Feeding Activated *B. infantis* EVC001 to VLBW Infants is Associated with Significant Reduction in Rates of Necrotizing Enterocolitis

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Objective

To measure NEC rates in cohorts of very low birth weight (VLBW) infants before and after introduction of *B. infantis* EVC001 in a single Level IV NICU.

Background

Necrotizing enterocolitis (NEC) is a leading cause of preterm infant morbidity and mortality[1]. Given the evidence for association of gut dysbiosis with NEC pathogenesis[2,3], we aimed to quantify the effects of feeding *B. infantis* EVC001 to VLBW infants at Oregon Health & Science University (OHSU), particularly on NEC rates.

Design / Methods

The study is single center, retrospective and observational. Chart review was used to evaluate two VLBW infant cohorts for demographics and NEC (Bell Stage 2 or above) at OHSU between Jan. 2014 and Oct. 2020. The reference group (n=329) did not receive a probiotic, while activated *B. infantis* EVC001 feeding was standard of care from June 2018 onward for the 'EVC001-fed' cohort (n=184). To qualify for inclusion in the EVC001-fed cohort, infants must have received more than 1 feed of EVC001. Both cohorts were fed a core diet including human milk and a period of trophic feeding.

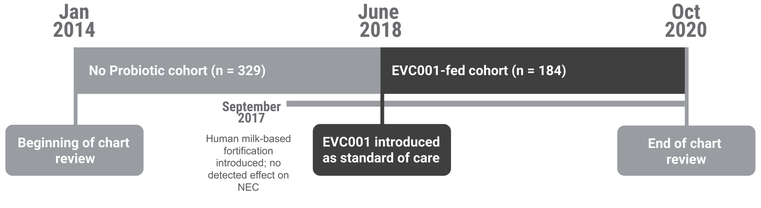

Figure 1. Study Design and Cohort Characteristics
From January 2014 to June 2018, 329 VLBW infants met eligibility criteria for inclusion in the No Probiotic cohort. There were 184 VLBW infants in the EVC001-fed cohort from June 2018 to Oct 2020. Aside from ANS, there were no differences between cohorts in patient demographics (Table 1) by Pearson's Chi-squared test.

Table 1. Patient Demographics

Characteristic	No Probiotic (n=329)	EVC001-fed (n=184)	P value
Female	50.5%	42.4%	p=0.079
Birth weight, mean (min, max)	1027 g (318 g – 1543 g)	1056 g (358 g – 1778 g)	p=0.410
Gestational age at birth, mean (min, max)	28.1 wks (23.1 wks – 35.3 wks)	28.4 wks (23.6 wks – 34.9 wks)	p=0.165
SGA (small for gestational age)	16.1%	14.7%	p=0.667
C-section delivery	76.0%	73.4%	p=0.511
CHD (congenital heart disease)	3.6%	7.1%	p=0.085
ANS (antenatal steroids)	89.7%	83.7%	p=0.050

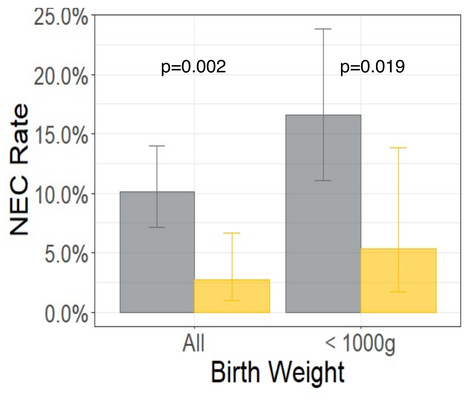

Figure 2. NEC Rates
The difference between cohorts in the rate of NEC was statistically significant: 10.0% (No Probiotic) vs. 2.7% (EVC001-fed), p=0.002.

Infants <1000g or ELBW analyzed as a subgroup also showed a statistically significant difference in NEC rates between cohorts (16.6% vs. 5.3%, p=0.019).

Error bars show the 95% confidence intervals around the estimates. Significance was determined by Fisher's exact test.

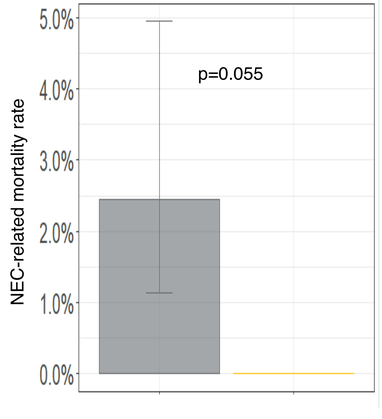

Figure 3. NEC Mortality
There was no NEC-related mortality in the EVC001-fed cohort compared to a NEC mortality rate of 2.4% in the No Probiotic cohort (p=0.055, Fisher's exact test).

Results

- Human milk-based fortification was introduced approximately 8.5 months prior to introduction of *B. infantis* EVC001 without detectable effect on NEC during that time period (Figure 1).
- There were 33 cases of NEC (10.0%) in the No Probiotic cohort (Figure 2). For infants who received more than 1 feed of EVC001, there were 5 cases of NEC in 184 VLBWs (2.7%).
- **The difference in NEC rates between the cohorts was significant (10.0% vs 2.7%, p=0.002)**, with an adjusted risk ratio (ARR) of 0.298 (95% CI 0.104, 0.680) and an **adjusted number needed to treat (NNT) of 14.2** (95% CI 11.2, 31.2). Infants <1000g at birth (ELBW) fed EVC001 and and exclusive human milk diet also showed a significantly lower rate of NEC (Figure 2).
- **There was no NEC-related mortality in infants who received EVC001** compared to a NEC mortality rate of 24% in the infants with NEC in the No Probiotic cohort. NEC mortality for the overall cohorts went from 2.4% to 0% (p = 0.055) (Figure 3).
- **No adverse effects were associated with *B. infantis* EVC001 administration**, including no cases of *B. infantis* infection of any type. Analysis is ongoing for rates of late onset sepsis and other secondary outcomes.

Conclusion

B. infantis EVC001 feeding was associated with a significant reduction in NEC rate in a single center, retrospective, observational study of 513 VLBW infants in a Level IV NICU. This magnitude of NEC prevention may not only reduce VLBW morbidity and mortality, but also provide reduced emotional impact of NEC on parents. Furthermore, it may also provide significant healthcare savings, as the cost of care for an infant with NEC can be over $100K[4].

References

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