

Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates (Review)

Ainsworth SB, Clerihew L, McGuire W



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TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	2
OBJECTIVES	3
CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW	3
SEARCH METHODS FOR IDENTIFICATION OF STUDIES	4
METHODS OF THE REVIEW	4
DESCRIPTION OF STUDIES	4
METHODOLOGICAL QUALITY	5
RESULTS	5
DISCUSSION	6
AUTHORS' CONCLUSIONS	7
POTENTIAL CONFLICT OF INTEREST	7
ACKNOWLEDGEMENTS	7
SOURCES OF SUPPORT	7
REFERENCES	7
TABLES	9
Characteristics of included studies	9
Characteristics of excluded studies	11
ANALYSES	11
Comparison 01. Percutaneous central venous catheter versus peripheral cannula	11
INDEX TERMS	11
COVER SHEET	12
GRAPHS AND OTHER TABLES	13
Analysis 01.01. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 01 Percentage deficit in nutrient delivery per infant	13
Analysis 01.02. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 02 Death before 28 days (all causes)	13
Analysis 01.03. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 03 Death before hospital discharge (all causes)	14
Analysis 01.04. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 04 Systemic bacterial and fungal infection	14
Analysis 01.05. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 05 Extravasation injury	15
Analysis 01.06. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 06 Number of cannulae/catheters per infant	15

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ABSTRACT

Background

Parenteral nutrition for neonates may be delivered via a short peripheral cannula or a central venous catheter. The latter may either be inserted via the umbilicus or percutaneously. Because of the complications associated with umbilical venous catheter use, many neonatal units prefer to use percutaneously inserted catheters following the initial stabilisation period. The method of parenteral nutrition delivery may affect nutrient input and consequently growth and development. Although potentially more difficult to place, percutaneous central venous catheters may be more stable than peripheral cannulae, and need less frequent replacement. These delivery methods may also be associated with different risks of adverse events, including acquired systemic infection and extravasation injury.

Objectives

To determine the effect of infusion via a percutaneous central venous catheter versus a peripheral cannula on nutrient input, growth and development, and complications including systemic infection, or extravasation injuries in newborn infants who require parenteral nutrition.

Search strategy

The standard search strategy of the Cochrane Neonatal Review Group was used. This included searches of the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2007), MEDLINE (1966 - February 2007), EMBASE (1980 - February 2007), conference proceedings, and previous reviews.

Selection criteria

Randomised controlled trials that compared the effect of delivering parenteral nutrition via a percutaneous central venous catheter versus a peripheral cannulae in neonates.

Data collection and analysis

Data were extracted the data using the standard methods of the Cochrane Neonatal Review Group, with separate evaluation of trial quality and data extraction by each author, and synthesis of data using relative risk, risk difference and mean difference.

Main results

Four trials eligible for inclusion were found. These trials recruited a total of 368 infants and reported a number of different outcomes. One study showed that the use of a percutaneous central venous catheter was associated with a decreased risk of cumulative nutritional deficit during the trial period: Mean difference in the percentage of the prescribed nutritional intake actually received: -7.1% (95% confidence interval -11.02, -3.2). In another trial, infants in the percutaneous central venous catheter group needed significantly fewer catheters/cannulae per infant during the trial period: Mean difference in the number of catheters/cannulae per infant: -3.2 (95% confidence interval -5.13, -1.27). Meta-analysis of data from all four trials did not find any evidence of an effect on the incidence of systemic infection: Typical relative risk: 0.94 (95% confidence interval 0.70, 1.25); typical risk difference: -0.02 (95% confidence interval -0.12, 0.08).

Authors' conclusions

Data from one small study suggest that the use of a percutaneous central venous catheter to deliver parenteral nutrition in newborn infants improves nutrient input. The significance of this in relation to long-term growth and developmental outcomes is unclear. Another study suggested that the use of a percutaneous central venous catheter rather than a peripheral cannula decreases the number of catheters/cannulae needed to deliver the nutrition. No evidence was found to suggest that percutaneous central venous catheter use increased the risk of adverse events, particularly systemic infection.

PLAIN LANGUAGE SUMMARY

More trials are needed to determine whether delivering intravenous nutrition into superficial or deep veins is better for newborn infants

Preterm or sick newborn infants are often fed with a special nutrient solution that is delivered directly into the veins. The solutions can either be given into a superficial vein through a standard short (peripheral) cannula or into a large deep vein via a long (central) catheter. This review found limited data from four small randomised controlled trials that compared the effects of using these two different methods of delivering nutrient solutions. There is some evidence from one study that infants who received the solution into a deep vein received more nutrition. The use of central catheters has been thought to increase the risk of bloodstream infection in newborn infants, but this review did not find any evidence that this was the case. More trials are needed to determine which method is better at improving growth and development in newborn infants.

BACKGROUND

The appropriate methods of feeding neonates vary with gestational age and clinical state. Some neonates, particularly those that are preterm or sick, are slow to tolerate the introduction of enteral feeds because of delayed gastric emptying and intestinal peristalsis. Since early postnatal nutrition may have a significant effect on important outcomes, including long-term neurodevelopment, these infants often receive parenteral (intravenous) nutrition during the establishment of enteral nutrition (Wilson 1997). Parenteral nutrition may also be delivered during periods when enteral nutrition is not possible, such as when there is lack of maternal expressed breast milk or when feeding is specifically contraindicated because of significant gastrointestinal disease such as necrotising enterocolitis. Because modern perinatal care has resulted in improved the survival rates of preterm and sick newborn infants, there has been an increase in the number of infants who require prolonged parenteral nutrition.

Parenteral nutrition usually consists of a glucose and electrolytes solution. More nutritionally complete formulations, "total parenteral nutrition", can also include an amino acid solution with minerals and vitamins in addition to fat as the principal non-protein energy source. The solutions are infused via either a short narrow-gauge peripheral venous cannula or a longer central venous catheter that extend into the larger veins such as the vena cavae (Shaw 1973; Trotter 1996).

Although it may be technically easier to site a peripheral cannula than to site a central venous catheter, peripheral cannulae are less stable and may require more frequent replacement. Once placed, a central venous catheter should remain in situ longer than a pe-

ripheral cannula (Shaw 1973), thus reducing the number of potentially painful procedures to which the infant is exposed. The need for frequent replacement of a peripheral cannula might also result in a significant cumulative period of interruption to the delivery of parenteral nutrition and in a nutrient deficit that which can have potential long-term consequences on growth and development (Embleton 2001). Another concern with the use of a peripheral cannula for delivering parenteral nutrition is the risk of extravasation injury. The subcutaneous infiltration of a hypertonic and irritant parenteral nutrition solution can cause local skin ulceration, secondary infection, and scarring.

In neonatal practice, a central venous catheter for the delivery of parenteral nutrition is usually placed percutaneously, although an umbilical venous or arterial catheter may also be used to deliver parenteral nutrition, particularly during the first week of life. Surgical placement, in which a deep vein is surgically exposed prior to cannulation and for which the infant may require a general anaesthetic, is less common. However, in infants in whom peripheral venous access is a major problem, often because of the frequency of previous cannulations, a surgically-placed central venous catheter may be the only option for the delivery of parenteral nutrition. This review will focus on the specific comparison of percutaneous central venous catheters versus peripheral cannulae.

The most common complication related to percutaneous central venous catheter use is nosocomial infection, which can include bacteraemia and invasive fungal infection. Micro-organisms can enter the bloodstream through the catheter entry site (Salzman 1995) or less commonly via the catheter hub (Salzman 1993). Catheter-associated thrombosis can act as a nidus for infection. It is often necessary to remove the catheter in order to clear the

infection (Karlłowicz 2002). The reported incidences of catheter-related sepsis in the neonatal intensive care unit vary from 5% (Neubauer 1995) to nearly 40% (Hruszkewycz 1991), depending on the criteria used to define catheter-related sepsis and the population studied. Extremely low birth weight infants (birth weight less than 1000 grams) are particularly at risk. Additional specific risk factors include prolonged use of parenteral nutrition and insertion of the catheter after the first week of life (Mahieu 2001). However, it is uncertain whether percutaneous central venous catheter use further increases the risk of infection in an “at-risk” population (Sohn 2001).

The use of a percutaneous central venous catheter to deliver parenteral nutrition may also be associated with iatrogenic injury, including embolism (air or thrombus) and infusate extravasation into tissue spaces. For example, there have been recent reports of cardiac tamponade following migration of the catheter tip to the pericardial space, and some authorities have recommended that central venous catheters should no longer be placed in the right atrium or ventricle because of this risk (Darling 2001).

Given that the choice of route for the delivery of parenteral nutrition may affect clinically important outcomes in neonates such as growth and development, the available evidence was systematically reviewed to determine if there are any implications for current practice or for future research.

OBJECTIVES

To determine the effect of infusion of parenteral nutrition via a percutaneous central venous catheter versus a peripheral catheter on nutrient input, growth and development and adverse consequences including bacteraemia or invasive fungal infection, cardiac tamponade, or other extravasation injuries in newborn infants who require parenteral nutrition.

The following sub-group analyses were performed:

1. preterm infants (less than 37 weeks gestation)
2. very low birth weight infants (less than 1500 grams)
3. extremely low birth weight infants (less than 1000 grams)

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Controlled trials utilizing either random or quasi-random patient allocation.

Types of participants

Neonates (newborn infants less than 28 days old at study entry) receiving parenteral nutrition, cared for in a hospital setting.

Types of intervention

Trials comparing parenteral nutrition delivered via a percutaneously inserted central venous catheter versus a peripheral cannula. Studies that compared delivery of parenteral nutrition via a surgically-placed central line (where the vein is surgically exposed prior to cannulation) or umbilical catheter will not be included. A minimum duration for trials was not specified.

Types of outcome measures

Primary outcomes: Nutrient input, growth and development:

1. Average daily input of parenteral calories (kilocalories per kilogram per day) and protein (grams per kilogram per day) during trial period
2. Average daily proportion of prescribed parenteral calories and protein that were actually delivered during trial period
3. Short-term (prior to discharge from hospital) growth parameters: weight gain (grams per day, or grams per kilogram per day), weight z-score at discharge, linear growth (millimetres per week), head growth (millimetres per week), skinfold thickness growth (millimetres per week)
4. Long-term (following discharge from hospital) growth parameters: weight gain (grams per day, or grams per kilogram per day), linear growth (millimetres per week), head growth (millimetres per week), skinfold thickness growth (millimetres per week)

5. Neurodevelopmental outcomes during infancy and beyond using validated assessment tools such as Bayley Scales of Infant Development, and classifications of disability, including auditory and visual disability. Severe neurodevelopmental disability was defined as any one or combination of the following: non-ambulant cerebral palsy, developmental delay (developmental quotient less than 70), auditory and visual impairment.

Secondary outcomes: Adverse events:

1. Death (all cause) before 28 days
2. Death (all cause) before discharge from hospital
3. Confirmed bacterial infection as determined by
 - a. culture from a normally sterile site: cerebrospinal fluid, blood (from peripheral sites, not from indwelling catheters), urine (obtained by sterile urethral catheterisation or supra-pubic bladder tap), bone or joint, peritoneum, pleural space, or central venous line tip
 - b. findings on autopsy examination consistent with invasive bacterial infection
4. Confirmed invasive fungal infection as determined by:
 - a. culture from a normally sterile site: cerebrospinal fluid, blood (from peripheral sites, not from indwelling catheters), urine (obtained by sterile urethral catheterisation or supra-pubic bladder tap), bone or joint, peritoneum, pleural space, or central venous line tip

- b. findings on autopsy examination consistent with invasive fungal infection
 - c. findings on ophthalmological examination consistent with fungal ophthalmitis or retinitis
 - d. pathognomonic findings on renal ultrasound examination: “renal fungal balls”
5. Extravasation injury as determined by:
- a. subcutaneous injury resulting in skin ulceration
 - b. “deep” extravasation resulting in limb swelling
 - b. “central” extravasation-infusate in the pleural, peritoneal, or pericardial space
6. Number of cannulae/catheters per child used to administer parenteral nutrition to each infant during trial period

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The standard search strategy of the Cochrane Neonatal Review Group was used, including electronic searches of The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2007), MEDLINE (1966 - February 2007) and EMBASE (1980 - February 2007). The search strategy included the following text words and MeSH subject headings: Infant-Newborn, infan\$, neonat\$, newborn, parenteral near3 nutrition, TPN, central near3 catheter, CVC, central near3 line, CVL. The search outputs will be limited with the relevant search filters for clinical trials. We did not apply any language restriction.

References in previous reviews and in studies identified as potentially relevant were examined. Abstracts presented at the Society for Pediatric Research and the European Society for Pediatric Research or published in the journal *Pediatric Research* between 1980 and 2006 inclusive were hand searched. Trials reported only as abstracts were eligible if sufficient information was available from the report, or from contact with the authors to fulfil the inclusion criteria.

METHODS OF THE REVIEW

1. William McGuire (WM) and Linda Clerihew (LC) screened the title and abstract of all studies identified by the above search strategy. All review authors screened the full text of the report of each study identified as of potential relevance. Only the studies that meet all of the pre-specified inclusion criteria were eligible for inclusion. The review authors resolved any disagreements by discussion until consensus was achieved.
2. The criteria and standard methods of the Cochrane Neonatal Review Group to assess the methodological quality of the included trials were used. The quality of the included trials in terms of

allocation concealment, blinding of parents or caregivers and assessors to intervention, and completeness of assessment in all randomised individuals. Additional information from the authors of included trials to clarify methodology and results was requested as necessary.

3. A data collection form to aid extraction of relevant information and data from each included study was used. LC and Sean Ainsworth (SA) extracted the data separately, compared the data, and resolve differences by consensus and discussion with WM.

4. The standard methods of the Cochrane Neonatal Review Group to analyse and synthesize the data was used. Outcomes per infant, rather than per catheter, or per catheter-unit time were considered. Outcomes for infants needed to have been reported on an intention-to-treat basis. For example, if an infant was randomly allocated to parenteral nutrition via a percutaneous central venous catheter but subsequently received nutrition via a peripheral cannula because central access was not achieved, the outcome for this infant was still considered in the percutaneous central venous catheter group. The treatment effects of individual trials were estimated and heterogeneity was examined between trial results using the I^2 test for dichotomous outcomes and ANOVA for continuous outcomes. A fixed effects model for meta-analyses was used. The effects seen for categorical data was expressed as relative risk, risk difference, and number needed to treat, with respective 95% confidence intervals. The effects seen for continuous data was expressed as weighted mean difference and 95% confidence interval.

DESCRIPTION OF STUDIES

Nine studies for potential inclusion were identified. Four of these studies, involving a total of 368 infants, fulfilled the inclusion criteria (Annibale 1995; Janes 2000; Ainsworth 2001; Wilson 2007). Details of these trials are presented in the Characteristics of Included Studies table. The other reports that were evaluated, but not included, were not randomised controlled trials (Cairns 1995; Parellada 1999; Liossis 2003) trials that compared outcomes in neonates and children (Schwengel 2004) or trials that did not compare percutaneous central venous catheters with peripheral cannulae (Childs 1995).

The included studies were undertaken in neonatal intensive care units in North America (Annibale 1995; Janes 2000; Wilson 2007) and the United Kingdom (Ainsworth 2001) during the 1990s and early 2000s. The average gestational age of participating infants was 26 weeks (Janes 2000), 27 weeks (Wilson 2007), 28 weeks (Ainsworth 2001) and 29 weeks (Annibale 1995). In all of the trials, infants were recruited within the first week after birth and follow-up continued until the infant no longer required intravenous access for delivery of parenteral nutrition (when the infant tolerated enteral intake).

Three of the studies did not report any data on the pre-specified primary outcomes for this review: nutritional input, growth, and development (Annibale 1995; Janes 2000; Wilson 2007). The lead investigators for these trials were contacted, in order to acquire the relevant data. Ainsworth 2001 reported the proportion of prescribed parenteral nutrition that was actually delivered during the trial period. All of the trials reported data on the incidence of bacteraemia or fungaemia. Two of the trials reported the number of insertion attempts and catheters required to maintain venous access, as well as the total duration of intravenous access (Annibale 1995; Janes 2000). Wilson 2007 report the number of skin punctures but not the duration of venous access. Although not primary outcomes for any of the studies, data on neonatal deaths and deaths prior to hospital discharge were available for three of the trials (Ainsworth 2001; Janes 2000; Wilson 2007).

Three of the excluded studies (Cairns 1995; Parellada 1999; Liosis 2003) reported outcomes between cohorts of infants who received parenteral nutrition via either a percutaneous catheters or a peripheral cannula. Although the groups were matched in terms of gestation and birth weights, the potential for bias at selection for these groups was high. For example, clinicians may have been more likely to use a peripheral cannula in those infants thought to require parenteral nutrition for shorter durations. The fourth excluded study (Schwengel 2004) examined outcomes in paediatric surgical patients and enrolled all age ranges from neonates through to 14 year olds. No stratification had been used in the study and it was not possible to extract the neonatal data.

METHODOLOGICAL QUALITY

Quality assessments are detailed in the Characteristics of Included Studies table. The methodology of the studies was generally good. Random allocation was concealed by using sealed opaque envelopes in three of the trials (Annibale 1995; Ainsworth 2001; Wilson 2007). It is unclear if a satisfactory method of allocation concealment was used in the fourth trial (Janes 2000). The lead investigator was contacted in order to seek clarification. None of the trials was able to blind caregivers to the intervention. Follow-up appears to have been complete for the outcomes reported.

RESULTS

PERCUTANEOUS CENTRAL VENOUS CATHETERS VERSUS PERIPHERAL CANNULA (COMPARISON 01):

Primary outcomes: Nutrient input, growth and development

1. Average daily input of parenteral calories:

None of the studies reported the average daily input of parenteral calories (kilocalories per kilogram per day) and protein (grams per kilogram per day) during the trial period.

2. Average daily proportion of prescribed parenteral calories and protein that were actually delivered during trial period (Outcome 01.01):

Ainsworth 2001 reported a statistically significant difference in the deficit of delivered parenteral nutrition (from that actually prescribed) during the trial period: 3.2% (standard deviation 6.8%) in the percutaneous central venous catheter group versus 10.3% (standard deviation 7.2%) in the peripheral cannula group: mean difference in the percentage of the prescribed nutritional intake actually received: -7.1% (95% confidence interval -11.02, -3.2).

3. Short-term growth parameters:

None of the studies reported any short-term (prior to discharge from hospital) growth parameters.

4. Long-term growth parameters:

None of the studies reported any long-term (following discharge from hospital) growth parameters.

5. Neurodevelopmental outcomes:

None of the studies reported any neurodevelopmental outcomes during infancy and beyond.

Secondary outcomes: Adverse events

1. Death (all causes) before 28 days (Outcome 01.02):

Three of the included studies report this outcome (Janes 2000; Ainsworth 2001; Wilson 2007). Seven of a total of 112 infants recruited to the three studies died. There was no statistically significant difference in the incidence of death before 28 days in either individual trial or on meta-analysis of the three trials: typical relative risk: 1.31 (95% confidence interval 0.36, 4.81); typical risk difference: -0.01 (95% confidence interval -0.04, 0.07). The lead investigator was contacted to inquire if the data on mortality are also available from the fourth trial (Annibale 1995).

2. Death (all cause) before discharge from hospital (Outcome 01.03):

Death before discharge from hospital: These data are identical to those for death before 28 days.

3. Confirmed bacterial infection and 4. Confirmed systemic fungal infection (Outcome 01.04):

Reported as bloodstream infections (sepsis) in all of the trials. Ainsworth 2001: 11 of 24 infants in the percutaneous central venous catheter group versus 10 of 25 infants in the peripheral cannula group had an episode of bloodstream infection: relative risk: 0.81 (95% confidence interval 0.51, 1.29); risk difference: -0.07 (95% confidence interval -0.22, 0.08).

Annibale 1995: 22 of 75 infants in the percutaneous central venous catheter group versus 27 of 75 infants in the peripheral cannula group had an episode of bloodstream infection: relative risk: 1.15 (95% confidence interval 0.6, 2.19); risk difference: 0.06 (95% confidence interval -0.22, 0.34).

Janes 2000 reported the total number of episodes of systemic infection in each group: 11 in the percutaneous central venous catheter

group versus 16 in the peripheral cannula group. However, some of the infants in each group had more than one episode of systemic infection during the trial period. The authors provided further information that 10 of 32 infants in the percutaneous central venous catheter group versus 13 of 31 infants in the peripheral cannula group had an episode of bloodstream infection: relative risk: 0.75 (95% confidence interval 0.39, 1.44); risk difference: -0.11 (95% confidence interval -0.34, 0.13).

Wilson 2007: 15 of 36 infants in the percutaneous central venous catheter group versus 13 of 50 infants in the peripheral cannula group had an episode of bloodstream infection: relative risk: 1.25 (95% confidence interval 0.67, 2.34); risk difference: 0.07 (95% confidence interval -0.12, 0.25).

Meta-analysis of the four trials did not detect any statistically significant difference in the incidence of systemic infection between the groups: typical relative risk: 0.94 (95% confidence interval 0.70, 1.25); typical risk difference: -0.02 (95% confidence interval -0.12, 0.08).

5. Extravasation injury (Outcome 01.05):

Three of the trials reported this outcome (Janes 2000; Ainsworth 2001; Wilson 2007). The lead investigator of the third trial was contacted to determine if the data were available (Annibale 1995).

Ainsworth 2001 reported that one infant in the percutaneous central venous catheter group versus none in the peripheral cannula group had an extravasation injury (a self-limiting episode of groin swelling). Janes 2000 reported that there were no episodes of significant subcutaneous infiltration in either of the study groups. Wilson 2007 reported none of the infants in the percutaneous central venous catheter group versus 5 of 50 in the peripheral cannula group had an extravasation injury. Meta-analysis of the three trials did not find any statistically significant difference: typical relative risk: 0.36 (95% confidence interval 0.07, 1.75); typical risk difference: -0.04 (95% confidence interval -0.09, 0.02).

6. Number of cannulae/catheters per infant used to administer parenteral nutrition during trial period (Outcome 01.06):

These data are not available from one of the trials (Ainsworth 2001). Janes 2000 reported that the mean number of cannulae/catheters used per infant was 4.8 (standard deviation 3.6) in the percutaneous central venous catheter group versus 8.0 (standard deviation 4.2) in the peripheral cannula group. Annibale 1995 reported that the number of catheters per infant did not differ between the two groups (average 4 versus 7). Wilson 2007 reported median and ranges for the number of skin punctures; the median (range) of skin puncture in the percutaneous central venous catheter group was 9 (1, 74) versus 14.5 (1, 111) in the peripheral cannula group. The authors of this study have been contacted for clarification about the means and standard deviations for these data. Meta-analysis of the Annibale 1995 and Janes 2000 studies shows a significant reduction in the number of number of cannu-

lae/catheters in the percutaneous central venous catheter group; weighted mean difference -3.06 (-4.11, -2.01).

Sub-group analyses:

Most infants participating in the four included trials were preterm. No sub-group analysis by birth weight was done.

DISCUSSION

Four randomised controlled trials comparing the use of percutaneous central venous catheters versus peripheral catheters for newborn infants who require parenteral nutrition were found. A total of 368 infants participated in the trials.

Limited data was found in the published reports on the pre-specified primary outcomes for this review. None of the trials assessed effects on growth or any longer term outcomes, nor did they plan to do so. Only one trial assessed nutrient input. Ainsworth 2001 found that infants randomly allocated to receive parenteral nutrition via peripheral cannulae had a statistically significantly higher nutritional deficit during the trial period than infants who received nutrition via a central venous catheter. The 7% difference in deficit seen would, if accumulated over the period of one week, result in the loss of one half of one day's nutrient requirements. The clinical significance of this finding is uncertain. Nutritional deficit during this very critical period of brain growth may have adverse consequences for long term neurodevelopmental outcomes. However, it may be that when enteral nutrition is introduced, catch-up growth can compensate for any deficiencies experienced during the early neonatal period.

All of the trials reported the incidence of systemic (bloodstream) bacterial or fungal infection. Meta-analysis did not demonstrate any statistically significant difference in the incidence of systemic infection between the groups. This finding should be interpreted with some caution as none of the trials blinded caregivers to the nature of the intervention and surveillance bias may have affected the results. Because percutaneous long lines are often considered risk factors for sepsis, caregivers may have had a lower threshold for investigating or diagnosing systemic infection in the percutaneous central venous catheter group. This situation is further compounded by the difficulty in diagnosing true systemic infection versus contamination of blood cultures with skin commensals. The reported systemic infection rates in the central venous catheter group might have been artificially high as caregivers, already more aware of the risks of sepsis might have, attributed symptoms to organisms isolated in contaminated cultures.

None of these studies reported the routine use of prophylactic antibiotics in the prevention of sepsis. Use of antibiotic prophylaxis to prevent sepsis when umbilical arterial and venous catheters are used has not been shown to be beneficial (Inglis 2004; Inglis 2005). Routine use of low dose vancomycin prophylaxis has been

shown to reduce the incidence of sepsis in preterm infants with and without percutaneous central venous catheters, although there are concerns that this may increase the numbers of vancomycin-resistant strains of bacteria (Ocete 1998; Craft 2000; Sherer 2005).

Percutaneous central venous cannulae are thought to be more stable than peripheral cannulae and, therefore, need to be replaced less frequently. Some evidence for this advantage was found. Both Janes 2000 and Annibale 1995 found that the mean number of cannulae/catheters used was statistically significantly lower in the percutaneous central venous catheter group compared with the peripheral cannula group. On average, infants needed about three fewer cannulae/catheters during the trial period. Wilson 2007 reported the number of number of skin punctures required to maintain venous access. It is unclear whether these data were for the actual numbers of catheters or cannulae or included 'failed' attempts. The data were also presented as a median and range. Further data from the lead investigator need to be obtained for inclusion in future updates. The number of catheter/cannulae may indirectly reflect the number of painful procedures in these infants. However, it is not clear whether insertion of a catheter (usually through a larger bore needle and technically more difficult) is more painful for the infant than the insertion of several peripheral cannulae over time. No study has specifically addressed the issue of pain or used pain scores in this respect.

The numbers of infants in these studies were too small to make any conclusions regarding the effects of either the catheters or cannulae on serious clinical adverse effects such as extravasation injuries and cardiac tamponade.

AUTHORS' CONCLUSIONS

Implications for practice

Limited data from one small study suggest that the use of a percutaneous central venous catheter rather than a peripheral cannula is associated with a statistically significant smaller deficit in delivered parenteral nutrition. Percutaneous central venous catheter

use resulted in fewer painful procedures (venepunctures) than peripheral cannula use. No evidence of an increased risk of adverse effects, particularly systemic infection was found. There were no data on long-term growth and developmental outcomes.

Implications for research

Further large randomised controlled trials are needed to determine whether the use of a percutaneous central venous catheter rather than a peripheral cannula for delivering parenteral nutrition has an important benefits for newborn infants. Trials should examine the effects of this intervention on growth and neurodevelopmental outcomes, particularly in very preterm infants where early nutritional intake may play an important role.

POTENTIAL CONFLICT OF INTEREST

Sean Ainsworth is the lead investigator of one of the included trials (Ainsworth 2001).

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TABLES

Characteristics of included studies

Study	Ainsworth 2001
Methods	Blinding of randomisation: Yes Blinding of intervention: No Complete follow-up: Yes Blinding of outcome measurement: Yes
Participants	49 infants cared for a regional neonatal intensive care unit who, in the opinion of the attending clinician were likely to need parenteral nutrition for greater than five days. Median gestation of recruited infants was 28 weeks. Infants excluded: Central venous catheter already in situ (except umbilical venous catheters which were removed at the time of recruitment). Percutaneous central venous catheter required for inotropic support. Royal Victoria Hospital, Newcastle, UK: 1998- 1999.
Interventions	Delivery of parenteral nutrition either via a percutaneous central venous catheter (N = 24), or a peripheral cannula (N = 25).
Outcomes	1. Episodes of "sepsis" - bacteraemia or fungaemia. 2. Proportion of prescribed parenteral nutrition actually delivered.
Notes	Infants in the two arms were of similar gestation and birth weight and age at randomisation. The infants in the percutaneous central venous catheter group were statistically significantly less likely to have had an umbilical line in situ and to have received parenteral antibiotics prior to randomisation. The study was stopped earlier than had been intended because interim analysis revealed a statistically significant difference in nutrient delivery between the groups. Further details on study methodology were available from the investigators.
Allocation concealment	A – Adequate
Study	Annibale 1995
Methods	Blinding of randomisation: Yes Blinding of intervention: No Complete follow-up: Yes Blinding of outcome measurement: Can't tell.

Characteristics of included studies (Continued)

Participants	150 neonates (less than 6 days old) cared for in a large neonatal unit, who were thought likely to require intra-venous access for at least 3 days. Exclusion criteria not stated. Children's Hospital, Charleston, South Carolina, USA: before 1995.
Interventions	Delivery of parenteral nutrition either via a percutaneous central venous catheter (N = 75), or a peripheral cannula (N = 75).
Outcomes	1. Incidence of bacterial or fungal sepsis. 2. Number of insertion attempts and catheters required for intra-venous access. 3. Duration of intra-venous access.
Notes	Trial reported in abstract form only. The lead investigator kindly provided further details of the trial methodology.
Allocation concealment	A – Adequate

Study Janes 2000

Methods	Blinding of randomisation: Can't tell Blinding of intervention: No Complete follow-up: Yes Blinding of outcome measurement: Can't tell
Participants	63 infants of birth weights less than 1251 grams, cared for in a neonatal intensive care unit, and likely to require intra-venous maintenance fluids or total parenteral nutrition at one week of age or when their umbilical venous catheter was removed. Children's Hospital and St Joseph's Hospital, Hamilton, Ontario, Canada: before 2000.
Interventions	Delivery of parenteral nutrition via a percutaneous central venous catheter (N = 32), versus a peripheral cannula (N = 31).
Outcomes	1. Incidence of bacterial or fungal sepsis 2. Number of insertion attempts and catheters required for intra-venous access. 3. Courses of antibiotics. 4. Duration of intra-venous access.
Notes	Random allocation was achieved using a "computer-generated block random number table". Further details on study outcomes were available from the investigators.
Allocation concealment	B – Unclear

Study Wilson 2007

Methods	Blinding of randomisation: Yes Blinding of intervention: No Complete follow-up: Yes Blinding of outcome measurement: Can't tell
Participants	96 infants of birth weights less than 1251 grams or gestation less than 32 weeks at birth, cared for in a neonatal intensive care unit, and likely to require intra-venous maintenance fluids or total parenteral nutrition for at least 5 days of age. Memorial Hermann Children's Hospital, Hamilton, Houston, USA: between 2000 and 2002. Mean gestation was 27.1 (CVCs) and 27.2 (cannula) weeks, mean birth weight was 914 grams and 971 grams respectively
Interventions	Delivery of parenteral nutrition via a percutaneous central venous catheter (N = 46), versus a peripheral cannula (N = 50).
Outcomes	1. Incidence of bacterial or fungal sepsis or death.

2. Number of insertion attempts and catheters required for intravenous access.
3. Extravasation episodes.

Notes	<p>Infants were of similar gestation, birth weights and age at randomisation.</p> <p>Percutaneous central venous catheters inserted by one of team of trained neonatal nurses. Same trained nurses also responsible for dressing changes and line manipulations.</p> <p>No prophylactic antibiotics used.</p> <p>Umbilical venous catheters (if used) were removed prior to enrolment.</p>
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
Cairns 1995	Not a randomised controlled trial. Matched historic cohorts.
Childs 1995	Comparison of percutaneous central venous catheters where the tip is sited either in a peripheral vein or a central vein (not percutaneous central venous catheters versus peripheral cannulae).
Liossis 2003	Not a randomised controlled trial. Matched historic cohorts.
Parellada 1999	Non-randomised comparison of infants with percutaneous central venous catheters and matched controls who had peripheral cannulae
Schwengel 2004	Randomised trial of percutaneous central venous catheters versus peripheral cannulae in neonates and children (ages ranging from neonatal through 14 years) without stratification by age group. We are seeking relevant subgroup data from the trial authors.

ANALYSES

Comparison 01. Percutaneous central venous catheter versus peripheral cannula

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Percentage deficit in nutrient delivery per infant	1	49	Weighted Mean Difference (Fixed) 95% CI	-7.10 [-11.02, -3.18]
02 Death before 28 days (all causes)	3	208	Relative Risk (Fixed) 95% CI	1.31 [0.36, 4.81]
03 Death before hospital discharge (all causes)	3	208	Relative Risk (Fixed) 95% CI	1.31 [0.36, 4.81]
04 Systemic bacterial and fungal infection	4	358	Relative Risk (Fixed) 95% CI	0.94 [0.70, 1.25]
05 Extravasation injury	3	208	Relative Risk (Fixed) 95% CI	0.36 [0.07, 1.75]
06 Number of cannulae/catheters per infant	2	213	Weighted Mean Difference (Fixed) 95% CI	-3.06 [-4.11, -2.01]

INDEX TERMS

Medical Subject Headings (MeSH)

Catheterization, Central Venous [*instrumentation]; Catheterization, Peripheral [*instrumentation]; *Infant, Newborn; Parenteral Nutrition [*instrumentation]; Randomized Controlled Trials

MeSH check words

Humans

COVER SHEET

Title	Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates
Authors	Ainsworth SB, Clerihew L, McGuire W
Contribution of author(s)	Sean Ainsworth (SA) and William McGuire (WM) developed the protocol for this review. All review authors screened the title and abstract of all studies identified by the search strategy. Linda Clerihew (LC) and SA screened the full text of the report of each study identified as of potential relevance. LC and SA extracted the data separately, compared data, and resolved differences by consensus, and with discussion with WM. SA and WM completed the final review.
Issue protocol first published	2003/2
Review first published	2004/2
Date of most recent amendment	21 May 2007
Date of most recent SUBSTANTIVE amendment	05 March 2007
What's New	This updates the review "Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates" published in the Cochrane Database of Systematic Reviews, The Cochrane Library, Issue 2, 2004 (Ainsworth 2004). Our updated search of the literature through February 2007 led to the inclusion of one additional trial (Wilson 2007). Additional data from study by Janes 2000 included.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Sean Ainsworth Consultant Neonatologist Directorate of Women and Children's Health NHS Fife (Acute Hospitals) Forth Park Hospital Bennochty Road Kirkcaldy Fife KY2 5RA UK E-mail: sean.ainsworth@faht.scot.nhs.uk Tel: +44 1592 643355 Fax: +44 1592 642376
DOI	10.1002/14651858.CD004219.pub3
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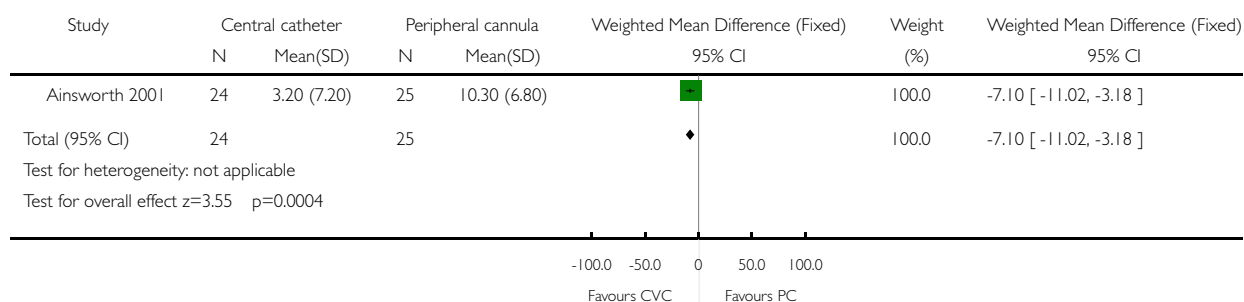
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 01 Percentage deficit in nutrient delivery per infant

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates

Comparison: 01 Percutaneous central venous catheter versus peripheral cannula

Outcome: 01 Percentage deficit in nutrient delivery per infant

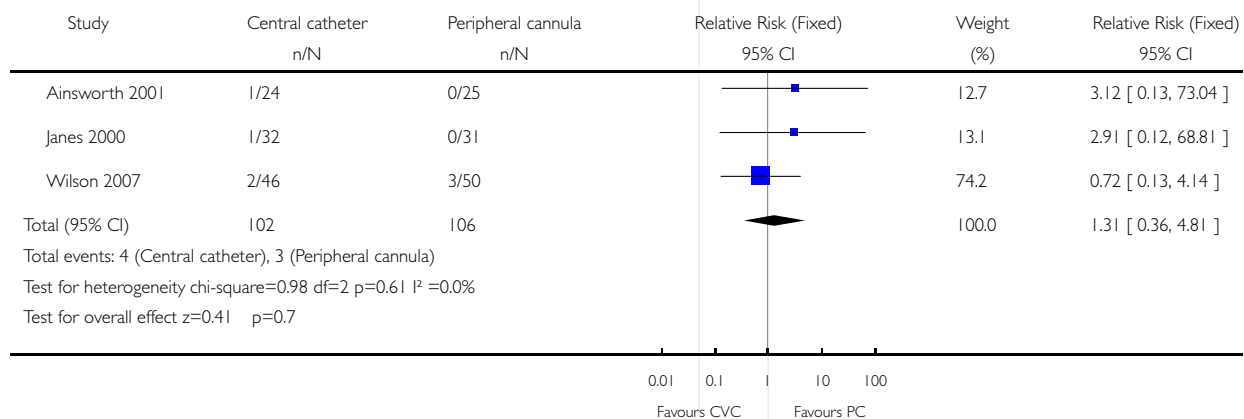


Analysis 01.02. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 02 Death before 28 days (all causes)

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates

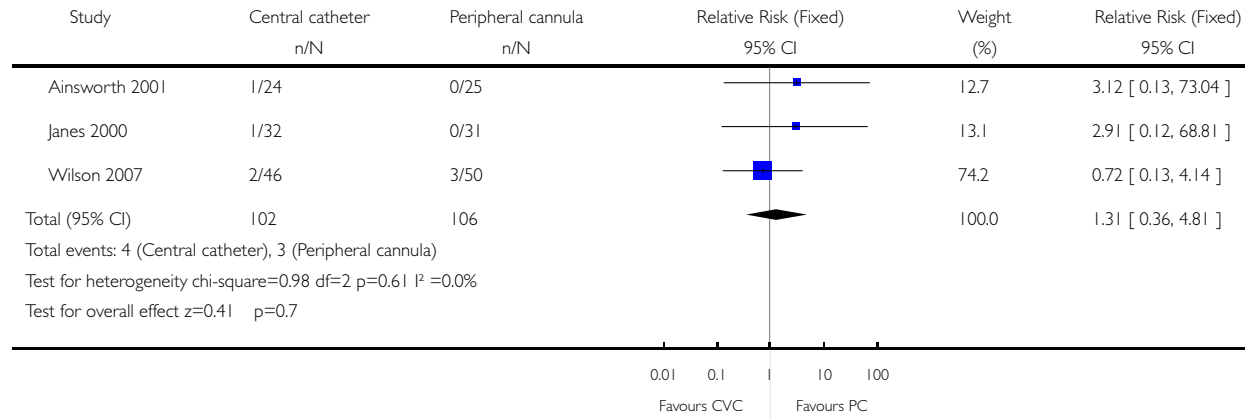
Comparison: 01 Percutaneous central venous catheter versus peripheral cannula

Outcome: 02 Death before 28 days (all causes)



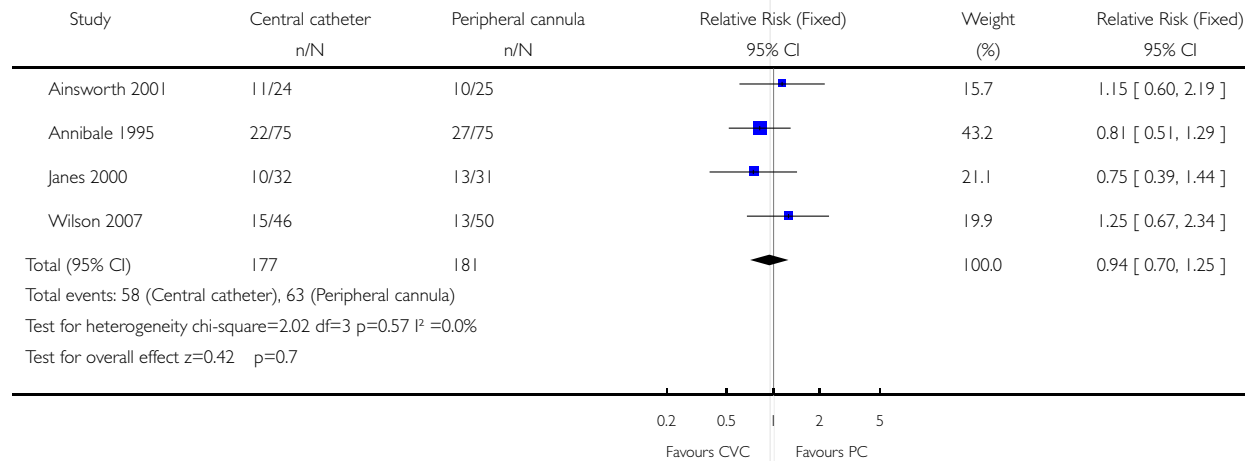
Analysis 01.03. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 03 Death before hospital discharge (all causes)

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates
 Comparison: 01 Percutaneous central venous catheter versus peripheral cannula
 Outcome: 03 Death before hospital discharge (all causes)



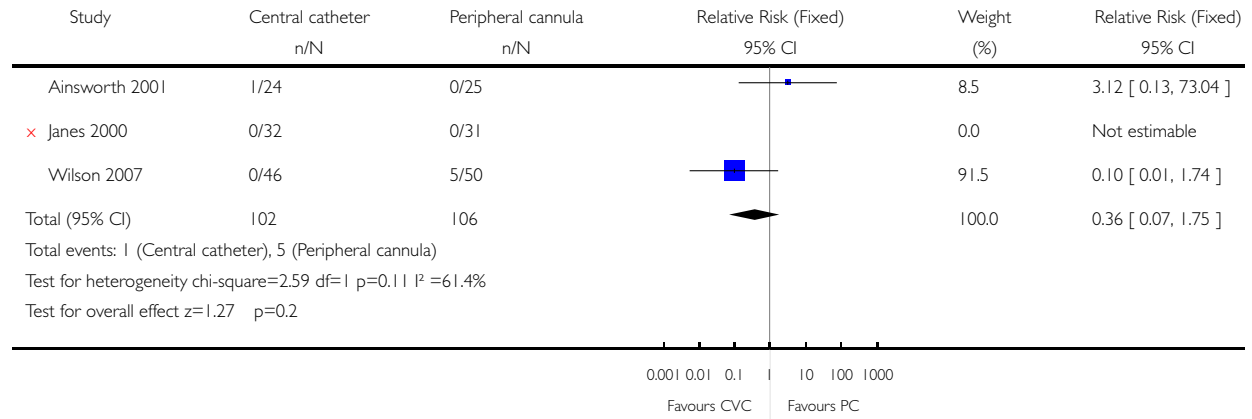
Analysis 01.04. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 04 Systemic bacterial and fungal infection

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates
 Comparison: 01 Percutaneous central venous catheter versus peripheral cannula
 Outcome: 04 Systemic bacterial and fungal infection



Analysis 01.05. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 05 Extravasation injury

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates
 Comparison: 01 Percutaneous central venous catheter versus peripheral cannula
 Outcome: 05 Extravasation injury



Analysis 01.06. Comparison 01 Percutaneous central venous catheter versus peripheral cannula, Outcome 06 Number of cannulae/catheters per infant

Review: Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates
 Comparison: 01 Percutaneous central venous catheter versus peripheral cannula
 Outcome: 06 Number of cannulae/catheters per infant

