REDUCTION IN PARENTERAL NUTRITION RELATED COMPLICATIONS IN THE NEWBORN

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ABSTRACT

A comparison of total parenteral nutrition (TPN) related complication in newboms was made between two study periods, namely, 1986 (Study A) and 1989-90 (Study B). A significant reduction was seen in all complications in Study B. Local complications (thrombophlebitis, gangrene, abscess) reduced from 80.0 to 29.4%, septicemia from 52.0 to 11.7% and metabolic complications from a computed mean of 1.6 episode per baby to 0.88 episode per baby.

The reduction in these complications has been attributed to the following additional inputs in the recent study (i) Additional staff (research officers, nurses, biochemist); (ii) Better training of resident staff; (iii) Use of a laminar flow system for mixing solutions; (iv) Specially designed locally manufactured intravenous sets and accessories; and (v) Use of well balanced nutrient solutions.

Outstanding problems perceived are–high incidence of TPN-related cholestasis (14.7%), azotemia (26.4%), central catheter-related sepsis (75.0%) and the falling, but yet high cost of the technique (Rs. 650 per day).

Key words: *Neonatal nutrition, Parenteral nutrition, TPN-related complications.*

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Parenteral nutrition, has perhaps been one of the most important recent advances responsible for the dramatic improvement in the survival of the small preterm infant in the developed world(1-3). Lack of funds, facilities and trained staff have no doubt been the main deterrants in the use and development of total parenteral nutrition (TPN) in India. At the same time, however, it has now increasingly become a 'felt need' in Neonatal Intensive Care Units all over the country, committed to the care of the small, low birthweight and malnourished baby.

In 1986, a preliminary study was carried out at our Neonatal Unit, to assess the feasibility of parenteral nutrition in our situation and to analyse its outcome and complications. The study concluded that although TPN was feasible in specialised centres with some additional demands to the existing infrastructure, the rate of complications was alarmingly high and the cost exhorbitant(4). This preliminary experience, however, conceived several newer inputs and adaptations, which were later introduced in a further study in 1989-90. This analysis evaluates the effectiveness of these improvisations in reducing TPN complications.

Material and Methods

The study comprises of a comparison of TPN-associated complications in neonates during two periods, namely, (*i*) 1986-87 (Study A); and (*ii*) 1989-90 (Study B).

In Study A, the patients were 25 neonates, whose clinical condition had precluded oral feeding for more than 5 days, and whose parents had afforded the cost; while in Study B the 34 neonates were very low birth weight (VLBW) babies (birthweight <1250 g), who were enrolled in a

randomized controlled manner for a research project. A few other neonates with feeding problems (necrotising enterocolitis, T-O fistula) were also included in this group.

Methodology

Study A (1986-87): The techniques, constituents, schedule and cost of parenteral nutrition employed during this study were as detailed earlier(4).

Study B (1989-90): During this period, the following additional features were introduced in the methodology described above: (*a*) *A laminar flow system:* This system which was available in an adjacent research laboratory was used for mixing of nutrient solutions (earlier this was being done in the ward itself). (*b*) *The nutrient solutions:* The crystalline aminoacid solution Aminoplasmal-paed (B. Braun) and the lipid emulsion Lipofundin 10% (B. Braun) were used for the study. These solutions were available in packs of 100 ml and were shared between neonates taken up for hyperalimentation on the same day. Bottles, once opened, were not used again on subsequent days. (*c*) *Infusion technique:* Disposable syringes and transfer sets were utilised for separation of nutrient solutions into sterile, empty evacuated containers (McGaw Laboratories). Specially designed (locally manufactured) intravenous sets with minimum number of units in the assembly were used with infusion pumps (*Fig. 1*). These sets were changed daily and peripheral lines were preferred for infusions. (*d*) *Additional staff:* As against a 'one man team' in the earlier study, an additional full-time research officer was now made available. The resident and nursing staff became more conversant with the technique of hyperalimentation. Special

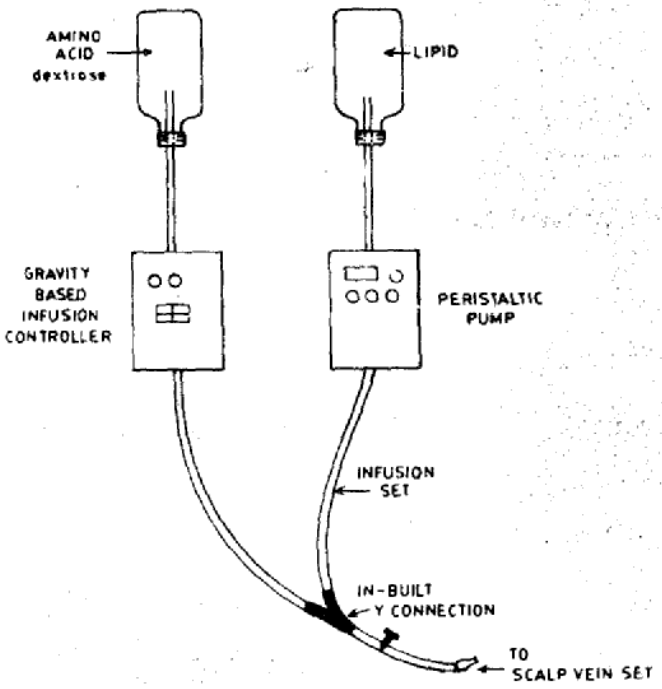

Fig. 1. Total parenteral nutrition infusion techniques

nurses were employed in certain cases in addition to the existing staff. A full-time biochemist (technician) with special responsibilities of monitoring TPN patients were added to the nursery staff. (*e*) *Monitoring:* Monitoring protocol was now strictly followed with additional investigations of triglycerides and serum ammonia.

Analysis

The complications in these two study periods were analysed by feeding the entire data in an IBM PC/XT computer, using software programmes based on dbase III plus. Comparisons between two periods were made by applying usual statistical tests of significance (Student 't' test, χ^2 test).

Results

A total of 25 newborns (Study A) and

34 newborns (Study B) were administered parenteral nutrition during the two study periods. The clinical features, hyperalimentation protocol and mortality of these babies is compared in *Table I*.

The mean birthweight and gestational age were lower in Study B. Further, babies in this group received TPN for a longer duration with higher aminoacid and lipid intakes. While all babies in Study A were given peripheral hyperalimentation, 6 babies (17%) in Study B received central hyperalimentation. Inspite of a distinctly higher risk in babies of Study B, the mortality was 52.9% which was lower than Study A (64%), though not reaching statistical significance ($p>0.05$).

The TPN-related complications seen in the 2 groups are analysed in *Table II*.

1. Local Complications

Complications related to intravenous

TABLE I — *Clinical Parameters of Newborns Receiving Parenteral Nutrition During Study A and Study B*

Parameters	Study A (1986-87)	Study B (1989-90)
1. Total number of cases (n)	25	34
2. Mean Birthweight in g × ±SD	1616 ± 653	1225 ± 328
(Range)	(800-2700)	(780-2000)
3. Mean gestational age in weeks ± SD	34.8 ± 4.9	31.7 ± 3
(Range)	(28-40)	(28-40)
4. Associated Problem: n (%)		
Uncomplicated VLBW	10 (40)	8 (23.5)
Septicemia	4 (16)	14 (41.1)
Necrotising enterocolitis	4 (16)	2 (5.8)
Surgical cases	6 (24)	11 (2.9)
Hyaline membrane disease	0 (0)	11 (32.6)
Others	1 (4)	6 (17.6)
5. Hyperalimentation Protocol:		
(*a*) Maximum protein intake in g/kg/day × ± SD	1.9 ± 0.6	2.45 ± 0.75
(Range)	(1.5-3)	(0.5-3.5)
(*b*) Maximum lipid intake in g/kg/day × ± SD	1.7 ± 0.5	2.16 ± 0.86
(Range)	(0.5-3)	(0.5-3)
(*c*) Duration of TPN in days × ± SD	6 ± 2.3	8.9 ± 3.2
(Range)	(2-8)	(2-16)
(*d*) Route of TPN	All Peripheral	Peripheral 83% Central 17%
6. Mortality		
n	16	18
%	(64)	(52.9)

TABLE II – *Comparison of TPN-Related Complications (%) in Study A and Study B*

Complications	Study A (1986-87)	Study B (1989-90)
1. Local	80*	29.4*
Thrombophlebitis	56.6	14.7
Cutaneous gangrene	16	5.8
Abscess at intravenous site	12	2.9
2. Infective (septicemia)	52*	11.7*
3. Fluid imbalance		
Overload, dehydration	36*	2.9*
4. Metabolic	1.6 episode per baby*	0.88 episode per baby*
Electrolyte imbalance	16	2.9
Metabolic acidosis	24	2.9
Hypoglycemia	–	8.8
Hyperglycemia	12	2.9
$CaPO_4$ imbalance	12	2.9
Hyperlipidemia	–	8.8
Hyperbilirubinemia	28	4.7
Azotemia	60	26.4
Elevated transaminases	4	2.9
5. Others		
Bleeding diathesis	24*	2.9*
Cholestasis	12	14.7
Thrombocytopenia	24*	0*

*Statistically significant ($p < 0.05$)

infusion sites (thrombophlebitis, cutaneous gangrene and abscess at intravenous site), were dramatically lesser in Study B as compared to Study A.

2. Septicemia

A significant decline in TPN-related septicemia was seen from 52% (Study A) to 11.7% (Study B).

In Study A, septicemia was a major cause of mortality (40%). Blood cultures grew pseudomonas(4), *Staphylococcus albus* (n=2), *E. coli* (n=1) and were sterile in the remaining 3 babies. In 2 babies, pseudomonas was also isolated from intravenous infusion site abscesses.

In Study B, 4 newborns developed fulminant sepsis, while on parenteral nutrition, of which 3 succumbed. Central line (umbilical vein) was used for hyperalimentation in three of these babies. Cultures of catheter tip done after the central line was removed, however, revealed no organisms.

3. Fluid Imbalance

Fluid overload or dehydration were seen in 9 patients in Study A, and only 1

patient in Study B (2.9%) ($p<0.001$).

4. Metabolic Complications

Electrolyte abnormalities (hyponatremia, hypokalemia, hyperkalemia), metabolic acidosis and azotemia were all significantly lesser in Study B. However, hypoglycemia and hyperlipidemia were more commonly encountered in Study B. Two newborns in Study A had metabolic abnormalities which could not be defined, namely, unexplained refractory seizures and sudden death, while on TPN.

As some babies had more than one metabolic problem during the course of their TPN, these complications were computed as mean episodes per baby, and were significantly lower in the latter study.

5. Other Complications

(*a*) *Coagulopathy:* Coagulopathy with disseminated bleeding was seen in 6 newborns (24%) in Study A, of which 4 who had associated septicemia succumbed. An abnormal coagulogram was detected in only one baby in Study B.

(*b*) *Cholestasis:* TPN-cholestasis was seen in 3 neonates in Study A (12%) and 5 neonates in Study B (14.7%). In Study A, all the 3 babies who developed colestasis succumbed. Postmortem liver biopsy done in one patient showed marked cholestasis with portal tract infiltration. In Study B, 4 babies developed cholestasis while on TPN, whereas one developed the complication 2 weeks after discharge. Three of these babies had clearing of jaundice and normal liver function within a month, whereas one baby died of hepatic failure (one newborn was lost to follow up).

Discussion

The proper use of parenteral nutrition in newborn has been of great benefit despite its potential hazards and complications. Further refinement, however, in its composition and application is necessary to maximise benefits and minimise risks. Our paper demonstrates that this can be achieved by technology transfer suitable to our situation and indigenisation of the various requirements.

Over the last four years, there has been a reduction in mortality in babies receiving hyperalimentation in our unit. Infact, the lower mortality (although not reaching statistically significant proportions) has been possible inspite of the distinctly higher risk in the later study. However, it is difficult to demonstrate the effectiveness of TPN in terms of reduction of mortality, as this, in any case will be high in these critically-ill newborns and deaths are often due to unrelated causes such as intracranial hemorrhage, hyaline membrane disease or necrotising entercolitis. It is, thus, the reduction in the TPN-related complications which gives a better perspective regarding the safety of the technique. It has been heartening to see a dramatic reduction in these complications in the later study.

Of all the positive inputs incorporated in the later study, four were perhaps most important: (*i*) Additional trained staff, (*ii*) Laminar flow system, (*iii*) Local adaptations of equipment and techniques, and (*iv*) More suitable nutrients.

In 1986, parenteral nutrition was started with a view to assess its feasibility in our set up. The author was single-handedly responsible for most of the jobs, usually done by a team of experts in the West (*viz.* Pharmacist, Biochemist, Nurse, Neonatologist, Microbiologist). As feasibility was

ensured, more staff was made available for this. With the addition of a full-time Research Officer and a Biochemist, clinical and biochemical monitoring improved. Resident doctors and nurses became more conversant with the techniques, leading to expertise in setting up and maintaining intravenous lines at peripheral sites. Motivated mothers were also pressed into service and trained to report extravasations at the earliest. There is no doubt that the addition of staff was responsible for bringing down the unacceptably high local complication rate from 80 to 29.4%. It is felt that with further training of the staff and more use of intravenous catheters, rather than needles, the rate will come down further.

The local adaptations of equipment and techniques were perhaps most responsible for reduction of the dangerous complication of sepsis. In the earlier study, the mixing of solutions (although with all aseptic precautions) was done in the ward itself. This is obviously unsatisfactory and a laminar flow hood appears to be an essential prerequisite for successful parenteral nutrition(7,8). This can often be located in laboratories or pharmacies of large hospitals (as we did), but it may be difficult for neonatal units to procure this equipment solely for the purpose of hyperalimentation as it costs Rs. 30,000-35,000. In the absence of the laminar flow system, it is recommended that the solution should be used in their original packs without external mixing, separation or sharing.

Specially designed intravenous sets, mixing sets and connectors were responsible for reduction in the risk of contamination of nutrient solutions. The process of separation and mixing of solutions was more convenient and safe. The sharing of solutions, thus possible, effectively cut down the cost, while still not compromising on safety. Infact, the current incidence of TPN-related septicemia compared quite favourable to Western studies of 6 to 33% (8-11). However, as septicemia is a hazardous and sometimes fatal complication of TPN, further efforts will have to be made in its reduction. An important consideration is, perhaps, the use of central lines. Of the 4 babies who died due to TPN-related sepsis in the later study, 3 had central lines (mortality 75%). Such severe catheter-related infections have been described from various centres(12-14) and as such central lines should be used only as a last resort in the complete non-availability of peripheral sites.

The significant decline in metabolic complications could no doubt be attributed to close biochemical monitoring, with early detection and prompt correction of abnormalities. But, perhaps, even more important was the nature of the aminoacid solution available for the later study (Aminoplasmal paed). This commercially available formulation appears to be more suited for neonates and is responsible for reduction in incidence of azotemia and metabolic acidosis. The incidence of these complications in the later study is similar to other western reports(15,16). Recently, crystalline aminoacid solution, Alamin N (Albert David Pvt. Ltd.) has become available. This Indian solution has an acceptable aminoacid constitution and is considerably cheaper as compared to the imported solutions. We are persuading the Indian manufacturers to make these solutions available in smaller packs for wider use.

Interestingly the above mentioned additional inputs in the technique of hyperalimentation effectively cut down the cost of TPN per day from Rs. 900/- to Rs. 650/- but obviously needs further reduction.

Of particular concern is the apparent increase in the incidence of cholestasis, hypoglycemia and hyperlipidemia. These could well have been detected more frequently because of better monitoring. This could also have been due to preselection of VLBW babies in whom these problems are known to be common. Even higher incidence of cholestasis (upto 50%) has been reported on prolonged administration of TPN in VLBWs. It is said to be of multifactorial etiology and the preventive steps could be balancing the use of aminoacids and lipids and by scrupulously avoiding TPN in established septicemia. Further improvement in the biochemical monitoring is needed with micromethod systems, serum ammonia and aminoacidograms.

It now appears that establishment of satisfactory techniques of TPN, though challenging, are feasible for the care of high risk neonates in our country. Technical problems and operational questions are abundant but apparently 'answerable' with use of local adaptations and technology transfer in a continuing manner. Perhaps, the overwhelmingly important guideline to be adapted from established centres in an effort to keep TPN within 'safe' limits is by an obsessional attention to detail!

In conclusion, the following recommendations can be suggested to Neonatal Special Care Units, contemplating TPN in the present situation; adequate, well trained staff, appropriate nutrient solutions and careful clinical and biochemical monitoring are a must. Mixing of solutions should be done only under a laminar flow hood. Central lines are to be avoided as far as possible. Local adaptations and indigenisations are essential to further bring down the cost of the technique.

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