

Prospective evaluation of a peripherally administered three-in-one parenteral nutrition product in dogs

OBJECTIVES: Peripheral parenteral nutrition is an option for short-term nutritional support in dogs which cannot be supported with enteral nutrition. The objective of this study was to examine the use of a three-in-one, 840 mOsmol/l peripheral parenteral nutrition product containing amino acids, lipids and glucose in separate compartments in dogs.

METHODS: Nine dogs were administered the three-in-one product, and two dogs were administered the amino acid part of the product, via a peripheral vein. Dogs were monitored for mechanical and metabolic complications.

RESULTS: Mechanical complications (apparent thrombus or thrombophlebitis) caused failure of infusion at a median of 36 hours. None of the dogs appeared to develop catheter-related sepsis. Using a 10-hour infusion period appeared to decrease the incidence of line failure. Mild and clinically non-significant hyperglycaemia was the only metabolic complication. In four of the dogs, serum folate, cobalamin and homocysteine concentrations were determined before and after peripheral parenteral nutrition administration. Oral and parenteral administration of methionine has been previously associated with lowered serum folate concentrations. Low serum folates and the subsequent hyperhomocysteinaemia have been associated with venous endothelial damage and venous thrombus in other species. Serum cobalamin also affects homocysteine metabolism. Median serum folate, cobalamin and homocysteine concentrations were not affected by the short-term administration of this three-in-one product.

CLINICAL SIGNIFICANCE: Using the product for 24 hours/day may require catheter replacement due to line failure. Other than line failure, which may be improved by 10- to 12-hour infusion times, this product was found to be safe and practical for short-term peripheral parenteral nutrition in dogs.

M. L. CHANDLER AND J. J. PAYNE-JAMES

Journal of Small Animal Practice (2006)
47, 518–523

Hospital for Small Animals, University of Edinburgh, Easter Bush Veterinary Centre, Roslin, Midlothian, Scotland EH25 9RG

J. J. Payne-James's current address is 19 Speldhurst Road, Victoria Park, London E9 7EH

INTRODUCTION

Parenteral nutrition is appropriate in patients in whom the gastrointestinal (GI) tract is not functional or where it is undesirable to use it for nutritional support (for example with severe malabsorption, prolonged ileus and postoperatively after some GI surgeries). Total parenteral nutrition (TPN) solutions are generally administered through a central vein to prevent peripheral vein thrombosis. Disadvantages of using TPN include cost, necessity of placing and maintaining a central venous catheter, risk of infection or central vein thrombus and metabolic disturbances. These difficulties and disadvantages limit the use of TPN in veterinary practices.

Peripheral parenteral nutrition (PPN) is the provision of nutritional supplementation through a peripheral vein. PPN accounts for almost 20 per cent of the parenteral nutrition used in the human populations in the UK, and it is estimated that with improved techniques, it could be used for 50 per cent (Anderson and others 2003). The goals of PPN are to spare endogenous protein by providing an energy source such as glucose or lipids and by providing amino acids, which are used for protein synthesis and may also be catabolised for energy. Sometimes, only part of an animal's nutritional needs can be met using a peripheral vein due to the lower osmolality of the solution used (Zsombor-Murray and Freeman 1999). This is sometimes termed partial parenteral nutrition; however, confusingly, partial parenteral nutrition is also sometimes delivered via a central vein (Chan and others 2002).

Possible candidates for PPN are those with non-functional GI tracts, those anticipated to require nutritional support for less than one week, those that may eventually have an enteral feeding tube placed (for example a jejunostomy tube in patients with pancreatitis) but who are not good anaesthetic risks at presentation and those who can tolerate a small amount

of enteral nutrition but may benefit from additional support. Debilitated patients should receive TPN via a central vein but are sometimes initially started on partial parenteral nutrition either via a peripheral or a central vein.

Potential advantages of using partial parenteral nutrition via a peripheral catheter include easier catheter placement, less metabolic complications and less intensive monitoring than TPN via a central vein. The primary disadvantage of PPN is the limitation in calories provided, as energy density decreases with the decreased osmolality thought to be necessary to prevent peripheral vein thrombophlebitis. In human beings, the incidence of thrombophlebitis has been decreased using the smallest catheter possible, using the least thrombogenic catheter and including lipids, which are thought to be veno-protective (Zsombor-Murray and Freeman 1999). In one study of PPN in human beings, the use of a very high-osmolality infusion did not increase the incidence of thrombophlebitis when a high lipid concentration was used (Kane and others 1996). These factors allow the use of a higher osmolality solution in PPN in human beings than has been used historically, thus providing total nutrient requirements.

Complications associated with parenteral nutrition include mechanical, septic and metabolic problems (Lippert and others 1993, Reuter and others 1998, Chan and others 2002). Mechanical complications are those which are associated with nutrient delivery and include thrombophlebitis, catheter occlusions, disconnected lines or any other technical problem with infusion delivery.

Chan and others (2002) found that the rate of mechanical complications for dogs receiving partial parenteral nutrition was 26 per cent; however, this study included 35 of 74 dogs with jugular vein placement of the catheter. The incidence of mechanical failure or thrombophlebitis in patients where parenteral nutrition was delivered via peripheral veins was not noted, but it was stated that the rate of mechanical complications was similar regardless of whether a central or a peripheral vein was used.

Septic complications are diagnosed by clinical suspicion of sepsis, a positive catheter tip culture and/or positive blood cul-

ture. An animal that has a febrile episode not attributable to the underlying disease occurring during parenteral nutrition delivery should be investigated for evidence of catheter-related sepsis. The rate of catheter-related sepsis during parenteral nutrition (using central or peripheral vein) has been reported as 1.25 per cent in dogs receiving partial parenteral nutrition (Chan and others 2002). Rates of sepsis of 12.4 per cent (Reuter and others 1998) and up to 42 per cent (Lippert and others 1993) have been reported for animals receiving TPN via a central vein.

Metabolic complications in dogs on parenteral nutrition include hyperglycaemia, hypertriglyceridaemia and increased serum urea concentrations in animals that initially had these serum chemistry parameters within the reference ranges (Lippert and others 1993, Reuter and others 1998, Chan and others 2002).

Chan and others (2002) reported a 27.5 per cent rate of metabolic complications in dogs on partial parenteral nutrition, of which 50 per cent was due to hyperglycaemia. Reuter and others (1998) reported early hyperglycaemia in 24 per cent of dogs on TPN, with approximately 32 per cent of the dogs developing hyperglycaemia after 24 hours of infusion.

Studies in human beings show that intravenous (iv) administration of amino acid solutions is associated with depression of serum folate concentrations within two days, probably due to metabolism of methionine (Connor and others 1978, Tennant and others 1981). A pilot study in three dogs receiving an amino acid solution iv also showed a marked decrease in the dogs' serum folate concentrations after four days (Chandler and others 2000).

Homocysteine is derived from dietary methionine. Normally, approximately 50 per cent of homocysteine is remethylated back to methionine, a process requiring the enzymes methionine synthase (MS) and methylenetetrahydrofolate reductase. The MS uses vitamin B12 (cobalamin) as a cofactor and 5-methyltetrahydrofolate as a methyl donor. Deficiencies of vitamin B12 and folate have been associated with elevated plasma homocysteine concentrations (Selhub and others 2000). Elevated homocysteine concentrations are present in individuals who develop atherosclerotic

vascular disease, coronary heart disease or peripheral vascular disease. The mechanism may be a direct angiotoxicity, involving endothelial and vascular smooth muscle cell injury and impaired thrombolysis (Wang 1999).

It is possible that a decreased folate and/or cobalamin concentration in patients on PPN could lead to increased serum homocysteine concentrations, which itself may contribute to peripheral venous thrombosis and failure of the iv administration of PPN.

The present study had two objectives. The first was to examine the incidence and timing of thrombophlebitis, iv line failure and metabolic disturbances (for example hyperglycaemia, hypertriglyceridaemia) when an all-in-one (glucose, amino acid and lipid) solution of 840 mOsmol/l Clinomel N4 (Baxter Healthcare) was delivered at a standard maintenance fluid rate of 2 ml/kg/hour via a peripheral vein. This product contains 630 kcal/l and provided 30 kcal/kg/day when given for 24 hours. If the product appeared to be safe and practical for clinical use, the second objective was to determine the serum folate, cobalamin and homocysteine concentrations before and after iv Clinomel N4 administration.

MATERIALS AND METHODS

Case inclusion criteria

The study included dogs that:

- had insufficient caloric intake determined as less than the estimated daily resting energy requirement (RER) for three days or longer, using: $([128 \times \text{bodyweight}^{0.75}] = \text{kcal RER})$;
- could not receive adequate nutrition via the enteral route;
- were not candidates for TPN via a central vein.

Dogs that were given any enteral nutritional support or a blood transfusion during the study were excluded from the study. The owners of the dogs gave informed permission for using PPN with Clinomel N4.

PPN solution

The parenteral formula used was Clinomel N4, a three-in-one product containing

separate compartments for glucose, amino acids and lipids. Separating the seams between the compartments results in sterile mixing of the components. This product includes electrolytes and contains 630 kcal/l and 840 mOsm/l (Table 1).

Protocol

A 25 to 32 mm 20 to 22 G polyurethane catheter was inserted into a cephalic or a saphenous vein after standard clipping of hair and skin preparation. The catheter was flushed with heparinised saline, secured by tape and covered with a protective bandage. The catheter was positioned so that the tip was not over a joint.

If dehydration was present, then it was corrected with an iv infusion appropriate for the patient before the administration of PPN. If a patient required additional iv fluids or medications, then they were administered using a different vein and catheter.

The all-in-one solution was administered via a giving set with an added 1.2 µm filter. An infusion pump was used and the infusion delivered at a rate of 2 ml/kg/hour. If infusion time was missed

due to diagnostic procedures or failure of the catheter, line or pump, the rate was still maintained at 2 ml/kg/hour. This rate provided 1.26 kcal/kg/hour.

The PPN was delivered continuously 24 hours/day during part 1 of the study. The patient and its leg and vein were checked at least every four to eight hours for evidence of mechanical complications or sepsis. The catheters were replaced as necessary due to catheter failure, thrombophlebitis or extravasation of fluid. The duration that each catheter successfully delivered the PPN solution was recorded. The patient's rectal temperature and heart and respiratory rates were taken at least twice a day. Blood samples were taken by standard venepuncture before and on each day during the PPN administration for monitoring the patient's metabolic status.

During part 2 of the study, the complete three-in-one PPN was delivered for 10 to 12 hours during the day, and an isotonic, crystalloid iv fluid was infused through the same catheter during the evening. Use of a 12-hour infusion for peripheral nutrition in human beings has been reported to decrease the incidence of phlebitis (May and others 1996). During the PPN infusion period, the patient and its leg were again checked several times each day as during part 1 of the study.

Parameters

Five dogs met the criteria and had the necessary data collected during the first part of

the study (Table 2). During part 1 of the study, serum sodium, potassium, triglycerides and blood glucose concentrations were measured before the initiation of PPN and on each day of infusion. Serum alanine aminotransferase (ALT) activity, serum urea and albumin concentrations were measured before the initiation of the PPN and on day 4 of infusion. Urine samples were checked daily for glucose using a reagent strip for urinalysis (Multistix 10 SG; Bayer Diagnostics). None of the dogs was found to be positive for urine glucose.

During part 2 of the study, blood samples were taken by standard venepuncture before and at the end of the 10- to 12-hour PPN delivery periods for assessment of serum cobalamin, folate and homocysteine concentrations. Two additional dogs (dogs 10 and 11) were given only the amino acid part of the Clinomel N4 to determine if this component used alone affected serum folate, cobalamin and homocysteine concentrations. Owing to the small number of dogs used in this study, comparative statistics were not performed.

RESULTS

Part 1

Mechanical complications The iv lines remained patent for a mean of 34.7 hours and a median of 36 hours, with a range of 11 to 51 hours (Table 3). The most

Table 1. Composition of Clinomel N4

Nutrient	Amount per litre
Nitrogen	3.6 g
Amino acids	22 g
Glucose	80 g
Glucose	220 kcal
Lipid	20 g
	(purified soybean oil)
Lipid	220 kcal
Amino acids	
L-alanine	4.56 g
L-arginine	2.53 g
Glycine	2.27 g
L-histidine	1.05 g
L-isoleucine	1.32 g
L-lysine	1.28 g
L-methionine	0.88 g
L-phenylalanine	1.23 g
L-proline	1.23 g
L-serine	1.10 g
L-threonine	0.92 g
L-tryptophan	0.39 g
L-tyrosine	0.09 g
L-valine	1.27 g
Electrolytes	
Sodium	28 mmol
Potassium	24 mmol
Magnesium	2 mmol
Phosphate	12 mmol
Chloride	32 mmol
Total energy	630 kcal
Osmolarity	840 mOsm

Table 2. Signalment and diagnoses of the dogs receiving peripheral parenteral nutrition (dogs 1 to 9) or amino acid solution only (dogs 10 and 11)

Dog	Signalment (age, sex, breed)	Diagnosis
Part 1		
1	Two years, F, golden retriever	Megaoesophagus with aspiration pneumonia
2	Six years, M, cocker spaniel	Pancreatic abscess
3	Six years, M, Weimaraner	Obstructive colonic granulomatous inflammatory bowel disease/partial colectomy
4	Four years, M, Irish setter	Hepatitis and anorexia
5	Seven years, M, Kerry blue terrier	Renal tumour/nephrectomy
Part 2		
6	12 years, MN, Border collie	Cholangiohepatopathy with bile duct obstruction
7	Five years, F, mastiff	Intestinal lymphoma
8	Six months, German shepherd dog	Pharyngeal dysphagia and aspiration pneumonia
9	Six years, M, West Highland white terrier	Gastroenteritis and aspiration pneumonia
10	12 years, F, Border terrier	Gastroenteritis
11	Four years, F, boxer	Anorexia, cause undetermined

F Female, M Male, MN Male neutered

common cause for failure of the iv line was apparent venous thrombus or thrombophlebitis, with swelling and/or redness of the leg, which resolved within 24 to 36 hours after removal of the catheter. No dog had evidence of fever unrelated to the underlying disease, although no blood cultures or catheter tip cultures were performed, so catheter-related sepsis cannot be excluded.

Metabolic complications All median and mean serum sodium and potassium concentrations were within the reference ranges before and throughout the PPN infusion (Table 4). Mean and median serum urea and triglyceride concentrations were also within the reference ranges before and on day 4 of PPN infusion. Dog 2, which had a pancreatic abscess, had a mildly elevated triglyceride concentration of 1.76 mmol/l (reference range 0.54 to 1.14 mmol/l) before PPN infusion, and over days 1 to 4 of infusion, his serum triglyceride concentrations were 1.85, 1.53, 1.0 and 2.35 mmol/l.

Median ALT values before infusion were 55 iu/l and 70 iu/l on day 4. Mean serum ALT decreased from 213.8 to 142.8 iu/l over three days, but this decrease was due to a dog with improving pancreatitis (Table 4) in which the values decreased from 463 to 70 iu/l. In dog 4, which had a hepatopathy, the initial and

day 3 ALT values were 488 and 451 iu/l, respectively.

Median albumin concentration before infusion was 19.9 g/l, with a range of 13.9 to 31.2 g/l. Median albumin concentration on day 4 was 20.9, with a range of 18.8 to 35.4 g/l. Mean serum albumin concentrations before infusion and on day 4 were 21.98 and 24.82 g/l, respectively (Table 4).

Median serum glucose concentrations on days 0 to 4 were 5.1, 4.6, 5.25, 5.8 and 5.5 mmol/l, respectively. Mean values for the same days were 5.6, 5.9, 5.6, 6.0 and 5.6 mmol/l, respectively (Table 4).

Part 2

During the second part of the study, the parenteral nutrition was infused for 10 to 12 hours during the day. There were no incidences of apparent thrombus, thrombophlebitis or line failure during this part of the study, although the longest infusion was only three days.

For the four dogs receiving the complete Clinomel N4 solution containing amino acids, lipids and glucose, the mean and median values for serum cobalamin concentration before PPN administration were 199.5 and 191.5 ng/l, respectively. After one day of PPN, the mean was 267.5 ng/l and the median value was 232 ng/l (Table 5).

For these dogs, the mean and median values for serum folate concentration before PPN administration were 5.73 and 5.85 µg/l, respectively. After one day of administration, the mean was 6.13 ng/l and the median was 5.65 ng/l. The mean and median values for serum homocysteine concentration before PPN administration were 6.25 and 6.26 µmol/l, respectively. After one day of administration, the mean serum homocysteine concentration was 4.88 µmol/l and the median was 3.79 µmol/l (Table 5).

For the two dogs (dogs 10 and 11) receiving only the amino acid solution, the serum cobalamin concentrations before PPN were 212 and 409 ng/l, respectively. After 12 hours of administration, the cobalamin concentration for dog 11 was 418 ng/l. After days 2 and 3, the cobalamin concentrations for dog 10 were 245 and 215 ng/l, respectively (Table 6).

The serum folate concentrations for dogs 10 and 11 before amino acid infusion were 16.8 and 18.3 µg/l, respectively. After 12 hours of PPN, the serum folate concentration for dog 11 was 12.3 ng/l. After day 2 and 3 of amino acid infusion, the folate concentrations for dog 10 were 18.1 and 15.3 ng/l, respectively (Table 6).

The serum homocysteine concentrations for dogs 10 and 11 before amino acid infusion were 7.42 and 7.66 µmol/l, respectively. After an amino acid infusion of three days (dog 10) and of one day (dog 11), the values were 11.0 and 8.61, respectively.

DISCUSSION

Part 1

Mechanical complications PPN with Clinomel N4 at 2 ml/kg/hour resulted

Table 3. Time to catheter or line failure in hours for part 1 of the study

Dog	Duration of first catheter (hours)	Duration of second catheter (hours)	Summary
1	48	51	
2	36	36	
3	36	24	
4	48	24	
5	11	33	
Mean	35.8	33.6	Overall mean, 34.7
Median	36	24	Overall median, 36

Table 4. Serum chemistry parameters for dogs on PPN with Clinomel N4

Parameter	Day 0 (before PPN), median (mean)	Day 1, median (mean)	Day 2, median (mean)	Day 3 median (mean)	Day 4 median (mean)	Reference range
Sodium (mmol/l)	149 (149)	147 (148)	147 (148)	154 (150)	154 (150)	139-154
Potassium (mmol/l)	4.3 (4.3)	4.3 (4.1)	4.0 (3.9)	4.1 (4.1)	4.3 (4.2)	3.6-5.6
Urea (mmol/l)	4.7 (4.5)	–	–	–	4.3 (4.3)	1.7-7.4
Triglycerides (mmol/l)	0.87 (0.80)	0.57 (1.02)	0.86 (1.01)	1.0 (0.92)	0.83 (1.1)	0.57-1.14
ALT (iu/l)	55.0 (213.8)	–	–	–	70.0 (142.8)	21-102
Albumin (g/l)	19.9 (22.0)	–	–	–	20.9 (24.8)	26-35
Glucose (mmol/l)	5.1 (5.6)	4.6 (5.9)	5.3 (5.6)	5.8 (6.0)	5.5 (5.6)	3.0-5.0

PPN Peripheral parenteral nutrition, ALT Alanine aminotransferase

Table 5. Mean and median serum cobalamin, folate and homocysteine concentrations for dogs on peripheral parenteral nutrition with Clinomel N4

Dog	Cobalamin (ng/l)			Folate ($\mu\text{g/l}$)			Homocysteine ($\mu\text{mol/l}$)		
	Day 0	Day 2	Day 3	Day 0	Day 2	Day 3	Day 0	Day 2	Day 3
6	198	226	–	6.6	7.0	–	8.12	8.26	–
7	172	390	–	5.1	4.3	–	5.75	3.87	–
8	243	238	256	4.1	4.0	7.2	4.35	3.67	2.62
9	185	216	–	7.1	9.2	–	6.76	3.71	–
Median	191.5	232	–	5.85	5.65	–	6.26	3.79	–
Mean	199.5	267.5	–	5.73	6.13	–	6.25	4.88	–

Day 0 is before infusion, days 2 and 3 are at the end of the 10- to 12-hour infusion period for the second and third days of infusion

Table 6. Mean and median serum cobalamin, folate and homocysteine concentrations for dogs infused with the amino acid solution only

Dog	Cobalamin (ng/l)				Folate ($\mu\text{g/l}$)				Homocysteine ($\mu\text{mol/l}$)			
	Day 0	Day 1	Day 2	Day 3	Day 0	Day 1	Day 2	Day 3	Day 0	Day 1	Day 2	Day 3
10	212	–	245	215	16.8	–	18.1	15.3	7.42	–	10.04	11.06
11	409	418	–	–	18.3	12.3	–	–	7.66	8.61	–	–

Day 0 is before infusion, days 1 to 3 are at the end of the 10- to 12-hour infusion period for the respective days of infusion

in a median time to failure of catheter patency of 36 hours. As the median duration of PPN support has been reported to be three days (Chan and others 2002), it is likely that use of this product would require at least one catheter change in most patients if administered for 24 hours/day.

Methods of obtaining a longer infusion time might include intermittent delivery or a slower rate of delivery, although either of these techniques would decrease the amount of calories provided. Use of a 12-hour infusion for peripheral nutrition in human beings has been reported to decrease phlebitis (May and others 1996), and infusion for 10 to 12 hours was used in the second part of the present study, with no line failures. This may result in preservation of venous access and be more feasible for some small animal clinics that are not staffed during the night. Use of a lower osmolality solution may provide a longer duration of infusion, and a similar three-in-one product (Oliclinomel N-4; Baxter Healthcare) with an osmolality of 750 mOsm/l and caloric content of 610 kcal/l is now available. While either of these changes in technique would result in provision of fewer calories, there would be a beneficial protein-sparing effect, as even the provision of 5 per cent glucose has been shown to

improve nitrogen balance (Craig and others 1977, Bernard and others 1986, Chandler and others 2000).

Metabolic complications In all dogs, excluding one with a pancreatic abscess, median and mean serum electrolytes, triglyceride and urea concentrations were within the reference ranges throughout the infusion time (Table 4). In the dog with the pancreatic abscess, the preinfusion serum triglyceride concentration was above the reference range at 1.76 mmol/l. This value increased to 1.85 on day 1, then decreased to 1.53 and 1.0 mmol/l on days 2 and 3, respectively, and increased to 2.46 mmol/l on the fourth day. The lipid infusion did not appear to consistently worsen the dog's serum triglyceride concentrations or his clinical signs. Infusion of lipid-containing products has been controversial in patients with pancreatitis. Parenteral nutrition is used in human beings with pancreatitis, with careful monitoring (Robin and others 1990), and a study in dogs and cats with pancreatitis supported the use of PPN in these patients (Freeman and others 1995). Patients with pancreatitis should, however, be fed enterally as soon as is feasible (McClave and others 1997, 1998, Qin and others 2002, Marik and Zaloga 2004).

Before and after infusion, median serum ALT activities were elevated, but

these results were skewed by dog 2 which had a pancreatic abscess and dog 4 which had a hepatopathy, both with high values before and during infusion. The ALT values for dog 2 did improve during treatment, but the effect of the parenteral nutrition on his improvement is difficult to evaluate. This dog's serum albumin and median and mean serum albumin concentrations also improved. The effect of the nutrition on the improvement in serum albumin concentrations is also difficult to evaluate. These improvements may be a reflection of nutritional support, increased production, decreased loss, an interstitial to intravascular shift or a decrease in the acute-phase reaction as the patient improved.

There were mild increases in median and mean blood glucose concentration before and throughout PPN infusion, but none of the dogs required insulin treatment and none of the dogs developed glucosuria. Hyperglycaemia is one of the most common sequela of parenteral nutrition, reported in about 12 to 32 per cent of dogs on parenteral nutrition (Lippert and others 1993, Reuter and others 1998, Chan and others 2002); however, it rarely requires cessation of the nutritional support. None of the dogs in the current study was hypoglycaemic at any of the measurement times.

Part 2

Although there are insufficient numbers of dogs for statistical analysis, no consistent trends in changes of serum folate, cobalamin or homocysteine concentrations were apparent either in the dogs given the three-in-one product or in the dogs given only the amino acid solution. The reason for the lack of decrease in folate concentration as seen in a previous study (Chandler and others 2000) in dogs on iv amino acid solution is not clear, but it may be due to the heterogeneous population of these clinical patients, shorter infusion time, slower infusion rate or some other property of the three-in-one product. The previous study was performed in research dogs that had similar previous management and feeding and may have had lower whole body concentrations of folate. Only a very small percentage of the body's folate is present in the serum, and serum values may not reflect whole body storage (Grant 1992). Serum folate concentrations can also be increased by intestinal bacterial synthesis or decreased by intestinal absorption disorders (Strombeck 1996), but neither of these factors is likely to have had an effect in the present study.

The Clinomel N4 and the amino acid solution used in the previous study (Chandler and others 2000) contain the same concentration of methionine (2.2 g/l). However, the infusion rate in the previous study was 6 ml/kg/hour for 10 hours for four days, whereas in the present study, the rate was 2 ml/kg/hour for 10 to 12 hours for one to three days. The more rapid rate or longer duration may have resulted in a methionine loading. In human beings, oral methionine supplementation ("loading") has been shown to result in a significant fall in serum folate concentration (Connor and others 1978) and an increase in homocysteine concentration (Bostom and others 1995), even in fed patients who previously had values within the reference ranges.

Conclusions

Short-term PPN with Clinomel N4 appears to be practical and safe in dogs and did not result in any consistent or significant changes in serum electrolytes or significant increases in serum triglycerides or glucose. There were also no consistent or significant decreases in serum cobalamin or folate concentrations or increases in homocysteine concentration. Further work in techniques to prolong the infusion times and decrease the incidence of venous thrombus will facilitate the use of PPN, especially using the convenient and safe three-in-one products.

Acknowledgement

The authors would like to thank the Waltham Centre for Pet Nutrition, for their generous financial support of this study, and Baxter, for provision of the Clinomel N4.

References

- ANDERSON, A. D., PALMER, D. & MACFIE, J. (2003) Peripheral parenteral nutrition. *British Journal of Surgery* **90**, 1048-1054
- BERNARD, M. A., JACOBS, D. O. & ROMBEAU, J. L. (1986) Nutritional and Metabolic Support of Hospitalized Patients. W. B. Saunders, Philadelphia, PA, USA
- BOSTOM, A. G., JACQUES, P. F., NADEAU, M. R., WILLIAMS, R. R., ELISON, R. C. & SELHUB, J. (1995) Post-methionine load hyperhomocysteinemia in persons with normal fasting total plasma homocysteine: initial results from the NHLBI Family Heart Study. *Atherosclerosis* **116**, 147-151
- CHAN, D. L., FREEMAN, L. M., LABATO, M. A. & RUSH, J. E. (2002) Retrospective evaluation of partial parenteral nutrition in dogs and cats. *Journal of Veterinary Internal Medicine* **16**, 440-445
- CHANDLER, M. L., GUILFORD, W. G., MAXWELL, A. & BARTER, L. (2000) A pilot study of protein sparing in healthy dogs using peripheral parenteral nutrition. *Research in Veterinary Science* **69**, 47-52
- CONNOR, H., NEWTON, D. J., PRESTON, F. E. & WOODS, H. F. (1978) Oral methionine loading as a cause of acute serum folate deficiency: its relevance to parenteral nutrition. *Postgraduate Medicine Journal* **54**, 318-320
- CRAIG, R. P., TWEEDLE, D., DAVIDSON, H. A. & JOHNSTON, I. D. A. (1977) Intravenous glucose, amino acids, and fat in the post operative period. *The Lancet* **2**, 8-11
- FREEMAN, L. M., LABATO, M. A., RUSH, J. E. & MURTAUGH, R. J. (1995) Nutritional support in pancreatitis: a retrospective study. *Journal of Veterinary Emergency and Critical Care* **5**, 2-41
- GRANT, J. P. (1992) Trace element requirements and deficiency syndromes. In: *Handbook of Total*

- Parenteral Nutrition*. 2nd edn. W. B. Saunders, Philadelphia, PA, USA. pp 275-309
- KANE, K. F., COLOGIOVANNI, L., MCKIERNAN, J., PANOS, M. Z., AYRES, R. C., LANGMAN, M. J. & LOWES, J. R. (1996) High osmolality feedings do not increase the incidence of thrombophlebitis during peripheral i.v. nutrition. *Journal of Parenteral and Enteral Nutrition* **20**, 194-197
- LIPPERT, A. C., FULTON, R. B. & PARR, A. M. (1993) A retrospective study of the use of total parenteral nutrition in dogs and cats. *Journal of Veterinary Internal Medicine* **7**, 52-64
- MCCLAIVE, S. A., GREENE, L. M., SNIDER, H. L., MAKK, L. J., CHEADLE, W. G., OWENS, N. A., DUKES, L. G. & GOLDSMITH, L. J. (1997) Comparison of the safety of early enteral versus enteral nutrition in mild acute pancreatitis. *Journal of Parenteral and Enteral Nutrition* **21**, 14-20
- MCCLAIVE, S. A., SPAIN, D. A. & SNIDER, H. L. (1998) Nutritional management in acute and chronic pancreatitis. *Gastroenterology Clinics of North America* **27**, 421-434
- MARIK, P. E. & ZALOGA, G. P. (2004) Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. *British Medical Journal* **328**, 1407-1416
- MAY, J., MURCHAN, P., MACFIE, J., SEDMAN, P., DONAT, R., PALMER, D. & MITCHELL, C. J. (1996) Prospective study of the aetiology of infusion phlebitis and line failure during peripheral parenteral nutrition. *British Journal of Surgery* **83**, 1091-1094
- QIN, H. L., SU, Z. D., GAO, Q. & LIN, Q. T. (2002) Early intrajejunal nutrition: bacterial translocation and gut barrier function of severe acute pancreatitis in dogs. *Hepatobiliary Pancreatic Disease International* **1**, 150-154
- REUTER, J. D., MARKS, S. L., ROGERS, Q. R. & FARVER, T. B. (1998) Use of total parenteral nutrition in dogs: 209 cases (1988-1995). *Journal of Veterinary Emergency and Critical Care* **8**, 201-213
- ROBIN, A. P., CAMPBELL, R., PALANI, C. K., LIN, K., DONOHUE, P. E. & NYHUS, L. M. (1990) Total parenteral nutrition during acute pancreatitis: clinical experience with 156 patients. *World Journal of Surgery* **4**, 579-572
- SELHUB, J., JACQUES, P. F., BOSTOM, A. G., WILSON, P. W. & ROSENBERG, I. H. (2000) Relationship between plasma homocysteine and vitamin status in the Framingham study population. Impact of folic acid fortification. *Public Health Review* **28**, 117-145
- STROMBECK, D. R. (1996) Small and large intestine: normal structure and function. In: *Strombeck's Small Animal Gastroenterology*. Eds W. G. Guilford, S. A. Center, D. R. Strombeck, D. A. Williams and D. J. Meyer. W. B. Saunders, Philadelphia, PA, USA. pp 318-350
- TENNANT, G. B., SMITH, R. C., LEINSTER, S. J., O'DONNELL, J. E. & WARDROP, C. A. (1981) Acute depression of serum folate in surgical patients during preoperative infusion on ethanol-free parenteral nutrition. *Scandinavian Journal of Haematology* **27**, 327-332
- WANG, X. (1999) A theory for the mechanism of homocysteine-induced vascular pathogenesis. *Medical Hypotheses* **53**, 386-394
- ZSOMBOR-MURRAY, E. & FREEMAN, L. M. (1999) Peripheral parenteral nutrition. *Compendium for Continuing Education of Practising Veterinarians* **21**, 512-523