

Medications for Gastroesophageal Reflux in Extremely Preterm Infants and Associations with Growth and Development



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Introduction

Reflux occurs commonly in premature infants and is often managed with acid-suppressive therapy. However, there is limited data on its impact on growth and development in the neonatal intensive care unit (NICU) population.

Objective

To determine associations of acid-suppressive therapy at discharge with growth and development in extremely preterm infants in a contemporary cohort.

Eligibility Criteria

- Infants with gestational age (GA) <27 weeks
- Born at a Neonatal Research Network (NRN) center between 2012-2019
- Completed 22-26 month corrected GA follow-up

Methods

- Divided infants into two groups based on receipt of **acid-suppressive therapy at discharge**
 - Acid-suppressive therapy defined as proton pump inhibitors and/or histamine-2 receptor antagonists
- Compared demographics, clinical features, and hospital outcomes
- Compared long term outcomes after **adjusting for confounders**
 - Adjustment Covariates: Birth year, SGA, and if relevant by the backward method, PVL, IVH, BPD, surgeries during NICU hospitalization, and surgeries after NICU discharge

Accounting for comorbidities, acid-suppressive therapy at discharge may be associated with poor growth and moderate/severe neurodevelopment impairment at follow-up.

Table 1. Demographics, clinical characteristics, and hospital outcomes of infants discharged home with and without acid-suppressive therapy

	Acid-suppressive therapy at discharge	
	No N= 2975	Yes N= 508
Gestational age (weeks), mean (SD)	24.8 (1)	24.8 (1)
Birthweight (grams), mean (SD)	757 (164)	727 (158)
SGA, n (%)	146 (5)	47 (9)
Male, n (%)	1,453 (49)	264 (52)
Race/Ethnicity, n(%)		
White	1,268/2,942 (43)	195/498 (39)
Black	1,051/2,942 (36)	187/498 (38)
Hispanic	508/2,942 (17)	74/498 (15)
Other	115/2,942 (4)	42/498 (8)
Significant bloodstream infection ¹ , n (%)	796 (27)	156 (30)
Diagnosis of NEC, n (%)	250/2,974 (8)	72/507 (14)
Diagnosis of SIP, n (%)	150 (5)	31 (6)
Diagnosis of short gut, n (%)	29 (1)	10 (2)
Diagnosis of BPD, grade II or III, n (%)	1,078/2,972 (36)	239/506 (47)
IVH, grade III or IV, n (%)	464/2,967 (16)	71/506 (14)
PVL, n (%)	169/2,974 (6)	37/508 (7)
Gastrostomy tube, n (%)	50 (2)	22 (4)
Nissen fundoplication, n (%)	5 (0.2)	6 (1)
Acid-suppressive therapy at follow up, n/N (%)	214/2,972 (7)	109/507 (22)

Abbreviations: SGA= Small for gestational age; NEC= Necrotizing enterocolitis; SIP= Spontaneous intestinal perforation; BPD= Bronchopulmonary dysplasia; IVH= Intraventricular hemorrhage; PVL= Periventricular leukomalacia
¹ defined by sepsis or bacteremia with positive blood culture
Note: Categorical variables are represented as n(%) or n/N (%) in case of missingness

Table 2. Unadjusted and adjusted outcomes at 22-26 months corrected GA follow up for acid-suppressive therapy use

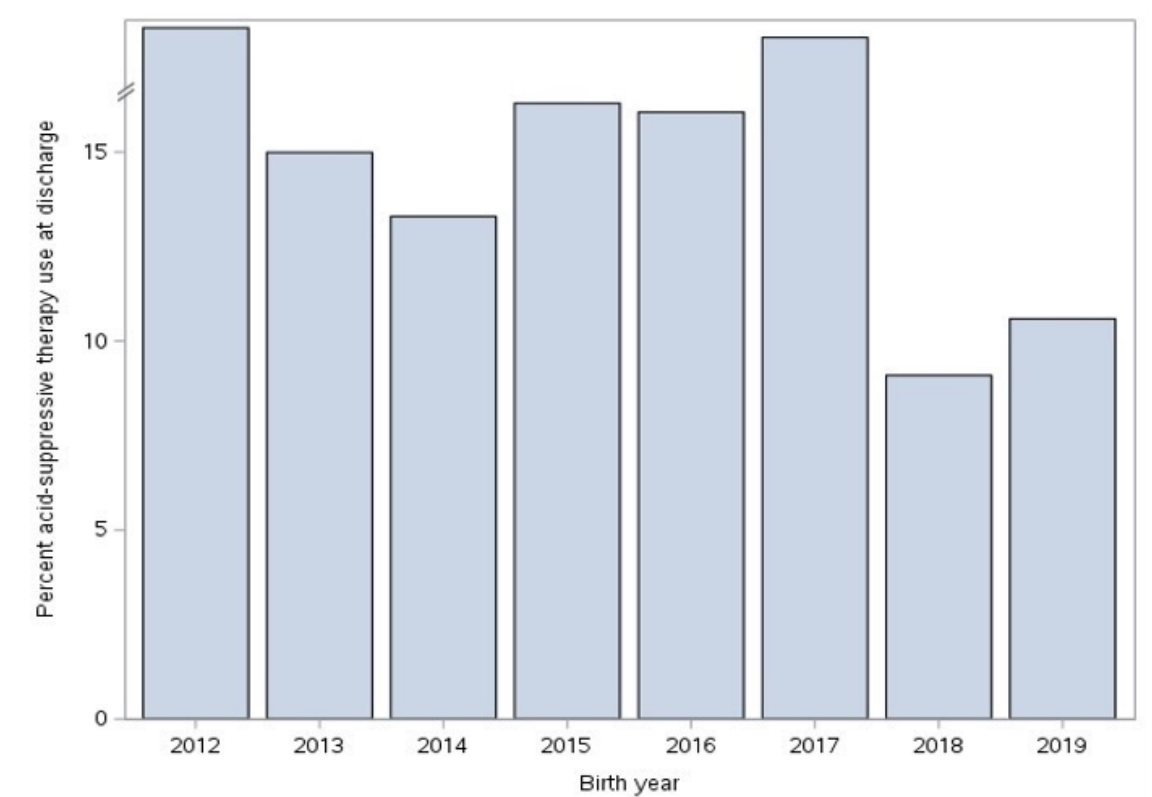
Acid-suppressive therapy at discharge	Unadjusted outcomes				Adjusted outcomes	
	No N= 2975	Yes N= 508	Absolute Mean Difference (95% CI)	p-value	Absolute Mean Difference (95% CI)	p-value
Follow-up weight z-score, mean (SD)	-0.2 (1.8)	-0.5 (1.2)	-0.33 (-0.45, -0.20)	<0.001	-0.18 (-0.35, 0.01)	0.03
Follow-up length z-score, mean (SD)	-0.7 (1.3)	-1.0 (1.3)	-0.30 (-0.42, -0.18)	<0.001	-0.12 (-0.25, 0.00)	0.05
Follow-up head circumference z-score, mean (SD)	-0.3 (1.5)	-0.5 (1.5)	-0.24 (-0.38, -0.10)	<0.001	-0.04 (-0.18, 0.10)	0.56
			Risk Ratio (95% CI)	p-value	Risk Ratio (95% CI)	p-value
Moderate/Severe neurodevelopmental impairment, n (%) ¹	1,188/2,893 (41)	252/497 (51)	1.23 (1.08, 1.41)	0.002	1.16 (1.01, 1.35)	0.04
Severe neurodevelopmental impairment, n (%) ²	511/2,911 (18)	116/498 (23)	1.33 (1.08, 1.62)	0.006	1.16 (0.93, 1.44)	0.19

¹Moderate to Severe Neurodevelopmental impairment (NDI) –Defined as one or more of the following: cognitive composite score of <85 on the Bayley-III; a GMFCS level ≥ 2; moderate-severe cerebral palsy (CP); severe blindness (<20/200 bilaterally); severe hearing impairment (deafness or need for bilateral amplification or cochlear implant)
²Severe NDI – Defined as one or more of the following: cognitive composite score of <70 on the Bayley-III; a GMFCS level ≥ 4; severe blindness (<20/200 bilaterally); severe hearing impairment (deafness or need for bilateral amplification or cochlear implant)
Abbreviations: SD= Standard deviation, CI= Confidence interval
P-values calculated by chi-squared test.
Note: Categorical variables are represented as n(%) or n/N (%) in case of missingness

Results

- 3,483 infants met inclusion criteria
- 508 (15%) were discharged on acid-suppressive therapy (Table 1)
- Acid-suppressive therapy use was more common in infants who were SGA or had complications including NEC (Table 1)
- **Use at discharge decreased** from 2012 to 2019 (Figure 1)
- 9% (323/3,479) of infants were on acid-suppressive therapy at follow up, **66% (214) of those were not discharged on it** (Table 1)
- **After adjustment, there was some association with growth and moderate/severe NDI at follow-up** (Table 2)

Figure 1. Acid-suppressive therapy use at discharge (%) by year (2012-2019)



P-value calculated with Cochran-Armitage test for trend over time, p-value = 0.01

Limitations

- Residual confounding



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Disclosures: The authors have no financial relationships to disclose or conflicts of interest to resolve. Any real or apparent conflicts of interest related to the content of this poster have been resolved. This poster does not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

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