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RESEARCH ARTICLE

The Effect of Granulocyte Colony Stimulating Factor Use in addition to Classical Treatment on Prognosis and Blood Values in Patients with Feline Panleukopenia

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ABSTRACT

Feline panleukopenia virus is a notable disease in cats and has a very contagious progression especially in young and not vaccinated individuals. Worse still, conventional treatments have a below 50 % success rate in treating this disease. This study investigated the prognostic success of administering a granulocyte colony-stimulating factor, filgrastim, with the conventional treatment for cats with feline infectious enteritis. The study had 48 sick individuals, 31 of whom had conventional + filgrastim treatment, whereas 17 had only conventional treatment (control group). A ratio of 93.61 % of all individuals showed leukopenia and 82.97 % of all individuals had neutropenia. The ratio of not vaccinated individuals in the study sample was 92.3 %. The recovery ratio in the study group in which filgrastim was administered was 72.41 %, whereas this ratio was 58.82 % in the control group, yet the difference was not statistically significant ($p>0.9999$). In the blood count values of the control group, there was no statistically significant difference between pre-treatment and post-treatment measurements. On the other hand, WBC, LYM, and NEU values were significantly different in the study group with additional filgrastim treatment ($p<0.001$). The study results indicated that vaccination is critical in protection against feline parvovirus, diarrhea, and vomiting symptoms in the first diagnosis are noteworthy, and using filgrastim in addition to the conventional treatment did not have a considerable impact on prognosis, although it did ameliorate blood values.
Keywords: Colony-stimulating factor, Feline panleukopenia Virus, Filgrastim, Leukopenia, Treatment

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Feline Panlökopeni Hastalarında Tedaviye Ek Koloni Stimüle Edici Faktör Kullanımının Kan Değerleri ve Prognostik Açıdan Önemi

ÖZ

Feline panlökopemi virüs özellikle genç ve aşısız bireylerde çok bulaşıcı seyreden, klasik tedaviler ile iyileşme oranları %50'nin altında olan, kedilerin önemli bir hastalığıdır. Bu çalışmada feline parvovirüs hastalarında klasik tedaviye ek olarak granülosit koloni sitümile edici faktör olarak filgrastim kullanımının prognostik başarısının incelenmesi amaçlanmıştır. Çalışmaya alınan 48 hastanın 31'inde filgrastim uygulaması yapılırken 17'si sadece klasik tedavi (kontrol grubu) yapılmıştır. Hastaların %93,61'inde lökopeni, %82,97'sinde ise nötropeni tespit edilmiştir. Hastaların %92,3'ünün aşısız olduğu görülmüştür. Filgrastim kullanılan grupta sağkalım %72,41 iken kontrol grubunda %58,82 dir ve aradaki fark istatistik yönden anlamsız bulunmuştur ($p>0,9999$). Kontrol grubunun tedavi öncesi ve sonrası kan değerlerindeki değişim anlamsız bulunurken filgrastim grubunda tedavi öncesi WBC, LYM, NEU değerlerinin tedavi sonrası değişimi istatistik olarak önemli bulunmuştur ($p<0,001$). Sonuç olarak feline parvovirüs hastalığından korunmada aşılamanın çok önemli olduğu, ilk muayenede ishal ve kusma gibi semptomların yanında lökopeninin dikkat çekici olduğu, tedavide klasik tedaviye ek olarak filgrastim kullanımının kan değerlerini yükselttiği ancak prognoza etkisinin olmadığı görülmüştür.
Anahtar kelimeler: Feline panlökopeni virus, Filgrastim, Lökopeni, Koloni sitümile edici faktör, Tedavi

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INTRODUCTION

Feline parvoviral enteritis, feline distemper, or more generally feline panleukopenia is a highly contagious and fatal disease for cats (Barker et al., 1983; Scott, 1987; Steinel et al., 2001). The factor is also known as Feline Panleukopenia Virus (FPV). This virus is in the Parvoviridae family, parvovirinae subfamily, protoparvovirus genus, and Carnivore protoparvovirus 1 species (Truyen et al., 1994). FPV has a single-stranded DNA without an envelope. Its genome is 18-22 nm in diameter, and 5 kb length. FPV is a small DNA virus with icosahedral symmetry (Miranda et al., 2017). FPV is highly resistant to environmental conditions and not vulnerable to a variety of chemical agents (e.g. alcohol, iodine, phenolic compounds, and chloroform). Nevertheless, sodium hypochlorite can quickly inactivate the virus (Rehme et al., 2022; Schultz and Scott, 1973). FPV is not sensitive to high or low environmental temperatures, and it can survive up to one year in room temperature conditions (Poole, 1972). The purpose of the treatment is to stimulate the immune system and facilitate active immunity. Generally, symptomatic treatments are preferred and applied. Parenteral liquid therapy is critical to re-establish the hydration, electrolyte, and acid-base equilibriums. Usually, the intravenous route is recommended (Rice, 2017). As long as vomiting continues, antiemetics should be administered, and oral feeding should be halted (Awad et al., 2019). Broad-spectrum antibiotics and the vitamin-B complex can be used (Hartmann and Hein, 2022; Rice, 2017). The most effective method to treat the disease and prevent it is vaccination and biosecurity precautions (Jacobson, 2021).

In recent years, granulocyte-colony stimulating factors (G-CSF), such as filgrastim, have been used in treating FPV disease. Thanks to these agents, higher treatment successes were reported (Rice, 2017). CSFs permit the generation of the primary cells from bone marrow and stimulate the blood cell processes. They are among the cytokines as growth factors (Akan, 1991). Nowadays, colony-stimulating factors can be genetically designed and administered as drugs. Filgrastim is the first known human recombinant G-CSF (Akan, 1991; Groblewska et al., 2004; Bolis et al., 2013). Moreover, in addition to its use in chemotherapy and Feline panleukopenia, veterinary medicine also utilizes filgrastim in lentivirus infections, e.g. FIV, and parvoviral enteritis in dogs (Bolis et al., 2013).

FPV disease is particularly prevalent in not vaccinated juvenile cats, or kittens. White blood cells decrease in number and immunity collapses in this disease. Hence, stimulating immunity is crucial in obtaining a successful treatment result. At this point, CSF agents, such as filgrastim, can be beneficial. This study aimed to uncover the impact of using filgrastim in addition to the conventional treatment applied to cats suffering from FPV disease.

MATERIALS AND METHOD

The study sample included 48 cats of both sexes and diverse races and 2-24 months old. Detailed general diagnosis of the cats brought to the clinics with depression, anorexia, diarrhea, vomiting, and fever symptoms and when the sick individuals were suspected of FPV disease, FPV quick diagnosis kit (Asan Easy Test® FPV Ag, ASAN PHARM. CO. LTD., Gyeonggi-do, Republic of Korea) were used. Individuals with positive test results for the disease were in the study sample.

The treatment for the disease included total parenteral nutrition, antibiotics, antiemetics, and stomach-protector medicines. Patients with FPV who were treated only with conventional treatment constituted the control group of this study. FPV patients who used filgrastim (FRAVEN® 30MIU/0.5 mL, ARVEN İlaç, Kırklareli, Turkey/Turkey) in their treatment in addition to conventional treatment formed the filgrastim group. Owner consent forms were obtained for the patients included in the study. Additionally, a retrospective (both retrospective and prospective data) scan using the disease monitoring program took place, and the data meeting the relevant criteria were in this study.

Filgrastim administration was in 6 μg/kg in the first, second, and third days subcutaneously. On the fourth day, a blood count test with the automatic tester device (Abacus Junior Vet 5, Hungary) was conducted, and for the individuals whose blood values rose back to the reference values, the treatment ended; otherwise, an additional two doses, in fifth and sixth days were also administered. Except for the one cat with agony and advanced dehydration, all cats had a blood count analysis in their first examination. The exceptional individual's treatment started immediately without a blood count test. Similarly, all individuals in the study (both study and control groups) had a blood count test on the fourth day. After the treatments, the study compared survival rates and pre and post-treatment blood values.

The evaluation of the results was done comparatively with percentage calculations for the symptoms observed from the individuals with FPV in the clinical examination and the impact of filgrastim use on survival. The check for the statistically significant difference between the survivals of the filgrastim and control group was done with chi-square tests. An independent t-test checked the difference in blood values before and after treatment.

RESULTS

Twenty-six of the 48 individuals in the study sample had information on vaccination: only two (7.7 %) were vaccinated. While forty-two individuals had racial information: twenty-two of them (52.38 %) were a mix, eleven (26.19 %) were tabby, three (7.14 %) were orange tabby, three (7.14 %) were British, one (2.38 %) was Bombay, one (2.38 %) was sphinx, and one (2.38 %) was Scottish. Finally, thirty-nine individuals had sex information, of which 21 (53.84 %) were female and eighteen (46.15 %) were male.

The first examination of the FPV cases with available clinical examination information had the following frequency of symptoms: 72.72 % vomiting, 45.45 % diarrhea, 93.93 % weakness and anorexia, and 3.03 % conjunctivitis. Twenty-six individuals had available information on their body temperature, and half had a value over 39.2°C . Blood count test results of the 47 FPV cases were available. The ratio of cases with leukopenia was 93.61 %, while it was 82.96 % for neutropenia.(Table 1).

According to the three age group divisions of the filgrastim group as younger than three months, between 3-12 months, and older than 12 months, the number of survivals to the total number in that group are as follows: 2/3 in younger than three months, 16/23 between 3-12 months, and 5/5 older than twelve months. The same division in the control group had the following survival outcomes: 2/4 in younger than three months, 7/11 between 3-12 months, and 1/2 older than twelve months. Considering the survival ratio according to the filgrastim use, the cases with filgrastim use had a survival ratio of 74.19 %, while the control group had 58.82 % (Table 2).

Table 1. Clinical symptoms observed in the first examination of the individuals with FPV diagnosis

Clinical symptom	Total Number of Sick Individuals	The Number of Individuals Showing the Clinical Symptom	The Frequency of the Clinical Symptom
Vomiting	33	24	72.72 %
Diarrhea	33	15	45.45 %
Fever	26	13	50.00 %
Weakness	33	31	93.93 %
Anorexia	33	31	93.93 %
Dehydration	33	12	36.36 %
Conjunctivitis	33	1	3.03 %
Leukopenia	47	44	93.61 %
Neutropenia	47	39	82.97 %

Table 2. The survival ratio of cats in different age groups according to the use of filgrastim

Age	Total	Survival	Death	Filgrastim
<3 months	3	2	1	Yes
3-12 months	23	16	7	Yes
>12 months	5	5	0	Yes
<3 months	4	2	2	No
3-12 months	11	7	4	No
>12 months	2	1	1	No
Total number of cats	48	33	15	-
Survived with filgrastim/Total filgrastim use	23/31	74.49 %	25.81 %	Yes
Survived without filgrastim/ Total of individuals without filgrastim	10/17	58.82 %	41.18 %	No

The comparison of the filgrastim group and control group according to the survival ratio did not yield statistically significant results (p=0.3364) (Figure 1).

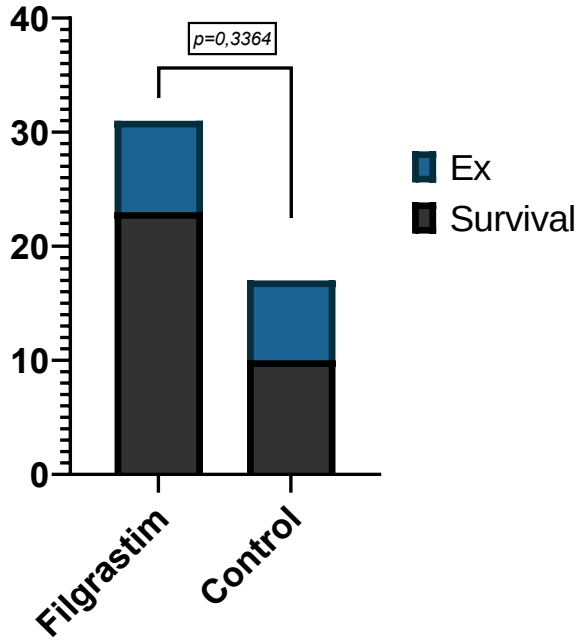

Figure 1. The evaluation of the filgrastim and control group in terms of prognosis

Comparing the filgrastim and control group's blood values in pre- and post-treatment periods; WBC, LYM, and NEU values were statistically significantly higher in the filgrastim group (p<0.001), while the differences between RBC and HCT values were not statistically significant (p>0.001). Whereas the difference in the corresponding values before and after the treatment in the control group was not statistically significant (p>0.001) (Table 3).

Table 3. The comparison of the filgrastim group and control group in terms of pre and post-treatment blood count values

	Filgrastim								
	Pre-treatment				Post-treatment				*p*
	n	Median	Mean	Std. Dev.	*n*	Median	Mean	Std. Dev.	
WBC	31	1.43	1.766129	1.696781	25	13.56	24.4284	24.72811	***p*>0.001**
LYM		0.59	0.666129	0.539065		2.82	3.8588	4.502287	***p*>0.001**
NEU		0.35	0.963548	1.421751		9.64	15.2796	15.194	***p*>0.001**
RBC		8.96	8.716129	3.192261		8.66	8.024	2.663145	*p*=0.389
HCT		33.9	34.19226	10.8136		32.08	31.754	9.892831	*p*=0.387
	Control								
	Pre-treatment				Post-treatment				*p*
	n	Median	Mean	Std. Dev.	*n*	Median	Mean	Std. Dev.	
WBC	16	1.665	6.69875	13.70496	10	11.165	11.327	7.518401	*p*=0.339
LYM		0.575	1.43125	2.306067		2.04	2.721	2.59193	*p*=0.198
NEU		0.525	4.517125	10.34071		6.045	6.9271	6.437099	*p*=0.516
RBC		7.955	7.628125	3.934362		8.13	7.859	1.602577	*p*=0.862
HCT		28.8	23.06125	20.35124		31.75	30.1881	12.39642	*p*=0.330

DISCUSSION

Generally, FPV is transmitted orally, and within 18-24 hours, it infests nasopharyngeal lymph nodes. Two-to-seven days later, it advances into the viremia state, and through the circulatory system, spreads all tissues and organs (Csiza et al., 1971). In the tissues with high mitotic activity, it infects the cells during the mitotic division (Garigliany et al., 2016; Parrish, 1995). It causes the destruction of the leukocytes in the bone marrow, spleen, and thymus. Thus, the infected individuals experience panleukopenia. Since the intestinal epithelial cells and crypts go through necrosis, malabsorption manifests. Disorders in absorption and ingestion result in diarrhea. Then, severe diarrhea leads to dehydration (Fei-Fei et al., 2017; Parrish, 1995).

FPV disease has been known since the beginning of the 20th century and has mostly been in cats without vaccination (Miranda et al., 2017). The effective vaccination procedure against FPV is as follows: first dose at the eighth-ninth weeks' old age, second dose after three to four weeks later, and third dose at 16-20 weeks old if the juvenile is in a high-risk environment. One year later, this procedure will be repeated, and the following vaccination periods will take place at three-year intervals (Truyen et al., 2009). Kruse et al. (2010) conducted a study including 244 cats with FPV. They reported that even if 39.7 % had a vaccination, none of them met the sample inclusion criteria of Truyen et al. (2009). Similar to that study, this study has mostly not vaccinated individuals (92.3 %). Considering the relevant literature and the results of this study, almost all individuals suffering from FPV are either not vaccinated or improperly vaccinated, which translates into the critical importance of vaccination in protection against FPV.

This study included mostly mixed and domestic short-hair races, with only approximately 15 % exotic ones. In the study of Kruse et al. (2010), over 90 % of the sick individuals were from domestic short-hair and mixed races. Citravoa et al. (2022) studied nine cats from domestic short-hair races. Among them, six had contact with the external environment, while three were shelter animals. At that point, their results were compatible with this study. Nevertheless, the fact that this study included a lower number of exotic race cases does not mean that such individuals are more resistant to FPV, but it is because there is a low number of exotic races in the cats brought to our clinics. Still more, exotic cats' street contact is generally limited, while a considerable fraction of the cats with FPV have extensive contact with the streets. In other words, a sampling bias might explain the race-related frequencies.

Juma (2023) reported that 40 % of the individuals with FPV were male and 60 % female. While Kruse et al. (2010) reported that 59.5 % of the sick individuals were male, while the remaining 40.5 % were female. This study sample had a similar sex distribution to other studies.

The clinical symptoms are particularly evident in this disease which is widespread globally and can impact a diverse set of races are intense gastroenteritis and leukopenia (Barrs, 2019). The first finding in the infected animals is leukopenia. The source of this problem is generally severe neutropenia. Moreover, fever, anorexia, weakness, and depression are present. Vomiting manifests most of the time. However, most cases may not show diarrhea (Addie et al., 1996; Greene, 2012; Litster and Benjanirut, 2013). This study observed the frequency of leukopenia in the sick individuals as 93.61 %, and 82.97 of all individuals had neutropenia. Approximately 93 % of the cases had anorexia and weakness. The prevalence of vomiting was 72.72 %, while diarrhea was present in 45.55 % of the cases. Half of the cases with body temperature measurements (13/36) had a fever. In the study of Citarova et al. (2022), which included nine cats, five had leukopenia, seven had mild apathy, eight had anorexia and intermittent vomiting, and all cases had a fever. However, no cases showed diarrhea in their early stage. Different from the literature, one cat had a different symptom, conjunctivitis. Nevertheless, this finding might not be directly related to FPV and may be a coexisting condition with another source.

The survival ratio in individuals with FPV older than six-to-eight weeks can vary according to the following: virus load, immunity, age, and infectious comorbidities developed with the FPV (Foley et al., 1999). Generally, recovering cases show hints of recovery in the first seven days of the treatment (Avad et al., 2019; Greene, 2012). Death generally develops after dehydration, septicemia, and disseminated intravascular coagulation (Litster and Benjanirus, 2013). The acute form of FPV has a varying fatality between 25-90 %, while the peracute form may have up to 100 % fatality (Addie et al., 1998; Cave et al., 2002). FPV, which progresses quite fatally in cats, had a varying survival ratio after the conventional treatment, changing between 11.2 % and 57.1 % (Kruse et al., 2011; Litster and Benjanirut, 2014; Porporato et al., 2018; Barrs, 2019; Isaya et al., 2021; Citarova et al., 2022). One study added Neupogen (filgrastim) to the treatment, and the recovery rate was almost three times higher compared to the control group (33 % vs. 91 %) (Rice, 2017). Rice (2017) attributed this very high success rate to the early diagnosis and additional filgrastim treatment to the aggressive symptomatic treatment. This study conducted a comparative case for that of Rice's study (2017) but did not observe a considerable difference in prognosis after using an additional filgrastim in the treatment schedule. While the survival ratio was 72.41 % in the filgrastim group, it was 58.82 % in the control. The literature values on the survival ratio of the control

group vary between 11.2-57.1 % and this study has a similar result. Even though the survival ratio in the filgrastim group is notably higher than the control group, the difference was low compared to Rice's (2017) study. One reason is that Rice (2017) excluded cases with agony from the calculations. In this study, even the cases that died right after 24 hours from the onset of the treatment, i.e. without successfully concluding the treatment, were present in the study. Without modifying the control group, excluding these cases from the filgrastim group, and then, making the calculations widens the gap in favor of the filgrastim use and changes the treatment efficiency statistics considerably.

The survival rate in individuals in the filgrastim group younger than three months and older than 12 months was the same, 50 %. However, this ratio was 70 % in cases in the filgrastim group between 3-12 months old. Rice (2017) reported a 100 % recovery in FPV cases younger than three months after filgrastim-included treatment. Whereas, only one case in the four older than three months responded negatively to the filgrastim treatment. This lost case brought in agony and treatment started in that condition (Rice, 2017). Previous studies did not uncover a statistically significant relationship between the severity of the clinical symptoms, and consequence of the disease, and the age of the case (Kruse et al., 2010). In short, both studies reported similar survival ratios in different age groups, and the results were in line with the previous studies.

Considering the blood count values, Kuffer and Frank (1999) reported a very positive impact of filgrastim use in cats with FPV on WBC count. While there was no statistically significant difference in prognosis ($p=0.3364$), pre and post-treatment blood count parameters WBC, LYM, and NEU values were significantly different ($p<0.001$).

CONCLUSION

As a result, vaccination is critical in protecting from FPV. Indeed, only a fraction of the cats with FPV were vaccinated. Anorexia, weakness, vomiting, diarrhea, fever, and dehydration are remarkable clinical outcomes in cats with FPV, and a very high prevalence of leukopenia is noteworthy. While the extra filgrastim administration did not significantly affect the survival ratio between the filgrastim and control groups, WBC, LYM, and NEU values from blood count tests were higher in the filgrastim group and this difference was statistically significant. Considering all the data, future studies including larger study samples on filgrastim use to treat FPV disease are promising to reach the targeted success ratio in FPV treatment.

Conflict of interest: The authors have no conflicts of interest to report.

Authors' Contributions: Authors contributed equally in the design, data collection, and manuscript preparation phases of this study.

Ethical approval: This study was approved by the Kırıkkale University Animal Experiments Local Ethics Committee (Approval no: 2022/07-42).

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REFERENCES

Akan, Ö.A. (1991). Koloni Stimüle Edici Faktörler. Mikrobiyoloji Bülteni 25, 285-293.

Awad, R.A., Hassan, S.A., Marets, B. (2019). Treatment of Feline panleukopenia virus infection in naturally infected cats and its assessment. J Biol. Sci., 19(2), 155-160. https://doi.org/10.3923/jbs.2019.155.160

Addie, D.D., Jarrett, O., Simpson, J., Thompson, H. (1996). Feline Parvovirus in Pedigree Kittens. Veterinary Record 138, 119.

Addie, D.D., Toth, S., Thompson, H., Greenwood, N., Jarrett, J.O. (1998). Detection of Feline Parvovirus in Dying Pedigree Kittens. Veterinary Record 142, 353-356.

Barker, I.K., Povey, R.C., Voigt, D.R. (1983). Response of Mink, Skunk, Red fox and Raccoon to İnoculation with Mink Virus Enteritis, Feline Panleukopenia and Canine Parvovirus and Prevalence of Antibody to Parvovirus in Wild Carnivores in Ontario. Canadian Journal of Comparative Medicine, 47, 188-197.

Barrs, V.R. (2019). Feline panleukopenia: a re-emergent disease. Veterinary Clinics: Small Animal Practice, 49(4), 651-670. https://doi.org/10.1016/j.cvsm.2019.02.006

Bolis, S., Cocorocchio, E., Corti, C., Ferreri, A.J.M., Frungillo, N., Grillo, G., Omodeo, E.S., Tedeschi, L., Zilioli, V.R. (2013). Clinical implications, safety, efficacy of recombinant human Granulocyte Colony-Stimulating Factors and pegylated equivalent. Epidemiology Biostatistics and Public Health, Volume 10, Number 4. https://doi.org/10.2427/8845

Cave, T.A., Thompson, H., Reid, S.W., Hodgson, D.R., Addie, D.D. (2002). Kitten Mortality in the United Kingdom: A Retrospective Analysis of 274 Histopathological Examinations (1986 to 2000). Veterinary Record 151, 497-501. https://doi.org/10.1136/vr.151.17.497

Citarova, A., Mojzisova, J., Vojtek, B., Zakutna, L., Drazovska, M. (2022). Nachweis von FPV, CPV-2a, CPV-2b und FCoV bei Katzen mit Symptomen der felinen Panleukopenie. Berliner und Münchener Tierärztliche Wochenschrift 135, 1–6. https://doi.org/10.2376/1439-0299-2022-13

Csiza, C.K., Scott, F.W., De Lahunta, A., Gillespie, J.H. (1971a). İmmune Carrier State of Feline Panleukopenia Virus-Infected Cats. American Journal of Veterinary Research 32, 419-426.

Csiza, C.K., Scott, F.W., De Lahunta, A., Gillespie, J.H. (1971). Pathogenesis of Feline Panleukopenia Virus in Susceptible Newborn Kittens. II. Pathology and Immunofluorescence. Infection and Immunity 3, 838-846.

Digangi, B.A., Gray, L.K., Levy, J.K., Dubovi, E.J., Tucker, S.J. (2011). Detection Protective Antibody Titers Against

Feline Panleukopenia Virus, Feline Herpesvirus-1 and Feline Calicivirus in Shelter Cats Using a Point-of-care an ELISA. Journal Feline Medicine and Surgery 13, 912- 918. https://doi.org/10.1016/j.jfms.2011.07.009

Digangi, B.A., Levy, J.K., Griffin, B., McGorray, S.P., Dubovi, E.J., Dingmann, P.A., Tucker, S.J. (2012). Prevalence of serum antibody titers against feline panleukopenia virus, feline herpesvirus 1, and feline calicivirus in cats entering a Florida animal shelter. JAVMA, 241(10), 1320-1325. **https://doi.org/10.2460/javma.241.10.1320**

Esfendiari, J., Klingeborn, B. (2000). A Comparative Study of a New Rapid and One-Step Test for The Detection of Parvovirus in Faeces from Dogs, Cats, and Mink. Journal of Veterinary Medicine. B, Infectious Diseases and Veterinary Public Health 47, 145-153.

Fei-Fei, D., Yong-Feng, Z., Jian-Li, W., Xue-Hua, W., Kai, C., Chuan-Yi, L., Zhi-Jing, X. (2017). Molecular characterization of feline panleukopenia virus isolated from mink and its pathogenesis in mink. Vet. Microbiol, 205, 92-98. **https://doi.org/10.1016/j.vetmic.2017.05.017**

Foley, J.E., Orgad, U., Hirsh, DC., Poland, A., Pedersen, N.C. (1999). Outbreak of Fatal Salmonellosis in Cats Following Use of A High-Titer Modified-live Panleucopenia Virus Vaccine. Journal of the American Veterinary Medical Association 214; 67-70, 43-64.

Garigliany, M., Gilliaux, G., Jolly, S., Casanova, T., Bayrou, C., Gommeren, K., Fett, T., Mauroy, A., Levy, E., Cassart, D., Peeters, D., Poncelet, L., Desmecht, D. (2016). Feline panleukopenia virus in cerebral neurons of young and adult cats. BMC Vet Res, 12(1), 1-9. https://doi.org/10.1186/s12917-016-0657-0

Greene, C.E. (2012). Feline enteric viral infections. In: Infectious diseases of the dog and cat, p. 80-91. 4th ed. St. Louis, Mo., Elsevier/Saunders.

Groblewska, M., Mroczko, B., Szmitkowski, M. (2004). Czynnik stymuluj1cy tworze- ni kolonii makrofagowych (M-CSF) i jego zastosowanie w praktyce klinicznej. Pol. Arch. Med. Wewn 111, 355-365.

Gür, S., Avdatek, K. (2016). A Serological İnvestigation for Feline Panleucopenia Virus in Cats in Afyonkarahisar. Kocatepe Veterinary Journal 9(3), 165-170. https://doi.org/10.5578/kvj.26547

Isaya, R., Ciccarelli, S., Enache, D., Specchi, S., Pesaresi, M., Ferri, F., Porporato. F., Auriemma, EB., Coppola, LM., Zini, E. (2021). Correction to: Gastrointestinal ultrasonographic findings in cats with Feline panleukopenia: a case series. BMC Vet Res 17(1), 143. https://doi.org/10.1186/s12917-020-02720-w

Jacobson, L.S., Janke, K.J., Giancinti, J., Weese J.S. (2021). Diagnostic testing for feline panleukopenia in a shelter setting: a prospective, observational study. J Feline Med Surg, 23(12), 1192-1199. https://doi.org/110.1177/1098612X211005301

Jumaa, MA. (2023). Feline Panlökopenide Tiyol Disülfit Dengesi Ve İskemi Modifiye Albümin (İma) Seviyelerinin Araştırılması. Yüksek Lisans Tezi, Ankara Üniversitesi Sağlık Bilimleri Enstitüsü, Ankara.

Kuffer-Frank, M., Jung, H., Kraft, W. (1999). Use of recombinant human granulocyte colony-stimulating factor (r-metHuG-CSF) in neutropenic cats. Tierarztliche Praxis Ausgabe K: Kleintiere – Heimtiere 27, 136-143.

Kruse, B.D., Unterer, S., Horlacher, K., Sauter-Louis, C., Hartmann, K. (2010). Prognostic Factors in Cats with Feline Panleucopenia. J Vet İntern Med 24, 1271-1276. https://doi.org/10.1111/j.1939-1676.2010.0604.x

Kruse, BD., Unterer, S., Horlacher, K., Sauter-Louis, C., Hartmann, K. (2011). Feline Panleukopenie – differierender Krankheitsverlauf bei Katzen im Alter von unter bzw. über 6 Monaten. Tierarztl Prax Kleintiere 39(04), 237–242. **https://doi.org/10.1055/s-0038-1623584**

Litster, A., Benjanirut, C. (2013). Case Series of Feline Panleucopenia Virus in An Animal Shelter. Journal of Feline Medicine and Surgery 16(4), 346-353. https://doi.org/10.1177/1098612X13497738

Meurs, K.M., Fox, P.R., Magnon, A.L., Liu, S., Towbin, J.A. (2000). Molecular Screening by Polymerase Chain Reaction Detects Panleukopenia Virus DNA in Formalin-Fixed Hearts From Cats with İdiopathic Cardiomyopathy and Myocarditis. Cardiovascular Pathology, 9, 119-126. https://doi.org/10.1016/S1054-8807(00)00031-4

Mende, K., Stuetzer, B., Mueller, R.S., Sauter Louis, C., Homeier Bachmann, T., Truyen, U., Hartmann, K. (2013). Prevalenz von Antikörpern Gegen Feline Parvoviren bei Katzen in Süddeutschland. Tierarztliche Praxis 2, A27.

Mende, K., Stuetzer, B., Truyen, U., Hartmann, K. (2014). Evaluation of An in-House Dot Enzyme Linked İmmunosorbent Assay to Detect Antibodies Against Feline Panleukopenia Virus. Journal of Feline Medicine and Surgery, 16(10), 805-811. doi: 10.1177/1098612X14520812

Mende, K., Stuetzer, B., Sauter-Louis, C., Homeier, T., Truyen, U., Hartmann, K. (2014). Prevalence of antibodies against feline panleukopenia virus in client-owned cats in Southern Germany. Vet J, 199(3), 419-423. https://doi.org/10.1016/j.tvjl.2013.12.023

Miranda, C., Viera, M.J., Silva, E., Carvalheira, J., Parrish, C.R., Thompson, G. (2017). Genetic Analysis of Feline Panleukopenia Virus Full-length VP 2 Gene in Domestic Cats Between 2006-2008 and 2012-2014, Portugal. Transboundary and Emerging Diseases, 64(4), 1178-1183. https://doi.org/10.1111/tbed.12483

Parrish, C.R. (1995). Pathogenesis of feline panleukopenia virus and canine parvovirus. Bailliere's Clinical Haematology, 8(1), 57-71.

Poole, G.M (1972). Stability of A Modified, Live Panleukopenia Virus Stored in Liquid Phase. Applied Microbiology 24, 663-664.

Porporato, F., Horzinek, MC., Hofmann-Lehmann, R., Ferri, F., Gerardi, G., Contiero, B., Vezzosi, T., Rocchi, P., Auriemma, E., Lutz, H., Zini, E. (2018). Survival estimates and outcome predictors for shelter cats with feline panleukopenia virus infection. J Am Vet Med Assoc 253(2), 188-195. https://doi.org/10.2460/javma.253.2.188

Proksch, A.L., Unterer, S., Truyen, U., Mueller, R.S., Hartmann, K. (2015). İnfluence of Clinical and Laboratory Variables on Fecal Antigen ELISA Results in Dog with Parvovirus infection. Journal of Veterinary İnternal Medicine 27, 721. https://doi.org/10.1016/j.tvjl.2015.03.009

Rehme, T., Hartmann, K., Truyen, U., Zablotski, Y., Bergmann, M. (2022). Feline Panleukopenia Outbreaks and Risk Factors in Cats in Animal Shelters. Viruses, 14(6), 1248. https://doi.org/10.3390/v14061248

Rice J.K., 2017. Successful Treatment of Feline Panleukopenia: A guideline for rescuers and veterinarians, Part I. J Vet Sci Med Diagn, 6, 2. https://doi.org/10.4172/2325-9590.1000223

Schatzberg, S.J., Haley, N.J., Barr, S.C., Parrish, C., Steingold, S., Summers, B.A., Delahunta, A., Kornegay, J.N., Sharp, N.J. (2003). Polymerase chain reactions (PCR) Amplication of parvoviral DNA from the

brains of dogs and cats with cerebellar hypoplasia. Journal of Veterinary İnternal Medicine 17, 538-544.

Schmitz, S., Coenen, C., Konig, M., Thiel, H.J., Neiger, R., (2009). Comparison of Three Rapid Commercial Canine Parvovirus Antigen Detection Tests with Electron Microscopy and Polymerase Chain Reaction. Journal of Veterinary Diagnostic İnvestigation 21, 344-345.

Schultz, R.D., Scott, F.W., (1973). Absence of an immune response after oral administration of attenuated feline panleukopenia virus. Infection and Immunity, 7(4), 547-549.

Schultz, R.D., Ford, R.B., Olsen, J. (2002). Titer Testing and Vaccinations: A New Look At Traditional Practices. Veterinary Medicine 1-13.

Scott, F.W., 1987. Viral Diseases: Panleukopenia. In: Holzworth, J. (Ed.), Diseases of the Cat: Medicine and Surgery, WB Saunders Co, Philadelphia, PA, USA, pp. 182-193.

Steinel, A., Parrish, C.R., Bloom, M.E., Truyen, U. (2001). Parvovirus Infections in Wild Carnivores. Journal of Wildlife Diseases 37, 594-607.

Truyen, U., Agbanddje, M., Parrish, C.R. (1994). Characterization of the feline host range and a specific epitope of feline panleukopenia virus. Virology, 200(2), 494-503.

Truyen, U., Addie, D., Belak, S., Boucraut-Baralon, C., Egberink, H., Frymus, T., Gruffydd-Jones, T., Hartman, K., Hosie, MJ., Lloret A., Lutz H., Marsilio, F., Pennisi, MG., Rodford,, AD., Thiry, E., Horzinek MC. (2009) Feline panleukopenia. ABCD guidelines on prevention and management. Journal of Feline Medicine &Surgery, 11(7), 538-546. https://doi.org/10.1016/j.jfms.2009.05.002