Shahid Bahonar University of Kerman

Veterinary and Comparative Biomedical Research

Original Research | ISSN: 3060-7663 | Doi: 10.22103/vcbr.2025.24710.1042

The Impacts of Folic Acid on Hematological Parameters in German Shepherd Dogs with Parvovirus-Induced Anemia

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Article history:

Received: 21 January 2025
Revised: 21 February 2025
Accepted: 20 March 2025
Published: 20 April 2025

Keywords:

Folic acid
Parvovirus
Anemia
Dog
German Shepherd

Abstract Canine parvovirus often causes anemia in dogs, presenting significant therapeutic challenges. This study evaluated the effectiveness of folic acid supplementation in improving hematological parameters in German Shepherd dogs with parvovirus-induced anemia. Forty German Shepherd dogs diagnosed with parvovirus-induced anemia were randomly assigned to two groups: the control group received standard treatment alone, and the experimental group was administered 5 mg of folic acid daily in addition to standard treatment for two weeks. Significant improvements were observed in hematocrit, hemoglobin, mean corpuscular volume, and mean corpuscular hemoglobin concentration in the experimental group ($p<0.05$). No significant differences were observed in mean corpuscular hemoglobin, white blood cell count, and thrombocyte count between the groups. Folic acid supplementation improved several hematological parameters in dogs with parvovirus-induced anemia, highlighting its potential as an adjunctive therapeutic approach.

Introduction

Folic acid (also known as folate, vitamin B_9, or folacin) is an essential vitamin for dogs, playing a critical role in DNA metabolism and red blood cell synthesis [1]. It facilitates the conversion of deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP), a pivotal step in DNA synthesis. Deficiency in folic acid leads to elevated dUMP levels, which can result in the substitution of uracil for thymine in DNA, which can result in chromosomal instability [2].

Folic acid is widely used to address folate deficiency in species such as dogs, cats, and horses, particularly in cases where gastrointestinal disorders impair nutrient absorption. As a water-soluble vitamin, the risk of toxicity from supplementation is low, as excess amounts are excreted via renal [1]. Clinically, folate deficiency is diagnosed through analysis of complete blood counts (CBC), alongside plasma vitamin B12 and folate concentrations [3, 4].

Canine parvovirus (CPV) is a highly contagious viral infection, predominantly affects young dogs aged 6 weeks to 6 months. It targets rapidly dividing cells, including intestinal epithelial cells, lymphoid tissues, and bone marrow progenitors. While adult dogs are typically resistant due to vaccination or natural immunity, young, unvaccinated dogs and breeds such as German Shepherds, Rottweilers, and Doberman Pinschers are at higher risk of severe infection [5 – 9].

CPV infection causes significant gastrointestinal damage, resulting in anemia due to blood and protein loss. Hematological findings in affected dogs typically demonstrate reduced hematocrit (Hct), hemoglobin (Hb), and red blood cell (RBC) counts. These complications necessitate intensive supportive care, including fluid therapy, antiemetic, and broad-spectrum antibiotics [10, 11]. This study evaluates the therapeutic potential of folic acid supplementation in managing parvovirus-induced anemia in German Shepherd dogs.

Materials and methods

Animals

A total of 40 German Shepherd dogs (aged 6 to 18 months) diagnosed with parvovirus-induced anemia were enrolled. The sample size was determined to ensure a 95% confidence level with a 15% margin of error. Inclusion criteria required dogs to be between 6 and 18 months old, weigh between 8 and 30 kg, and have a confirmed diagnosis of parvovirus-induced anemia. Dogs were randomly assigned to control and experimental groups, ensuring no significant differences in baseline characteristics.

Dietary management

All dogs received a balanced diet prepared in a controlled environment. The diet included: white rice (45%), lean skinless white meat (35%), carrots (15%), and boiled egg whites (10%), administered at 3% of the dogs' body weight divided into two daily portions. The dietary sources of folic acid, listed in descending order of their content, are as follows: egg white: 10 µg, carrot: 5 µg, white rice: 2 µg, and lean skinless white meat: 2 µg.

Study protocol

The study was conducted over seven months, with each dog being monitored for a 14-day period. Throughout the observation period, the dogs received standard parvovirus treatments and being evaluated for the effects of folic acid on anemia. Hematological parameters were measured and analyzed at the beginning and end of the study period. Parvovirus infection was confirmed using a CPV Ag test kit. Baseline hematological parameters, including RBC count, Hb, and Hct were measured using an Auto 3-part Hematology Analyzer (BK-3200, China).

Treatment protocol

Both groups received standard treatment for parvovirus without folic acid supplementation. Supportive care included: crystalloids at 50–80 ml/kg/day intravenously based on dehydration level, Ondansetron: 0.1–0.2 mg/kg/ q 12 hours intravenously, ceftriaxone: 20–40 mg/kg / q 12 hours intravenously, metronidazole: 10–20 mg/kg / q 12 hours intravenously. None of these medications interfered with folic acid absorption or anemia status. Dogs in the experimental group received 5 mg of folic acid intramuscularly once daily for two weeks. The control group did not receive folic acid supplementation.

Hematological evaluation

After two weeks, blood samples were collected from all dogs, and hematological parameters, including red blood cell (RBC), Hematocrit (Hct), Hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell (WBC), and thrombocyte (PLT) levels were re-evaluated.

Statistical analysis

Statistical analysis was performed with SPSS Version 21 statistic software package. Data normality was assessed using the Kolmogorov-Smirnov test. An independent t-test was used to assess differences between the groups, with $p<0.05$ considered statistically significant.

Results

The results confirmed that all hematological parameters followed a normal distribution. Additionally, variance homogeneity was observed for all indices in both experimental and control groups ($p>0.05$), validating the application of parametric t-tests for mean comparisons between groups.

The results revealed both significant and non-significant differences in hematological parameters between the control and treatment groups. The mean RBC count was slightly lower in the control group (5.1×10^6 /µL) compared to the treatment group (5.5×10^6 /µL), but this difference was not statistically significant ($p > 0.05$). Similarly, no significant differences were observed in mean corpuscular hemoglobin, white blood cell count or thrombocyte count between the two groups ($p>0.05$).

Table 1. Hematological parameters before treatment in the 40 German Shepherd dogs

Parameter	Control	Treatment
RBC ($\times10^6$/µl)	4.5 ± 0.2*	4.4 ± 0.3
Hematocrit (%)	29.5 ± 1.6	29.1 ± 1.8
Hemoglobin (g/dl)	10.3 ± 0.6	10.4 ± 0.9
MCV (fl)	64.8 ± 0.7	65.1 ± 0.8
MCH (pg)	21.8 ± 0.2	21.2 ± 0.4
MCHC (g/dl)	34.3 ± 0.7	33.8 ± 1
WBC ($\times10^3$/µl)	9.9 ± 1	10.1 ± 1.1
Thrombocyte ($\times10^3$/µl)	441.1 ± 34.2	421.4 ± 30.7

*Mean ± Standard deviation

In contrast, several parameters showed statistically significant differences ($p<0.05$), indicating the impact of folic acid supplementation. Hematocrit levels were higher in the treatment group compared to the control group, as were hemoglobin levels. Additionally, the treatment group exhibited significantly higher mean corpuscular volume and mean corpuscular hemoglobin concentration. These findings suggest that folic acid supplementation effectively improved key hematological parameters, particularly Hct, Hb, MCV, and MCHC, in dogs with parvovirus-induced anemia. However, no statistically significant changes were observed in RBC count, WBC count, or PLT count.

Table 2. Comparison of hematological parameters after treatment in the two study groups

Parameter	Control*	Treatment
RBC ($\times10^6/\mu$l)	5.1± 0.67	5.5 ± 0.77
Hematocrit (%)	33.7± 3.5 [a]	38.3 ± 3.2 [a]
Hemoglobin (g/dl)	11.95 ± 1.2[b]	12.76 ± 1.1[b]
MCV (fl)	66.53 ± 4.3[c]	70.28 ± 6.2 [c]
MCH (pg)	23,62 ± 1.8	23.46 ± 1.8
MCHC (g/dl)	35.59 ± 3.1[d]	33.47 ± 2.4 [d]
WBC ($\times10^3/\mu$l)	9.80 ± 1.3	9.95 ± 0.5
Thrombocyte ($\times10^3/\mu$l)	377.6 ± 40.1	356 ± 43.8

*Mean ± Standard deviation

Similar alphabetic superscripts (a, b, c and d) in each row show significant differences between control and treatment groups

Discussion

CPV is a significant cause of acute gastrointestinal inflammation in dogs; with novel genetic variants (such as CPV-2a, CPV-2b, and CPV-2c) further complicating the clinical presentation. Clinical signs of CPV range from mild gastroenteritis to severe hemorrhagic diarrhea, influenced by factors such as breed, age, and immune status [12 – 15].

The relationship between folic acid and canine anemia is particularly significant, as folic acid is essential for the production of RBCs, and its deficiency can hinder the recovery of dogs with parvovirus-induced anemia [16 – 20]. Folic acid is essential for erythropoiesis (RBC formation), DNA synthesis, and erythroblast maturation [2].

Hematological and biochemical evaluations are crucial for diagnosing and monitoring

parvovirus infections, providing valuable insights into differential diagnosis, treatment response, and clinical outcomes, although they might not fully elucidate the underlying causes of gastrointestinal disease [13, 17].

The present study supports previous findings that CPV infection leads to significant hematological abnormalities including anemia, leukopenia, lymphopenia, thrombocytopenia, hypoglycemia, and hypoproteinemia [21, 22]. In the present study, infected dogs exhibit significantly reduced Hct, Hb, and RBC levels compared to healthy dogs. Moreover, acute enteritis caused by CPV can be particularly severe in certain breeds, such as German Shepherds, Rottweilers, and Doberman Pinschers, indicating a breed predisposition to the disease [21].

Previous research has demonstrated significant hematological differences between parvovirus-infected and healthy dogs. Infected dogs have significantly lower mean HGB levels (10.30 ± 0.35 g/dl) compared to healthy dogs (13.13 ± 0.20 g/dl), as well as Hct levels (36.96 ± 0.92% vs. 41.75 ± 0.53%) and RBC counts (5.52 ± 0.17 million/µl vs. 6.14 ± 0.09 million/µl) [18].

Similarly, the concentrations of serum protein such as albumin and globulin were significantly decreased in dogs infected with CPV, highlighting the impact of intestinal protein loss. The activity of enzymes such as alkaline phosphatase and aspartate amino transferase was elevated in infected dogs, indicating potential hepatic involvement during the infection [18].

Studies on folic acid deficiency in dogs have shown the significant impact of folate on hematological health. Folic acid deficiency in dogs can lead to progressive anemia, weight loss, and glossitis, with notable improvement observed after folic acid supplementation [1]. Furthermore, Zoya et al. (2022) found a positive relationship between HCT levels and serum folate concentrations, highlighting the critical role of folate in managing anemia [23].

The present study supports previous findings by showing significant enhancements in hematological indices, such as Hct, Hb, MCV, and MCHC in the group supplemented with folic acid. However, some parameters like RBC count, MCH, WBC count, and PLT count did not exhibit significant differences between the control and treatment groups. This indicates that while folic acid supplementation is effective in improving anemia-related indices, its effects on other hematological parameters may be limited.

The present study has limitations including a small sample size and a focus on a single breed (German Shepherds), which may restrict the generalizability of the findings to other breeds or populations. Moreover, the two-week treatment duration may not provide a comprehensive understanding of the long-term benefits or potential side effects of folic acid supplementation.

Conclusion

The current study highlights the potential of folic acid as a supplementary treatment for parvovirus-induced anemia in German Shepherd dogs. The treatment group showed significant improvements in Hct, Hb, MCV, and MCHC, indicating the effectiveness of folic acid in managing anemia ($p<0.05$). However, the lack of significant changes in parameters such as RBC count, MCH, WBC count, and PLT count suggests the need for further investigation into the broader hematological effects of folic acid supplementation.

Future studies with larger sample sizes, longer treatment durations, and a variety of dog breeds are essential to validate these findings and to provide veterinary practitioners with comprehensive insights into managing parvovirus-induced anemia. This research could lead to more targeted and evidence-based therapeutic approaches in veterinary medicine.

Acknowledgements

The authors express their gratitude to the Islamic Azad University, Baft branch, for their financial support of this research.

Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

All phases of sample collection, processing, and analysis were performed in strict accordance with established ethical guidelines for research. Adherence to these standards ensured the integrity of the study and upheld ethical responsibility throughout the research process

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How to cite this article:
Erfan Fadaie, Hossein Iravani, Mohammad Mazrouei Sebdani, The Impacts of Folic Acid on Hematological Parameters in German Shepherd Dogs with Parvovirus-Induced Anemia. Veterinary and Comparative Biomedical Research, 2025, 2(1): 66 – 71. http://doi.org/10.22103/vcbr.2025.24710.1042