

Randomized Trial of Routine vs Selective Human Milk Fortification in Extremely Preterm Infants

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Background

- Fortified maternal breastmilk is considered the ideal feeding for extremely preterm infants.
- The optimal timing, complications and long-term benefits of fortification are unclear.

Objective

To compare feeding-related morbidities, growth and developmental outcomes in extremely preterm infants fed preterm milk either with fortification added routinely or with fortification added subsequently only for poor weight gain.

Methods

This is a prospective randomized controlled trial of extremely preterm infants admitted to the Regional Perinatal Center in Syracuse, NY from Feb 2020 to Dec 2022

Inclusion Criteria:

- Gestational Age (GA) ≤ 27 weeks
- Admitted to our NICU prior to day 7 of life and first enteral feeding

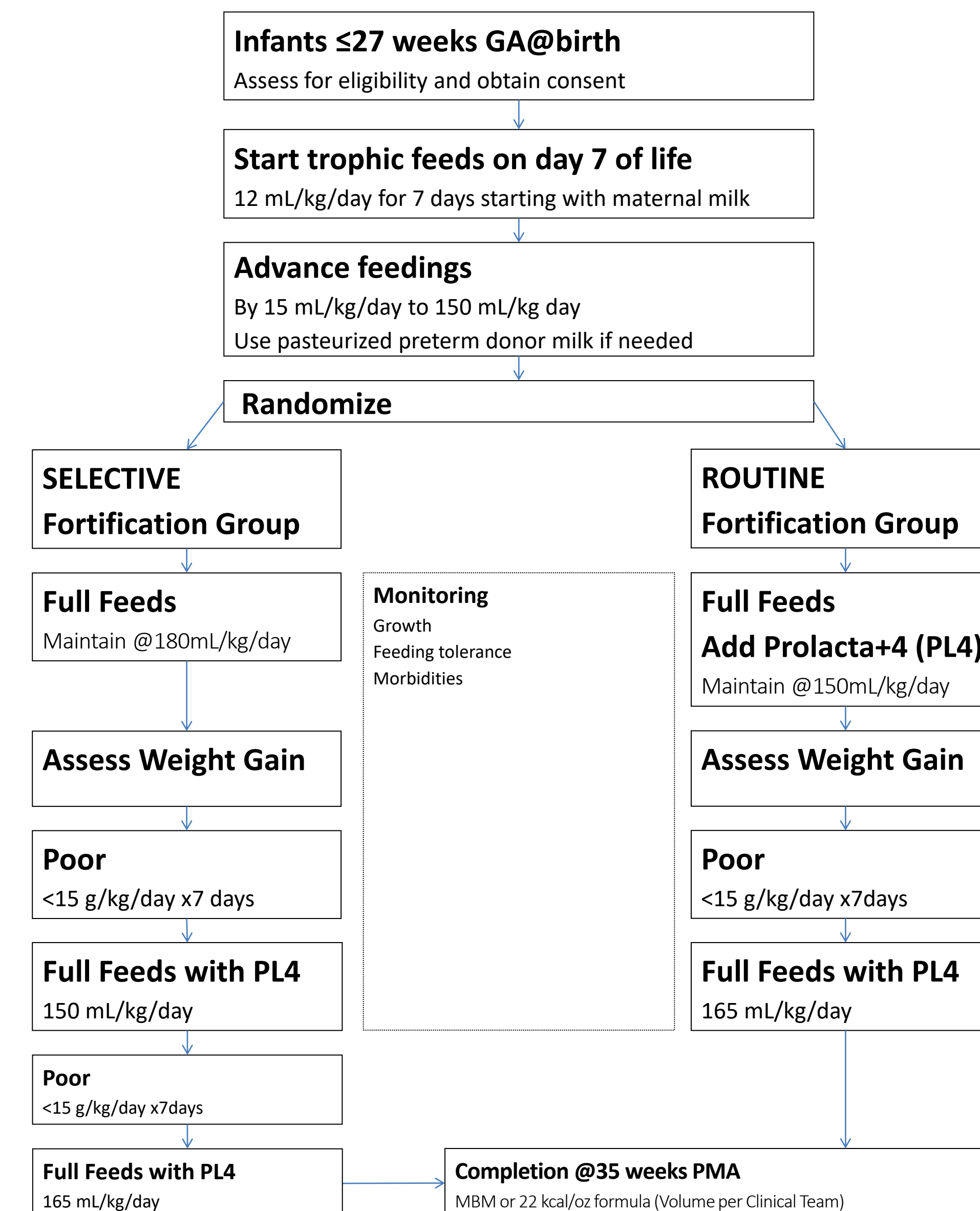
Exclusion Criteria:

- Severe congenital anomalies
- Severe intraventricular hemorrhage
- No availability of maternal milk

Primary Outcomes: rates of necrotizing enterocolitis (NEC), sepsis, death and anthropomorphic measures at 35 weeks postmenstrual age (PMA)

Disclosures: There are no conflicts of interest to disclose.

Study Protocol



Exclusive Human Milk Diet

- Following randomization, both study groups received 120 kcal/kg/day.
- All of the infants in the ROUTINE group received nutritional fortification with ProLacta+4 H²MF (ProLacta Biosciences, City of Industry, CA).
- Infants the SELECTIVE group received nutritional fortification with ProLacta+4 only in the case of poor growth: < 15 g/kg/day for one week.
- An in-house milk bank comprised of donors who delivered preterm allowed all to receive exclusive preterm human milk until 35 weeks PMA.

Results

Demographics: The two groups were similar at admission to the NICU as shown below.

	Routine n=65	Selective n=68	p-value
Birth Weight (g)	812 \pm 230	824 \pm 195	0.753
GA (weeks)	25.5 \pm 1.3	25.3 \pm 1.4	0.433
Male Sex (%)	36 (55)	39 (57)	0.862
White Race (%)	43 (66)	44 (65)	1.000
Inborn (%)	60 (92)	58 (85)	0.237
Maternal Betamethasone (%)	61 (94)	63 (93)	1.000
C-Section (%)	48 (74)	50 (74)	1.000
Apgar @5 min <7	17 (27)*	17 (25)	0.845

Nutritional Fortification

- While all of the infants in the ROUTINE group received ProLacta+4, only 39 (57%) received ProLacta+4 in the SELECTIVE group.
- Twenty-nine (43%) in the SELECTIVE group never had weight gain < 15 g/kg/day.

Outcomes

	Routine	Selective	p-value
NEC (%)	4 (6)	0 (0)	0.054
Sepsis after Randomization	1 (1.5)	2 (2.9)	1.00
Death and/or NEC	5 (7.7)	0	0.026

- Two infants in the ROUTINE study group died prior to 35 weeks, one from NEC.

Anthropomorphic Measures

Birth	Routine n=65	Selective n=68	p-value
SGA (%)	10 (15)	5 (7)	0.176
Length (cm)	32.6 \pm 3.1	32.6 \pm 2.4	0.957
Head (cm)	23.2 \pm 2.2	23.0 \pm 1.7	0.661
Weight (Z-score)	-0.13 \pm 0.97	0.11 \pm 0.89	0.147
Length (Z-score)	-0.35 \pm 1.1	-0.24 \pm 0.89	0.521
Head (Z-score)	-0.24 \pm 1.3	-0.22 \pm 0.84	0.913

35 weeks PMA	Routine n=63	Selective n=68	p-value
SGA (%)	56 (89)	65 (96)	0.195
Weight (cm)	1560 \pm 343	1586 \pm 265	0.632
Length (cm)	39.1 \pm 3.2	39.2 \pm 2.6	0.868
Head (cm)	29.2 \pm 1.6	29.3 \pm 1.3	0.568
Weight (Z-score)	-2.48 \pm 0.90	-2.39 \pm 0.7	0.534
Length (Z-score)	-2.83 \pm 1.3	-2.81 \pm 1.1	0.922
Head (Z-score)	-1.99 \pm 1.0	-1.90 \pm 0.89	0.577
Birth Weight Regained to 35 weeks (g/kg/day)	14.4 \pm 4.7	15.0 \pm 4.5	0.476

Conclusions

- Delayed human milk fortification based on weight gain reduces morbidity without significant effect on growth.
- Long-term follow-up for growth and neurodevelopment is on-going.