Cover page

Title of study

Maternal role in sensory motor stimulation for Oral Feed Establishment in preterm neonates: MSMS trial

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Maternal role in sensory motor stimulation for Oral Feed Establishment in preterm neonates: MSMS trial

Oral feed establishment is one of the most challenging milestones for preterm neonates. It is becoming an emerging challenge for neonatologists with an improvement in the survival of preterm neonates. A successful transition from full gavage (tube) feeding to independent oral feeding is considered an important milestone of neonatal neurodevelopment maturation. It has been estimated that about 40% of preterm neonates face difficulty transitioning from gavage to oral feeding (1).

Tube feeding-related problems are commonly observed in neonates. A literature review regarding the safety profile of having a feeding tube shows that it is not risk-free. Major problems enlisted are mechanical, functional, nutritional, biological and neurodevelopmental (mental motor delay) (2-5).

According to Heidelise Als' "Synactive Theory" in growing fetus and neonate, developmental maturation is done by integrating neonatal internal physiological status and functional demands with multisensory inputs from the environment (6,7). In preterm neonates, synergistic effects of combined oral and non-oral sensorimotor (tactile/kinesthetic) interventions have shown promising results (8). It helps augment their experience to exercise their innate (sucking) reflex that ultimately decreases transition time from introduction to safe full independent oral feeding (9). Feeders and grower neonates are ideal for oral stimulation for oral feed establishment.

The ideal time to start oral feeding in preterm neonates is still debatable. In developing fetus shows sucking, swallowing and breathing at 15, 14 and 10 weeks of gestation, respectively (10). Feeding development undergoes maturational processes throughout gestation, from non-coordinated sucking and swallowing movements to fully coordinated suck-swallow-breathe, usually occurring after 34 weeks. Unlike the term sucking reflex, preterm neonates have a predominant expression pattern of sucking with no suction. Lau et al. demonstrated that around 30 weeks of post-menstrual age (PMA), healthy preterm neonates could complete their successful oral feeding within 20 minutes using an immature sucking reflex (11).

Family-centred care (FCC) is, in fact, developmentally supportive care that helps develop bonding (12). Intermittent kangaroo mother, as a part of FCC, benefits from maternal-neonatal bonding (13). Similarly, the role of maternal involvement in pre-feeding sensorimotor stimulation is a hidden corner in research. To our knowledge, not even a single international or national study is available in this regard.

In resource-constrained setups with limited properly trained speech therapists and neonatal nurses, mothers can be involved in pre-feeding sensory motor stimulation after training and teaching to improve their feeding performance. Within this context, the current study aims to determine the following: 1) the maternal role in sensory-motor stimulation for oral feed establishment in preterm neonates, 2) determine the effect of sensory-motor stimulation offered by the mother on the onset of oral feeding, and 3) the efficiency of mother-mediated stimulation techniques on oral feeding compared to trained nurses.

Keywords

Prematurity sensory-motor stimulation oral feed establishment, feeding intervention

Material and methods

An interventional, prospective, randomized control trial was conducted after ethical approval from the Institutional Review Board of Fatima Memorial Hospital (FMH-07-2021-IRB-929-M). The authors confirm that this intervention's ongoing and related trials are registered in the ClinicalTrials.gov platform–accession number NCT05484726. The study protocol can be accessed at https://www.clinicaltrials.gov/ct2/show/NCT05484726.

Study hypothesised that preterm babies who receive sensory motor stimulation from their mothers as compared to trained nurses, are

- Start taking oral feed at the same time as compared to the control group
- Take the same amount of milk at the commencement of oral feeding
- Take milk with equal efficiency
- Not face more adverse effects

The study period spans 16 months, from March 2022 to july 2023, in the department of Neonatology, Fatima Memorial Hospital, Lahore. We enrolled all preterm neonates of gestation age 28 to 34 weeks who were admitted to NICU during the study period after seeking consent from parents or guardians. All these neonates were haemodynamically stable, established gavage feed, had no respiratory distress, no need for respiratory support except LFNC and did not receive any kind of analgesics at time of enrollment.

However, all those neonates having major anomalies incompatible with life, major malformations, syndromic babies, cleft lip and palate, genetic disorders, haemodynamically unstable babies including IVH (grade III & IV), haemodynamically significant PDA (HsPDA) requiring antifailue therapy, NEC (stage II & III) or anemia requiring blood transfusion. All those neonates with adverse events including cough with chocking, breath holding, chocking, aspiration, tachycardia HR > 200/min, bradycardia HR < 100/min, apnea > 15 sec, tachypnea RR > 70/min while stimulation or feeding were excluded.

Protocol

Interventional Study Model: Factorial Assignment

- Maternal involvement in perioral sensory-motor stimulation be in three stages
  - Observer status
  - Performing under supervision
  - Independent
- Intervention period: 5 days as
  - Training phase (T): T1 and T2 (for mothers by the nurse)
  - Direct feeding phase (D): F1, 2, and 3 (oral feed was offered to neonate)
- Stimulation for 7 minutes and 15 minutes before feeding twice a day at 1100 and 1700 hrs.
- Two groups
  - Intervention group (GI): by mothers
  - Control group (G II): by staff nurses

Number of Arms: 2

Masking: Single (Care Provider)

The mothers, medical staff involved in general care, nursing staff involved in the intervention, and doctors conducting the assessment of oral feeding skills (OFS) were all blinded to allocation. The nursing staff was informed at the time of intervention that participating infants received either sensory motor stimulation or sham oral stimulation depending on group allocation.

Allocation
Randomization was done using a random Alloc Software environment. Gestation age-based stratification was done using 3 blocks design of 28 to 30, 30+1 to 32 & 32+1 to 34. Random allocation of neonates into the intervention or control groups by stratum using lottery method.

Blinding

The mothers, medical staff involved in general care, nursing staff involved in intervention and doctors conducting the assessment of oral feeding skills (OFS) were all blinded to allocation. The nursing staff was informed at the time of intervention that participating infants received either sensory motor stimulation or sham oral stimulation depending on group allocation.

Sample size
The sample size was 46 (23 each in interventional and control groups) and calculated with a 95% confidence level, 10% margin of error and 5% level of significance by taking feeding-related problems as 40%. It was done by using openepi.com.
Initially only 46 neonates were enrolled in study. But later an immense maternal response was observed. Mothers were ready to learn and involve in sensory motor stimulation of their neonates. Hence, the final total study population size was 97 with 49 in experimental and 48 in control group.

Procedure of intervention
- The study intermediation was started not before 30 weeks of postmenstrual age when full gavage feeding was established with the addition of supplements.
- All mothers in this study was involved in gavage feeding before involvement in the procedure.
- Trained nurses tought details of sensory-motor stimulation to mothers in easily understandable languages (annexure 1 in (a) English and (b) Urdu). This procedure has been adapted from modified from PIOMI and Fucile (14,15).
- Stimulation was done for 7 minutes and at least 15 minutes before feeding twice daily at 1100 and 1700 hrs till full oral feed establishment (expected time 28 days chronological age)
- Oral feeding was offered using a bottle with a slow-flow nipple.
- Time monitoring for feeding was strictly followed
- Infants was fed for a maximum of 20 min, and feeding wias discontinued early if adverse events occur.

Arms and intervention
- Study groups for sensory motor stimulation (5 minutes) + pacifier (2 minutes)
  - Intervention group (G1) : by mothers
  - Control group (G 2) : by staff nurses

Experimental: Intervention group (Group 1)
- Maternal involvement was done in three stages for the intervention group as
  - Observer status
    - T1: Nurses performing all steps while mother observer status
    - T2: Nurses perform all steps in front of the mother and a pacifier was offered by the mother
  - Performing under supervision
    - D1: Mother performs all steps and oral milk was offered by the nurse while the mother observes.
    - D2: Mother performing all steps and offering oral milk while the nurse is supervising

- Independent
  - D3: Mother performing all steps independently
- Study groups for sensory motor stimulation

  Assigned intervention perioral sensory motor stimulation Step 1 - 6 over 5 minutes + pacifier 2 minutes for total duration of 7 minutes.
  - Step 1: With the help of the index finger, on the external surface of the cheek, make a circle starting from the angle of the mouth towards the ear then back 7x each cheek
  - Step 2: While holding both sides of the cheek with help of the thumb and index finger repeat step 1 7x each cheek
  - Step 3: Move index finger from one corner to opposite one over both lips separately 7x each lip
  - Step 4: Gentle massage and compress the gums from center to back of mouth 7x each half of the gum
  - Step 5: Move the finger from front to back on the hard palate while applying gentle pressure 7x
  - Step 6: Displace the center of the tongue with gentle pressure 7x
  - Offer pacifier at the end 2 minutes Note: 7x means 7 times

Control group / Sham Comparator (Group II)

All steps were same as intervention group and was performed by trained staff nurses

Data Collection

All relevant maternal and neonatal data (baseline measures) were collected on a specially designed proforma.

Baseline measures

- Maternal demographic and clinical data include
  - Age in years
  - Gravidity / number of pregnancies measured in numbers as primigravida (PG), 2-3 or ≥ 4)
  - Educational qualification as uneducated, primary, secondary or higher
  - Previous preterm baby measured as yes or no
  - Job status as working-lady or home-maker
  - Diabetes mellitus, hypertensive disorders and anemia as yes or no
- Neonatal demographic data includes
  - Gender as male or female
  - Gestation age measured in weeks
  - Mode of delivery as spontaneous vaginal delivery (SVD) or low segment caesarian section (LSCS)
  - Birth weight measured in kg
  - Weight for gestation age. It can be appropriate for gestation age (AGA), small for gestation age (SGA) or large for gestation age (LGA)
  - Place of birth as inborn or out-born
  - Neonates with respiratory failure may need respiratory support that was measured as
    - Requirement of invasive mechanical ventilation (IMV) along with duration in days as median with IQR

        - Non invasive ventilation (NIV) along with duration in days as median with IQR
        - Oxygen as low flow nasal cannula (LFNC) along with duration in days as median with IQR
        - Neonates with prophylactic caffeine therapy given to all neonates < 32 weeks of gestation age
        - Respiratory distress syndrome (RDS) was diagnosed on clinical and radiological features of reticulo-nodular shadowing
        - Apnea was diagnosed on basis of breath holding spells for > 20 second
        - Hemodynamically significant patent ductus arteriosus (HsPDA) diagnosed by echocardiography
        - Necrotizing enterocolitis (NEC) diagnosed using modified Bell's scoring (stage 1)
        - Feeding intolerance diagnosed as aspirates > 20% of previous feed ± abdominal distension of > 2cm from base line
        - Sepsis (leukocytosis or leukopenia or ANC<150 along with raised CRP and platelets <100 and or positive blood culture)
        - Seizures
        - Discharge weight in kg
        - Duration of stay in NICU in days
- Neonatal feeding characteristics at time of enrollment in study include
    - Postmenstrual age (PMA) measured in weeks
    - Chronological age (ChA)measured in weeks
    - Time/duration to achieve full gavage/tube feed measured in days
    - Daily milk intake (ml/kg/day) when sensory motor stimulation was started
    - Volume of feed prescribed for each feed (ml)

The **outcome** measured were documented daily twice a day (11.00 and 17.00 hrs) until achievement of full oral feed. Full oral feed was volume of 120-140ml/kg/day taken orally. However, to make calculations concise, for both groups, all outcome parameters were documented on proforma for fixed time (11.00 am) for D1, D2, D3, D5, D7 and D14.

- Primary Outcome Measure
    - Transition time to full oral feeding is the time interval between commencement of perioral sensory stimulation on D1 to establishment of full oral feed in both groups.It was done daily till 14th day of perioral sensory motor stimulation. Transition time to full oral feeding was the day at which baby was able to take oral feed of volume of 120-140ml/kg/day.
    - Improvement (change) in efficiency oral feed establishment in terms of amount and time. It was classified into four levels depending upon the level of maturity in ascending order as follows:
        - Level 1: PRO < 30% and RT < 1.5 ml/min
        - Level 2: PRO < 30% and RT ≥ 1.5 ml/min
        - Level 3: PRO ≥ 30% and RT < 1.5 ml/min
        - Level 4: PRO ≥ 30% and RT ≥ 1.5 ml/min

      For our RCT, efficacy was measured as the achievement of L4 for the intervention group vs the control group.

- Adverse outcome monitoring was done for every neonate from first day of enrollment in study (D1) till establishment of full oral feed (by D14 expected). These include non-life threatening adverse events including cough, tachycardia HR 180-200/min, bradycardia HR120 - 100/min, , tachypnea RR 60 - 70/min while maintaining SpO2 of >90% at room air

- Secondary Outcome Measure:
  - Total volume (TV) taken during each feed
  - Volume taken during the first 5 min (TV_5) out of total feed taken orally
  - Rate of transfer (RT) ml/min i.e., how long it neonate takes to finish oral feed.
  - Overall transfer (OT percent) volume taken/total volume prescribed. It shows trend towards oral feed establishment.
  - Proficiency (PRO percent) volume taken during the first 5 min/total volume prescribed.
  - SSB (Suck Swallow Breaths) coordination coordinated, developed pattern of suck swallow and breathe. It is a subjective assessment.

Statistical analysis

The statistical software IBM SPSS Statistics version 21 (SPSS, Chicago, IL) was used for the statistical analysis of the data. Appropriate bivariate analysis was performed to identify the unadjusted differences between the cases and controls. Categorical variables were expressed as frequencies and percentages. According to Shapiro Wilk test all continuous variables were asymmetrically distributed. Mann–Whitney U test was used for nonparametric continuous variables and were described as medians and inter quartile range (IQR). Fisher exact/Chi square test was used to compare categorical variables. Mann- Whitney test was used to compare continuous variables. The p-value of < 0.05 was taken as statistically significant.

Results

During the research period, 1009 newborns were admitted to the Neonatal Intensive Care Unit (NICU). Among them, 142 were born prematurely, with gestational ages falling between 28 and 34 weeks. Out of the preterm neonates, a total of 130 were eligible for the study, as 12 had to be excluded for various reasons. These exclusions included 2 cases where mothers experienced serious postnatal complications, 1 instance of parental refusal to participate, 1 case with incomplete data, and 8 cases that did not meet the inclusion criteria due to different reasons such as syndromic features, cleft lip and palate, suspected inborn error of metabolism (IEM), intraventricular hemorrhage (grade IV), and hemodynamically significant patent ductus arteriosus (HsPDA). Consequently, 130 neonates were included in the study and randomly assigned, with 65 in each group for intervention and control. Sensory motor stimulation (SMS) was administered to 107 of these neonates, and the study was completed with 97 neonates (as illustrated in Figure 1).

The sociodemographic and clinical characteristics of both mothers and neonates are shown in Table 1. There were no statistically significant differences between groups regarding maternal age, gravidity, education, previous preterm neonates, job status and pregnancy related issues (hypertensive disorder of pregnancy, gestational diabetes, and anemia). Similarly, neonatal characteristics regarding gender, mode of delivery, gestation age, birth weight, weight for gestation age, place of delivery, need and duration of invasive mechanical ventilation (IMV), non

invasive ventilation (NIV) and low flow nasal cannula (LFNC), apnea, RDS, use of caffeine, HsPDA, NEC stage 1, feed intolerance, sepsis, and seizures. (Table 1).

There was also no significant difference in feeding characteristics The feeding characteristics assessed were postmenstrual (PMA), chronological (ChA) age, and weight at enrollment, time to full gavage feed establishment, amount of milk feed advised for each feed and day on D1, D2,D3, D5, D7 and D14. (Table 2).

Table 3 provides an overview of both the primary and secondary outcomes observed in both study groups. When examining the primary outcome measures, there were no significant differences observed in terms of the time it took to establish full oral feeding, adverse events, or the effectiveness observed during oral assessments. The findings indicate that neonates in the experimental group demonstrated oral feeding skills that were comparable to those in the control group. These skills were measured in terms of volume (both total and during the initial 5 minutes of feeding), feeding rate, overall transfer, proficiency, and the coordination of suck, swallow, and breath (Table 3).

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Figure 1: Consort diagram

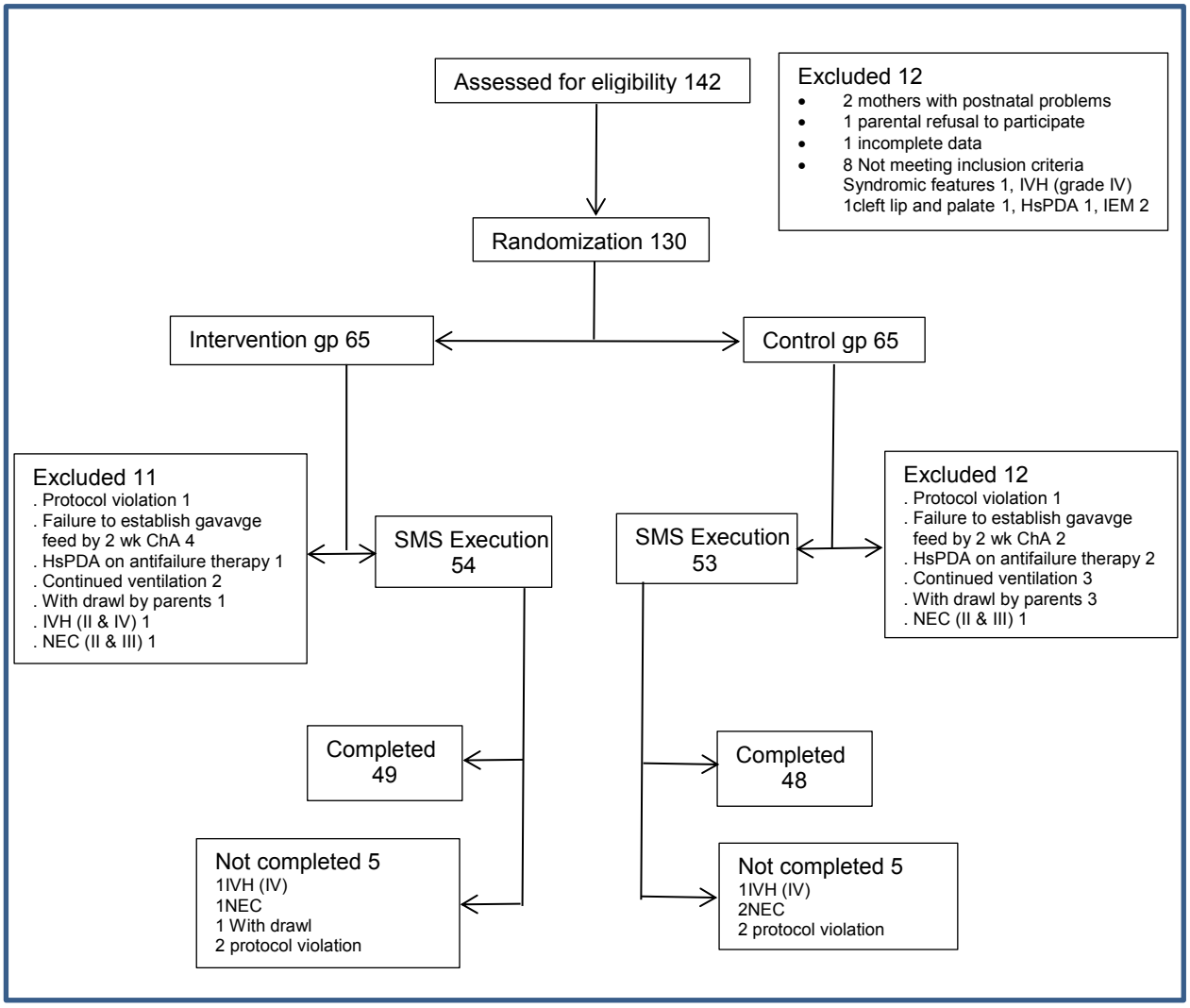

Table 1: Maternal and neonatal characteristics

Characteristics			Experimental group (n=49)	Control group (n = 48)	p-value
NEONATAL	Gender (Male) [a]		27 (55.1%)	22 (44.9%)	0.239
	Gestational age (week) [b]		30 (29 – 32)	31 (29.3 – 32)	0.543
	Mode of delivery (SVD) [a]		26 (47.3%)	29 (52.7%)	0.300
	Birth weight [b]		1.29 (1.20 – 1.52)	1.34 (1.15 – 1.67)	0.744
	Weight for GA [a]	AGA	27 (47.4%)	30 (52.6%)	0.554
		SGA	16 (51.6%)	15 (48.4%)	
		LGA	6 (66.7%)	3 (33.3%)	
	Inborn [a]		30 (67.6%)	33 (52.4%)	0.287
	IMV [a]		26 (46.4%)	30 (53.6%)	0.231
	Duration of IMV (days) [b]		1 (0 – 4)	2 (0 – 5)	0.463
	NIV [a]		45 (48.4%)	48 (51.6%)	0.061
	Duration of NIV (days) [b]		3 (1 – 7)	4 (2 – 6.75)	0.509
	LFNC [a]		47 (52.2%)	43 (47.8%)	0.209
	Duration of LFNC (days) [b]		4 (2 – 5)	3.5 (2 – 5)	0.716
	Apnea [a]		18 (47.4%)	20 (52.6%)	0.386
	RDS [a]		25 (50.0%)	25 (50.0%)	0.539
	Caffeine [a]		28 (50.0%)	28 (50.0%)	0.535
	HsPDA [a]		17 (45.9%)	20 (54.1%)	0.309
	NEC (stage I) [a]		9 (42.9%)	12 (57.1%)	0.293
	Feeding intolerance [a]		20 (44.4%)	25 (55.6%)	0.182
	Sepsis [a]		43 (51.2%)	41 (48.8%)	0.484
	Seizures [a]		7 (58.3%)	5 (41.7%)	0.394
MATERNAL	Age [b]		29 (26 - 32)	30 (26.5 – 33)	0.138
	Gravidity [a]	Primigravida	20 (43.5%)	26 (56.5%)	0.350
		2-3	22 (59.5%)	15 (40.5%)	
		≥ 4	7 (50.0%)	7 (50.0%)	
	Education [a]	Uneducated	2 (50.0%)	2 (50.0%)	0.699
		Primary	11 (52.4%)	10 (47.6)	
		Secondary	15 (42.9%)	20 (57.1%)	
		Higher	21 (56.8%)	16 (43.2%)	
	Previous preterm (yes) [a]		42 (52.5%)	38 (47.5%)	0.281
	Job status (Housewife) [a]		29 (48.3%)	31 (51.7%)	0.368
	Hypertensive disorder [a]		29 (47.5%)	32 (52.5%)	0.290
	DM [a]		17 (50.0%)	17 (50.0%)	0.555
	Anemia [a]		25 (54.3%)	21 (45.7%)	0.304

Table 2 : Feeding charteristics

Feeding characteristics	**Experimental group (n=49)**	**Control group (n = 48)**	**p-value**
PMA at enrollment (week)	32 (31 – 33)	32 (31 – 33)	0.787
ChA at enrollment (days)	13 (6 – 14)	9 (7 – 16)	0.925
Time to full gavage feed (days)	7 (5.5 – 13.5)	7 (6 – 14)	0.726
Discharge weight (kg)	1.48 (1.42 – 1.66)	1.48 (1.43 – 1.75)	0.698
Weight at enrollment (kg)	1.35 (1.25 – 1.54)	1.35 (1.21 – 1.60)	0.610
Duration of stay in NICU (days)	21 (15 – 29.5)	30 (16 – 30.75)	0.848
Milk Feed (ml/kg/day)			
Milk feed D1	120 (120 – 120)	120 (120 – 120)	0.302
Milk feed D2	120 (120 – 140)	120 (120 – 140)	0.871
Milk feed D3	140 (140 – 140)	140 (140 – 157.50)	0.109
Milk feed D5	150 (150 – 160)	160 (150 – 160)	0.361
Milk feed D7	160 (160 – 160)	160 (160 – 160)	0.184
Milk feed D14	160 (160 – 180)	160 (160 – 180)	0.758
Volume of feed prescribed (ml/feed)			
Volume prescribed D1	14 (12 – 15.5)	14 (12 – 16)	0.670
Volume prescribed D2	14 (12 – 17.5)	12.5 (12.25 – 19)	0.825
Volume prescribed D3	16 (14 – 17.5)	14 (14 – 20)	0.569
Volume prescribed D5	17 (15 – 19)	17 (15 – 21)	0.758
Volume prescribed D7	18 (16 – 20.5)	18 (16 – 22)	0.614
Volume prescribed D14	18 (16 – 22)	18 (16 – 24)	0.933

Table 3 : Study outcome

Outcome		Experimental gp (n=49)	Control gp (n=48)	p-value
Time to full oral feed (days)		10 (7 – 13)	9 (7 – 13)	0.531
Adverse events	D1	36 (53.7%)	31 (46.3%)	0.234
	D2	14 (50.0%)	14 (50.0%)	0.563
	D3	12 (50.0%)	12 (50.0%)	0.570
	D5	2 (100%)	0 (00%)	0.253
	D7 & 14	0 (00%)	0 (00%)	NA
L4 Efficacy on	D 1 -3	0 (00%)	0 (00%)	NA
	D5	12 (57.1%)	9 (42.9%)	0.331
	D7	16 (51.6%)	15 (48.4%)	0.528
	D14	35 (49.3%)	36 (50.7%)	0.434
Volume Taken Each feed	D1	2.0 (2.0 -7.0)	2.0 (2.0 -7.0)	0.803
	D2	5.0 (2.0 - 9.0)	3.0 (2.0 – 7.0)	0.558
	D3	7.0 (3.0 – 11)	4.0 (3.0 – 10.0)	0.540
	D5	8.0 (5.0 – 15)	6.5 (5.0 – 15)	0.521
	D7	9.0 (7.0 – 18)	7.5 (7.0 – 20)	0.951
	D14	15 (13 – 20.5)	15.5 (14 – 22)	0.737
Volume taken in first 5 mins	D1	2.0 (1.0 – 4.5)	2.0 (1.25 – 4.0)	0.938
	D2	3.0 (2.0 – 6.0)	3.0 (2.0 – 5.0)	0.988
	D3	3.0 (2.0 – 7.0)	3.0 (2.0 – 7.0)	0.723
	D5	5.0 (4.0 – 9.0)	5.0 (4.0 – 8 .0)	0.817
	D7	7.0 (5.5 – 11)	7.0 (6.0 – 10)	0.895
	D14	10 (9.0 – 12.5)	10 (9.0 – 10)	0.618
RT %	D1	0.42 (0.24 – 0.85)	0.42 (0.28 – 0.70)	0.835
	D2	0.70 (0.59 – 1.0)	0.71 (0.70 – 1.0)	0.663
	D3	0.70 (0.40 – 1.0)	0.70 (0.40 – 1.0)	0.941
	D5	0.83 (0.50 – 1.45)	0.90 (0.50 – 1.2)	0.645
	D7	1.0 (0.68 – 1.6)	1.0 (0.67 – 1.7)	0.584
	D14	1.6 (1.10 – 2.1)	1.6 (1.10 – 2.1)	0.913
OT%	D1	21 (15 – 36)	21 (15.3 – 36)	0.936
	D2	36 (15 – 44)	35.7 (15 – 36)	0.422
	D3	43.8 (21 – 55.5)	43.8 (21 – 50)	0.551
	D5	48 (33 – 65)	48 (33 – 65)	0.700
	D7	60 (46 – 73.5)	56 (46 – 100)	0.950
	D14	91 (87 – 100)	95.5 (87.9 – 100)	0.521
PRO%	D1	16 (7.8 – 24)	16 (9.2 – 21)	0.948
	D2	21.6 (15 – 32.5)	21 (15 – 27)	0.847
	D3	23 (14 – 37)	19.5 (14 – 31)	0.499
	D5	30 (25 – 39)	29 (24.5 – 39)	0.629
	D7	39 (33 – 49.5)	39 (32 – 46)	0.872
	D14	56 (50 – 60)	55.8 (46 – 56)	0.630
Neonates SSB coordinated feeding	D1	23 (51.1%)	22 (48.9%)	0.538
	D2	33 (55.0%)	27 (45.0%)	0.180
	D3	33 (50.8%)	32 (49.2%)	0.746
	D5	40 (51.9%)	37 (48.1%)	0.381
	D7	39 (52.0%)	36 (48.0%)	0.383
	D14	49 (50.5%)	48 (49.5%)	NA