

ORIGINAL RESEARCH

Early Exclusive Enteral Feeding Versus Conventional Feeding In Stable Very Low Birth Weight Premies

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Abstract:

Background: Most commonly preterm very low birth weight babies require thermal support, infection control, surfactant support and nutritional support. One of the most challenging issues in the management of preterm very low birth weight infants is providing standard nutritional support. Optimal nutrition has been identified as a fundamental factor in reducing mortality and long term morbidities like extra-uterine growth restriction and poor neurodevelopmental outcome in preterm very low birth weight infants. So, the study is to determine the beneficial effects of early exclusive enteral feeding in stable very low birth weight babies.

Results: Each group included 51 neonates. The incidence of feeding intolerance and sepsis was 15.7% and 5.9% in exclusive enteral feeding group where as in conventional feeding group the incidence of feeding intolerance and sepsis was 27.1 and 29.2. The difference was statistically significant when exclusive enteral feeding group was compared with conventional feeding group with p values 0.002 and 0.003 respectively. Duration of antibiotic therapy is also less in exclusive enteral feeding group. More babies of exclusive enteral feeding group does not received intravenous fluids where as in conventional feeding group all the babies received intravenous fluids so time taken to achieve total enteral feeds also high. The duration of hospital stay was less in exclusive enteral feeding group compared with conventional feeding group. Mean duration of hospital stay for exclusive enteral feeding group was 10.35 ± 4.93 where as in conventional feeding group was 13.88 ± 3.33 . The difference was statistically significant with p value < 0.001 .

Conclusion: our study it was concluded that we can start exclusive enteral feeding without using intravenous fluids from the day one of life. The incidence of feeding intolerance and sepsis is also decreased in infants on exclusive enteral feeding. The need for central lines, antibiotic therapy and intravenous fluids can be decreased in infants on exclusive enteral feeding as compared to infants on conventional feeding. We can successfully start exclusive enteral feeding in stable very low birth weight infants, it is useful for early discharge of the infants without increasing the risk of sepsis and NEC.

Keywords: Enteral feeding, Sepsis, NEC.

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Introduction

Most commonly preterm very low birth weight babies require thermal support, infection control, surfactant support and nutritional support. One of the most challenging issues in the management of preterm very low birth weight infants is providing standard nutritional support. Optimal nutrition has been identified as a fundamental factor in reducing mortality and long term morbidities like extra-uterine growth restriction and poor neurodevelopmental outcome in preterm very low

birth weight infants. Providing regular nutritional assistance to preterm newborns is one of the most difficult problems to solve [1]. Early, optimal feeding is essential for reducing sepsis and potentially even retinopathy of prematurity [2-4]. The functional adaptability of the gastrointestinal system is lessened by this delay, which may also lengthen the time spent receiving parenteral nourishment with all of its associated infections and metabolic hazards [6,7]. Infants born prematurely benefit from early start and rapid advancement of enteral feeding, which

enhances gut development and lowers the incidence of NEC [5,8,9].

Methods

The study was an open labelled Randomized controlled trial carried out at Special Newborn Care Unit, Neonatal Intensive Care Unit, department of Pediatrics, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, in the Department of Pediatrics from January 2021 to October 2022. Approval was received from institutional ethical committee vide approval no.089-2022/I-S-O/75. As per the previous study Nangia et al, the sample size included minimum 80% power, and 5% significance level (significant at 95% confidence interval) the sample in each group should be 51. term neonates, babies with congenital malformations, syndromic babies, infant of diabetic mother etc. were excluded. The stable very low birth weight babies were assigned randomly to either exclusive enteral feeding group (study group) or conventional feeding group (control group). The neonates allocated to the exclusive enteral feeding group received total enteral feeding on the first day (80 m L/kg/day) with expressed breast milk, which was advanced by 20 m L/kg each day until maximum enteral feeding of 150 m L/kg/day was attained and maintained for 24 hours. This group did not receive any intravenous fluids. In the conventional feeding group, feeding was initiated with 20 m L/kg of expressed breast milk, and the remaining requirement was provided as intravenous fluids through a peripheral line. The feeds were advanced by 10- 20 m L/kg/day for the 2 subsequent days and then by 20-30 m L/kg/day for the next 3 days along with the remaining daily requirement as intravenous fluid until enteral feeding of 150 m L/kg/day was reached and maintained for 24 hours. Clinical examinations were done in both groups till their discharge from SNCU and NICU.

Results

A total of 3226 neonates were admitted in SNCU and NICU unit in our hospital over a period of twelve months. Amongst them, 382 neonates were VLBW neonates. 156 babies were eligible for the study from which 54 neonates were excluded. One hundred and two neonates who fulfilled the inclusion criteria were enrolled in the study. The mean and the standard deviation for all the variables taken in the study were calculated for both the groups and t-statistics, chi square were calculated to find the p value for statistical significance where p value below 0.05 was defined to be significant. Mean gestational age

for exclusive enteral feeding group is 32.04 ± 1.44 weeks while mean gestational age for conventional feeding group is 31.86 ± 1.42 weeks. Socioeconomic status distribution was observed between two groups. In exclusive enteral feeding group and conventional feeding group most of the patients belong to lower middle and upper lower class of SES. There was no significant difference between two groups with p value 0.97. In exclusive enteral feeding group antenatal risk factors were observed in 9.8% of the babies while in conventional feeding group presence of antenatal risk factors was 20.8%. There was no significant difference between two groups p value 1.0. Comparison between two groups according to antenatal steroid prophylaxis. 84.3% of the patient mothers received antenatal steroids in exclusive enteral feeding group while in conventional feeding group 82.0% of the patient mothers received antenatal steroids there is no significant difference between two groups p value 1.0. Gender distribution was observed in two groups in exclusive enteral feeding group 56.9% of babies were males while 44.0% of the babies were females. While in conventional feeding group 56.3% of the babies were males and 43.7% of the babies were females. In this study comparison of mode of delivery between two groups is observed. Under exclusive enteral feeding group 51.1% of the patients had vaginal delivery (NVD and AVD) and 48.9% of the patients had LSCS (emergency and elective). Similarly, under conventional feeding group 41.7% of the patients had LSCS delivery, while 58.3% of the patients had vaginal delivery. Mean birth weight under exclusive enteral feeding group is 1339.75 ± 102 grams while mean birth weight under conventional feeding group was 1335.52 ± 111 grams. In exclusive enteral feeding group 64.7% of the babies were AGA and 35.3% of the babies were SGA. Similarly in conventional feeding group 64.6% of the babies were AGA and 35.4% of the babies were SGA. There was no significant difference between two groups with p value 1.0. In exclusive enteral feeding group 41.2% of the patients were primipara, 39.2% of the patients were P2 (para 2) and 19.6% of the patients were multi para. In conventional feeding group 45.8% of the patients were primi para, 29.2% of the patients were P2 and 25.0% of the patients were multi para. Comparison of mean age at attainment of full feeding between two groups. In exclusive enteral feeding group mean age at attainment of full feeds is 2.2 ± 0.37 while in conventional feeding group was 8.5 ± 0.48 .

Table 1: Baseline characteristics of the study participants

Variables	Frequency/Mean	Percentage/SD
Mean Gestational age (weeks) \pm SD	32.02	1.4
Gender, n (%)		
Male	56	56.6
Female	43	43.4

Variables	Frequency/Mean	Percentage/SD
Mean birth weight (gms) ± SD	1338	105.7
Mode of delivery, n (%)		
Normal Vaginal delivery	44	44.4
Assisted Vaginal delivery	10	10.1
Emergency LSCS	36	36.4
Elective LSCS	9	9.1
Presence of AGA, n (%)	64	64.6
Presence of SGA, n (%)	35	35.4
Parity, n (%)		
1	43	43.4
2	34	34.3
≥3	22	22.2
Socio-economic status, n (%)		
Upper	6	6.1
Upper-middle	8	8.1
Lower-middle	31	31.3
Upper-lower	32	32.3
Lower	22	22.2
Presence of antenatal risk factor, n (%)	15	15.2

There was significant difference in distribution of age at attainment of the full feeds in exclusive enteral feeding group when compared with conventional feeding group with P value <0.001. Comparison of feeding intolerance distribution between the two groups in exclusive enteral feeding group 15.7% of the patients develop feeding intolerance while in conventional feeding group 35.4% of the patients develop feeding intolerance. There was significant difference in feeding intolerance distribution when

exclusive enteral feeding group is compared with conventional feeding group with p value of 0.024. In our study sepsis (clinical and culture proven) was observed in 5.9% of the patients in exclusive enteral feeding group while 29.2% of the patients in conventional feeding group. There was significant difference in sepsis distribution when exclusive enteral feeding group was compared with conventional feeding group with P value 0.003.

Table 2: Head to head comparison of enteral feeding and conventional feeding on other neonatal outcomes

Variables	Exclusive enteral feeding (n=51) n (%)	Conventional feeding (n=48) n (%)	χ^2 (df)	OR (95% CI)	p-value
Feeding intolerance	8 (15.7)	17 (35.4)	5.1 (1)	2.94 (1.13-7.69)	0.03*
Clinical sepsis	2 (3.9)	13 (27.1)	10.1 (1)	9.1 (19.3- 42.9)	0.002*
Culture proven sepsis	1 (2.0)	4 (8.3)	2.1 (1)	4.5 (0.5- 42.2)	0.19
Clinical and Culture proven sepsis	3 (5.9)	14 (29.2)	9.4 (1)	6.6 (1.8- 24.7)	0.003*

Mean duration of antibiotic therapy was observed between two groups. In exclusive enteral feeding group mean duration of antibiotics was 1.24 ± 2.9 while in conventional feeding group was 3.56 ± 4.6 . There was significant difference in distribution of patients according to mean duration of antibiotics when exclusive enteral feeding group is compared with conventional feeding group with P value 0.003. Duration of IV fluids also less in exclusive enteral feeding group when compared with conventional feeding group with p value <0.001. In exclusive enteral feeding groups 56.8% of the patient regain birth weight between 14- 17 days and 48.2% of patients between 18-21 days. While in conventional feeding group 43.1% of the patients regain birth weight between 14-17 days and 50.9% of the patients

between 18-21 days. Duration of hospital stay is also less in exclusive enteral feeding group when compared with conventional feeding group. Mean duration of hospital stay for exclusive enteral feeding group is 10.35 ± 4.93 days while mean duration of hospital stay for conventional feeding group was 13.88 ± 3.33 . There was a significant difference in duration of hospital stay when exclusive enteral feeding group was compared with conventional feeding group with P value <0.001. More babies of exclusive enteral feeding group does not received intravenous fluids where as in conventional feeding group all the babies received intravenous fluids so time taken to achieve total enteral feeds also high. The duration of hospital stay was less in exclusive enteral feeding group compared with conventional feeding

group. Mean duration of hospital stay for exclusive enteral feeding group was 10.35 ± 4.93 where as in conventional feeding group was 13.88 ± 3.33 . The difference was statistically significant with p value < 0.001 .

Table 3: Comparison between two groups according to outcomes

Variables	Exclusive enteral feeding (n=51) mean (SD)	Conventional feeding (n=48) mean (SD)	t-test (df)	Mean difference (95% CI)	p-value
Postnatal age at attainment of full feeds	2.24 (2.5)	8.6 (2.0)	-13.8 (97)	-6.34 (-7.3 to -5.4)	<0.001*
Duration of antibiotics	1.24 ± 2.9	3.56 ± 4.6	-3.0 (97)	-2.3 (-3.87 to -0.78)	0.003*
Duration of IVF	1.27 ± 2.45	8.4 ± 2.42	-14.7 (97)	-7.1 (-8.1 to -6.1)	<0.001*
Duration to regain birth weight in days	17.25 ± 2.3	18.0 ± 2.2	-1.65 (97)	-0.74 (-1.6 to 0.74)	0.1
Duration of hospital stay, days	10.35 ± 4.93	13.88 ± 3.33	-4.13 (97)	-3.53 (-5.21 to -1.83)	<0.001*

Discussion

Our study suggest that early introduction of enteral feeding in stable very low birth weight infants (1000-1499 gm) results in early achievement of full feeds with no increase in risk of NEC. Early introduction and rapid achievement of full enteral feeding reduce the need for central lines and parenteral nutrition and thus the infection risk(11)and length of hospital stay. In contrast delayed introduction and slow increments lead to impairment of functional adaptation of the gastrointestinal tract in preterm infants (12). This two year Randomized controlled trial was conducted In VIMSAR: Burla during the period from November 2020 to October2022. A total of 102 stable VLBW neonates were included in the study. Out of 102 babies 51 babies were given exclusive enteral feeding and 51 babies were given conventional feeding. Previous study also done on enteral feeding Sanghvi at el, Salhotra et al, Krishnamurthy and team et al, Dinerstein et al, Nangia at el etc., Mean gestational age for exclusive enteral feeding group is 32.04 ± 1.44 weeks while mean gestational age for conventional feeding group is 31.86 ± 1.42 weeks. There was no Significant difference in mean gestational age when exclusive enteral feeding group was compared with conventional feeding group with P value 0.532 same as in Sanghvi et al 2013(16) where mean GA was 31.8 ± 2.4 and 31.8 ± 1.8 weeks P value 0.26 and salhotra et al(14) and Ann Dsilna lindh et al . Socioeconomic status distribution was observed between two groups. In exclusive enteral feeding group and conventional feeding group most of the patients belongs to lower middle and upper lower class of SES. There was no significant difference between two groups with p value 0.97 same as in Ann Dsilna lindh et al. In exclusive enteral feeding group antenatal risk factors were observed in 9.8% of the babies while in conventional feeding

group presence of antenatal risk factors was 20.8%. There was no significant difference between two groups p value 1.0 same as in Nangia et al(13)and Dinerstein et al(15) where there was no significant difference. Comparison between two groups according to antenatal steroid prophylaxis. 84.3% of the patient mothers received antenatal steroids in exclusive enteral feeding group while in conventional feeding group 82.0% of the patient mothers received antenatal steroids there is no significant difference between two groups (p value 1.0) same as in Sanghvi et al(16), Krisnamurthy and team et al(17), Salhotra et al(14) where there was also no statistical significant with p value 0.65. Gender distribution was observed in two groups in exclusive enteral feeding group 56.9% of babies were males while 44.0% of the babies were females. While in conventional feeding group 56.3% of the babies were males and 43.7% of the babies were females. There was no significant difference in gender distribution of babies when exclusive enteral feeding group is compared with conventional feeding group with p value is 0.092 same as in Nangia et al(13), Ann Dsilna lindh et al where the difference was not significant where p value was 0.47. In this study comparison of mode of delivery between two groups is observed. Under exclusive enteral feeding group 51.1% of the patients had vaginal delivery (NVD and AVD) and 48.9% of the patients had LSCS (emergency and elective). Similarly, under conventional feeding group 41.7% of the patients had LSCS delivery, while 58.3% of the patients had vaginal delivery. It was observed that there was no significant difference in mode of delivery when exclusive enteral feeding groups compared with conventional feeding group with p value 0.7 as Sanghvi et al 2013(16), Nangia et al(13) and Ann Dsilna et al where there was no significance with p value is 1.00. Mean birth weight under

exclusive enteral feeding group is 1339.75 ± 102 grams while mean birth weight under conventional feeding group was 1335.52 ± 111 grams. It was observed that there was no significant difference in mean birth weight when exclusive enteral feeding groups is compared with conventional feeding group with P value 0.84 as in previous studies Sanghvi et al 2013(16), Nangia et al(13) and Krishnamurthy and team(17) and Ann Dsilna lindh et al where mean birth weight in study group is 1350 gms and contral group was 1320 gm with P value 0.26. In exclusive enteral feeding group 64.7% of the babies were AGA and 35.3% of the babies were SGA. Similarly in conventional feeding group 64.6% of the babies were AGA and 35.4% of the babies were SGA. There was no significant difference between two groups with p value 1.0 same as in Nangia et al(13) and Sanghvi et al(16) where p value is 1.0 In exclusive enteral feeding group 41.2% of the patients were primipara, 39.2% of the patients were P2 (para 2) and 19.6% of the patients were multi para. In conventional feeding group 45.8% of the patients were primi para, 29.2% of the patients were P2 and 25.0% of the patients were multi para. There was no significant difference according to parity when exclusive enteral feeding group was compared with conventional feeding group with p value 0.55 Comparison of mean age at attainment of full feeding between two groups. In exclusive enteral feeding group mean age at attainment of full feeds is 2.2 ± 0.37 while in conventional feeding group was 8.5 ± 0.48 . There was significant difference in distribution of age at attainment of the full feeds in exclusive enteral feeding group when compared with conventional feeding group with P value <0.001 which is consistent with previous study Nangia et al(13) where p value was <0.001 and Ann Dsilna et al where p value was 0.027 which correlates with my study. Comparison of feeding intolerance distribution between the two groups in exclusive enteral feeding group 15.7% of the patients develop feeding intolerance while in conventional feeding group 35.4% of the patients develop feeding intolerance. There was significant difference in feeding intolerance distribution when exclusive enteral feeding group is compared with conventional feeding group with p value of 0.024. This is consistent with Nangia et al(13) in which feeding intolerance occurs in enteral feeding group is 15.9% of the patients while in conventional feeding group was 30.2% of patients with P value 0.002 which correlates with my study. In Sanghvi et al(16) no statistical significance in incidence feeding intolerance with p value 0.45. In our study sepsis (clinical and culture proven) was observed in 5.9% of the patients in exclusive enteral feeding group while 29.2% of the patients in conventional feeding group. There was significant difference in sepsis distribution when exclusive enteral feeding group was compared with conventional feeding group with P value 0.003. It is

consistent with Nangia et al(13) where p value was <0.001 . the study done by Sanghvi et al(16) shows no sepsis was observed in study group but sepsis was observed in 13% of patients in control group. There was no statistical significance with p value 0.23 because the sample size was small. Ann Dsilna lindh et al and krishnamurthy and team(17) also shows no significant difference. Mean duration of antibiotic therapy was observed between two groups. In exclusive enteral feeding group mean duration of antibiotics was 1.24 ± 2.9 while in conventional feeding group was 3.56 ± 4.6 . There was significant difference in distribution of patients according to mean duration of antibiotics when exclusive enteral feeding group is compared with conventional feeding group with P value 0.003. In previous study Nangia et al(13) the difference was not significant with p value 0.97. Necrotizing enterocolitis was observed in 2.0% of the babies in exclusive enteral feeding group while in conventional feeding group the incidence of NEC was 6.8%. No significant difference in incidence of NEC between two groups with p value 0.35 same as in Nangia et al(13), krishnamurthy and team(17), and Ann Dsilna lindh et al where p value was 0.12. In Sanghvi et al(16) there was no incidence of NEC. Incidence of apnea was observed in 5.9% of the patients in exclusive enteral feeding group while 18.8% of patients in conventional feeding group. There was no significant difference between two groups with p value 0.06 same as in Nangia et al(13) where p value was 0.005. Incidence of IVH not observed in exclusive enteral feeding group while incidence of IVH in conventional feeding group is 4.0% which is not significant between two groups. Sanghvi et al(16), Dinerstein et al(15) shows no incidence of IVH. Incidence of hypoglycemia was observed in 3.9% of the patients in exclusive enteral feeding group while 14.6% of the patients in conventional feeding group which was not significant with p value 0.08. Incidence of shock was observed in 5.9% of the patients in exclusive enteral feeding group whereas in conventional feeding group it was 12.5%. There was no significant difference between two groups with p value 0.3. Previous studies shows no incidence of Apnea, shock, hypoglycemia and NEC in study groups. But there is incidence of shock, apnea, hypoglycemia and NEC in both groups which were predominantly, associated with feeding intolerance. But there was no significant difference between two groups.

Duration of IV fluids also less in exclusive enteral feeding group when compared with conventional feeding group with p value <0.001 . This is consistent with Nangia et al(13) where p value was 0.02 which correlates with my study. In exclusive enteral feeding groups 56.8% of the patient regain birth weight between 14- 17 days and 48.2% of patients between 18-21 days. While in conventional feeding group 43.1% of the patients regain birth weight between 14-17 days and 50.9% of the patients between 18-21 days. There

was no significant difference according to duration to regain birth weight when exclusive enteral feeding group compared with conventional feeding group with p value 0.1. Same as in Nangia et al(13) and Ann Dsilna lindh et al where p value was 0.40. Early introduction and faster advancement of feeds leads to faster regaining of birth weight between 11-21 days.(7,9,10). Duration of hospital stay is also less in exclusive enteral feeding group when compared with conventional feeding group. Mean duration of hospital stay for exclusive enteral feeding group is 10.35 ± 4.93 days while mean duration of hospital stay for conventional feeding group was 13.88 ± 3.33 . There was a significant difference in duration of hospital stay when exclusive enteral feeding group was compared with conventional feeding group with P value <0.001 . This is consistent with Nangia et al and sanghvi et al. In Nangia et al duration of hospital stay is 14 days for enteral feeding group and 18 days for conventional feeding group in Sanghvi et al duration of hospital stay was 15 ± 2.56 for study group and 28 ± 6.75 for control group.

Conclusion

Early initiation of exclusive enteral feeding is strongly associated with lower incidence of feeding intolerance, clinical sepsis, duration of hospital stay and there is early regain of birth weight. However there is comparable incidence of apnea, hypoglycemia, shock, NEC and IVH in exclusive early enteral feeding and conventional feeding practice in preterm neonates.

Abbreviations

1. NEC- necrotising enterocolitis
2. AGA-appropriate for gestational age
3. SGA- small for gestational age
4. LGA- large for gestational age
5. VLBW- very low birth weight
6. IVH- intra ventricular hemorrhage
7. LSCS- lower segment cesarean section
8. NVD- normal vaginal delivery
9. AVD- assisted vaginal delivery
10. SES- socioeconomic status
11. SNCU- special newborn care unit
12. NICU- neonatal intensive care unit

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Authors contribution

Siva Naik collected the data, analysed the results of the two intervention group and wrote the final manuscript. SP participated in patients clinical assessment in addition to data analysis and interpretation. PCP contributed to the conception of

the work and designed frame of work. CKP, JNK, PM, SD edited the manuscript in the data collection and analysis. All authors read and approved final manuscript.

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Availability of data and materials

All the data supporting the results can be found with in the article

Declarations

Ethical approval and consent to participate

The study was approved by institutional research and ethical committee, Veer Surendra Sai Institute of Medical Sciences and Research. Guardians of eligible children signed and written informed consent before study enrolment.

Consent for publication

A written informed consent for publication was obtained from the guardian of eligible children.

Competing interests

The authors declare that they have no competing interests.

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