

Umbilical vs Peripheral Vein Catheterization for Parenteral Nutrition in Sick Premature Neonates

Gilberto R. Pereira, Baek-Keun Lim¹, Christopher Ing
and Helosia F. Medeiros

The efficacy and safety of using umbilical venous catheters vs. peripheral venous catheters for the delivery of parenteral nutrition was studied in 129 critically ill premature infants who were treated in a neonatal intensive care unit for the first 3 weeks of life. Infants who received parenteral nutrition by umbilical venous catheter had greater parenteral caloric intake, lower physiologic weight loss and greater weight gain during the study as compared to infants who received parenteral nutrition by peripheral vein. While the overall incidence of sepsis was comparable in both groups (19% vs 19.7%), benign and transient episodes of hyperglycemia were seen more commonly in infants receiving parenteral nutrition by umbilical catheters. None of the hyperglycemic infants, however, required insulin therapy. The incidence of other metabolic complication was comparable in both groups. At follow up, no evidence of portal hypertension was detected in any of the infants up to 66 months of age treated with umbilical venous catheters. We conclude that the use of umbilical venous catheter allows for a comparably safe and a more appropriate parenteral nutrition support than peripheral catheters in critically ill premature neonates.

Key Words: Umbilical catheterization, parenteral nutrition, neonates, premature infants

Parenteral nutrition is routinely administered to sick neonates until enteral feedings can solely provide appropriate nutritional support. Parenteral nutrition can be delivered by central or peripheral vein catheters depending on the patients' venous accessibility, caloric requirement and expected duration of therapy (Pereira and Ziegler 1989). In the neonatal period, the umbilical vein can be easily cannulated at the bedside and used as a durable and reliable conduit for the delivery of parenteral nutrition solution of high caloric density. However, it is generally believed that the use of umbilical venous catheter can be associated with a high risk of

thrombosis, especially if the catheter is placed in the portal or hepatic vein or if hyperosmolar solutions are rapidly infused through the catheter (Schmidt and Zipursky 1984). At the present time, the risk of using umbilical vein catheters which are placed above the diaphragm and used for continuous delivery of parenteral nutrition solution is not known.

The purpose of this study is to compare the efficacy and the safety of using either umbilical or peripheral venous catheters for the delivery of parenteral nutrition to critically ill premature infants.

MATERIAL AND METHODS

We studied retrospectively 129 premature infants admitted to the Infant Intensive Care Unit at Children's Hospital of Philadelphia from September 1984 to August 1987. All infants were critically ill, receiving mechanical ventilation for the treatment

Division of Neonatology, Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania, School of Medicine, Philadelphia, PA, 19104, U.S.A.

Department of Pediatrics¹, Yonsei University Wonju College of Medicine, Wonju, Kangwon, Korea

Address reprint requests to Dr. B K Lim, Department of Pediatrics, Yonsei University Wonju College of Medicine, 162 Ilsandong, Wonju, Kangwon, Korea, 220-701

Table 1. Clinical characteristics of infants receiving parenteral nutrition by umbilical vein (UV) and peripheral vein (PV) catheters

	UV group (n=63)	PV group (n=66)	
Birth weight (g)	1254±605	1370±418	NS
Head Circumference (cm)	26.2±3.7	26.7±2.5	NS
Length (cm)	36.7±8	37.8±7.2	NS
Gestation age (wk)	29.1±4.5	30.1±2.7	NS
Sex, male/female	37/26	35/31	NS
Duration of mechanical ventilation (days)	32.8±28.2	18.5±23.1	p<0.005
Age of initiation of enteral feeding (days)	16.5±8.2	11.2±4.9	p<0.005

Values are mean±SD.

NS, not significant

of respiratory distress syndrome. Clinical characteristics of these infants are presented in Table 1. Parenteral nutrition was started in all patients by the third day of life either by umbilical vein catheter (n=63) or by peripheral vein catheter (n=66). Decisions to place an umbilical vein catheter were made by the physician caring for these infants based on the severity of illness, the anticipated duration of parenteral nutrition therapy (greater than 1-2 weeks) and on patients' poor venous accessibility. Parenteral nutrition by peripheral vein was utilized in all other infants and also in those selected for umbilical venous catheterization in whom the tip of the catheter could not be advanced and placed at the junction of the inferior vena cava and right atrium; in all of these patients, the umbilical vein catheter was removed. The duration of parenteral nutrition, the time of initiation of enteral feeding and the rate of feeding advancement were also decided by the physicians caring for these premature infants and not by our group of investigators.

The umbilical vein catheters were inserted under aseptic conditions, and the length of the catheter inserted corresponded to the distance between the shoulder and the umbilicus added to the length of the umbilical stump; this distance has been shown to make possible the placing of the tip of the umbilical vein catheter above the diaphragm (Dunn 1966). In all instances the location of the catheter tip was documented radiologically prior to the initiation of parenteral nutrition, and then the catheter was sutured to the umbilical stump to prevent displacement. The umbilical stump was kept uncov-

Table 2. Composition of standard parenteral nutrition solution per 500 ml

Protein solution	1.5/2/2.5/3/3.5
Protein ^a	10 (PV), 15/20 (UV)
Dextrose ^b	20
Na (mEq)	10
K (mEq)	23
Cl (mEq)	300
Ca (mg)	7
Phos (mEq)	2
Mg (mEq)	2500
Zn (mcg)	300
Cu (mcg)	0.85
Cr (mcg)	25
Mn (mcg)	15
Se (mcg)	40
I (mcg)	0.5 ^c
Fe (mg)	500
Heparin (u)	

^aAvailable standard protein concentration (g/100 ml)^bAvailable standard dextrose concentrations (g/100 ml)^cIron is added for all infants, including premature infants, after 4 weeks of life.

PV, peripheral vein, UV, umbilical vein

ered and dry. Application of povidone iodine solution to the umbilical stump at the site of entry of the catheter was routinely performed three times daily by the nursing staff. The peripheral vein catheters were inserted by the house staff or the intravenous therapy team and replaced at 2 to 3 day in-

tervals. The umbilical vein and peripheral vein catheters were used solely for the administration of parenteral nutrition solutions. All parenteral nutrition solutions were delivered by constant infusion pumps, and all tubings were changed every 24 hours. All infants received parenteral nutrition solutions with an initial dextrose concentration of 10%. The dextrose concentration was increased to 15% and to 20% in infants with umbilical vein catheters and it was maintained at 10% in infants with peripheral catheters. The composition of the solutions used for parenteral nutrition are presented in Table 2.

Enteral feedings were started and advanced according to the infants' clinical status and tolerance. Enteral feeding included own mother's human milk, and premature infant formula (Special care, Ross Lab). All feedings were initially delivered by continuously or intermittent gavage through nasogastric tubes. Parenteral nutrition was discontinued when enteral feedings provided a minimum of 85 Kcal/kg/day.

Data collected from each patient included: daily weights, weekly length and head circumferences, and daily intakes of calories, dextrose, amino acids, and fat emulsion. Dextrostix were done three times daily, and blood glucose determination was obtained whenever dextrostix values ranged from 120 to 180 mg/dL or above. Hyperglycemia was defined as a blood glucose determination above

150 mg/dL. Serum triglyceride were measured weekly and hypertriglyceridemia was defined as serum triglyceride greater than 250 mg/dL. All infants were also observed for clinical signs of sepsis and necrotizing enterocolitis. The criteria to define sepsis included the presence of suggestive clinical and laboratory findings documented by one or more positive blood cultures obtained from peripheral veins. The criteria to define catheter related sepsis include: 1) The above described criteria, 2) The presence of positive blood culture drawn through the catheter, and 3) the absence of any documented focus of infection. Necrotizing enterocolitis was defined by the presence of 1) clinical signs of bloody stool, abdominal distension, feeding intolerance and 2) radiological sign of pneumatosis intestinalis, pneumoperitoneum, and portal vein air.

Data obtained from patients receiving parenteral nutrition by umbilical vein and peripheral vein catheters were compared by chi square analysis and Student's t-test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Of the 129 infants studied, 63 received parenteral nutrition by umbilical vein catheters and 66 by peripheral vein catheters. As shown in Table 1,

Table 3. Parenteral, enteral, and total caloric intakes in infants receiving parenteral nutrition by umbilical vein (UV) and by peripheral vein (PV) catheters

		1st wk (UV, n=63 PV, n=66)	2nd wk (UV, n=40 PV, n=48)	3rd wk (UV, n=16 PV, n=16)
Parenteral Caloric intake (Kcal/kg/d)	UV	61.9±15.3	77.0±23.6	72.0±30.0
	PV	50.1±15.9 p<0.0005	58.9±29.3 p<0.001	50.9±34.2 p<0.05
Enteral Caloric intake (Kcal/kg/d)	UV	1.8±5.8	5.3±10.3	17.2±19.8
	PV	9.8±16.2 p<0.0005	32.1±30.5 p<0.0005	59.6±68.1 p<0.01
Total Caloric intake (Kcal/kg/d)	UV	63.8±16.0	82.2±20.2	89.2±30.8
	PV	58.9±20.6 NS	88.4±32.3 NS	110.5±48.8 NS

Values are mean±SD

NS, not significant

there were no significant differences in birth weight, head circumference, length, gestational age, and sex ratio between the 2 groups. The duration of mechanical ventilation was significantly longer in the umbilical catheter group than in the peripheral catheter group (32.8 ± 28.2 vs 18.5 ± 23.1 days, $p < 0.005$). Infants receiving parenteral nutrition by umbilical vein catheter were started on enteral feedings at a greater postnatal age than those receiving parenteral nutrition by peripheral vein (16.5 ± 8.2 vs 11.2 ± 4.9 days).

Table 3 displays the mean caloric intakes of infants receiving parenteral nutrition by umbilical and peripheral veins during the 3 weeks of the study. Infants receiving parenteral nutrition by umbilical vein had a greater parenteral caloric intake during the whole study as compared to infants in the peripheral catheter group. However, infants who received parenteral nutrition by peripheral vein had a significantly greater enteral intake during the 3 weeks of the study. The total caloric intake (parenteral and enteral) between the two groups was comparable during the study.

Table 4 displays parenteral intakes of dextrose, amino acids, and fat emulsion of the two study groups. Infants receiving parenteral nutrition by umbilical vein had a greater parenteral intake of dextrose during the three weeks of the study period and a greater intake of amino acids and fat emulsion during the second and the third week of the

study.

Table 5 shows changes in weight, length and head circumference in the two groups of infants during the study. Infants who received parenteral nutrition by umbilical vein had a lower per cent of weight loss during the first week and a greater per cent of weight gain during the second and third week of the study as compared to infants who received parenteral nutrition by peripheral vein. There were no significant differences in weekly changes in length or head circumference between the two groups during the study period.

The complications of parenteral nutrition observed in the two groups of infants are presented in table 6. Sepsis occurred in a comparable number of patients from each group (19.7% vs 19%, NS). The incidence of sepsis was noted to increase with the duration of parenteral nutrition during the three weeks of the study: it increased from 8% during the first week, to 10% during the second week, and to 19% during the third week in the umbilical vein group, and it increased from 3% during the first week, to 15% during the second week, to 25% during the third week in the peripheral vein group. Primary catheter sepsis was observed in 2 patients in the umbilical vein group at 2 and 4 days after initiation of parenteral nutrition. Staphylococcus epidermidis was the most common organism causing sepsis in the two groups (19/25 instances). Other organisms causing sepsis on a single instance

Table 4. Parenteral caloric intake from dextrose, amino acids and fat emulsion in infant receiving parenteral nutrition by umbilical vein (UV) and peripheral vein (PV) catheters during the 3 weeks of the study

		1st wk (UV, n=63 PV, n=66)	2nd wk (UV, n=40 PV, n=48)	3rd wk (UV, n=16 PV, n=16)
Dextrose (mg/kg/min)	UV	7.3 ± 2.3	8.9 ± 4	7.8 ± 5.1
	PV	5.8 ± 1.7	6.0 ± 2.8	4.8 ± 3.1
		$p < 0.0005$	$p < 0.00005$	$p < 0.05$
Amino acids (g/kg/d)	UV	1.7 ± 0.5	2.4 ± 0.7	2.4 ± 1.1
	PV	1.6 ± 1.2	2.0 ± 0.9	1.7 ± 1.2
		NS	$p < 0.025$	$p < 0.05$
Fat emulsion (g/kg/d)	UV	1.3 ± 0.6	2.0 ± 0.8	2.2 ± 0.7
	PV	1.3 ± 0.7	1.6 ± 0.9	1.5 ± 1.1
		NS	$p < 0.025$	$p < 0.05$

Values are mean \pm SD.

NS, not significant

Table 5. Percent changes in Weight, Length, and Head circumference in infants in the umbilical vein (UV) and peripheral vein (PV) catheters during the 3 weeks of the study

		1st wk (UV, n=63 PV, n=66)	2nd wk (UV, n=40 PV, n=48)	3rd wk (UV, n=16 PV, n=16)
% change in weight	UV	0.01 ± 11.6	5.2 ± 12.1	14.4 ± 13.5
	PV	-5.2 ± 8.0 p < 0.005	-0.7 ± 10.1 p < 0.01	6.4 ± 11.4 p < 0.05
% change in length	UV	1.3 ± 2.7	3.2 ± 4.8	1.9 ± 1.7
	PV	1.0 ± 2.3 NS	2.1 ± 2.5 NS	5.3 ± 4.9 NS
% change in head circumference	UV	0.5 ± 2.4	2.0 ± 3.5	5.3 ± 5.9
	PV	-0.3 ± 3.2 NS	1.6 ± 4.8 NS	4.9 ± 6.3 NS

Values are mean ± SD.

NS, not significant

Table 6. Complications of parenteral nutrition in infants receiving parenteral nutrition by umbilical vein (UV) and peripheral vein (PV) catheters

	UV group (n=63)	PV group (n=66)	
Sepsis(%)	19	19.7	NS
Hyperglycemia (%)	30	9	p < 0.05
Hypertriglyceridemia (%)	3.2	0	NS
Necrotizing enterocolitis (%)	10.6	4.8	NS

NS, not significant

included: *Candida albicans*, *Streptococcus* species, *Enterobacter* species, *Acinetobacter* species, *Klebsiella* species and *Pseudomonas* species. Transient hyperglycemia occurred more frequently in infants receiving parenteral nutrition by umbilical vein catheters and required a temporary reduction in either the rate or the concentration of dextrose infused; none of the affected infants required insulin therapy. There were no significant difference in the incidence of hypertriglyceridemia or necrotizing enterocolitis between the two study groups.

Follow up data was evaluated for the 63 infants in the umbilical catheter group. 15 infants expired during the neonatal period from complications unrelated to parenteral nutrition. Of the 48 survivors, 9 were lost to follow up and 39 were followed for a

mean of 27.8 ± 16 months (range 4-66 months). None of these infants had any symptoms or signs of portal hypertension such as abdominal distension, ascites, splenomegaly or gastrointestinal bleeding. Hepatomegaly was observed in 3 asymptomatic infants. An autopsy was performed on 6 of the 15 infants who expired. In one of those patients several fibrin thrombi were detected in the liver and lung, and in another patient a mural thrombi was noted in the left atrial septal wall. These thrombi were unexpected autopsy findings which caused no significant venous obstruction or any other symptomatology to the patients.

DISCUSSION

The catheterization of the umbilical vein in neonates has several advantages over the catheterization of the peripheral vein including the ease with which the umbilical vein can be cannulated, the minimum time and handling of patients required to perform this procedure, and the reliability and durability of the catheter as a conduit for intravenous therapy (Balagtas et al. 1971). In addition, if the tip of the umbilical vein catheter is placed at the junction of the inferior vena cava and right atrium it can be used as a central line for the delivery of parenteral nutrition solutions of high caloric density. Parenteral nutrition solutions for peripheral catheteriza-

tion contain dextrose at a maximal concentration of 10% to prevent the occurrence of skin sloughs which may result from infiltration of hypertonic solution into the subcutaneous tissue. Even with the additional use of fat emulsion, peripheral nutrition solutions provide a maximum intake of 80 to 90 Kcal/kg/day. Therefore, when the neonate require a caloric intake greater than 90 kcal/kg/day, the delivery of parenteral nutrition solution by a central rather than a peripheral line should be considered (Pereira and Ziegler 1989). Other indications for the use of central lines for parenteral nutrition include patients who have poor peripheral venous access or those who are anticipated to need longterm parenteral support.

In our study there were no significant differences between the birth weight or gestational age of infants who received parenteral nutrition by umbilical or by peripheral veins. However, the duration of mechanical ventilation and the age of initiation of enteral feeding in infant receiving parenteral nutrition by umbilical vein were greater than in those who received parenteral nutrition by peripheral vein. These findings indicate that infants who received parenteral nutrition by umbilical vein were sicker than those who received parenteral nutrition by peripheral vein. Since infants in our study were not randomly assigned to the treated with either umbilical or peripheral venous catheters, we concluded that the severity of illness was a significant factor which influenced the physician to use the umbilical venous catheters for nutritional support.

Our study also shows that the parenteral caloric intake provided to infants in the umbilical vein group was greater than that provided to infants in the peripheral vein group during the 3 weeks of the study. However, because of the greater enteral intake observed in infants receiving parenteral nutrition by peripheral vein, the mean total caloric intakes in both groups were comparable. We concluded that the presence of the umbilical vein catheter allowed for the provision of appropriate nutritional support to sicker infants in whom the initiation and advancement of enteral feedings were delayed.

The main goal of parenteral nutrition in neonates is to provide adequate nutritional support to maintain postnatal growth (Adamkin 1986). It was interesting to observe that despite comparable total energy intake (enteral plus parenteral), infants who received parenteral nutrition by umbilical vein regained birth weight within one week of the study while infants who received parenteral nutrition by

peripheral vein had not regained birth weight until the second week of the study. Additionally, differences in weight gain between the two groups were noted until the third week of the study. This data indicates that lower energy requirements are needed during parenteral nutrition, as compared to enteral nutrition possibly because during parenteral nutrition energy is neither utilized for intestinal digestion and absorption (specific dynamic action) nor lost in the stools of premature infants.

Sepsis associated with umbilical vein catheterization has been described by Scott (1965) who reported septic emboli to the liver and lung in the autopsies of 20% of infants with umbilical vein catheters. Balagtas *et al.* (1972) reported a sepsis rate of 8% in newborns treated with umbilical vein catheters whose mean birth weight greater than 2,400 gm. Bryan *et al.* (1973) reported a 17% sepsis rate in low birth weight infants (<1,300 gm) who received parenteral nutrition via umbilical vein catheters for the first five days after birth and then by peripheral vein catheters. The rate of sepsis associated with the use of peripheral vein catheters for parenteral nutrition ranges from 0 to 10% in children and adults (Tager *et al.* 1983, Ziegler *et al.* 1980). Our study showed that the rates of sepsis associated with peripheral vein catheterization and umbilical vein catheterization were higher than those of older children but comparable to other reports including low birth weight neonates. Although sepsis was associated with umbilical catheterization in two of our patients, it is difficult to exclude the contribution of other predisposing factors such as the umbilical arterial catheters, endotracheal tubes and invasive monitoring device. The high incidence of sepsis in our study population may well be related to their very low birth weight and gestational age, and the associated immaturity of their immune system (Grisoni *et al.* 1986). Similarly to recent reports (Ziegler *et al.* 1980; Grisoni *et al.* 1986), *Staphylococcus epidermidis* was the most frequent organism causing sepsis in our patients. *Candida* septicemia occurred in one of our patients without the development of mural thrombi or valvular endocarditis (Nagwell and Marchildon 1989; Johnson *et al.* 1981). Our data also show that the increased duration of parenteral nutrition was associated with a greater incidence of infection in both groups of infants, as been previously reported (Filler *et al.* 1975).

Thrombosis is a serious complication associated with the catheterization of the umbilical vein which has been reported in 20 to 65% of autopsies

(Symansky and Fox 1972; Scott 1965). Past studies showed that the sequelae of thrombosis associated with catheterization of the umbilical vein include portal hypertension (Osiki et al. 1963), splenic vein thrombosis (Vos et al. 1974), hepatic necrosis (Wigger et al. 1970) and pulmonary embolism (Sanerkin et al. 1966). However, a review of these studies clearly indicates the presence of 2 confounding variables, each of which increases the risk of thrombosis. The first is the placement of the umbilical venous catheter in either the portal or the hepatic vein and the second is the infusion of hyperosmolar solutions. In two of these previous studies all cases of thrombosis and hepatic necrosis were related to umbilical catheters which had not been placed beyond the ductus venosus (Wiedesberg and Pawlowski 1979; Wigger et al. 1970). In addition, all cases of portal vein thrombosis in one of these studies were noted only in patients who received rapid injection of either sodium bicarbonate or 50% dextrose solutions through the catheter (Wigger et al. 1970). In most of these reports, radiological documentation of the position of the umbilical venous catheter was not routinely obtained. Therefore, it can be argued that the incidence of thrombosis associated with umbilical vein catheterization is either reduced or eliminated if the tip of the catheter is positioned above the diaphragm and the delivery of parenteral nutrition solutions provided by slow and continuous infusions. Our data showed no evidence of portal vein thrombosis or hypertension in either the postmortem examinations of infants who expired in the newborn period or in follow up of the survivors up to 66 months of age.

The most common metabolic complication of parenteral nutrition in neonates is hyperglycemia (James et al. 1979). The incidence of hyperglycemia was higher in infants in the umbilical vein group who were treated with higher dextrose concentrations, but in no instance did it impose any difficulty for the clinical management of these patients. Hypertriglyceridemia occurred at low frequency in the two groups, possibly due to the prolonged period administration of fat infusion (Spear et al. 1988).

In summary, these study indicated that the catheterization of umbilical vein for parenteral nutrition is an easy and effective method to provide nutritional support to sick neonates. With appropriate placement and management of the umbilical venous catheter, it seems that the greater nutritional benefits outweigh the complications as compared to the use of parenteral nutrition by peripheral veins.

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