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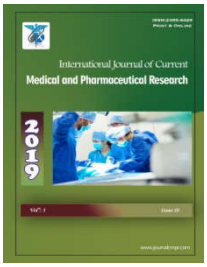

Research Article

A STUDY ON COMPARISON OF VOLUME AND FREQUENCY BASED FEEDING PROTOCOL IN VERY LOW BIRTH WEIGHT BABY

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ABSTRACT

Introduction: Very Low Birth Weight (VLBW) neonates are increased risk for potential nutritional compromise. These infants are born with limited nutrient reserves, immature metabolic pathways and increased nutrient demands. These neonates require specialized nutritional support due to their biochemical immaturity, faster growth rates and increased metabolic demand. These demands results from increased risk of several problems such as respiratory distress syndrome, sepsis, gastro-oesophageal reflux, apnoea and other factors related to feeding intolerance. Providing optimal enteral nutrition to high risk premature neonates is a difficult clinical challenge. Material &Method: The study was conducted from October 2016 to September 2018 at Newborn wards and SNCU, Department of Paediatrics SCB MCH and SVPGIP, Cuttack. 200 babies were included in our study. It was a randomised prospective study Result: Babies of Volume advancement group regain birth weight earlier (mean of 7.27days) than the babies of frequency advancement group (mean of 8.05 days).Gain of weight on D10 and on D15 was more in the babies of VA group than the babies of FA group (p=0.001, p=0.001 respectively). Days of attainment of full enteral feeding was earlier in volume advancement (VA) group (mean of 8.25days) than the frequency advancement (FA) group (mean of 15.40 days). Conclusion: Volume advancement feeding protocol is found to be better than frequency advancement feeding protocol considering the benefits of rapid weight gain in volume advancement group, earlier attainment of full enteral nutrition, lesser duration of hospital stay and lower incidence of feeding interruption.

INTRODUCTION

Backgrounds*:* Providing optimal enteral nutrition to high risk premature neonates, very low birth weight is a difficult clinical challenge. These infants are born with limited nutrient reserves, immature metabolic pathways and increased nutrient demands. These neonates require specialized nutritional support due to their biochemical immaturity, faster growth rates and increased metabolic demand .These demands results from increased risk of several problems such as respiratory distress syndrome, sepsis, gastro esophageal reflux, apnea and other factors related to feeding intolerance[1]. The structural and functional integrity of GI tract is dependent upon the provision of enteral nutrition. With holding enteral feeding after birth places the infant at risk for all the complications associated with luminal starvation, including mucosal thinning, flattening of the villi, bacterial translocation. There have also been several reports about early imitation of enteral feeding to achieve an early catch-up growth and avoid gut atrophy [2]. Early enteral feeding enhances maturation of the motor responses of the small intestine of the preterm babies compared with infants receiving exclusively parenteral nutrition.[3] Optimal growth of preterm infants has yet o be determined, and, thus, cannot have been achieved, but the general objective remains consistent -to achieve postnatal growth and body composition equivalent o those of normally growing, healthy human foetuses of the same gestational age [4].Most preterm infants fail to grow after birth for days, often weeks and once they start to grow they do not keep up with normal rates of intrauterine growth [5]. This problem is worse for smaller, more preterm infants, and even more so for infants who have serious illness with marked physiological instability [6]. As a result, most preterm infants do not achieve normal size, anthropometric indices, or body composition by term gestation. This problem is compounded for infants with intrauterine growth restriction (IUGR) from inadequate foetal nutrition who are born small for gestational age and are even more susceptible to postnatal nutritional deficits [7, 8]. The recommended goal of nutritional support for VLBW from birth to term is to match the in utero growth rates of the normally growing foetus coupled with satisfactory functional development [9]. The postnatal nutrition in preterm infants is designed to mimic the growth and body composition of the healthy foetus growing in the uterus. Some recent evidence has demonstrated that inadequate nutrition in premature infants in the first week results in growth retardation and may lead to Permanent detrimental effects [10, 11]. Malnutrition is a cause of morbidity and mortality in VLBW infants receiving les

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nutrition in the first week of life. Therefore, parenteral nutrition is required until full enteral nutrition can be established [12]. Now the survival rates of VLBW infants have improved with use of mechanical ventilation and exogenous surfactant [13], preterm infants are faced with another challenge in nutrition. Extra uterine growth retardation is associated with adverse outcomes including chronic lung disease, increased risk to infection, severe retinopathy, and abnormal neurodevelopment outcome [14-16]. To achieve weight gain of preterm infants who are appropriate for gestational age without adverse effect, there should be no interruption in delivery of nutrients from time of birth [17, 18]. It is difficult for most VLBW infants to reach this suggested caloric and protein intake because of fluid restriction, intolerance, delay in imitation of nutrition, immaturity of intestinal functions, and slow progress of enteral feeding.[19-21] Much controversy about initiation and advancement of feeding of VLBW babies. Implementation of a standardized feeding regimen for very low birth weight babies reduces variations in the practitioners and may enhance early recognition of feeding intolerance and reduce the rate of Necrotizing enterocolitis [23]. The advantage of frequency advancement feeding is by giving les frequent meals, will help feeding tolerance, provide enough time for the gut to metabolize the meal, and reduce the stagnation of the feed. This feeding approach will reduce the risk of feeding intolerance and development of Necrotizing enterocolitis. This is based on the fact that VLBW newborn has immature gut motility, low enzymatic activity which leads to an inability to digest and absorb properly [22-24]. Volume advancement feeding approach is carried out by increasing the feed and reducing parenteral nutrition. With this, it is hoped that there will be a shortened in the total days on intravenous parenteral nutrition, which may eliminate the catheters associated problems. [25] It is believed that those VLBW neonates in volume advancement feeding protocol will take less time to reach full feeds and have better weight gain after discharge. [26]

Aim and objectives*:* To compare two strategies for the advancement of enteral feeding in very low birth weight babies that is volume advancement and frequency advancement enteral feeding protocol and different complication arising there on & to find the most preferable feeding protocol. There are very limited studies and data to support any of these feeding protocols to be optimal.

Two studies were done previously comparing the volume and frequency based feeding advancement feeding protocol [28,29].

Dr Amal Zubani et al[28], a randomised prospective study was done in Dept of paediatric, King Faisal Specialist Hospital and Research Centre,Saudi Arabia, during December 2010 till June 2014, taking VLBW neonates(haemodynamically stable) as study population. All babies in both groups were started on minimal enteral feeding as gastrointestinal priming after 24hrsof birth for 3 days with expressed breast milk or premature formula at rate of 1ml/kg/day(every 8hr in FA group and every 4hr in VA group). FA group were started at 8hourly feeding intervals and the frequency was gradually increased to every 3hourly intervals with increase in volume by only 10ml/kg/day.

The VA group, feeds were started at 2hourly intervals and the feeds were increased gradually every 2 hr with an increase in volume by 20-25 ml/kg/day. Results found as Full feed achieved in VA group was significantly earlier than FA group (p-value <0.001). No significant difference in the length of hospital stay in both group (p-value=0.221). TPN days (p<0.001) Feed interruptions (p-value=0.02) Days on ventilation (p-value=0.034). Number of infections (p-value=0.042) was in favour of VA group. No significant differences in the weight on discharge (p-value=0.376) and the weight at 30 days post discharge from the hospital (p-value=0.322).

Another study was done by Dr Afaq Hussain et al[29] in Children Hospital Multan during February 2017 to August 2017, taking VLBW babies as study population. The protocol for frequency advancement (FA) group was to give 1ml/kg/ human milk or pre-formula milk after every 8hrs and in volume advancement (VA) group after every 3hrs initially. After 3days, in FA group duration of feeds was decreased gradually from 8 to 2 hours & feed volume of 10ml/kg/day until full recommended dose of feeding i.e 150ml/kg/day reached. While in VA group, volume of 20ml/kg/day was given until full recommended dose of feeding reached. In their study they found VA feeding was better as compared to FA feeding in VLBW neonates.

MATERIAL & METHOD

The study was conducted from October 2016 to September 2018 at Newborn wards and SNCU, Department of Paediatrics SCB MCH and SVPPGIP, CUTTACK, with approval from institutional ethical committee of the hospital. It was a randomised prospective study. After obtaining written consent from the legal guardian to participate in this study, samples were included in the study. The babies were randomized into two groups: volume advancement (VA) and frequency advancement (FA) with the alteration of sequence of admission. All VLBW neonates of birth weight (up to and 1499g) born in our hospital and referred from other hospital before initiating feeding and who were haemodyanamicaly stable were included in the study.

Inclusion criteria*:* All very low birth weight baby both AGA and SGA who were hemodynamically stable.

Exclusion criteria*:* Baby with 1.congenital abnormalities, 2.Disaminated Intravascular Coagulation, 3.Intra Ventricular Haemorrhage, 4. Hypoxic Ischemic Encephalopathy, 5.Proven sepsis, 6. Suspected or proven NEC, 6. Cardio respiratory compromised, 7. Respiratory distress, 8. Shocks were excluded from the study. Out of total newborn admitted to the hospital 200 babies were enrolled in the study fulfilling the protocol criteria. The babies were randomized into two groups volume advancement (VA) and frequency advancement (FA) with the alteration of sequence of admission. All neonates in both groups were started feeding with 10 ml kg-1 with expressed breast milk on D1. Frequency group were started at 8 hourly feeding intervals and volume advancement group were started at 2 hourly feeding intervals. Then gradually, in frequency advancement group, feeding interval was decreased from 8 hourly feeding to 2hourly feeding, with increase in volume by 10 ml kg-1day-1. In the volume advancement group feeding volume was increased by 20mlkg-1day-1 with feeding interval remaining the same 2hours. In both the groups, feeding volume was increased until recommended full fed had been reached i.e. 150 ml kg-1 day-1 Birth weight, birth length and birth head circumference were measured and recorded. Daily

weight of all the babies were measured and recorded. Length and head circumference were measured weekly. Blood glucose, transcutaneous bilirubine, urine output were monitored. Babies were screened for sepsis. Babies were vigilantly monitored for feeding intolerance, and appearance of any signs of necrotising enterocolits. A chart of feeding volume, feeding time interval, feeding interruption, number of times and amount baby vomited, pre feeding gastric residuals, pre feeding abdominal girth were maintained. Vitals of the babies were monitored; development of hypoglycaemia, seizure, neonatal hyperbilirubinemia and the requirement of double surface phototherapy (dspt) /double volume exchange transfusion (dvet) were recorded. Babies were discharged when able to maintain temperature without radiant warmer and Haemodynamicaly stable & have documented weight gain for three consecutive days. All data collected were entered in master chart and statistical analysis was done. Both the groups were comparable in terms of baseline characters (gestational age, birth weight, sex). Mean, standard deviation, chi square were calculated and then p value was calculated. P value <0.05 is considered significant.

OBSERVATION & RESULTS

This study includes 200 patients admitted over two years (October 2016-september2018) in our hospital. All babies included were haemo-dynamically stable VLBW. All included neonates were divided randomly in two groups volume advancement (VA) and frequency advancement (FA) in our current study(C).

The two groups were comparable for gender, birth weight, gestational age, head circumference, birth length at the initiation of the protocol. There are two study available by Amal Zubani et al (AZ)[28] in 2016 and by Afaq Husain et al(AH)[29] in 2018.

Citation has been done only where the data of previous study is available.

Table 1 Gender of the two study groups (Volume advancement & frequency advancement)[28.29].

			Group								
			V A			F A			Total		
			C	AZ	AH	C	AZ	AH	C	AZ	AH
Gender	Male	Count	50	22	24	52	16	23	102	38	47
		%	50	46.9	54.5	52	42.1	53.4	51	44.7	54
	Female	Count	50	25	20	48	22	20	98	47	40
		%	50	53.1	45.5	48	57.9	46.6	49	55.3	46
Total		Count	100	47	44	100	38	43	200	85	87
		%	100	100	100	100	100	100	100	100	100

Shows gender of all the neonates which were included in the two study groups were comparable. In VA group total number of females was 50 and in FA group total number of females were 52. In VA group total numbers of males was 50 and in FA group total number of males were 48.Total numbers of female in the study were 102 and total number of male in the study were 98.

Analysis :(chi square=0.08 ,p value= 0.777 ,statistically not significant)

Hence one of the baseline characteristics of these two study groups were comparable.

Table 2 Different parameters of the babies included in the two study groups (Volume advancement & frequency advancement)[28,29].

Group		Study group	N	Mean	Std. Deviation	p value
Gestational age(weeks)	Volume advancement	C	100	32.32	2.220	0.924
		AZ	47	29.15	-	
		AH	44	29.72	-	
	Frequency advancement	C	100	32.35	2.199	
		AZ	38	29.21	-	
		AH	43	29.76	-	
Birth weight	Volume advancement	C	100	1273.50	112.908	0.691
		AZ	47	1147.8	-	
		AH	44	1148	-	
	Frequency advancement	C	100	1267.10	114.312	
		AZ	38	114.8	-	
		AH	43	1179	-	
HC(cm)on D1	Volume advancement		100	28.97	2.110	0.810
	Frequency advancement		100	28.90	2.003	
length(cm) on D1	Volume advancement		100	40.75	3.013	0.648
	Frequency advancement		100	40.56	2.865	

Gestational weeks of the babies included in both the study group vary from 28 weeks to 39 weeks.

Mean gestational age of the neonates in the volume advancement group was 32.32 weeks. Mean gestational age of the neonates in the frequency advancement group was 32.35 weeks. P value =0.924, statistically not significant. Gestational age, another baseline character was also comparable in both the groups.

Birth weight of the babies in volume advancement (VA) group varies from 1010 g to 1450g. Mean birth weight of neonates in volume advancement group was 1273.50grams. Birth weight of the babies in frequency advancement group varies from 1010 g to 1470g.Mean birth weight of neonates in frequency advancement group was 1267.312 grams. P value=0.691, statistically not significant.

Birth weight another baseline character was also comparable in both the study group.

Table 3 Baseline antenatal risk factors (Volume advancement & frequency advancement).

Parameter		Group		Total	P value
		Volume Advancement	Frequency Advancement		
Preeclampsia	Count	2	4	6	0.407
	%	2	4	3	
GDM	Count	2	3	5	0.651
	%	2	3	2.5	
Placental insufficiency	Count	4	4	8	1.0
	%	4	4	4	
Oligohydramnious	Count	7	4	11	0.352
	%	7	4	5.5	

Baseline antenatal factor were comparable in both the groups statistically significant difference was not found.

Table 4 Prelacteal feed comparison (Volume advancement & frequency advancement).

Prelacteal feed		Group		Total	P value
		Volume Advancement	Frequency Advancement		
Yes	Count	3	2	5	0.651
	%	3	3	2.5	
No	Count	97	98	195	
	%	97	98	97.5	
Total	Count	100	100	200	
	%	100	100	100	

In volume advancement group, out of total neonates 3 babies have prelacteal feed and in volume advancement group, out of total neonates 2 babies have prelacteal feed. Statistical analysis: chi square is 0.205, p-value =0.651 i.e. statistical not significant.

Table 5 Changes in different parameter on day 15 of life (Volume advancement & frequency advancement)[28,29].

Group			N	Mean	Standard deviation	P value
Change in head circumference	Volume Advancement		99	0.700	0.2559	0.257
	Frequency Advancement		98	0.655	0.2076	
Change in Length	Volume Advancement		99	1.019192	0.2801883	0.873
	Frequency Advancement		98	1.014	0.1292	
Gain in weight	Volume Advancement		99	104.55	22.373	0.0001
	Frequency Advancement		98	40.20	16.053	
Gain of wt D10 (gm)	Volume Advancement		99	32.32	14.202	0.001
	Frequency Advancement		98	11.02	9.791	
Gain of wt D15 (gm)	Volume Advancement	C	99	104.44	22.737	0.0001
		AZ	47	134.68		0.001
		AH	44	299		0.001
	Frequency Advancement	C	98	40.20	16.053	
		AZ	38	398.26		
		AH	43	105		
Days of regaining birth weight	Volume Advancement	C	99	7.27	0.855	0.001
		AZ	47	7.88		0.260
	Frequency Advancement	C	98	8.05	0.854	
		AZ	38	8.03		
Days of attaining full feeding	Volume Advancement	C	99	8.25	0.675	0.0001
		AZ	47	10.32		<0.001
		AH	44	11.04		<0.001
	Frequency Advancement	C	98	15.40	1.023	
		AZ	38	22.53		
		AH	43	15.76		

As one baby from VA group had died on day 7, n=9. Mean change in head circumference on day 15 of life in VA group was 0.70cm whereas mean change in head circumference on day 15 of life in FA group was 0.65cm. P value= 0.257, statistically not significant. Hence there was no effect of the type feeding protocols on change in head circumference on day 15 of life.

Mean change in length on D15 of life in babies of VA group was 1.019 cm whereas mean change in length on D15 of life in babies of FA group was 1.014cm. P value=0.873, which is not significant statistically. Hence there was no statistically significant difference in change in length on day 15 of life in these two study groups.

Mean gain in weight on day 10 of life in volume advancement group was 32.32gms whereas mean gain in weight on day 10 of life in frequency advancement group was 1.02 grams. P value=0.001, significant statistically. Average gain in weight on day 10 of life was significantly more in the volume advancement group. Average change in weight on day 15 of life in babies of volume advancement group was 104.5grams. Average change in weight on day 15 of life in babies of frequency advancement group was 40.20 grams. P value =0.001, significant statistically. Weight gain in babies of VA group was god than the babies in FA group. Volume advancement group, babies had regained their birth weight in 6 to 9 days whereas in frequency advancement, babies regained their birth weight in 6 to 10 days. Majority of the babies took 8 to 9 days. In volume advancement group, mean days to regain birth weight was 7.27 days. In frequency advancement group, mean days to regain birth weight was 8.05 days. p-value=0.01 ,statistically significant. In volume advancement group, babies attained their full enteral feeding in 8 to 12 days whereas babies in frequency advancement group, babies took 15 to 18 days for attaining full enteral feeding. Mean days of attaining full fed in volume advancement group was 8.25 days. In frequency advancement group mean days of attaining full fed was 15.40days. P value =0.001, which is statistically significant. Babies in volume advancement group attained their full fed earlier than the babies in the frequency advancement group.

Table 6 Feeding interrupted& intolerance in number of babies in both group (Volume advancement & frequency advancement)[28,29].

Parameter			Group		Total	P value	
			V A C	F A		C	AZ
Feeding Interrupted	Yes	Count	17	32	49	0.011	0.025
		%	17	32.7	24.7		
	No	Count	83	66	149		
		%	83	67.375.3			
	Total	Count	100	98	198		
		%	100	100	100		
Feeding Intolerance	Yes	Count	4	7	11	0.334	
		%	4	7.1	5.6		
	No	Count	96	91	187		
		%	96	92.9	94.4		
	Total	Count	100	98	198		
		%	100	100	100		

In volume advancement group, 17 babies had interrupted feeding and in frequency advancement group 32 babies had interrupted feeding. Statistical analysis: chi square =6.512, p value=0.01(statistically significant).Hence babies of frequency advancement feeding protocol feeding had more interruption of feeding as compared to the babies of volume advancement feeding protocol group.

In volume advancement group 4 neonates had feeding intolerance but in frequency advancement group 7 neonates had feeding intolerance. Statistical analysis: chi square =0.9318, p value =0.334 i.e. statistically not significant. Feeding intolerance was not affected by any of these two feeding protocols.

Table 7 Different complication in both the study group (Volume advancement & frequency advancement)[28,29,30].

Parameter			Group		Total	P value	
			Volume advancement	Frequency advancement		C	AZ
Sepsis	Yes	Count	4	8	12	0.146	0.042
		%	4	8.2	6.1		
	No	Count	96	90	186		
		%	96	91.8	93.9		
	Total	Count	100	98	198		
		%	100	100	100		
Seizure	Yes	Count	1	1	2	0.988	
		%	1	1.02	1.01		
	No	Count	99	97	196		
		%	100	98.98	98.99		
	Total	Count	100	98	198		
		%	100	100	100		
Hypoglycemia	Yes	Count	9	5	14	0.284	
		%	9	5.1	7.1		
	No	Count	91	93	184		
		%	91	94.9	92.9		
	Total	Count	100	98	198		
		%	100	100	100		
NEC	Yes	Count	2	1	3(C) 1(AZ) 1(AH)	0.572	
		%	2	1	1.5		
	No	Count	98	97	195		
		%	98	98.98	98.5		
	Total	Count	100	98	198		
		%	100	100	100		

NNHB	Yes	Count	95	97	192	0.102
		%	95	99	97	
	No	Count	5	1	6	
		%	5	1	3	
	Total	Count	100	98	198	
		%	100	100	100	
DSPT/ DVET	Yes	Count	95	96	191	0.259
		%	95	97.96	96.5	
	No	Count	5	2	7	
		%	5	2.04	3.5	
	Total	Count	100	98	198	
		%	100	100	100	
AKI	Yes	Count	1	0	1	0.100
		%	1	0	0.5	
	No	Count	99	98	197	
		%	99	100	99.5	
	Total	Count	100	98	198	
		%	100	100	100	

Out of total babies in volume advancement group, 4 had developed sepsis and out of total babies in frequency advancement 9 had developed sepsis. Statically analysis: chi square =1.5068, p value= 0.219 (statistically not significant). Developments of sepsis in the babies of both the groups were not statistically significant. Sepsis was not influenced by the type of feeding protocols. Seizure developed in one baby of volume advancement group as well as in one baby of frequency advancement group. Statistical analysis: chi square=0.002, p value=0.988(statistically not significant). Development of seizures had not influenced by the type of feeding protocols.

In volume advancement group, 9 babies had hypoglycemia and infrequency advancement group 5 babies had hypoglycemia. Statistical analysis: chi square =1.14, p value =0.284 (statistically not significant). Hypoglycemia in neonates was not affected by the type of feeding protocols.

In volume advancement group, 2 babies had developed NEC and in frequency advancement group 1 baby had developed NEC. Statistical analysis: chi square=0.318, p value=0.572(statistically non significant). Types of feeding protocol had no influence on development of NEC.

95 babies out of 10 babies in volume advancement group had neonatal hyperbilrubinemia whereas in frequency advancement group 97 babies out of 98 babies had NNHB. Statistical analysis: chi square =2.67 ,p value =0.102. Neonatal hyperbilrubinemia was not affected by the type of feeding protocol. There was no statistical significant difference in the development of neonatal hyperbilrubinemia (NNHB) in both the groups.

In volume advanced group, 95 babies out of 10 babies received phototherapy/DVET and in frequency advancement group, 96 babies out of 98 babies had received phototherapy/DVET. Statistical analysis: chi square=1.2709, p value=0.259 (statistical non significant).There was no significant difference in two study groups in terms of receiving phototherapy or DVET.

Only one baby in volume advancement group had AKI, no baby in frequency advancement group had developed acute kidney injury. Acute kidney injury was diagnosed by monitoring the urine output. Development of AKI was not affected by the type of feeding protocols followed.

Table 8 Outcome in terms of death and survival in study groups[28,29].

Parameter			Group		Total
			Volume Advancement	Frequency Advancement	
Outcome	Survival	Count	99	98	197
		%	99	98	99.5
	Death	Count	1	0	1
		%	1	0	0.5
Total		Count	100	98	198
		%	100	100	100

Only one baby in volume advancement group had died on day 7 of life and no death had occurred in frequency advancement group.

Table 9 Comparing the length of stay in hospital in both the study groups.[28,29,30,31]

Group statistics			Mean(days)			Std. Deviation	P value		
			C	AZ	AH		C	AZ	AH
Duration of hospital stay	V A	99	16.08	38.55	41.20	1.085	0.0001	0.221	0.34
	F A	98	23.95	50.71	42.62	2.672			

In volume advancement group (VA) group babies stayed in hospital in the range of 15 to 20 days. However babies in frequency advancement group length of hospitalization ranges from 21 days to 30 days. In volume advancement group, mean days of hospital stay was 16.08 days and in frequency advancement group mean days of hospital stay was 23.95 days. Babies of frequency advancement group had longer duration of hospital stay as compared to the babies in volume advancement group. Statistical analysis: p value =0.001(statistically significant). Babies of volume advancement group discharged earlier from the hospital as they fulfilled the discharge criteria (consecutive 3 days of weight gain) earlier.

DISCUSSION

All included new born were divided into two groups as volume advancement (VA) group and frequency advancement (FA) group. The two groups were comparable for gender, birth weight, gestational age, head circumference, birth length at the initiation of the protocol. There are two study available by Amal Zubani et al[28] in 2016 and by Afaq Husain et al[29] in 2018.

As only two studies are available for comparison of our study and not all aspect have been studied by previous author citation are not available for all the tables.

Citation to Table-1

The baseline demographic parameter of sex distribution shows there is slight female predominance in both volume advancement and frequency advancement study, comparable with the study done by Amal Zubani et al[28] in 2016 and differ from the study done by Afaq Husain et al[29] in 2018 showing male predominance.

Citation to Table-2:

The study done by Amal Zubani et al[28] in 2016 and Afaq Husain et al[29] in 2018 , the mean gestational age was aroung 29 weeks where as current study having mean gestational age of 32 weeks. So also in mean birth weight is low (1150grams) as compared to current study(1250grams)

Citation to Table-3&4: Baseline antenatal risk factors & Prelacteal feed comparison

This aspect of study has not done by any of the previous author, citation not available.

Citation to Table-5:

In volume advancement group birth weight was regained in 7.27 days (mean) whereas birth weight was regained in 8.05 days (mean) in frequency advancement group, which was statistically significant, with p value of 0.01. However, when this was compared with other similar studies, the time of regaining birth weight was not significantly different in the two groups.

Mean head circumference (HC) in VA group on day 1 of life was 28.97 cm whereas mean head circumference in FA group on day 1 of life was 28.90 cm. P value=0.810, which was not statistically significant. Mean length in VA group on day 1 of life was 40.75cm where as mean head circumference in FA group on day 1 of life was 40.56 cm. P value=0.648, statistically not significant.

In Amal Zubani et al study[28], both groups have regained their birth weight within 7-10days, babies in frequency advancement group attained birth weight at day 8.03(mean) of life as compared with 7.8day (mean) of life in volume advancement group, which was not statistically significant. In volume advancement group weight gain on D10 & ON D15 of life is more than that of frequency advancement group. It was mostly due to more daily feeding volume increment i.e. 20ml/kg/day in VA group versus 10ml/kg/day in FA group. In Afaq Husain et al[29] study, weight gain was significantly more in VA group (p=0.01).

In Amal Zubani et al study [28], weight gain was more in favor of FA group as compared to VA group which was in contrast o the present study. The reason most probably was due to the fact that babies in FA group had spent more days on TPN. Days to reach full feeding was significantly different in two groups, babies of VA group attain full feeding much earlier than babies in FA group.

VA group had taken a mean of 8.25 days whereas FA group had taken mean of 15.40 days. (p=0.001)

Afaq Husain et al[29] study also found les days to reach full fed in VA group as compared to FA group just like this present study. In contrast Amal Zubani et al[28] study had shown an average difference of about 12 days in attaining full feed in both the groups (p<0.01). FA group reached full fed earlier than VA group.

Citation to Table -6

Feeding was interrupted more in FA group than VA group and statistically significant (p=0.01).

In previous study by Amal Zubani et al[28] feeding interruption was also statistically significant more in FA group. (p =0.025)

Feeding intolerance was not significantly different in both groups which indicate that as if feeding intolerance was not influenced by the feeding protocols chosen in the present study.

Citation to Table- 7

Sepsis in both groups were not statistically significant.(p=0.146) mostly due to following the universal aseptic measures. In Amal Zubani et al[28] study ,sepsis was statistically significant (p=0.042)and was found to be associated more in FA group.

It is a well known fact hat parenteral nutrition also increases the risk of catheter elated blood stream infections, it seems a reasonable explanation for association of more sepsis in the study by Amal Zubani et al[28]. Bombell S et al[30] concluded that early enteral feeding increases the GI motility, prevent normal flora and reduces the risk the risk of infections. In this study total duration of iv fluid was longer in FA group as compared to VA group. Therefore, though volume advancement group should have les incidence of sepsis, we did not found any statistically significant association of sepsis in any of the said groups. Strict adherence to universal method of sepsis prevention may be the reasonable explanation.

Seizure in both groups was not significantly different (p=0.98), one baby from each group had developed seizure which was associated with hypoglycemia and hypocalcaemia. However seizure as a variable was not taken into consideration in previous studies Comparing incidence of hypoglycemia in both the groups, it was no found statistically significant. There was no effect of feeding protocols in blood glucose level in neonates (p=0.284).

Two babies in volume advancement group had developed NEC whereas in frequency advancement group one baby had developed NEC. This difference was not statistically significant (p=0.572).

In Amal Zubani et al[28] study, only one neonate of VA group had NEC. In Afaq Husain et al[29] study, also one patient had NEC which was in VA group. Recent systematic reviews have also concluded that VA did not increases the risk of NEC in neonates and is a safe option.

Number of babies who had developed neonatal hyperbilrubinemia (NNHB) and received phototherapy was more in FA group than VA group but he difference was not found statistically significant (p=0.102, p=0.259 respectively). In previous studies NNHB was not taken as a comparing parameter.

There was only one patient from VA group who had developed AKI of stage 1, the baby had improved gradually over 12hrs with conservative management. In previous studies no such report was mentioned regarding AKI in study groups.

Citation to Table-8:

Unfortunately, there was one death in the study groups that belonged to VA group. The baby was of 29 weeks gestational age developed sepsis on DAY 4 of life with multiorgan dysfunction in form of gastrointestinal bleeding sclerema, had NEC with gut perforation, had apnea for which baby got intubated, was in shock and was on vasopresors and died on Day 7 of life.

Citation to Table-9

As compared to the babies of VA group with mean duration of hospital stay 16.08 days, babies of FA group had longer duration of hospital with a mean of 23.95 days. Total length of hospital stay in FA group was statistically significant more than the VA group as evidenced from the p value=0.001.

As days to reach full enteral feed was longer in FA group , consecutive days of weight gain in FA was slow and as per the discharge criteria that is 3 consecutive days of weight gain,

babies got discharged slow, hence length of hospitalization increases.

In Amal Zubani et al[28] study, there was no significant difference in length of hospital stay in two groups (p=0.21).In Afaq Husain et al study[29], there were similar duration of hospital stay in both groups (p=0.34). Recent Cochrane database review have concluded that VA feeding is better than FA feeding because it takes less to reach full feed, rapid weight gain. In addition, it has no adverse effects on NEC. Furthermore, some researchers have found that VA feeding also has beneficial effects on the development of neural outcomes.[30,31]

Summary

Babies of Volume advancement group regain birth weight earlier, Gain of weight on D10 and on D15 , attainment of full enteral feeding was more in the babies of VA group than the frequency advancement (FA) group (mean of 15.40 days). Feeding interruption was more in frequency advancement group than the babies in volume advancement group (p=0.01). Feeding intolerance, Feeding protocols, incidence of sepsis in both the groups were not statistically significant. One baby from each group had seizure which was associated with hypoglycemia .Seizure in both the groups were statistically non-significant (p=0.98).Difference in both the groups in terms of number of babies, who had developed hypoglycemia was not significant (p=0.284). There was no significant difference in both the groups regarding development of neonatal hyperbilrubinemia (p=0.10) and number of babies who had received phototherapy/DVET (p=0.25). Only one baby in VA group had acute kidney injury of stage-1, which got improved with conservative management. Two babies of VA group had developed NEC whereas only one baby of FA group had NEC, this difference was not significant statistically(p=0.57). Unfortunately there was one baby from VA group who had died on day 7 of life with sepsis, multi organ dysfunction, with extreme prematurity. Rest of the neonates in both groups were discharged successfully. Babies of frequency advancement group stayed for a longer period(mean 23.95 days) in the hospital in comparison to the babies of volume advancement group (mean 16.08 days).Difference in length of stay in hospital was statistically significant (p=0.001).

CONCLUSION

Volume advancement feeding protocol is found to be better than frequency advancement feeding protocol considering the benefits of rapid weight gain in volume advancement group, earlier attainment of full enteral nutrition, lesser duration of hospital stay and lower incidence of feeding interruption. The incidence of associated adverse events like feeding intolerance, development of necrotising enterocolits (NEC), sepsis, seizure, acute kidney injury, neonatal hyperbilrubinemia and receiver of phototherapy/DVET were not statistically significant among the two groups. Hence volume advancement feeding protocol should be considered as the preferred feeding protocol.

Limitation of our Study: Due to small sample size we cannot reach in a conclusion about the significance of these associations. Further studies with large number of samples, multi centric study are required to draw any inference for validation.

What is the existing knowledge till date : Many of the developing country in their nursery still using frequency advancement of feeding practice for the very Low birth weight, small for gestational age baby for the feeding the baby. What this study add to existing knowledge: The present study contributes to the knowledge of feeding in very low birth weight and small for gestational age that Volume advancement feeding protocol is found to be better than frequency advancement feeding protocol in all the parameter of the development.

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Contributionship statement

Dr Pradeep Kumar Jena: Concept and design , revising critically for intellectual contents, final approval and agreement to be accountable.

Dr Sudipta Sahoo: Data analysis and interpretation, drafting the work, final approval and agreement to be accountable .
Dr. Mangal Charan Murmu: Drafting the work, Manuscript writing, validation of data, final approval and agreement to be accountable.

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