Short reports

Total parenteral nutrition and sepsis

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SUMMARY In 1279 very premature or very low birthweight infants the use and duration of treatment with total parenteral nutrition were associated with short gestational age and low birth weight. Infants treated with total parenteral nutrition had a higher risk of sepsis usually caused by *Staphylococcus epidermidis* or *Staphylococcus aureus*.

In very low birthweight (VLBW) infants sepsis is a major problem and an important cause of mortality. Recently changes in incidence and causative organisms have been reported^{1 2} duplicating hospital acquired organisms, particularly *Staphylococcus epidermidis* and *Staphylococcus aureus*.^{1 3} These organisms are often isolated from children who have long term indwelling intravenous catheters in situ.^{1 4}

Few reports have focused on very low birthweight infants. We therefore used the Project on Preterm and Small for Gestational Age Infants to collect prospective data on 1338 infants born alive in 1983 with a gestational age of less than 32 weeks or a birth weight of less than 1500 g, or both.⁵ We studied the use and duration of total parenteral nutrition, the incidence and nature of the sepsis, and the association between them.

Patients and methods

Data on total parenteral nutrition (defined as the infusion of glucose, amino acids, and fat solution intravenously for more than 24 hours) were available for 1279 infants; the remaining infants had died shortly after birth.

Firstly, we investigated the use and duration of total parenteral nutrition, the incidence of bacteriologically confirmed sepsis (defined as a positive blood culture and identification of the causative organism) and clinical sepsis (clinical symptoms and haematological changes such as leucocytosis, neutropenia, an increased number of band cells, or thrombocytopenia) and the association among these

factors, using the non-parametric Kruskal-Wallis analysis of variance. Secondly, we analysed the association between total parenteral nutrition and sepsis using logistic regression analysis. Total parenteral nutrition was entered into the logistic regression equation as an input variable, sepsis as an outcome variable, and gestational age and birth weight as potential confounding factors. The odds ratio was calculated as a measure, comparing the risk of developing sepsis when the infants were or were not treated with total parenteral nutrition.

Results

A total of 822 infants (64%) were treated with total parenteral nutrition. The incidence of treatment was highest (over 80%) in infants with birth weights below 1000 g and gestational ages of 28-32 weeks. More than half the infants were treated for longer than a week, 53 infants for more than four weeks (table 1). The duration of total parenteral nutrition was positively and significantly associated with a lower mean gestational age ($p < 0.0005$) and lower mean birth weight ($p < 0.0001$).

Clinical sepsis was present in 486 cases (38.0%), and bacteriologically confirmed sepsis in 138 (10.8%). Both were clearly associated with the duration of total parenteral nutrition (table 1). No association

Table 1 Duration of total parenteral nutrition, clinical sepsis, and bacteriologically confirmed sepsis

Duration of total parenteral nutrition (days)	No of infants (%)	No with clinical sepsis (%)	No with bacteriologically confirmed sepsis (%)
0	457 (36)	99 (20)	28 (20)
1-7	396 (31)	126 (26)	33 (24)
8-28	373 (29)	222 (46)	65 (47)
>28	53 (4)	39 (8)	12 (9)
Total	1279 (100)	486 (38)	138 (11)

Table 2 Causative organisms in bacteriologically confirmed sepsis

Organism	Patients not receiving total parenteral nutrition No (%)	Patients receiving total parenteral nutrition No (%)
<i>S epidermidis</i>	1 (4)	40 (36)
<i>S aureus</i>	3 (11)	21 (19)
<i>E coli</i>	7 (25)	17 (16)
Streptococcus group B	8 (29)	10 (9)
Other	9 (32)	22 (20)
Total	28 (100)	110 (100)

was found between sepsis and gestational age or birth weight.

Logistic regression analysis with total parenteral nutrition as an input variable, clinical sepsis as an outcome variable, and gestational age and birth weight as potential confounding factors, showed that infants treated with total parenteral nutrition had a significantly higher risk of sepsis (odds ratio 3.1; 95% confidence interval 2.4 to 4.0; $p < 0.0001$) than infants not so treated. Total parenteral nutrition for more than seven days was even more strongly associated with sepsis (odds ratio 4.4; 95% confidence interval 3.4 to 5.6; $p < 0.0001$), compared with those who had received it for seven days or less, or those who had not received it at all.

The bacteria isolated from the blood cultures in cases of bacteriologically confirmed sepsis in treated infants showed a pattern different from that in infants not given total parenteral nutrition; with *S epidermidis* and *S aureus* outnumbering other micro-organisms (table 2).

Discussion

Between 1977 and 1978 La Gamma *et al* found that 48% of infants with birth weights below 1000 g received partial and 37% received total parenteral nutrition.⁶

In our study population 64% of infants were treated with total parenteral nutrition, a doubling of its use over five years. The widespread use of this kind of intensive treatment reflects the fact that the commercially available solutions have been adapted for premature newborn infants.

The association between indwelling catheters and the occurrence of sepsis, described in reports on smaller study populations, was confirmed in our large survey.¹⁻⁶ The association between the use of total parenteral nutrition and sepsis was clear, as was the association between the duration of total

parenteral nutrition and sepsis. The amount of perinatal data available enabled us to take the most important potential confounding factors into consideration when we further analysed this association by a multivariate statistical technique. Low gestational age might have been in itself associated with sepsis, and because its association with the duration of total parenteral nutrition is clear it might have caused the 'crude' differences we found. By including gestational age in the logistic regression analysis, the calculated odds ratio (3.1) is corrected for gestational age; that means that the increased risk of sepsis is associated with total parenteral nutrition.

As far as causative organisms are concerned, *S epidermidis* and *S aureus* were found in 47% (65 of 138) of all cases of bacteriologically confirmed sepsis, which is in keeping with the findings in a smaller study group.⁶ In our infants treated with total parenteral nutrition this was the case in 55% (61 of 110), increasing from 46% of infants given total parenteral nutrition for less than a week to 84% of infants treated for more than four weeks. Sepsis in infants not so treated was more often caused by *E coli* and streptococcus group B.

The present study has shown that the use of total parenteral nutrition is widespread in The Netherlands. Although the risk of sepsis seemed to be significantly increased by total parenteral nutrition, the causative organisms were fairly benign. We suggest that the advantages of total parenteral nutrition outweigh the disadvantages of sepsis in this group of infants.

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