Revisión Bibliográfica

Junio – Julio 2020

- Jama / Jama Pediatrics
- NEJM (newborn, colecciones)
- Lancet
- BMJ

17-07-2020

Dr. Javier Cifuentes.

INDISA
CLINICA DE FAMILIA

Neo Red

Cycled Phototherapy Dose-Finding Study for Extremely Low-Birth-Weight Infants. A Randomized Clinical Trial.

Cody Arnold, MD, MSc; Jon E. Tyson, MD, MPH; Claudia Pedroza, PhD;Wally F. Carlo, MD; David K. Stevenson, MD; RonaldWong, PhD;Allison Dempsey, PhD; Amir Khan, MD; Rafael Fonseca, MD; MyraWyckoff, MD; Alvaro Moreira, MD, MSc; Robert Lasky, PhD.

IMPORTANCE Cycled (intermittent) phototherapy (PT) might adequately control peak total serum bilirubin (TSB) level and avoid mortality associated with usual care (continuous PT) among extremely low-birth-weight (ELBW) infants (401-1000 g).

OBJECTIVE To identify a cycled PT regimen that substantially reduces PT exposure, with an increase in mean peak TSB level lower than 1.5 mg/dL in ELBW infants.

DESIGN, SETTING, AND PARTICIPANTS This dose-finding randomized clinical trial of cycled PT vs continuous PT among 305 ELBW infants in 6 US newborn intensive care units was conducted from March 12, 2014, to November 14, 2018.

INTERVENTIONS Two cycled PT regimens (≥15 min/h and ≥30 min/h) were provided using a simple, commercially available timer to titrate PT minutes per hour against TSB level. The comparator arm was usual care (continuous PT).

MAIN OUTCOMES AND MEASURES Mean peak TSB level and total PT hours through day 14 in all 6 centers and predischarge brainstem auditory-evoked response wave V latency in 1 center. Mortality and major morbidities were secondary outcomes despite limited power.

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- Fototerapia en ELBW puede asociarse a un aumento de:
  - Mortalidad.
  - Epilepsia
  - Cáncer
- Mecanismo;
  - Daño oxidativo
  - Peroxidación de lípidos
  - Daños en DNA

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Cycled Phototherapy Dose-Finding Study for Extremely Low-Birth-Weight Infants. A Randomized Clinical Trial.

- Estudio Randomizado: 6 centros
- Randomización: Estratificada por centro y grupo:
  - Alto riesgo: ≤ 750 g y en VM. Bajo riesgo: > 750 g o sin VM
- Hipótesis:
  - La fototerapia (F) ciclada (cl) puede usarse con seguridad en ELBW para disminuir el tiempo de F contínua (con) manteniendo el promedio del peak de bilirrubina sérica 1,5 mg dentro del promedio logrado con la Fcon y no > a 8 mg/dl
  - BERA sin diferencia entre grupos
- Variable principal:
  - Peak Bilirrubinemia
  - Promedio
  - Bera

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- Criterios Inclusión:
  - RN 400 – 1000 g
  - < 24 h de vida
- Exclusión:
  - Enfermedad hemolítica
  - Infección evidente
  - Anomalía congénita mayor
  - Moribundo: pH < 6.8 por > 2 h

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Table 1. Phototherapy Administration Protocol

TSB level, mg/dL	Phototherapy, min/h			Irradiance, all groups, μW/cm²/nm
	Continuous	Cycled ≥30	Cycled ≥15	
BW ≤750 g				
<5.0[a]	0	0	0	NA
5.0-7.9	60	30	15	22
8.0-9.9	60	60	30	22
10.0-12.9	60	60	60	33
≥13.0	60	60	60	40
BW 751-1000 g				
<5.0 or <7.0[a]	0	0	0	NA
5.0 or 7.0-9.9[a]	60	30	15	22
10.0-11.9	60	60	30	22
12.0-14.9	60	60	60	33
≥15.0	60	60	60	40

Cycled Phototherapy Dose-Finding Study for Extremely Low-Birth-Weight Infants. A Randomized Clinical Trial.

- Randomización:
  - Inicial (primeros100 RN) a 3 grupos (1:1:1):
    Fcon - Fcl: 30 min/h - Fcl: 15 min/h
  - Después el análisis interino: 2 grupos
    Fcon - Fcl: 15 min/h
- Protocolo:
  - 1 bili al día por primeros 7 días. Segunda semana: al inicio y término F
  - Fototerapia: luz azul (irradianza: 22-33 $\mu W/cm^2/nm$)
  - Inicio si bili > 5 mg/dl
  - Suspensión y reinicio según tabla
  - Exanguíneo: $\leq$ 750: bili $\geq$13 mg/dl, $\geq$ 750g: $\geq$ 15 mg/dl. Después de 8 h de F

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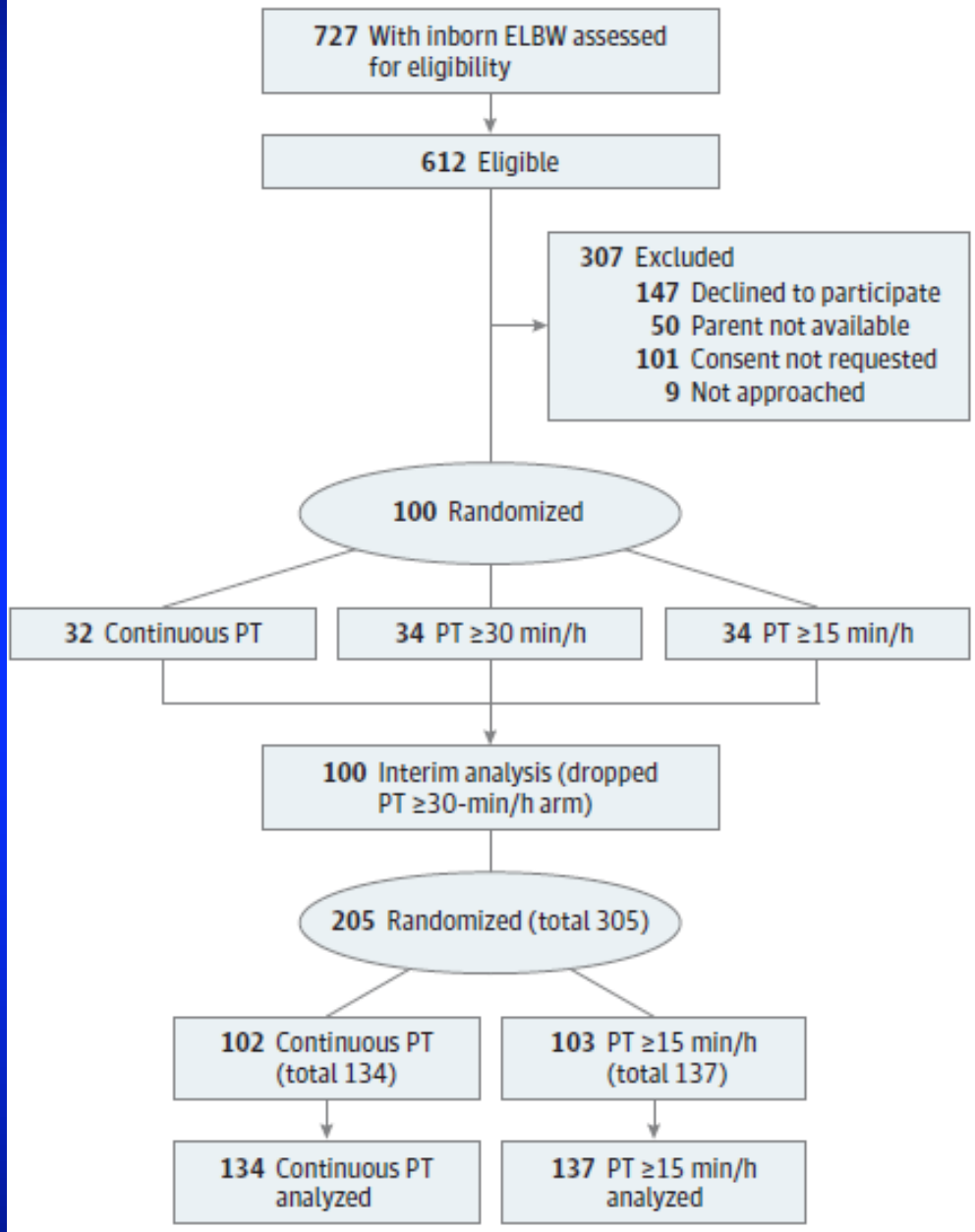
Figure 1. Consort Diagram



ELBW indicates extremely low birth weight; PT, phototherapy.

Characteristic	No. (%) of patients	
	Continuous PT (n = 134)	Cycled PT ≥15 min/h (n = 137)
Gestational age, mean (SD), wk	26.1 (1.9)	26.1 (1.9)
Birth weight, mean (SD), g	736 (151)	754 (149)
Male sex	64 (48)	63 (46)
Race/ethnicity		
White	75 (56)	77 (56)
Black	51 (38)	50 (37)
Hispanic	47 (35)	52 (38)
Antenatal steroid	125 (93)	119 (87)
Magnesium sulfate	125 (93)	119 (87)
Multiple birth	27 (20)	40 (29)
Cesarean delivery	113 (84)	104 (76)
Apgar score, median (IQR)		
1 min	4 (4)	4 (4)
5 min	7 (3)	7 (3)
Baseline hematocrit, mean (SD)		
%	43.6 (6.9)	42.3 (7.1)
Age, h	2.5 (2.8)	2.1 (2.8)
Baseline TSB level, mean (SD), mg/dL	3.4 (1.0)	3.6 (1.1)
Baseline TSB age, mean (SD), h	11.7 (5.7)	11.9 (5.8)
High risk	60 (45)	61 (45)
Intubated at randomization, No./total No. (%)	60/60 (100)	61/61 (100)
Birth weight ≤750 g, No./total No. (%)	60/60 (100)	61/61 (100)
Birth weight, mean (SD), g	629 (99)	626 (86)
Gestational age, mean (SD), wk	25.0 (1.4)	24.8 (1.5)
Low risk	74 (55)	76 (55)
Intubated at randomization, No./total No. (%)	27/74 (37)	36/76 (47)
Birth weight ≤750 g, No./total No. (%)	16/74 (22)	11/76 (14)
Birth weight, mean (SD), g	823 (129)	857 (103)
Gestational age, mean (SD), wk	27.0 (1.7)	27.1 (1.7)

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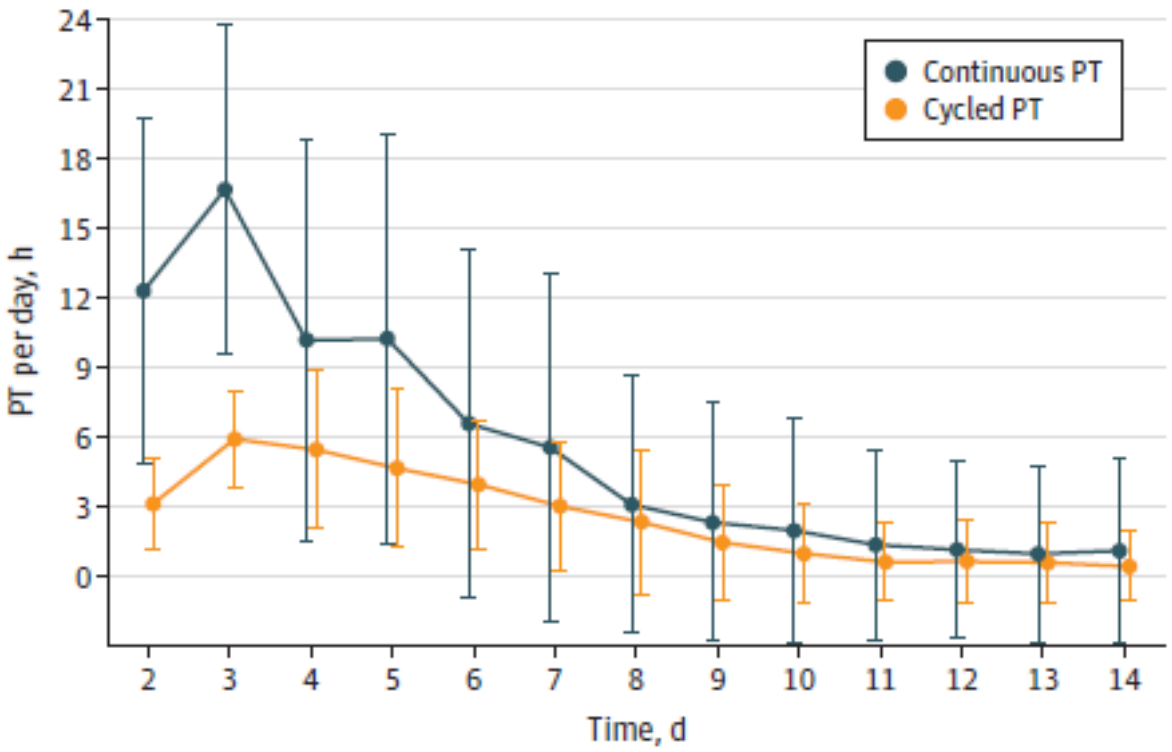
Figure 2. Phototherapy (PT) Hours per Day



Markers represent mean PT hours per day; error bars, 1 SD.

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Table 3. Main Outcomes

Outcome	Phototherapy		Adjusted difference (95% CI)[a,b]
	Continuous	≥15 min/h	
Primary outcomes			
Peak TSB level, mg/dL[c]			
All patients, No.[d]	128	128	
Mean (SD)	6.4 (1.4)	7.1 (1.7)	0.7 (0.4 to 1.1)
High risk, No.	55	53	
Mean (SD)	6.2 (1.2)	6.6 (1.4)	0.4 (−0.1 to 0.8)
Low risk, No.	73	75	
Mean (SD)	6.5 (1.5)	7.5 (1.9)	1.0 (0.5 to 1.6)
Phototherapy, h[c]			
All patients, No.	128	128	
Mean (SD)	72 (34)	34 (19)	−39 (−45 to −32)
High risk, No.	55	53	
Mean (SD)	70 (30)	31 (20)	−39 (−49 to −29)
Low risk, No.	73	75	
Mean (SD)	75 (36)	36 (18)	−39 (−48 to −30)
Secondary outcome of mortality, No./total No. (%)	18/134 (13.4%)	14/137 (10.2%)	−4.5% (−10.9 to 2.0)
Adjusted relative risk (95% CI)[a,e]			0.79 (0.40 to 1.54)

Early-Onset Neonatal Sepsis 2015 to 2017, the Rise of *Escherichia coli*, and the Need for Novel Prevention Strategies. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

IMPORTANCE Early-onset sepsis (EOS) remains a potentially fatal newborn condition. Ongoing surveillance is critical to optimize prevention and treatment strategies.

OBJECTIVE To describe the current incidence, microbiology, morbidity, and mortality of EOS among a cohort of term and preterm infants.

DESIGN, SETTING, AND PARTICIPANTS This prospective surveillance study included a cohort of infants born at a gestational age (GA) of at least 22 weeks and birth weight of greater than 400 g from 18 centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network from April 1, 2015, to March 31, 2017. Data were analyzed from June 14, 2019, to January 28, 2020.

MAIN OUTCOMES AND MEASURES Early-onset sepsis defined by isolation of pathogenic species from blood or cerebrospinal fluid culture within 72 hours of birth and antibiotic treatment for at least 5 days or until death.

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CONCLUSIONS AND RELEVANCE In this study, EOS incidence and associated mortality disproportionately occurred in preterm infants. Contemporary cases have demonstrated the limitations of current GBS prevention strategies. The increase in *E coli* infections among very low-birth-weight infants warrants continued study. Ampicillin and gentamicin remained effective antibiotics in most cases, but ongoing surveillance should monitor antibiotic susceptibilities of EOS pathogens.

Key Points

Question What is the incidence and microbiology of contemporary cases of neonatal early-onset sepsis?

Findings This cohort study of 217 480 infants identified 235 cases of early-onset sepsis from 2015 to 2017; *Escherichia coli* (86 [36.6%]) and group B streptococcus (71 [30.2%]) were the most common pathogens, with *E coli* most frequent among preterm infants and group B streptococcus most frequent among term infants. Of note, 6 of 77 *E coli* isolates (7.8%) were resistant to both ampicillin and gentamicin, the most commonly used agents for empirical therapy.

Meaning These findings suggest that early-onset sepsis persists despite recommended prevention strategies and requires ongoing surveillance for shifts in etiologic agents and antimicrobial resistance.

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Table 1. Pathogens Associated With EOS and EOM

Pathogen[a]	Infant Group, No. (%)					
	All		Preterm (GA 22-36 wk)		Term (GA ≥37 wk)	
	EOS	EOM[b]	EOS	EOM	EOS	EOM
Gram-positive	120 (51.1)	3 (50.0)	38 (29.0)	1 (25.0)	82 (78.8)	2 (100)
GBS	70 (29.8)	1 (16.7)	17 (13.0)	0	53 (51.0)	1 (50.0)
Enterococcus species	13 (5.5)	0	4 (3.1)	0	9 (8.7)	0
Group A streptococcus	9 (3.8)	0	3 (2.3)	0	6 (5.8)	0
Viridans streptococci	7 (3.0)	0	4 (3.1)	0	3 (2.9)	0
Streptococcus bovis	6 (2.6)	1 (16.7)	2 (1.5)	0	4 (3.8)	1 (50.0)
Streptococcus species	5 (2.1)	0	2 (1.5)	0	3 (2.9)	0
Streptococcus pneumoniae	3 (1.3)	0	1 (0.8)	0	2 (1.9)	0
Coagulase-negative staphylococci	2 (0.9)	1 (16.7)	1 (0.8)	1 (25.0)	1 (1.0)	0
Listeria monocytogenes	2 (0.9)	0	2 (1.5)	0	0	0
Staphylococcus aureus	2 (0.9)	0	2 (1.5)	0	0	0
S aureus (methicillin-resistant)	1 (0.4)	0		0	1 (1.0)	0
Gram-negative	107 (45.5)	3 (50.0)	87 (66.4)	3 (75.0)	20 (19.2)	0
Escherichia coli	83 (35.3)	1 (16.7)	67 (51.1)	1 (25.0)	16 (15.4)	0
Haemophilus species	9 (3.8)	0	7 (5.3)	0	2 (1.9)	0
Klebsiella species	7 (3.0)	0	7 (5.3)	0	0	0
Morganella morganii	3 (1.3)	1 (16.7)	3 (2.3)	1 (25.0)	0	0
Citrobacter species	1 (0.4)	1 (16.7)	1 (0.8)	1 (25.0)	0	0
Enterobacter species	1 (0.4)	0	0	0	1 (1.0)	0
Flavobacterium species	1 (0.4)	0	1 (0.8)	0	0	0
Proteus species	1 (0.4)	0	1 (0.8)	0	0	0
Pseudomonas species	1 (0.4)	0	0	0	1 (1.0)	0
Fungi	4 (1.7)	0	4 (3.1)	0	0	0
Candida albicans	4 (1.7)	0	4 (3.1)	0	0	0

Table 2. Rates of EOS per 1000 Live Births

Variable	All pathogens		GBS		*Escherichia coli*	
	No./total No.	Rate (95% CI)[a]	No./total No.	Rate (95% CI)[a]	No./total No.	Rate (95% CI)[a]
All	235/217 480	1.08 (0.95-1.23)	71/217 480	0.33 (0.26-0.41)	86/217 480	0.40 (0.32-0.49)
By birth weight, g						
401-1500	88/6322	13.92 (11.31-17.12)	10/6322	1.58 (0.86-2.91)	51/6322	8.07 (6.14-10.59)
1501-2500	39/20 743	1.88 (1.38-2.57)	7/20 743	0.34 (0.16-0.70)	14/20 743	0.67 (0.40-1.13)
>2501	108/190 415	0.57 (0.47-0.68)	54/190 415	0.28 (0.22-0.37)	21/190 415	0.11 (0.07-0.17)
By GA, wk						
22-28	67/3628	18.47 (14.57-23.38)	5/3628	1.38 (0.59-3.22)	44/3628	12.13 (9.05-16.24)
29-33	50/8056	6.21 (4.71-8.17)	9/8056	1.12 (0.59-2.12)	20/8056	2.48 (1.61-3.83)
34-36	14/19 195	0.73 (0.43-1.22)	3/19 195	0.16 (0.05-0.46)	4/19 195	0.21 (0.08-0.54)
≥37	104/185 970	0.56 (0.46-0.68)	54/185 970	0.29 (0.22-0.38)	18/185 970	0.10 (0.06-0.15)
By sex						
Male	127/111 543	1.14 (0.96-1.35)	39/111 543	0.35 (0.26-0.48)	50/111 543	0.45 (0.34-0.59)
Female	108/105 977	1.02 (0.84-1.23)	32/105 977	0.30 (0.21-0.43)	36/105 977	0.34 (0.25-0.47)
Total (sites included in rates by race)[b]	137/127 740	1.07 (0.91-1.27)	37/127 740	0.29 (0.21-0.40)	52/127 740	0.41 (0.31-0.53)
By race						
Black	47/40 250	1.17 (0.88-1.55)	12/40 250	0.30 (0.17-0.52)	19/40 250	0.47 (0.30-0.74)
White	70/69 140	1.01 (0.80-1.28)	20/69 140	0.29 (0.19-0.45)	26/69 140	0.38 (0.26-0.55)
Other, unknown, or not reported	20/18 089	1.11 (0.72-1.71)	5/18 089	0.28 (0.12-0.65)	7/18 089	0.39 (0.19-0.80)
Total (sites included in rates by ethnicity)[c]	176/155 831	1.13 (0.97-1.31)	56/155 831	0.36 (0.28-0.47)	59/155 831	0.38 (0.29-0.49)
By ethnicity						
Hispanic	46/39 798	1.16 (0.87-1.54)	15/39 798	0.38 (0.23-0.62)	16/39 798	0.40 (0.25-0.65)
Non-Hispanic	125/111 725	1.12 (0.94-1.33)	40/111 725	0.36 (0.26-0.49)	41/111 725	0.37 (0.27-0.50)
Unknown or not reported	5/4393	1.14 (0.49-2.66)	1/4393	0.23 (0.04-1.29)	2/4393	0.46 (0.12-1.66)

Table 2. Rates of EOS per 1000 Live Births

Variable	All pathogens		GBS		*Escherichia coli*	
	No./total No.	Rate (95% CI)[a]	No./total No.	Rate (95% CI)[a]	No./total No.	Rate (95% CI)[a]
All	235/217 480	1.08 (0.95-1.23)	71/217 480	0.33 (0.26-0.41)	86/217 480	0.40 (0.32-0.49)
By birth weight, g						
401-1500	88/6322	13.92 (11.31-17.12)	10/6322	1.58 (0.86-2.91)	51/6322	8.07 (6.14-10.59)
1501-2500	39/20 743	1.88 (1.38-2.57)	7/20 743	0.34 (0.16-0.70)	14/20 743	0.67 (0.40-1.13)
>2501	108/190 415	0.57 (0.47-0.68)	54/190 415	0.28 (0.22-0.37)	21/190 415	0.11 (0.07-0.17)
By GA, wk						
22-28	67/3628	18.47 (14.57-23.38)	5/3628	1.38 (0.59-3.22)	44/3628	12.13 (9.05-16.24)
29-33	50/8056	6.21 (4.71-8.17)	9/8056	1.12 (0.59-2.12)	20/8056	2.48 (1.61-3.83)
34-36	14/19 195	0.73 (0.43-1.22)	3/19 195	0.16 (0.05-0.46)	4/19 195	0.21 (0.08-0.54)
≥37	104/185 970	0.56 (0.46-0.68)	54/185 970	0.29 (0.22-0.38)	18/185 970	0.10 (0.06-0.15)

Abbreviations: EOS, early-onset sepsis; GA, gestational age; GBS, group B streptococcus.

[a] Wilson 95% CIs are reported.

[b] Data were excluded from calculations if the number of births was not reported by race (1 center) or if the number of births recorded as other, unknown, or not reported was more than 20% of the total live births reported (4 centers, 1 hospital at each of 2 additional centers) unless more than 20% of infants at the center were thought to have maternal race other than white or black as determined by center infants born 2015 to 2017 enrolled in the Neonatal Research Network high-risk registry (1 center that was 27% Asian and 1 center that was 29% American Indian/Alaskan Native were not excluded).

[c] Data were excluded from calculations if the number of births was not reported by ethnicity (2 centers, 1 hospital at each of 2 additional centers) or if the number of births recorded as unknown or not reported was more than 20% of the total live births reported (1 hospital at each of 2 centers).

Table 3. Maternal GBS Screening and Indications for IAP for Infants With EOS

Variable	Infant group[a]				
		GA of infants with GBS, wk[c]			
	All (N = 235)[b]	22-34 (n = 14)	35-37 (n = 13)	≥38 (n = 43)	Overall (n = 70)
Screened for GBS					
Yes	158 (67.2)	10 (71.4)	10 (76.9)	25 (58.1)	45 (64.3)
No	68 (28.9)	4 (28.6)	2 (15.4)	17 (39.5)	23 (32.9)
Unknown	9 (3.8)	0	1 (7.7)	1 (2.3)	2 (2.9)
GBS screen result[d]					
Positive	41 (25.9)	9 (90.0)	5 (50.0)	7 (28.0)	21 (46.7)
Negative	115 (72.8)	1 (10.0)	5 (50.0)	18 (72.0)	24 (53.3)
Unknown	2 (1.3)	0	0	0	0
Intrapartum antibiotics given[e]					
GBS prophylaxis (with or without another indication)	47 (20.1)	3 (21.4)	2 (15.4)	2 (4.7)	7 (10.0)
Chorioamnionitis or other non-GBS indication	114 (48.7)	7 (50.0)	3 (23.1)	18 (41.9)	28 (40.0)
No intrapartum antibiotics given	73 (31.2)	4 (28.6)	8 (61.5)	23 (53.5)	35 (50.0)

ble	All (N = 235)[b]	GA of infants with GBS, wk[c] 22-34 (n = 14)	35-37 (n = 13)	≥38 (n = 43)	Overall (n = 70)
per CDC 2010 guidelines					
Previous infant with GBS, No. of mothers	1	0	0	0	0
Antibiotics given	1 (100)	0	0	0	0
Maternal GBS bacteriuria (without CD performed before onset of labor or ROM), No. of mothers	17	2	3	5	10
Antibiotics given	11 (64.7)	2 (100)	2 (66.7)	1 (20.0)	5 (50.0)
Positive GBS screening culture (without CD performed before onset of labor or ROM), No. of mothers	25	7	2	3	12
Antibiotics given	21 (84.0)	6 (85.7)	0	2 (66.7)	8 (66.7)
Unknown GBS status with maternal risk factor, No of mothers.[f]	62	4	0	14	18
Antibiotics given	49 (79.0)	2 (50.0)	0	10 (71.4)	12 (66.7)
Negative GBS screen >5 wk before delivery, no repeat of test, with preterm ROM, and/or labor, No. of mothers[g]	1	0	0	0	0
Antibiotics given	1 (100)	0	0	0	0
Intrapartum prophylaxis not indicated per CDC 2010 guidelines					
Negative GBS screen ≤5 wk before delivery or CD in the absence of labor or ROM, No. of mothers	99	1	4	10	15
Antibiotics given	69 (69.7)	0	1 (25.0)	6 (60.0)	7 (46.7)
Other clinical scenarios					
Negative GBS screen >5 wk before delivery without maternal risk factor, No. of mothers	4	0	0	2	2
Antibiotics given	0	0	0	0	0
Negative GBS screen result, timing unknown, with or without maternal risk factor, No. of mothers[h]	10	0	1	5	6
Antibiotics given	2 (20.0)	0	0	0	0
Unknown GBS status without maternal risk factor, No. of mothers	16	0	3	4	7
Antibiotics given	8 (50.0)	0	2 (66.7)	3 (75.0)	3 (42.8)

Characteristic	All (N = 235)[a]	Preterm (GA 22-36 wk) with GBS or *E coli*		Term (GA ≥37 wk) with GBS or *E coli*		All with GBS or *E coli*		*P* value[b]	
		GBS (n = 17)	*E coli* (n = 68)	GBS (n = 53)	*E coli* (n = 17)	GBS (n = 70)	*E coli* (n = 85)	Unadjusted	Adjusted
Birth weight, g									
401-1500	88 (37.4)	10 (58.8)	51 (75.0)	0	0	10 (14.3)	51 (60.0)	<.001	.67
1501-2500	39 (16.6)	6 (35.3)	14 (20.6)	1 (1.9)	0	7 (10.0)	14 (16.5)		
>2500	108 (46.0)	1 (5.9)	3 (4.4)	52 (98.1)	17 (100)	53 (75.7)	20 (23.5)		
Sex									
Male	127 (54.0)	9 (52.9)	41 (60.3)	30 (56.6)	9 (52.9)	39 (55.7)	50 (58.8)	.75	.79
Female	108 (46.0)	8 (47.1)	27 (39.7)	23 (43.4)	8 (47.1)	31 (44.3)	35 (41.2)		
Antibiotics within 72 h before delivery	162 (68.9)	11 (64.7)	62 (91.2)	24 (45.3)	10 (58.8)	35 (50.0)	72 (84.7)	<.001	.01
Antenatal corticosteroids within 72 h before delivery	85 (36.2)	10 (58.8)	44 (64.7)	NA	NA	NA	NA	.78	.91[c]
ROM ≥18 h before delivery	115 (48.9)	8 (47.1)	53 (77.9)	14 (26.4)	10 (58.8)	22 (31.4)	63 (74.1)	<.001	<.001
Spontaneous ROM with or without labor before 37 weeks	93 (39.6)	12 (70.6)	57 (83.8)	NA	NA	NA	NA	.30	.16[d]
Symptoms within 72 h before delivery									
Maternal temperature ≥38.0 °C	72 (30.6)	3 (17.6)	22 (32.4)	20 (37.7)	8 (47.1)	23 (32.9)	30 (35.3)	.87	.16
Uterine or abdominal tenderness	34 (14.5)	0	23 (33.8)	1 (1.9)	0	1 (1.4)	23 (27.1)	<.001	.03
Foul-smelling vaginal discharge or amniotic fluid	20 (8.5)	1 (5.9)	10 (14.7)	3 (5.7)	1 (5.9)	4 (5.7)	11 (12.9)	.17	.55
Maternal tachycardia (>100 bpm)	135 (57.4)	10 (58.8)	46 (67.6)	20 (37.7)	11 (64.7)	30 (42.9)	57 (67.1)	.003	.05
Fetal tachycardia (>160 bpm)	94 (40.2)	3 (17.6)	35 (52.2)	22 (41.5)	3 (17.6)	25 (35.7)	38 (45.2)	.25	.34
Chorioamnionitis documented in the medical record	103 (43.8)	5 (29.4)	40 (58.8)	23 (43.4)	8 (47.1)	28 (40.0)	48 (56.5)	.05	.09

Characteristic	All (N = 235)[a]	Preterm (GA 22-36 wk) with GBS or *E coli*		Term (GA ≥37 wk) with GBS or *E coli*		All with GBS or *E coli*		*P* value[b]	
		GBS (n = 17)	*E coli* (n = 68)	GBS (n = 53)	*E coli* (n = 17)	GBS (n = 70)	*E coli* (n = 85)	Unadjusted	Adjusted
Highest care level									
Well-baby nursery	25 (10.6)	0	2 (2.9)	13 (24.5)	2 (11.8)	13 (18.6)	4 (4.7)	.02	.31
Intermediate, step-down, or transitional	12 (5.1)	0	2 (2.9)	4 (7.5)	2 (11.8)	4 (5.7)	4 (4.7)		
Intensive care	198 (84.3)	17 (100)	64 (94.1)	36 (67.9)	13 (76.5)	53 (75.7)	77 (90.6)		
Any signs of sepsis in the first 72 h									
Yes	220 (93.6)	17 (100)	67 (98.5)	45 (84.9)	16 (94.1)	62 (88.6)	83 (97.6)	.04	.58
No	15 (6.4)	0	1 (1.5)	8 (15.1)	1 (5.9)	8 (11.4)	2 (2.4)		

Characteristic	All (N = 235)[a]	Preterm (GA 22-36 wk) with GBS or *E coli*		Term (GA ≥37 wk) with GBS or *E coli*		All with GBS or *E coli*		*P* value[b]	
		GBS (n = 17)	*E coli* (n = 68)	GBS (n = 53)	*E coli* (n = 17)	GBS (n = 70)	*E coli* (n = 85)	Unadjusted	Adjusted
Signs of sepsis[f]									
Temperature ≥38.0 °C	42 (19.1)	1 (5.9)	13 (19.4)	10 (22.2)	4 (25.0)	11 (17.7)	17 (20.5)	.83	.17
Temperature ≤36.0 °C	40 (18.2)	2 (11.8)	17 (25.4)	6 (13.3)	3 (18.8)	8 (12.9)	20 (24.1)	.14	.32
Cyanosis with use of supplemental oxygen (>60 min)	90 (40.9)	7 (41.2)	36 (53.7)	11 (24.4)	3 (18.8)	18 (29.0)	39 (47.0)	.04	.92
Tachypnea (respiratory rate >60 breaths/min) for ≥30 min documented twice	132 (60.0)	11 (64.7)	38 (56.7)	27 (60.0)	9 (56.3)	38 (61.3)	47 (56.6)	.61	.57
Grunting, flaring, retractions	144 (65.5)	11 (64.7)	45 (67.2)	27 (60.0)	8 (50.0)	38 (61.3)	53 (63.9)	.86	.63
Hypotension[g]	92 (41.8)	8 (47.1)	41 (61.2)	12 (26.7)	6 (37.5)	20 (32.3)	47 (56.6)	.004	.19
Acidosis[h]	116 (52.7)	10 (58.8)	50 (74.6)	16 (35.5)	3 (18.8)	26 (41.9)	53 (63.9)	.01	.89
Tachycardia (heart rate >160 bpm)	154 (70.0)	12 (70.6)	59 (88.1)	20 (44.4)	9 (56.3)	32 (51.6)	68 (81.9)	<.001	.15
Apnea and/or intermittent bradycardia	69 (31.4)	5 (29.4)	32 (47.8)	6 (13.3)	3 (18.8)	11 (17.7)	35 (42.2)	.002	.15
Lethargy	51 (23.2)	5 (29.4)	21 (31.3)	12 (26.7)	1 (6.3)	17 (27.4)	22 (26.5)	>.99	.41
Irritability	31 (14.1)	4 (23.5)	5 (7.5)	4 (8.9)	3 (18.8)	8 (12.9)	8 (9.6)	.60	.74
Hypoglycemia (lowest blood glucose level <40 mg/dL)	61 (27.7)	2 (11.8)	24 (35.8)	13 (28.9)	6 (37.5)	15 (24.2)	30 (36.1)	.15	.09
Neutropenia (ANC<1000/μL)	44 (20.0)	5 (29.4)	20 (29.9)	4 (8.9)	3 (18.8)	9 (14.5)	23 (27.7)	.07	.46
Bleeding, petechiae, thrombocytopenia (platelets < × 10^3/μL)	42 (19.1)	2 (11.8)	20 (29.9)	8 (17.8)	2 (12.5)	10 (16.1)	22 (26.5)	.16	.98
Abdominal distention or >1 episode of bilious emesis	11 (5.0)	1 (5.9)	7 (10.4)	0	0	1 (1.6)	7 (8.4)	.14	.21
Clinical seizures (proven or suspect)	9 (4.1)	0	6 (9.0)	2 (4.4)	0	2 (3.2)	6 (7.2)	.47	.35

- E Coli: 86 (36,6%)
- SGB: 71 (30,2%)

- Gram negativos: Más frecuentes en RNpT
- Gram positivos: Maás frecuentes en RNT
- No hay casos de cultivo + solo en LCR
- Hemocultivo: 85% en primeras 24 h
- Cultivo LCR: ≥ 2 días. 95% recibiendo antibióticos

- EOS: 1.08 CI (0.95 – 1.23)/1000 RN
- 22-28 s: 18.47 CI (14.57 – 23.38)/1000 RN
- E. Coli: 0.40 CI (0.32 – 049)/1000 RN
- SGB: 0.33 CI (0.26 – 0.41)/1000 RN
- 22-28 s. 12.13 CI (9.05 – 16.24) v/s 1.38 CI (0.59 – 3.22)/1000 RN

- Tiempo a la positividad del cultivo:
  - 17.6 h (95% percentil: 65.9 h).
  - Gram positivos: 19.3 (95% percentil: 71.3 h)
  - Gram negativos: 14.7 (95% percentil: 43.3 h)
  - Hongoss: 49.7 (95% percentil: 66.3 h)

- E. Coli: 90% susceptibles para gentamicina.
- 7.8% E. coli resistentes a Ampi y Genta
- Screening para SGB y uso de antibióticos intraparto (AIP):
- 158/235 (67.2%). 41/158 (25.9%) colonizado
- 83/106 (78%) de RN con indicación recibieron AIP
- RN con SGB:
  - 45/70 madres (64.3%) recibieron screening
  - 24/45 screening negativo15/40 /37.5%) no recibieron AIP a pesar de tener al menos una indicación.

Características Clínicas:

- 79% E.coli en RNpT. EG: 28 (25-33) s. Peso: 1230 (800-2090) g.
- 76% SGB en RNT EG: 39 (37-40) s. Peso: 3199 (2550-3440) g.
- E. Coli v/s SGB:
  - > uso de antibióticos prenatal (72 h)- 84% v/s 50%.
  - RPM ≥ 18 h: 74% v/s 31%
  - Corioamnionitis clínica: 53%
- Signos clínicos:
- Inestabilidad clínica en < 72 h: 93.6%
- RN con EOS nacidos de madres con corioamnionitis 59/60 signos al nacer
- < 37s: 97,6% parto vaginal o cesárea con RPM o inicio de trabajo de parto. 2.3% cesárea sin RPM o inicio de trabajo de parto

- 198/235 (84.3%) recibieron cuidados intensivos.
- RNT: 21% manejado en salacuna
- 22/104 EOS en RNT fueron manejados en nursery
- Antibióticos:
- 234/235 recibieron antibióticos.
- 182/234 recibieron 2 antibióticos (ampicilina/gentamicina)
- 138/234 (59%) cambiaron antibiótico según cultivo
- EOS RNT: mayoría en RN con screening negativo
- Mortalidad:
  - 195/235 (83%) sobrevida
  - 22 - 36 s: 71% sobrevida. (E coli: 60%)
  - ≥ 36 s: 100% sobrevida
  - 2 RN fallecidos con resitencia a Ampi y Genta

- 2006-2009 v/s 2019 -2020
- Tasa de infección:
- 1.16 (1.01-1.33) v/s 1.0 (0.9-1.1)/1000 (p: 0.08)
- VLBW:
- 15.05 (12.08-18.74) v/s 11.0 (9.26-13.06)
- Tasa de SGB sin cambios
- E. Coli en VLBW: 8.68 (6.50-11.60) v/s 5.07 (3.93-6.53). p_:0.008.
- Sin cambios en mortalidad.