Impact of a new aggressive nutrition policy incorporating early introduction of parenteral nutrition and mother's own milk on growth of preterm infants

Chuen Siang Low, Jacqueline J Ho, Revathy Nallusamy
Penang, Malaysia

Background: **Most of the evidence on early feeding of preterm infants was derived from high income settings, it is equally important to evaluate whether it can be successfully implemented into less resourced settings. This study aimed to compare growth and feeding of preterm infants before and after the introduction of a new aggressive feeding policy in Penang Hospital, a tertiary referral hospital in a middle income country.**

Methods: **The new aggressive feeding policy was developed mainly from Cochrane review evidence, using early parenteral and enteral nutrition with standardized breastfeeding counselling aimed at empowering mothers to provide early expressed milk. A total of 80 preterm babies (34 weeks and below) discharged from NICU were included (40 pre- and 40 post-intervention). Pre and post-intervention data were compared. The primary outcome was growth at day 7, 14, 21 and at discharge and secondary outcomes were time to full oral feeding, breastfeeding rates, and adverse events.**

Results: **Complete data were available for all babies to discharge. One baby was discharged prior to day 14 and 10 babies before day 21, so growth data for these babies were unavailable. Baseline data were similar in the two groups. There was no significant weight difference at 7, 14, 21 days and at discharge. More post-intervention babies were breastfed at discharge than pre-intervention babies (21 *vs.* 8, *P*=0.005). Nosocomial infection (11 *vs.* 4, *P*=0.045), and blood transfusion were significantly lower in the post-intervention babies than in the pre-intervention babies (31 *vs.* 13, *P*=0.01). The post-intervention babies were more likely to achieve shorter median days (interquartile range) to full oral feeding [11 (6) days *vs.* 13 (11) days, *P*=0.058] and with lower number affecting necrotising enterocolitis (0 *vs.* 5, *P*=0.055).**

Conclusions: **Early aggressive parenteral nutrition and early provision of mother's milk did not result in improved growth as evidenced by weight gain at discharge. However we found more breastfeeding babies, lower nosocomial infection and transfusion rates. Our findings suggest that implementing a more aggressive feeding policy supported by high level scientific evidence is able to improve important outcomes**

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Introduction

One of the goals of nutrition in preterm babies is to achieve a postnatal growth and nutrient accretion rate that is equal or near to that of intrauterine rates.[1] However, this is often hard to achieve due to numerous factors relating to prematurity. Recent years have seen changes in the feeding of preterm infants. Traditionally, enteral feeds of very low birth weight or ill preterm babies were delayed for days or even weeks after birth,[2] while overly aggressive feeding was thought to be associated with problems such as necrotising enterocolitis (NEC), feed intolerance and intolerance to parenteral nutrition components.[3,4] However, evidence for early feeding has become increasingly strong and it now appears that the benefits outweigh the potential harms.[5-8] There is evidence of an important association between early introduction of protein and energy and an increased Mental Development Index scores at 18 months postnatal age.[9] In addition, early aggressive feeding, both parenteral and enteral is associated with

Author Affiliations: Penang Medical College, Penang 10450, Malaysia (Low CS); Department of Pediatrics, Penang Medical College, Penang, Malaysia (Ho JJ); Department of Pediatrics, Penang Hospital, Penang, Malaysia (Nallusamy R)

Corresponding Author: Chuen Siang Low, Penang Medical College, Penang 10450, Malaysia (Email: Eugenelcs33@hotmail.com)

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a 66% reduction in risk of postnatal malnutrition at 40 weeks postmenstrual age.[10] Studies have also suggested that early feeding does not increase the risk of NEC.[11-13] There has been an increasing emphasis on the use of breastmilk for preterm babies. Breastmilk was associated with reduced rates of NEC and nosocomial infection.[8]

A new aggressive feeding policy for preterm infants admitted to the Neonatal Intensive Care Unit (NICU) was adopted by Penang Hospital in July 2011. It aimed to provide early parenteral and enteral feeding as well as the early provision of mothers' own milk for preterm babies.

We carried out an audit by examining the growth and feeding of the preterm babies before and after the introduction of the new policy. Since most of the evidence on early feeding was derived from high income settings, it is equally important to evaluate whether it can be successfully implemented into less resourced settings. The aim of this retrospective audit was to examine whether growth, feeding tolerance and breastfeeding rates had improved without adverse events.

Methods

Study setting

The study took place in the NICU of Penang Hospital, a tertiary referral Hospital in Penang, Malaysia (a middle income country) serving a population of 1.5 million people. The NICU is a 10-intensive care bed unit that serves 5000 inborn deliveries per year as well as referred babies from surrounding hospitals. Approximately 60% of admissions are inborn.

Inclusion criteria

All preterm babies (34 weeks or below) admitted to the NICU who required parenteral nutrition (PN) as judged by the attending physician were included. Only babies who were discharged before the first week or those who died before discharge were excluded.

Study design

The study was a before and after study design. Data from 80 preterm babies (40 pre intervention and 40 post intervention) admitted into the NICU between July 2009 and October 2012 were collected for the study. Babies were selected from the Malaysian Neonatal Registry (MNNR), a prospective registry of babies admitted to all NICUs in Malaysia including Penang Hospital. The new feeding policy was implemented in July 2011 with an implementation period of 6 months (3 months before and after) during which hospital staffs were trained on the new feeding policy. Therefore the pre intervention population consisted of babies born before April 2011 (recruited consecutively from that date backwards) and post-intervention babies were recruited consecutively forwards from October 2011. A power calculation showed that this number could detect a weight difference of 150 g at 3 weeks of age between the two groups. The primary outcome was growth at day 7, 14, 21 and at discharge and secondary outcomes were time to full oral feeding, breastfeeding on discharge, and adverse events.

Description of the new feeding policy

During the period prior to the new policy, PN was prescribed on an individual basis starting with low levels of proteins such as 0.5g/kg/day and lipids and building up by 0.5 g/kg/day over several days. Protein provided by PN would be started usually on day three of life and lipid would be started a day later. There was no policy for the initiation of oral feeding. Oral feeding was generally started at the earliest by day 2 and sometimes as late as day 5. Mother's breast milk was preferred but attempts to obtain it were not consistent.

The new policy was developed mainly from Cochrane review evidence.[5-8] It included a standardized PN formula aimed at providing early PN in the form of calories and amino acids built up to 3g/kg/day within the first 24 to 72 hours of life, as well as the early introduction of mother's own milk. This would be as soon as the infant was considered stable enough to feed and mothers own milk was available. The policy was implemented by firstly developing the written policy, secondly by establishing standardized PN and a checklist of key breastfeeding messages to be delivered in stages to mothers of preterm babies and thirdly a half day structured training session using the SCORPIO technique[14] which was delivered to all staff of the NICU. The training session covered the evidence for early feeding, use of the key messages checklist, breastfeeding counselling skills and an overview and discussion on how to implement the policy.

Data collection and analysis

Data were collected from the MNNR, as well as the individual medical records of included babies. Length of hospital stay, respiratory support and adverse outcomes which included nosocomial infection, NEC, patent ductus arteriosus (PDA) and oxygen dependency were obtained from the MNNR. Nosocomial infection was defined as sepsis beyond 3 days of age, either the finding of a positive blood culture or antibiotic prescription extending beyond 72 hours. Respiratory support was defined as the total number of days the infant was on either continuous positive airway pressure

(CPAP) or intermittent positive pressure ventilation (IPPV). Data on growth and feeding were obtained retrospectively from the case notes. Weight at day 7, 14, 21 and at discharge were recorded. Feeding data (day of life of onset of feeding, day of life full enteral feeding achieved, and type of feeding on discharge) were obtained from the daily feeding chart. PN data, obtained from PN request forms, consisted of day of life PN was started, maximum dose was achieved and the total days of PN. Full oral feeding was defined as 150 mL/kg/day while full PN was considered achieved when amino acids levels were 3.0 g/kg/day and lipids at least 2.5 g/kg/day.

Data were analysed using SPSS (IBM version 18). Pre-intervention data were compared with post intervention data. Normal continuous data were expressed as means and standard deviation (SD) and analysed using an independent *T*-test. Non-normal data were expressed as medians and interquartile range (IQR) and analysed using the Man-Whitney-*U* test. Categorical data were cross tabulated and analysed using Chi Square or Fisher's Exact Test when applicable. A *P* value of <0.05 was taken to be significant.

Ethics statement

Ethics approval for this study was obtained from the Malaysian Research Ethics Committee (MREC) (NMRR-13-482-16305). As this was a retrospective case audit we were granted a waiver of the need for individual written consent from next of kin or caretakers of included babies. All data were collected onto a data extraction form specially designed for the study. No identifying data were recorded.

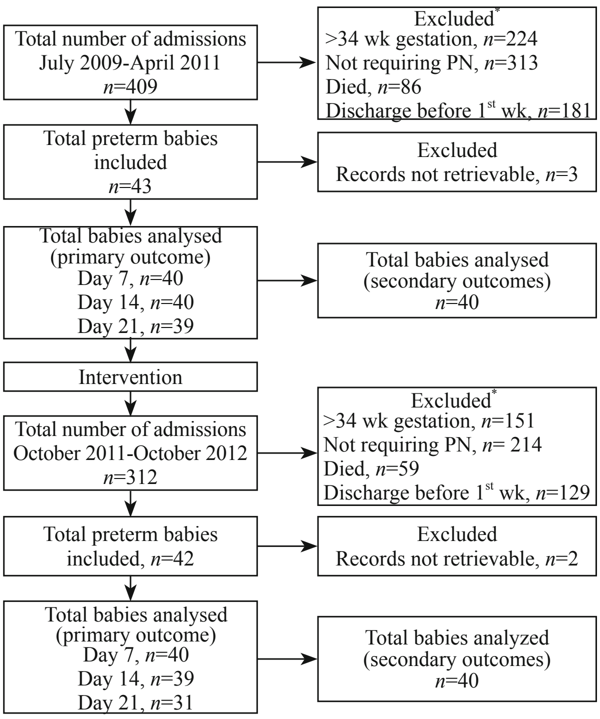

Fig. 1. Flow chart showing numbers of infants who were eligible for inclusion. *: Babies may be excluded for more than one reason.

Results

We included 40 babies pre-intervention and 40 babies post-intervention. Fig. 1 shows the numbers of infants eligible and the reasons for exclusion. Data obtained

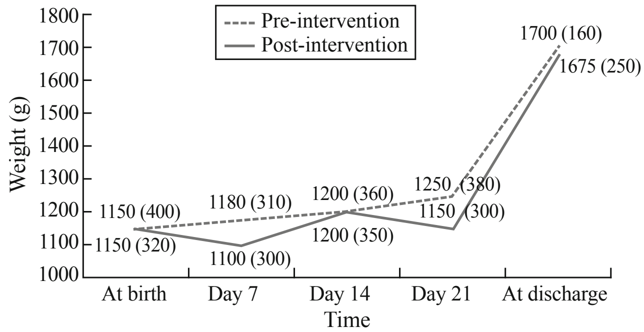

Fig. 2. Median body weight at birth, on day 7, 14, 21 and discharge for pre and post intervention babies. Numbers in brackets represent interquartile ranges.

Table 1. Baseline characteristic of included babies

Baseline characteristics	Pre-intervention (*n*=40)	Post-intervention (*n*=40)
Mean mother's age (y)	31.28±5.58	31.63±5.78
Gestation (wk)		
24-28, *n*	12	8
29-32, *n*	25	31
33-34, *n*	3	1
Birthweight (g)		
0-749, *n*	0	2
750-999, *n*	4	6
1000-1499, *n*	30	23
1500-2499, *n*	6	9
Male, *n*	15	18
Median days of respiratory support*, d	9.5 (13.5)	8.5 (11.8)
Median highest FiO_2† (%)	21 (8)	30 (19)

All numbers in brackets denotes interquartile range (IQR). FiO_2: fraction of inspired oxygen. *: respiratory support includes mechanical ventilation via endotracheal tube and nasal continuous positive airway pressure; †: *P*=0.01.

Table 2. Feeding of preterm babies before and after the new policy

Feeding data	Pre-intervention (IQR) (*n*=40)	Post-intervention (IQR) (*n*=40)
Day of life feeding started *	3 (2)	2 (1)
Day of life full oral feeding achieved†	13 (11)	11 (6)
Day of life PN started	2 (1)	2 (1)
Day of life full PN achieved‡	7 (4)	2 (1)
Duration of PN	9 (8)	7 (5)

All data are shown as medians and interquartile range (IQR). *: *P* =0.006; †: *P*=0.058; ‡: *P*<0.001. PN: parenteral nutrition.

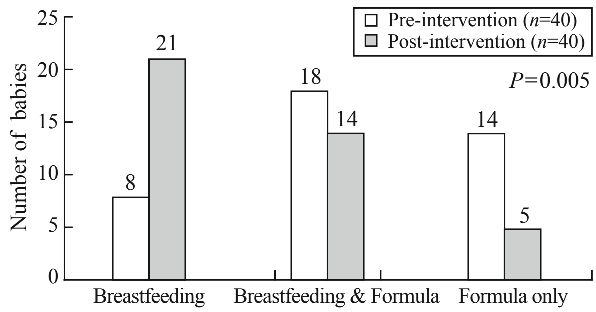

Fig. 3. Type of feeding upon discharge.

Table 3. Adverse outcomes in the pre and post intervention group

Complications	Pre-intervention (*n*=40)	Post-intervention (*n*=40)
Nosocomial infection*	11	4
Patent ductus arteriosus	11	14
Necrotising enterocolitis†	5	0
Blood transfusion‡		
None	9	27
One or more	31	13
Oxygen dependency beyond 28 d	7	7
Oxygen dependency beyond 36 wk	4	5

*: P=0.045; †: P=0.055; ‡: P=0.01.

retrospectively were remarkably complete. One baby was discharged prior to day 14 and 10 babies before day 21 so growth data at these data points for these babies were not available. There was no significant difference in baseline characteristics except post-intervention babies had a higher median highest fraction of inspired oxygen (FiO_2) (Table 1).

There was no overall difference in weight between the two groups (Fig. 2). Weight difference at birth, day 7, day 14, day 21 and at discharge were not significantly different.

Enteral feeding was started significantly earlier in the post-intervention group than in the pre-intervention group [median days (IQR) 2(1) *vs.* 3(2), P=0.006)] (Table 2). A trend was also observed for earlier achievement of full oral feeding in the post-intervention group (P=0.058). There was no significant difference in the day of life PN was started and the total days of PN. However, the median day of life full PN was achieved significantly earlier in the post-intervention group than that in the pre-intervention group [7(4) *vs.* 2(1), P=0.000].

There was a significant difference in the type of feeding upon discharge for the two groups of babies (P=0.005; Fig. 3). Significantly more babies were discharged on exclusive breastfeeding and any breastfeeding in the pre-intervention group than that in the post-intervention group (21 *vs.* 8, P=0.005; 35 *vs.* 29, P=0.034).

There was a significant reduction in nosocomial infection in the post intervention group (4 *vs.* 10, P=0.045). A trend for reduced incidence of NEC was also observed in the post intervention group (0 *vs.* 5, P=0.055). Less post intervention babies required one or more blood transfusions (13 *vs.* 31, P=0.01; Table 3).

Discussion

We found that the implementation of a new aggressive feeding policy for preterm infants did not improve growth as evidenced by weight gain prior to discharge but did result in other benefits. The policy did result in earlier initiation of feeds, earlier achievement of full oral feeds and earlier achievement of full PN indicating successful implementation of the policy. This was associated with reduced nosocomial infection and an increase in breastfeeding at discharge. There was also a suggestion of reduced NEC.

We chose a sample size of 40 babies pre and post intervention. Since our power calculation showed that this number could only detect a weight difference of 150 g at 3 weeks of age between before and after intervention group it is possible that we were underpowered to show smaller differences and hence open to chance findings. However this sample size was chosen as a compromise between small study sample and overly long study duration. The study duration was about 2 years. A limitation of the before and after study design is that there is a chance that other unrecognised changes in patients or management, not included in the intervention could account for the changes seen. Certainly over a two year study period this is possible. However, this is less likely than a longer study with a larger sample size. Another limitation to the study was PN data were collected from request forms. We were not able to substantiate whether the requested amount was actually administered. We believe that the amount requested would be based on the intake of the previous day and in most cases would reflect the amount actually given. We also found that the mean highest FiO_2 was greater in the post intervention group. Since this is a before and after audit it might represent an unrelated change in practice that we are not aware of or it could be due to chance. In fact we found that two babies in the post intervention period required extremely high oxygen concentrations on the first day of life. However since these two post intervention babies were sicker at baseline this would be unlikely to explain the improved outcomes found in the post intervention group.

Some of the data were collected prospectively and

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entered into a data base. Other data were retrospectively extracted from the case notes. However this retrospective data were remarkably complete with the only missing data being due to early discharge.

Our finding of no improvements in growth, measured as body weight at 7, 14, 21 days and at discharge is similar to a previous report.[15] Ibrahim et al[15] studied early full PN versus delayed introduction with a gradual increase to full PN but without an early oral feeding policy. In our study, we introduced early parenteral nutrition as well as early oral feeding and strongly promoted the use of mother's own milk. Banked milk is not available in our NICU. Human milk fortifier was used but not consistently during the study period. It is well known that preterm babies on human milk have slower growth compared to those fed formula. This occurs not only with banked milk but also with mother's own milk.[8] However, there is evidence that this slower growth is associated with lower total body fat and better tissue differentiation.[16]

Therefore a possible explanation for our failure to show a growth difference could be due at least in part to the increased use of human milk in the post intervention group. Thirty-five of 40 babies received breastfeeding at discharge post intervention compared with only 26 in the pre-intervention group. It is likely that the observed reduction in nosocomial infection and possible reduction in NEC could also both be attributed to the increased use of human milk. We excluded ten babies who were discharged before 21 days (and hence body weight data were not available). Nine of these infants were in the post intervention sample and is a possible explanation why no improvement in weight gain was seen. It is possible that these infants were discharged due to earlier weight gain and improved secondary outcomes.

We observed a reduction in the use of blood transfusion post intervention. We are not sure why this occurred but it could possibly be partly explained by the observed reduction in infections and NEC.

In summary our findings suggest that implementing a more aggressive feeding policy supported by high level scientific evidence is able to improve important outcomes.

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Competing interest: The authors have no competing interest to declare.

Contributors: Ho JJ and Nallusamy R conceived the project. Low CS and Ho JJ designed and performed the data collection and analysis. Low CS drafted the final paper and all authors had equal input into writing the final manuscript. All authors approved the final version of the manuscript to be published.

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