endoplasmic reticulum), after that, in the mid-phase of macrogamete development, rounded electron dense granules show in the cytoplasm (Mai et al., 2009). Research in recent decades has greatly expanded ideas about the epizootiology and specific prevention of parvovirus enteritis as a mono-infection (Nandi and Kumar, 2010). However, the modern principle of studying animal diseases lies in the principles of parasitocenoses, evolutionary-ecological aspects, and poly morbidity the microbiocenoses of dogs with parvovirus enteritis remain unexplored. Such important issues as the features of the epizootic process, pathogenesis, and treatment of dogs with parvovirus enteritis complicated by associations of coccidia remain poorly studied, which is an important area of scientific research.

The aim of the work is to investigate the effectiveness of a method for treating dogs with parvovirus enteritis complicated by associations of coccidia in a severe form of the disease in special area (Al-Muthanna city) and can be applicable in everywhere around the world.

## MATERIALS AND METHODS

The study was carried on in Veterinary Medicine Hospital

of Al-Muthanna Province, south of Iraq. If puppies have diarrhea or loose stools, coccidiosis should be suspected. Veterinarians can confirm the diagnosis by microscopic examination of the feces, revealing the oocysts.

The suspected cases were diagnosed by using a rapid test for parvovirus. Canine parvovirus and coronavirus rapid antigen test using the Anigen kit for dogs. This was produced by Modern Veterinary Therapeutics. For the qualitative detection of Canine Parvovirus antigen and Coronavirus antigen in canine feces, a chromatographic immunoassay like the one provided by the Canine Parvovirus-Coronavirus Antigen Test Kit was used. The Test line and Control line on the Anigen Quick Canine Parvovirus-Coronavirus Ag Test Kit are marked by the letter's "T" and "C," respectively. Before applying any samples, neither the test line nor the control line in the result window will be displayed. To ensure that the test method is being carried out correctly and that the control line's test reagents are functioning, it is necessary to observe the appearance of the control line. If the material contains detectable levels of Canine Parvovirus antigen and/or Canine Coronavirus antigen, a purple test line will appear in the result window.

The effectiveness of the method of therapy for dogs with parvovirus enteritis complicated by associations of coccidia in a severe form of the course of the disease was evaluated in two stages. The first stage was carried out at the time of the appointment of treatment, and the second stage after 14 days.

Globcan-5 was used subcutaneously at a dose of 3.0 ml three times at an interval of 12–24 hours. Suprastin was used intramuscularly at a dose of 1–2 mg/kg 15–30 minutes before immunoglobulin administration. Fosprenil was used subcutaneously at a dose of 1.0 ml/kg body weight once a day for 5 days. Gamavit-forte was administered at a dose of 1.0 ml/kg body weight once a day for 5 days. Levofloxacin was used subcutaneously at a dose of 15–20 mg/kg (with a mild form of the disease) 1 time per day for 5 days or intravenously drops at a dose of 15 mg/kg (with a moderate and severe form of the disease) 1 time per day for 5 days. Gordox was administered intravenously at a dose of 1500–2000 IU/kg once a day for 5 days. Okrestatin subcutaneously at a 5–7 mcg/kg dose once a day for 5 days. Lactobifadol was administered orally at a dose of 0.2 g/kg of animal weight 2 times a day for 14 days. Polyoxidonium was used intramuscularly at a dose of 3–6 mg once a day for 3 days. Ringer's solution at a dose of 17–20 ml/kg, 5% glucose solution at a dose of 17–20 ml/kg, rheosorbilact at a dose of 17–20 ml/kg once a day for 5–7 days, and stabilizol were used as infusion therapy. at a dose of 3–6 ml/kg once a day for 5–7 days.

The hemoglobin concentration in dogs' blood was determined by the hemoglobin cyanide method; the number of erythrocytes and leukocytes was counted in a chamber with a Goryaev grid, ESR was determined using the Panchenkov apparatus, a leukogram was taken in blood smears stained according to Romanovsky-Giemsa (Kondrakhin et al., 2004). The concentration of total protein in the blood serum of dogs was determined by the biuret reaction, protein fractions by the nephelometric method, urea by a color reaction with diacetylmonoxime, creatinine- by the Jaffe color reaction,  $\alpha$ -amylase activity by the Caraway method, ALAT and AsAT- by Reitman and Frenkel, bilirubin concentration – Jendrashik (Kondrakhin et al., 2004). A/G ratio and de Ritis coefficient (AsAT/ALAT) were calculated. To carry out the above studies, a BioChem SA semiautomatic biochemical analyzer (High Technology Inc., USA) was used. The total number of T-lymphocytes was determined by the method of spontaneous rosette formation with ram erythrocytes modified by AI Cheredeev. Theophyllin sensitivity and resistance of T-cells to theophylline were studied (Reisner et al., 1981, 1983). The number of theophylline-sensitive T-lymphocytes (T-suppressors) was determined by the difference between the number of theophylline-resistant T-cells (T-helpers) and T-lymphocytes. The immunoregulatory index (IRI) was calculated from the T-helper/T-suppressor ratio. The number of O-cells was calculated from the difference between the sum of the number of T-lymphocytes and B-lymphocytes according to the method of complementary rosette formation from the total number of lymphocytes. The total level of circulating immune complexes (CIC) and their fractional composition were determined by molecular weight (Mavligit and Wong, 1982; Novak et al., 2005; Fratrić et al., 2012). All calculations were performed on a personal computer using the statistical program GraphPad Prism 9.

## RESULTS AND DISCUSSION

### THE CLINICAL SIGNS OF COCCIDIA

Five dogs were diagnosed with coccidiosis. The recorded clinical signs were diarrhea as the most noticeable symptom of coccidiosis in tested dogs. Diarrhea ranged from moderate to severe. In severe situations, there was blood and mucus. Dogs with severe cases of the disease showed vomiting, loss of appetite, and dehydration.

### IDENTIFIED COCCIDIANS

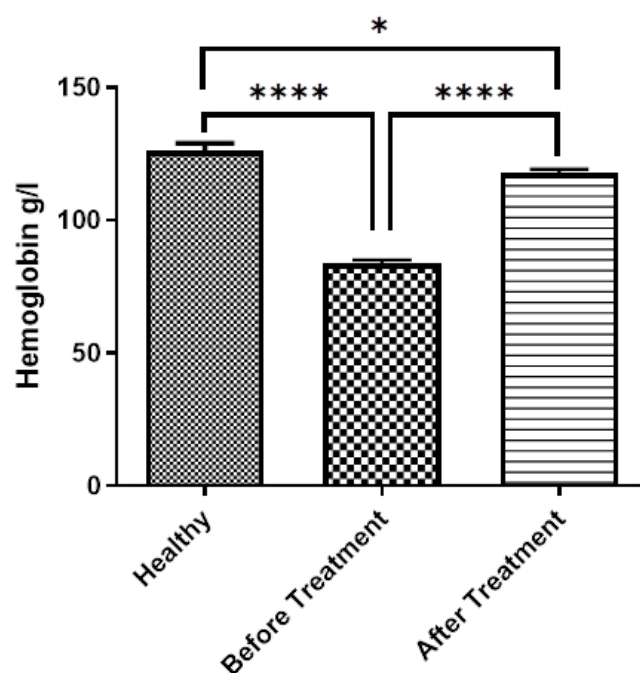
Oocysts of *Cystoisospora canis* were identified in two out of twelve (16%). The measurements of oocysts ranged from 38  $\mu$ m to 43.7  $\mu$ m by 33.2  $\mu$ m to 35.8  $\mu$ m. It was thick and the oocyst wall was smooth and a very light brown color. There was no micropyle or polar cup. Sporulated Oocysts had two daughters sporocysts, which ranged in shape from

elliptical to avoid.

### TREATMENT OF AFFECTED DOGS

The effectiveness of treatment of seven dogs with parvovirus enteritis complicated by associations with coccidia with a severe course of the disease was evaluated. Experimental dogs were treated according to a single scheme, in particular, they used Glocan-5, suprastin, fosprenil, gamavit-forte, levofloxacin, Gordox, intravenous infusions of Ringer's solution, 5% glucose solution and reosorbilact, stabizol, lactobifadol. Also, sick dogs have been prescribed the most powerful immunostimulant drug- polyoxidonium, which was used intramuscularly at a dose of 3-6 mg once a day for 3 days.

For coccidian cases treatment, the researchers used sulfadimethoxine to eliminate the parasitic infection and IV fluids for dehydration treatment. The recommendations were spraying the entire animal house or the owner's home with diluted chlorine bleach. In addition to using diarrhea stop to control diarrhea.



**Figure 1:** Concentration of Hemoglobin g/l.

It should be noted that in the process of treatment in the body of dogs with parvovirus enteritis, complicated by associations of coccidia with a severe course of the disease, positive changes occur, which are characterized by an improvement in the general clinical condition, a decrease in body temperature, elimination of vomiting, diarrhea, gastrointestinal bleeding, syndromes of intoxication and dehydration, normalization of the concentration of hemoglobin in the blood as in Figure 1, erythrocytes, ESR, leukocytes as in Figure 2, 3 and 4, respectively, total protein, albumin, urea, creatinine, total bilirubin,  $\alpha$ -amylase in

blood serum as Shaw in Figures 5, 6, 7, 8, 9 and 10, CEC, the activity of ALT, AST as in Figures 11, 12 and 13, T- and B-lymphocytes, T-helpers and O-cells as in Figures 14, 15, 16 and 17, respectively.

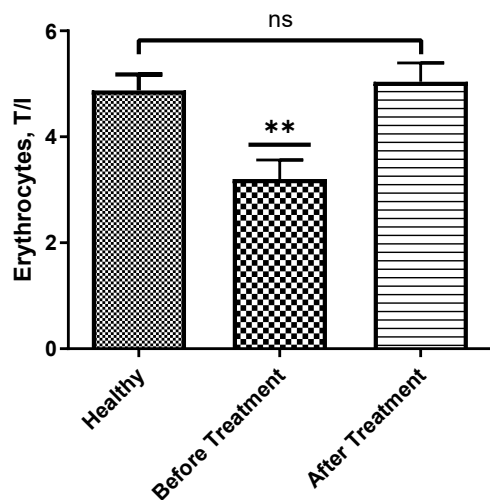


Figure 2: Total number of Erythrocytes, T/l.

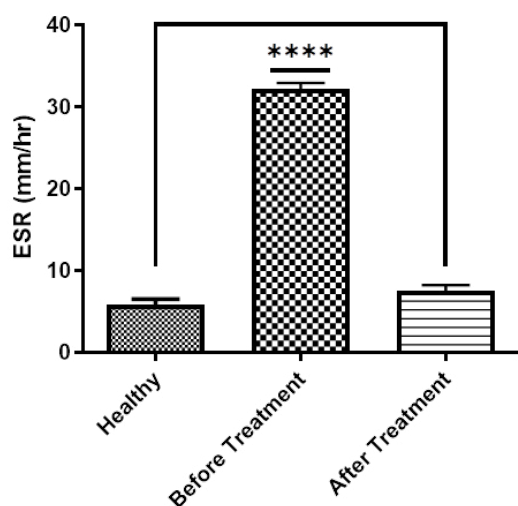


Figure 3: ESR, mm/h.

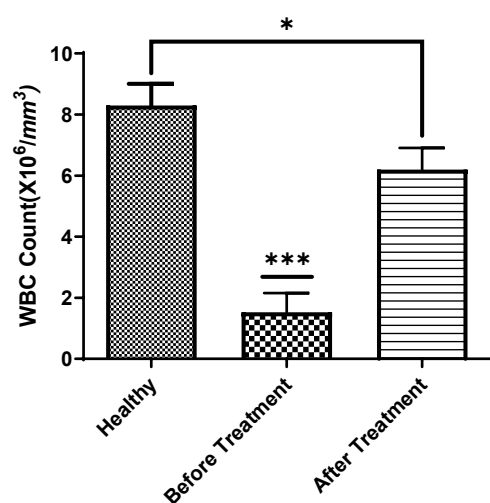


Figure 4: Total number of leucocyte.

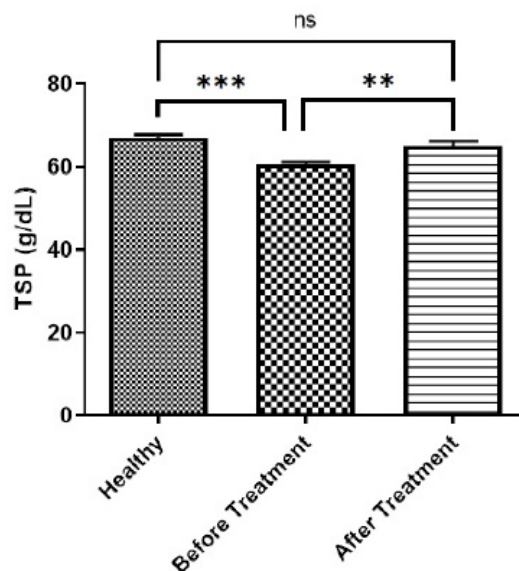


Figure 5: Concentration of Total serum protein (g/dl).

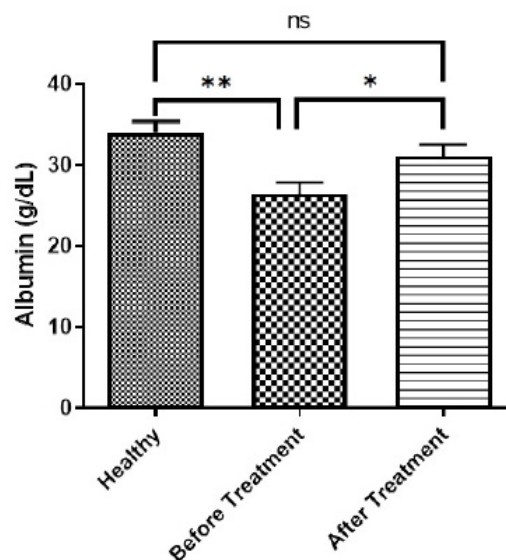


Figure 6: Concentration of Albumin (g/dl).

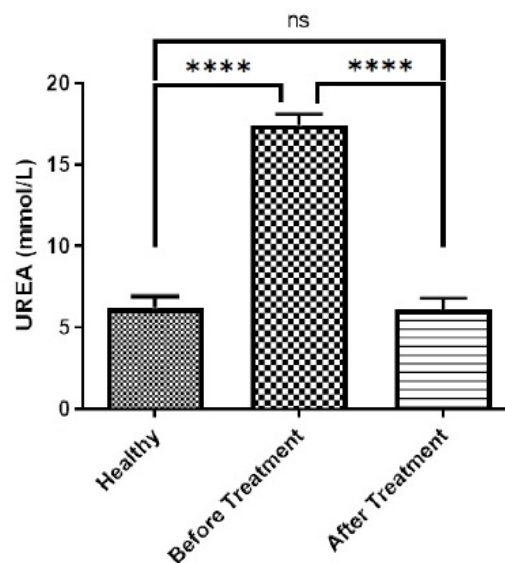


Figure 7: Concentration of UREA (mmol/L).



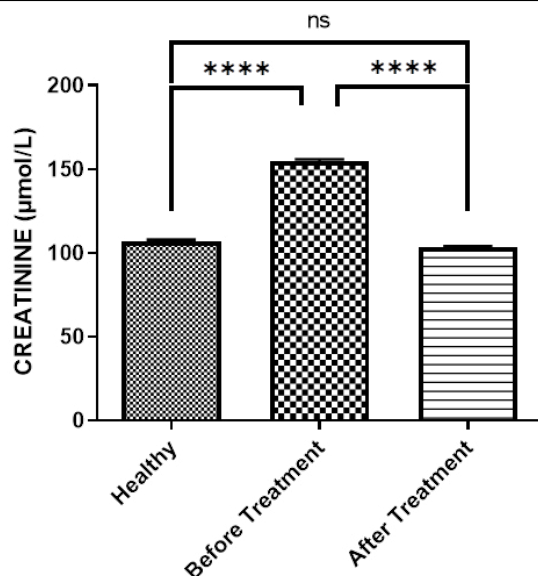


Figure 8: Concentration of Creatinine (μmol/l).

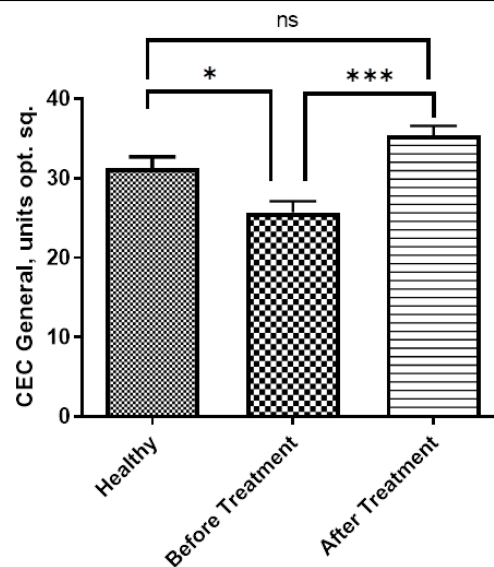


Figure 11: CEC general, units opt. sq.

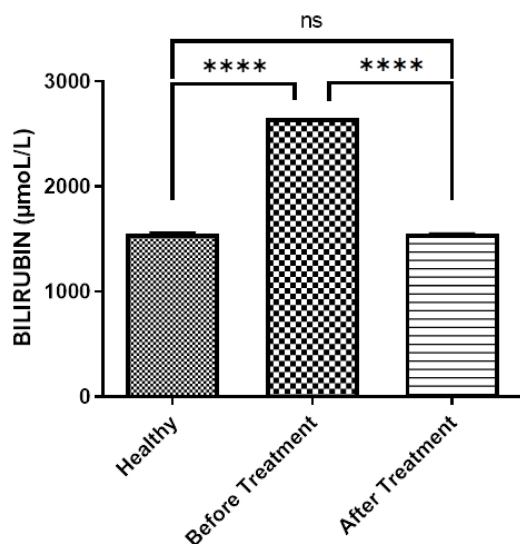


Figure 9: Concentration of bilirubin (μmol/l).

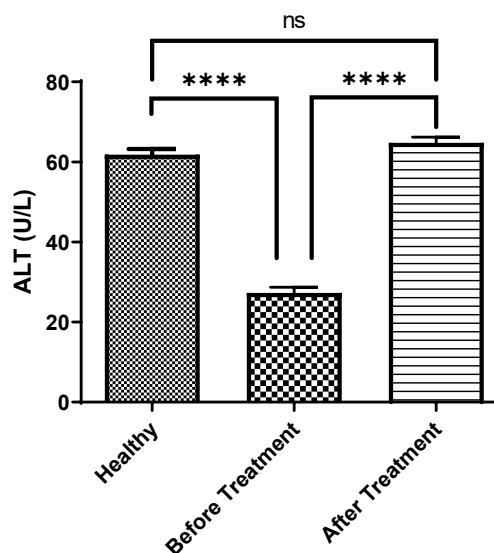


Figure 12: Concentration of alanine aminotransferases (U/L).

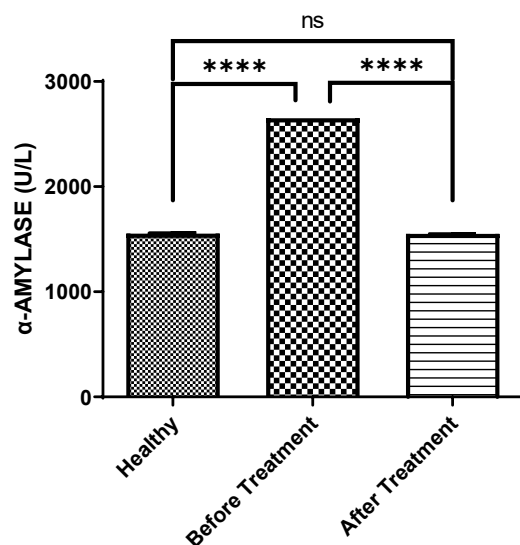


Figure 10: Concentration of α-amylase (U/L), CEC, the activity of ALT, AST as in Figures 11,12 and 13.

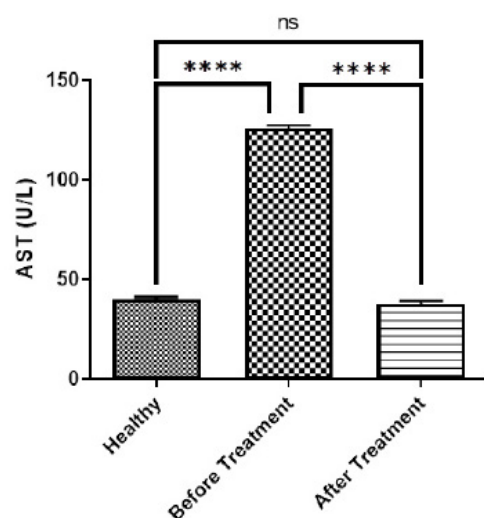
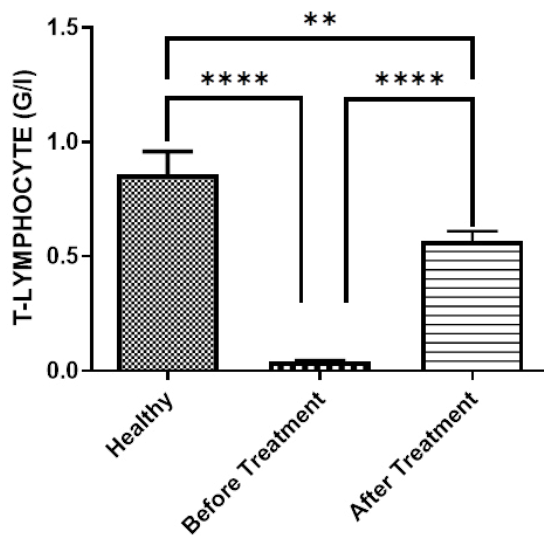
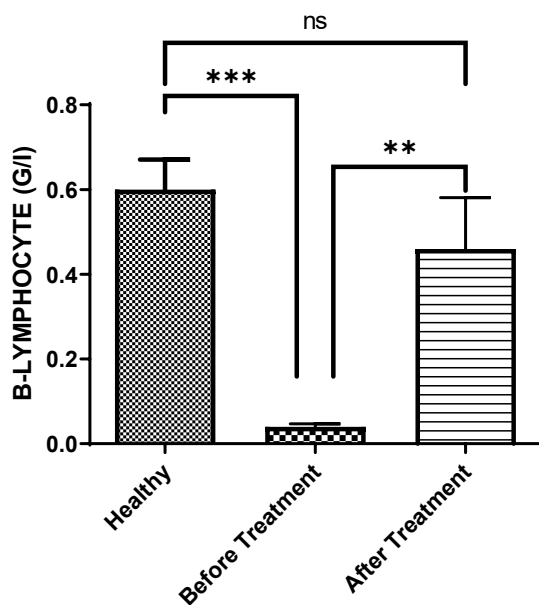


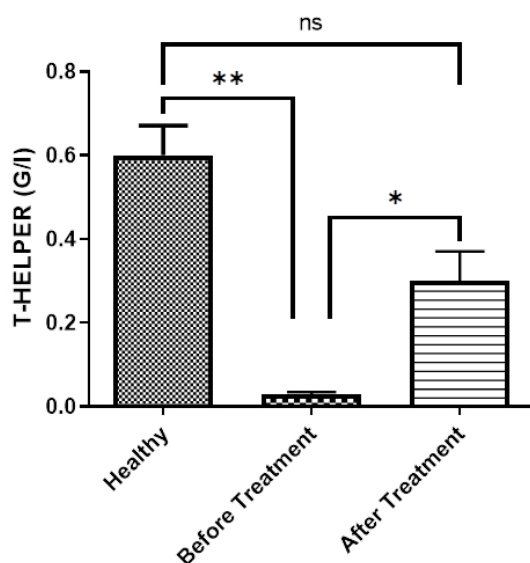
Figure 13: Concentration of Aspartic i aminotransferases (U/L).



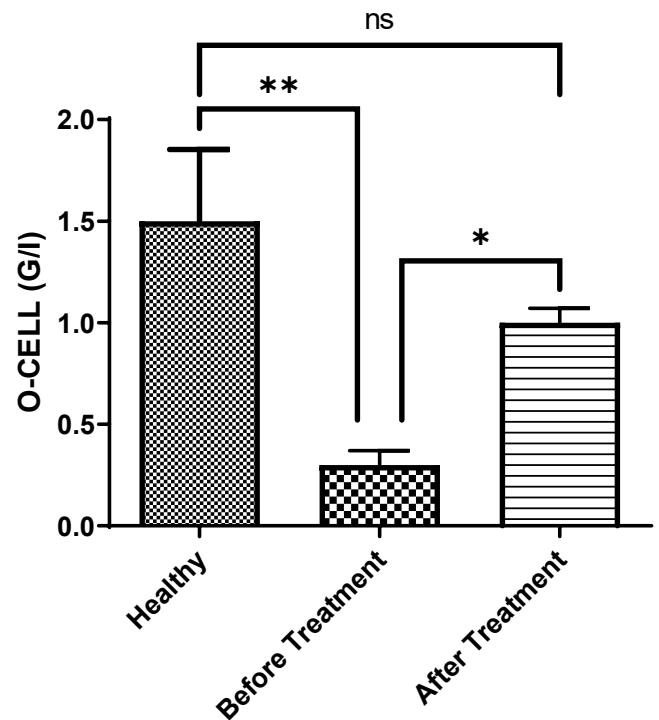
**Figure 14:** Total number of T. Lymphocyte (G/L).



**Figure 15:** Total number of B. Lymphocyte (G/L).



**Figure 16:** Total number of T. Helper (G/L).



**Figure 17:** Total number of O-cells (G/L).

Note: \* –  $p \leq 0.05$ ; \*\* –  $p \leq 0.01$ ; \*\*\* –  $p \leq 0.001$  (Reliability of the difference between the indicators of sick dogs before and after treatment).

One of the predisposing factors of Canine parvovirus is intestinal parasitism (Da Silva et al., 2001; De Castro et al., 2007). Furthermore, the infected dogs without treatment died in other studies recorded by Otto et al., (2001). As well as, Other studies reported by Thwiny et al. (2022), Alsaadawi et al. (2022a) and Hameed et al. (2022) they examined sixty-four diarrheic dogs and puppies in the Veterinary Teaching Hospitals in Samawah. Age, sex, owner's living places, and main clinical signs were recorded. The number of female puppies was higher than males. The infection rate with rotavirus was the highest in both sexes, while the protozoan infection was the lowest. From our recordings, there were many cases diagnosed as unknown diarrhea as the diagnosis revealed no pathogenic agent. This is one of the biggest limitations of our study. We recommend establishing a new unit for dealing with unknown cases in all medical aspects of the province as transitional diseases are considered nowadays a big part of global health.

In addition, our study included also the evaluation of infection rates according to the age of examined animals. The results showed the highest infection rates were in the youngest animals. this can be attributed to the weak immune system at this age as the immunity tends to be more active during subsequent ages, this explaining was agreed with Alsaadawi et al. (2022b). However, the later ages showed lower infection rates which seems to start developing immune resistance against infectious agents.

In addition, to the new active acquired immunity that is acquired from vaccination.

In the present study, the positive dynamics of the course of the disease were noted with the improvement of the general clinical condition, the cessation of vomiting and diarrhea, the appearance of appetite, the normalization of skin turgor, and the restoration of body weight. Negative dynamics were noted with the progression of parvovirus enteritis, complicated by associations of *Coccidia*, the increase in intoxication, and dehydration syndromes, followed by a fatal outcome of the disease. Particularly unfavorable in terms of prognosis symptoms were profuse intestinal bleeding, coma, and intestinal paresis. Three animals died during the treatment of dogs with severe parvovirus enteritis, complicated by associations of coccidia (mortality rate 42.9%). In the remaining animals of this group, recovery occurred on average for  $11.7 \pm 0.92$  days. It should also be noted that the hemorrhagic syndrome in surviving dogs was eliminated on the  $3.4 \pm 0.87$  days.

General clinical, biochemical, and immunological parameters of the blood of dogs with parvovirus enteritis, complicated by associations of *Coccidia*, with a severe course of the disease during their treatment. The dogs treated with *Coccidia* drugs showed further diarrhea.

Several studies showed the positive effect of treatment in case of canine parvovirus (Khatiri et al., 2017; Tabary, 2020; Horecka et al., 2020). The treatment regimen proved to be effective. With additional intramuscular use of polyoxidonium, the survival rate of dogs with parvovirus enteritis complicated by associations of *Coccidia* with a severe course of the disease was 57.1%. The high therapeutic efficacy of the treatment can be explained by the powerful immunostimulatory effect of polyoxidonium. Polyoxidonium increases the body's resistance to bacterial, fungal, and viral infections. The basis of the mechanism of the immunomodulatory action of polyoxidonium is a direct effect on phagocytic cells and natural killers, as well as stimulation of antibody production. Along with the immunomodulatory effect, polyoxidonium has a pronounced detoxifying and antioxidant activity.

## CONCLUSIONS AND RECOMMENDATIONS

Treatment of dogs with severe forms of parvovirus enteritis, complicated by associations of *Cystoisospora canis*, is based on the use of globcan-5 at a dose of 3.0 ml, suprastin (1–2 mg/kg), fosprenil (1.0 ml/kg), gamavit-forte (1.0 ml/kg), lactobifadol (0.2 g/kg), levofloxacin (15–20 mg/kg), Gordox (1500–2000 U/kg), ocreastatin (5–7 µg/kg), polyoxidonium (3–6 mg), infusions of Ringer's solution

(10–17 ml/kg), glucose (10–17 ml/kg), rheosorbilact (10–17 ml/kg) and stabilizol (3–6 ml/kg). In the process of treating sick dogs, positive changes occur, which are characterized by an improvement in the general clinical condition, a decrease in body temperature, elimination of vomiting, diarrhea, gastrointestinal bleeding, intoxication and dehydration syndromes, normalization of the concentration of hemoglobin in the blood, total protein, albumin, urea, creatinine, total bilirubin, circulating immune complexes, the activity of alanine, aspartic aminotransferases,  $\alpha$ -amylase in blood serum, the number of erythrocytes, leukocytes, T- and B-lymphocytes, O-cells, and T-helpers in the blood.

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## NOVELTY STATEMENT

The novelty of the study is focus on the suitable and drug of choice in the treatment of parvoviral infections in canine associated with *Coccidia* parasitic infection according to the laboratory estimations of the studied cases.

## AUTHOR'S CONTRIBUTION

NJA: Acquisition of data and drafting the article, preparing, and reading the histopathology slides, collecting the samples, and designing the study and methodology.

MAA: The conception and design of the study, interpretation of data.

MA: Final approval of the version to be submitted and collecting the samples and designing the study.

## DATA AVAILABILITY

Not applicable

## CONSENT TO PARTICIPATE

Not applicable.

## FUNDING

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## ETHICAL APPROVAL

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Veterinary Medicine College Ethical Approval Committee (Application Number: 12032023).

## CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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