

Comparison of The Effects of Classical Fluid Therapy and Total Parenteral Nutrition in The Treatment of Dogs With Gastroenteritis

Zeki YILMAZ* Sezgin ŞENTÜRK* Esin GÖLCÜ* Ebru YALÇIN*
Yeşim İLÇÖL** Serhat TORUN* Mutlu TEMİZEL*

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Summary: In the study, it was aimed to compare the effect of classical fluid therapy and total parenteral nutrition (TPN) in the management of dogs with gastroenteritis. Seventeen dogs with gastroenteritis were divided into 2 groups at the treatment stage: TPN group (n=10) and control group (n=7). Solution of TPN group included an aminoacids solution (8.5% Fre-Amine), a lipid solution (20% lipovenouse), a dextrose solution (20% Dextrose), a balanced electrolyte solution (Lactated Ringers) and a vitamin solution (Polybion). The combination of lactated ringers and dextrose (5%) solutions were administered to dogs in control group. Solutions were administered for 2 days in each group.

Clinical and laboratory examination were carried out, before and at 24th, 48th and 72nd hr after initiation of the treatment. Body temperature was gradually decreased in the control and TPN groups. The alterations of heart and respiratory rates were similar in each group. Capillary filling time was gradually decreased and within normal limits at 72nd hr in both group (p<0.05). Hematologic parameters, except from PLT count, were higher at baseline in the TPN group than in the control group.

While total protein and albumin concentrations were decreased from baseline to the 48th hr, they increased at 72nd hr in the control group. Urea and Cr values were decreased after the treatment in both groups. Cholestrerol and TG concentrations were decreased at 72nd hr after the discontinued infusion in the TPN group. While alanine transaminase enzyme activity was increased from base line to at 48th hr, it decreased at 72nd hr in the TPN group. Glucose concentration at 24th hr in the control group was significantly lower than in the TPN group (p<0.05). Plasma osmolality was lower in the TPN group throughtout the study (p<0.01). Sodium and chloride concentrations in the TPN group were lower than the control group at 24 hr (p<0.05). Potassium concentrations in serum samples of the TPN applied group were lower through the study than those of control group (p<0.05).

As a result, it was concluded that the total parenteral nutrition could be used effectively and safety for 2 days in the management of dogs with gastroenteritis.

Key Word: Total parenteral nutrition, dog

Gastroenteritisli Köpeklerin Tedavilerinde Klasik Sıvı Tedavisi ve Total Parantral Beslemenin Etkilerinin Karşılaştırılması

Özet: Bu çalışmada gastroenteritisli köpeklerin tedavisinde klasik sıvı tedavisi ile total parenteral beslemenin (TPN) etkilerinin karşılaştırılması amaçlandı. On yedi gastroenteritisli köpek tedavi aşamasında iki gruba ayrıldı: TPN grubu (n=10) ve kontrol grubu (n=7). TPN solusyonu bir aminoasid (%8,5 Fre-Amine), bir lipid (%20 lipovenouse), bir dextrose (%20 Dextrose), bir dengeli elektrolit (Laktalı Ringer) ve bir vitamin solusyonu (Polybion) içermekteydi. Kontrol grubundaki köpeklere de laktatlı ringer ve dextrose (%5) kombinasyonu uygulandı. Her iki gruptaki solusyonlar iki gün süreyle kullanıldı.

* Dep. of Internal Medicine, Veterinary Faculty, University of Uludag, Bursa-TURKEY

** Laboratory of Biochemical, Medical Faculty, University of Uludag, Bursa-TURKEY

Klinik ve laboratuvar muayeneleri tedavi öncesi ve tedavinin başlatılmasından sonraki 24, 48 ve 72'nci saatlerde gerçekleştirildi. Beden ısısı kontrol ve TPN gruplarında dereceli olarak azaldı. Kalp ve solunum sayısındaki değişimler her bir grupta birbirine benzerdi. Kapıllar dolum süresi her iki grupta dereceli olarak azaldı ve 72'nci saatte normal sınırlara geldi ($p<0.05$). TPN grubunda PLT dışındaki bazal hematolojik parametreler kontrol grubundan daha yüksekti.

Total protein ve albumin konsantrasyonu kontrol grubunda bazal değerden 48'nci saate kadar azalırken, 78'nci saatte arttı. Üre ve kreatinin konsantrasyonu her iki grupta tedaviden sonra azaldı. TPN grubunda kolesterol ve trigliserid konsantrasyonu infüzyonun kesilmesinden sonra 72'nci saatte azaldı. Alanine transaminase enzim aktivitesi TPN grubunda bazal değerden 48'nci saate kadar artarken, kontrol grubunda 72'nci saate kadar azaldı. Kontrol grubunda 24'ncü saattaki glukoz konsantrasyonu TPN grubuna göre anlamlı bir şekilde düşüktü ($p<0.05$). Plasma osmolaritesi TPN grubunda çalışma boyunca kontrol grubundan daha düşüktü ($p<0.01$). TPN grubundaki sodyum ve klor konsantrasyonları 24'ncü saatte kontrol grubundan daha düşüktü ($p<0.05$). TPN uygulanan gruptaki potasyum konsantrasyonu çalışma süresince kontrol grubundan daha düşüktü ($p<0.05$).

Sonuç olarak, gastroenteritisli köpeklerin tedavilerinde, 2 gün süreyle, TPN'nin etkili ve güvenli bir şekilde kullanılabilceği kanısına varılmıştır.

Anahtar Kelimeler: Total parenteral besleme, köpek

Introduction

Parenteral nutritional support, more commonly referred as total parenteral nutrition (TPN), entails providing all necessary nutrients via administration through a central, periferal, or portal vein^{1,2}. The major indication for TPN is functional failure of the gastrointestinal tract³. The other indications for TPN include intestinal obstruction, extreme gastrointestinal resection, wasting diseases, burns and trauma. In addition, TPN may be particularly benefit in animals with severe pancreatitis, severe inflammatory bowel disease with protein-losing enteropathy, neurologic states such as coma or semicoma, large open wounds or open abdomen in which significant protein loss is expected, acute renal failure¹ and obstructive jaundice^{4,5}. Normally, the portion of nutrients reaching the systemic circulation is modified by the bowel and liver, but in TPN all of the nutrients infused are delivered directly to systemic circulation³.

TPN is a combination of dextrose and amino acids with or without a lipid source, vitamins and trace elements⁶. The energy should be supplied both fat and carbohydrate. Clinical trials in humans have shown that there is a limit to the protein sparing effect of glucose, and if glucose is provided as the sole calorie source protein repletion cannot be achieved⁶. Glucose is required by the brain, red blood cells, and nervous tissue, and its has also anabolic effects³. Furthermore, fat solution provide a source of essential fatty acids and lower the osmolality of the parenteral solution due to its high caloric density⁶. Lipid solution contains soybean oil and its isotonicity is achieved by adding glyserol.

After the infusion of a fat emulsion, transient hyperlipidemia invariably occurs^{1,3}.

TPN is best administered when 24-hr observation is available¹. The nutritional solution is initially administered slowly. Hematocrit, total protein, serum electrolyte and glucose concentrations should be followed closely. The most important complication of parenteral nutrition is sepsis⁷. Metabolic complications include hyperglycemia, hypokalemia, hypophosphatemia, hypernatremia, hypertriglyceridemia^{1,3,6,7} and gallstones⁸.

In the study, it was aimed to compare the effect of classical fluid therapy and total parenteral nutrition (TPN) in the management of dogs with gastroenteritis.

Materials and Methods

In this study, 17 dogs with gastroenteritis, of different age (8 months-7 years), weight (6-15Kg) and sex (11male and 6 female), were used as materials, as in previous studies^{2,4}. The duration of gastroenteritis before the study began were ranged from 3 to 6 days in all dogs. Any medical history of the sick dogs was not reported prior to study. Gastroenteritis was diagnosed on the bases of clinical examinations such as vomiting, diarrhea, anorexia, depression and poor condition. At the treatment state, regardless of etiological factors, dogs were divided into 2 groups: TPN group (n=10) and control group (n=7). The solutions of TPN included an amino acids solution (8.5% Fre-Amine[®], Baxter), a lipid solution (20% Ivelip[®], Baxter), a dextrose solution (20% Dextrose[®], Baxter), a balanced

electrolyte solution (Lactated Ringers[®], Baxter) and a vitamin solution (Polybion[®], Merck), as in published nutrient recommendation^{1,3,6,7}. A combination of Lactated Ringers and Dextrose (5%) solutions (50-100ml/kg/iv) was administered to the dogs in the control group. Therapy was supported by use of antibiotics (penicillin+gentamycin) and antiemetic (metaclopramide) as needed in two groups. The requirements of TPN were calculated, as follows³:

- 1- Calculate resting energy requirement (**RER**) = $\{30 \times \text{BW (Kg)}\} + 70 \text{ kcal/day}$
- 2- Calculate illness energy requirement (**IER**) = $1.4 \times \text{RER kcal/day}$
- 3- Calculate protein requirement (**PR**) = $4\text{-}8\text{g}/100 \text{ kcal} \times \text{IER (100 kcal/day)}$
- 4- Calculate non-protein calorie requirement (**NPCR**) = $\text{IER} - 4 \times \text{PR kcal/day}$
- 5- Calculate fluid quantities to meet NPCR
 $\text{NPCR} \times 50\% = \text{kcal/day from dextrose} \div \text{caloric density} = \text{mls dextrose}$
 $\text{NPCR} \times 50\% = \text{kcal/day from lipid} \div \text{caloric density} = \text{mls lipid}$
- 6- Calculate total daily volume (TDV) = dextrose + lipid + aminoacids with electrolytes + balanced multielectrolyte solution + vitamin B complex (1-2ml)

Solutions were slowly administered, 4 times daily, for 2 days in two groups. Dogs were not allowed to feed via enteral route for 2 days in both groups. After the fluid therapy, dogs were fed twice daily and water was provided ad libitum.

Sample collection and measurements:

Clinical (temperature, heart and respiratory rates, capillary filling time-CFT etc) and laboratory examination (complete blood count and serum biochemical analysis) were carried out

at pre-treatment to establish base-line, and at 24th, 48th and 72nd hr after initiation of the treatment. Food tolerance was also monitored after the discontinued infusion. Angio-cath was placed into vena cephalica antebrae for the serial fluid therapy and sample collection. Fluid administrations were discontinued at 48th hr in each group. Serum biochemical analysis such as glucose, urea, creatinin (Cr), sodium (Na), potassium (K), chloride (Cl), total cholesterol (Chol), triglyceride (TG), total protein, albumin (Alb) and ALT enzyme activity were determined at the same times of measurements, using Tecnichon Dax-72, in Biochemistry Laboratory of Medical Faculty. Plasma osmolality (P.O.) was calculated, using the formul⁹, as shown below:

$$\text{P.O. (mOsm/L)} = 2 (\text{Na} + \text{K mEq/L}) + \text{Urea (mg/L)} + \text{Glucose (mg/L)}$$

Statistical analysis:

Data including the results of clinical, hematological and serum biochemical examination in each group were compared, using one-factor analysis of variance (ANOVA) in the Minitab Statistically Programme. Duncan's test was also used to show a difference between control and TPN groups. The difference between parameters was considered statistically significant at $p < 0.05$ ¹⁰.

Results

The results of routine clinical and hematological examination are seen in Table I and Table II, respectively. All dogs had non-specific clinical findings such as weakness, depression, anorexia or inappetence, poor condition and weight loss, typical signs such as vomiting and diarrhea associated with gastroenteritis, according to owner. Body temperature was gradually decreased and roughly

Table I. Findings in control and TPN groups

Parameter	Group	Baseline Mean±SD	24 th hr Mean±SD	48 th hr Mean±SD	72 nd hr Mean±SD	Reference ⁽⁹⁾
Temperature C	Control	39.8±0.5	39.4±0.7	39.4±0.9	39.5±0.8	37-39.3
	TPN	40.1±1.1	40.0±1.0	39.7±0.9	39.6±1.2	
Heart Rate bpm	Control	155.0±6.6 ^{ab}	151.0±9.5 ^{ab}	156.0±6.6 ^a	149.0±4.5 ^{b*}	80-140
	TPN	164.0±2.1	161.5±7.2	166.0±8.1	152.5±4.6	
Respiration /min	Control	38.0±6.7	39.5±5.4	37.0±5.4	37.0±5.7	10-30
	TPN	37.0±5.0	39.0±6.0	36.5±1.8	37.0±5.8	
CFT /sc	Control	2.5±0.5 ^a	1.7±0.5 ^a	1.5±0.5 ^b	1.5±0.5 ^{b*}	1-2
	TPN	2.7±0.5 ^a	2.0±0.5 ^{ab}	1.7±0.5 ^{ab}	1.5±0.5 ^{b*}	

* $p < 0.05$

a, b, c : Differences between the values involving different letters on the same line are found to be important.

A, B : Differences between the values involving different letters on the same column are found to be important

same at 72nd hr in the control and TPN groups. The alterations of heart and respiratory rates were similar in each group. After initiation of the treatment, CFT was gradually decreased and return to normal limits at 72nd hr in both group ($p<0.05$). Hematologic parameters, except PLT count, were higher in the TPN group than that observed in the control group, compared with base line values.

Total protein and albumin concentrations were decreased from base line at 48th hr, and

continuously increased at 72nd hr in the control group, whereas total protein concentration continuously decreased in the TPN group (Table III). Na and Cl concentrations in the TPN group were lower at 24th hr ($p<0.05$) and at 72nd hr than in the control group. K concentration of TPN administered group was lower throughout the study, except from base line, than that of control group ($p<0.05$). Urea and Cr values were decreased after the treatment in both groups. Cholestrerol concentrations was increased in the

Table II. Some hematological parameters in control and TPN groups

Parameter	Group	Baseline Mean±SD	24 th hr Mean±SD	48 th hr Mean±SD	72 nd hr Mean±SD	Reference ⁽³⁾
WBC	Control	14.5±1.1	15.7±2.3	13.3±3.1	12.5±2.1	6-15 x10 ³ /μl
	TPN	16.6±3.2	15.5±2.9	15.7±4.3	11.2±3.1	
PCV	Control	41.2±3.5	39.4±3.6	40.6±4.1	42.1±5.7	37-54 %
	TPN	43.4±6.2 ^a	37.1±4.2 ^b	38.4±5.6 ^{ab}	41.1±3.5 ^{ab*}	
HGB	Control	13.4±2.1	12.9±3.1	13.0±1.1	13.9±3.3	12-18 gr/dl
	TPN	14.6±2.5 ^a	12.3±2.5 ^b	12.9±4.0 ^{ab}	13.1±3.1 ^{ab**}	
PLT	Control	2.2±0.1	2.1±0.1	1.8±0.4	2.2±0.1	2-9x 10 ⁵ /μl
	TPN	1.8±0.1	1.8±0.2	2.2±0.2	2.3±0.1	

* $p<0.05$ ** $p<0.01$

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A, B: Differences between the values involving different letters on the same colum are found to be important.

Table III. Serum biochemical paremeters of control and TPN groups.

Parameter	Group	Baseline Mean±SD	24 th hr Mean±SD	48 th hr Mean±SD	72 nd hr Mean±SD	Reference ⁽³⁾
T. Protein g/dl	Control	5.8±0.7	5.4±0.9	5.0±1.1	6.9±1.9	5.4-7.7
	TPN	5.9±0.9	5.2±0.9	5.8±1.4	5.6±1.1	
Alb g/dl	Control	2.5±0.3	2.2±0.3	2.3±0.6	3.1±0.0	2.3-3.8
	TPN	2.6±0.6	2.3±0.6	2.7±0.5	2.6±0.9	
Na mEq/l	Control	144.8±1.9	144.8±5.0 ^A	144.2±8.0	142.0±0.8	141-153
	TPN	142.1±5.5 ^a	131.4±11.7 ^{bB*}	140.2±9.6 ^{ab}	139.2±9.6 ^{ab*}	
K mEq/l	Control	4.4±0.7	4.4±0.1 ^A	4.3±0.3 ^A	4.3±0.4 ^A	3.7-5.8
	TPN	4.3±0.4 ^a	3.2±0.4 ^{bB*}	3.6±0.2 ^{bB*}	3.8±0.2 ^{bB*}	
Cl mEq/l	Control	101.0±3.6	106.8±3.2 ^A	105.2±6.3 ^A	99.0±1.0	105-115
	TPN	97.6±4.2	92.5±13.1 ^{B*}	95.0±7.7 ^{B*}	99.6±4.2	
Urea mg/dl	Control	32.5±27.0	22.8±3.7	19.2±11.5	16.6±0.5	20-40
	TPN	42.5±17.0	31.5±15.9	30.3±16.3	30.0±11.8	
SCr mg/dl	Control	0.5±0.1	0.5±0.2	0.6±0.3	0.4±0.0	0.5-1.5
	TPN	0.9±0.3	1.1±0.5	0.9±0.4	0.7±0.3	
Chol mg/dl	Control	195.0±65.8	243±91.6	197.6±34.8	203.3±5.7	125-270
	TPN	267.7±105.3	210.1±71.4	317.6±134.3	188.2±38.5	
TG mg/dl	Control	99.4±46.6	86.6±32.2	70.2±29.8	77.6±21.1	20-112
	TPN	111.0±48.9	120.2±68.1	86.5±73.0	80.2±35.1	
ALT U/l	Control	35.2±9.5	27.4±6.7	22.5±4.5	26.3±5.6	10-88
	TPN	26.1±15.9	32.4±28.1	36.1±22.5	31.8±11.9	
Glucose mg/dl	Control	90.2±6.34 ^a	144.3±35.1 ^{bcA}	132.3±24.9 ^c	110.6±14.3 ^a	60-110
	TPN	88.2±10.0 ^a	177.2±17.2 ^{bB*}	164.3±30.5 ^b	102.6±0.5 ^{ab**}	
P.O. mOsm/L	Control	310.6±8.2	308.3±4.3 ^A	310.3±7.1	304.4±6.6	291-315
	TPN	306.2±4.1 ^a	286.7±10 ^{bB***}	303.8±5.0 ^{ab}	300.0±3.2 ^{ab**}	

* $p<0.05$ ** $p<0.01$ *** $p<0.001$

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control group, although it was decreased in the TPN group, at 72nd hr of the study as compared to baseline value. TG concentration was increased in the TPN group, but was decreased in the control group after the first measurements, as compared to baseline values. Alanine transaminase (ALT) enzyme activity were increased from base line to at 48th hr but decreased at 72nd hr in the TPN group, whereas decreased from base line to at 72nd hr in the control group. Glucose concentration was significantly lower in the control group than in the TPN group, at 24th hr of the study ($p < 0.05$). Plasma osmolality was lower in the TPN group throughout the study ($p < 0.01$). There was no death in both group. Phlebitis and edema formation were occurred during the TPN administration in one case.

Oral feeding started spontaneously just after 48th hr of the study in dogs treated with TPN, whereas it was good after the 72nd and/or later in the control group.

Discussion

Nutritional support indicates in patient that are malnourished, unlikely to eat for more than 3 days, or at risk of developing malnutrition because of profound, ongoing protein losses⁷. In this study, dogs with gastroenteritis and anorectic for at least 3 days were used as materials. Cephalic vein was preferred for fluid and TPN administration, as reported by Payne-James and Khawaja¹¹, but central vein should be recommended generally. Regardless of etiological factors, total parenteral nutrition or classical fluid therapy was performed in the TPN and control groups, respectively. In our study, TPN's solutions consisted of an aminoacid solution, a lipid solution and glucose solution, as well as lactated Ringers solution, as in published nutrient recommendation. In the control group, 5% dextrose in combination with lactated ringers solution were preferred to compare with TPN group.

On the first clinical examination, all dogs with gastroenteritis had non-specific or specific findings such as anorexia, dehydration, weakness, depression, weight loss, vomiting and diarrhea. Additionally, pyrexia, increased heart and respiratory rates, prolonged CFT, and also increased the number of total WBC count in both groups (especially in TPN group) revealed that systemic inflammatory response syndrome was

possibly occurred by bacterial infection. Bjarnosan et al¹² reported that increased protein catabolism due, for example, to sepsis, had been improved with TPN. Lang et al¹³ determined that insulin-like growth factor (IGF-I) levels and net hepatic IGF-I output were decreased at 48 hr after induction of infection. These data may be explain what is the reason of weight loss or poor condition in concomitant with infection in dogs of the study. Also glutamin deficiency that is caused by infectious gastrointestinal problems may be considered as an another possible cause of poor condition reported by the owner in the present study. This consideration is supported by the studies of Roth et al¹⁴, Molinez et al¹⁵ and Morlion et al¹⁶.

Although sepsis has been reported to the most important complication of parenteral nutrition⁷, body temperature was gradually decreased and roughly same at 72nd hr in the control and TPN groups. In addition to the similar alterations of heart and respiratory rates, WBC counts were decreased gradually and reached to normal limits at 72nd hr in each group. These data is suggested that dogs with gastroenteritis are treated successfully by antibacterial in conjunctive with fluid therapy or TPN administrations.

Most animals requires TPN because of gastrointestinal dysfunction, and more than half of them gains weight during TPN administration¹⁷. Oral feeding started spontaneously just after 48th hr of the study in dogs treated with TPN, whereas it was good after the 72nd and/or later in the control group. This alteration of appetite may be explained on results of the study of Lee et al¹⁸, reported that continuous parenteral nutrition significantly increased neuropeptid Y (NPY) receptor density in the rat brain suggesting that TPN may impact feeding via the regulation of NPY receptor-mediated effects. Additionally, Lane et al¹⁹ determined that short-term parenteral nutrition hastened normalisation of serum proteins, resulation of diarrhae, and weight gain. Total protein concentrations were reached to normal limits at 48th hr in TPN group but at 72nd in control group. Total protein concentration of control group was higher at 72nd hr than that of TPN group. This result may be explained by having no oncotic properties of isotonic cristalloid solutions, as well as possible ongoing loses of fluid due to diarrhae and/or vomiting^{1,3,6,7}.

Prolonged CFT at base line was interpreted as a sign of peripheral circulatory failure in both, especially TPN group. After initiation of the treatment, CFT was gradually decreased and within normal limits at 72nd hr in both groups ($p < 0.05$). The reason for this is more likely to the efficacy of fluid or parenteral nutrition's solution, which is supported by decreasing urea and Cr concentrations, as well as decreased hematocrit value. Although hyperglycemia, hyperosmolality, hypernatremia and hypertriglyceridemia has been reported as metabolic complications due to TPN administration in animals^{7,15}, these complications were not determined in the TPN group in this study. The reason why the hyperosmolality was not determined in the TPN group is most likely to lipid's effects such as decreasing of hyperosmolality that can be occurred by aminoacide solutions^{3,6}. Thus, lipid solutions should be recommended in parenteral nutritional support^{3,7}. Also, Moens and Remedios¹⁵ reported that hyperosmolar hyperglycemic syndrome in a dog resulting from parenteral nutrition overload. As agreement with the study of Kramer et al²⁰, hypokalemia determined at all times was considered as a minor side effect of TPN, except from base line in the TPN group. Additional common complications are often catheter-related and include thrombophlebitis, edema, cellulitis, thromboembolism, catheter occlusion, line disconnection on breakage and an inability to recatheterize the animal^{1,7}. In only one case, phlebitis and edema formations were occurred due to extravasation of parenteral nutrition's solution. This complication was completely recovered at the 48 hr after the TPN, and furosemid administration. If TPN is administered slowly when 24-hr observation is available, minimal complication has been reported¹, as agreement with the our study.

Hematocrit, total protein, serum electrolyte and glucose concentrations should be followed closely during parenteral nutrition⁷. If the serum glucose concentration exceeds 300mg/dl, the rate should be temporarily reduced⁶. Glucose concentration after at 24th of initiation of the treatment was higher from base line value in both groups ($p < 0.05$) but it remained in normal limits. This data probably showed that patients developed a tolerance for the glucose (serum concentration decrease). This explanation may be supported by the study of Donmayer et al²¹, reported that more glucose is utilized by

peripheral tissue because of hyperinsulinemia and reduced net-hepatic glucose uptake, which are occurred by infection.

Increase of ALT enzyme activity was not statistically significant from base line to at 48th hr in the TPN group. On the other hand, TPN decreased bacterial translocation to liver⁴. This may be explained by the side effects of TPN including hemolysis and erythrocyte abnormalities, as well as precipitated cholestasis. This may be supported by decreased ALT activity after discontinued of TPN (at 72nd hr of the study). DNA synthesis in the activity in the mucosa of the stomach, jejunum and ileum decrease after TPN for 3 weeks, and these changes recover after oral refeeding^{22,23}. In this study oral refeeding tolerated well because of short-duration of TPN administration.

As a result, it was concluded that TPN solution, infused by slowly and short-duration periods (2 days), could be effectively used without complications as classical fluid therapy in the management of dogs with gastroenteritis.

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