Brief Report

Use and Abuse of Antibiotics in Latin American Neonatal Units in the EpicLatino Database Eight Years of Experience

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Use and Abuse of Antibiotics in Latin American Neonatal Units in the EpicLatino Database Eight Years of Experience

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Abstract: The use of antibiotics in neonatal units worldwide varies significantly. We included data from 2015-2022 from the EpicLatino database, which comprises a network of 32 units in Latin America and the Caribbean with gestational age at birth (GA) of ≤ 32 weeks. A questionnaire was sent to the EpicLatino units, to correlate practice with outcomes. Negative binomial regression with standard errors and confidence intervals computed for incidence-rate ratios (IRRs) was used for comparative statistics on antibiotic days per 1000 patient-days between units. All units that responded had 1-6 differences with the reference unit (Unit 2) with the best results, but there was no clear association with the IRR. Each EpicLatino unit should review its statistics to explore possibilities for reducing antibiotic usage.

Keywords: antibiotic use in neonatal units; preterm infants; EpicLatino database

Introduction

The use of antibiotics in neonatal units worldwide varies significantly,[1] and there are ethical and practical limitations that hinder its study. In Latin America, similar variability in antibiotic use occurs, as reflected in the annual reports from EpicLatino.[2]

Materials and Methods:

We included data from 2015-2022 from the EpicLatino database, which comprises a network of 32 units in Latin America and the Caribbean (Table 1), with gestational age at birth (GA) of ≤ 32 weeks. A questionnaire was sent to the EpicLatino units, to correlate practice with outcomes (Table 2).

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Table 1. Units belonging to the EpicLatino network.

UNITS	CITY/COUNTRY
Centenario H. de Esp. Miguel Hidalgo	Aguascalientes, Mexico
Clínica Dávila	Santiago, Chile
Clínica de Santa María de Santiago	Santiago, Chile
Clínica del Country	Bogotá, Colombia
Clínica la Colina	Bogotá, Colombia
Clínica Materno Infantil San Luis	Bucaramanga, Colombia
Clínica San Felipe	Lima, Perú
Clínica Santa Bárbara	Quito, Ecuador
Clínica Somer	Rio Negro, Colombia
Clínica Universitaria Colombia	Bogotá, Colombia
Clínica Vespucio	Santiago, Chile
Colsanitas – Clínica Pediátrica UCI Neonatal	Bogotá, Colombia
Curaçao Medical Center	Willemstad, Curaçao
H Regional DR Rafael Pascacio Gamboa	Tuxtla Gutiérrez, México
Hospital Central Dr. Ignacio Morones Prieto	San Luis Potosí, México
Hospital Civil de Ipiales E.S.E	Ipiales, Colombia
Hospital de los Valles	Quito, Ecuador
Hospital Departamental San Vicente de Paul	Garzón, Huila, Colombia
Hospital Dr. Florencio Escardó	Tigre, Argentina
Hospital Español de Mendoza	Mendoza, Argentina
Hospital General EISS de Manta	Manta, Ecuador
Hospital Italiano de La Plata	La Plata, Argentina
Hospital Luis Lagomaggiore	Mendoza, Argentina
Hospital Metropolitano	Quito, Ecuador
Hospital Militar Central	Bogotá, Colombia
Hospital Regional Universitario de Colima	Colima, México
Hospital San Francisco de Quito	Quito, Ecuador
Hospital San José	Bogotá, Colombia
Hospital Santísima Trinidad	Asunción, Paraguay
Los Cobos Medical Center	Bogotá, Colombia
Maternidad Nuestra Sra. de las Mercedes	Tucumán, Argentina
S.E.S. Hospital de Caldas	Manizales, Colombia

Negative binomial regression with standard errors and confidence intervals computed for incidence-rate ratios[3,4] (IRRs) was used for comparative statistics on antibiotic days per 1000 patient-days between units. We used for the statistics Stata 18, StataCorp LLC, Texas, USA. The variables used to adjust the regression analysis were necrotizing enterocolitis (NEC), GA, infected patients (positive blood or cerebrospinal fluid cultures), length of stay, time period (before/after 2020) and mortality.

Table 2. Questionnaire sent to the EpicLatino units, to correlate practice with outcomes.

1. Do you initiate antibiotics in premature infants ≤ 32 weeks gestation as follows:
A) Initiate antibiotics in all or almost all premature infants[5] ≤ 32 weeks gestational age after birth due to the risk of infection?
B) Select premature infants ≤ 32 weeks gestation for antibiotic administration based on risk factors or laboratory tests.
2. If premature infants ≤ 32 weeks gestation are born outside[6] your institution, do you manage them the same as those born in your institution?

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A) Yes

B) No

3. If the mother has received prenatal antibiotics, do you use the same criteria to initiate antibiotics in premature infants ≤ 32 weeks gestation?

A) Yes

B) No

4. Do you take blood cultures, if possible, for all premature infants who are going to receive antibiotics?

A) Yes

B) No

5. If you select the premature infants to whom antibiotics will be administered at birth (skip this question if you administer them to almost all infants):

A) Select premature infants based on risk factors.

B) Select premature infants based on laboratory results obtained within the first 24 hours.

C) Do not perform tests and rely on clinical follow-up.

D) Both A and B.

6. For premature infants who undergo blood cultures:

A) If the premature infant is stable and the blood cultures are negative, antibiotics are discontinued within 24 to 72 hours.

B) Despite negative results, antibiotics are often continued for 5 to 10 days due to a lack of confidence in the results.

7. In addition to blood cultures, what laboratory tests do you use to decide whether to initiate/continue antibiotics?

A) Complete blood count

B) C-reactive protein

C) A and B, or A and D

D) Procalcitonin

E) No tests are used to make this decision

F) Other tests not listed

Antibiotics initiated after the second day of life:

8. If a premature infant deteriorates (increased apnea, dusky color, lethargy, persistent vomiting, abdominal distension, among others):

A) Blood cultures are taken, and antibiotics are initiated regardless of the results of other tests, if performed.

B) Blood cultures and other tests are taken, and antibiotics are initiated based on the results of the other tests.

C) Antibiotics are initiated before taking blood cultures or other tests, if performed.

9. For premature infants who received antibiotics:[7]

A) If the premature infant is stable, there have been no changes in the laboratory findings, and blood cultures are negative, antibiotics are discontinued within 24 to 72 hours.

B) Despite negative blood cultures, antibiotics are often continued for more than 72 hours due to a lack of confidence in the results.

10. Duration of antibiotic treatment in premature infants[8] ≤ 32 weeks gestation with positive blood cultures:

A) Antibiotics are discontinued when symptoms resolve or 2-3 days later, regardless of the treatment duration.

B) Antibiotics are only discontinued if a new blood culture is negative and/or the previously positive laboratory tests completely normalize, regardless of symptoms.

C) The duration depends on the type of organism.

D) The established treatment duration in the unit is always completed (7, 10, 14, 21 days).

E) Options C and D include our management in the unit.

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11. Use of antibiotics in premature infants ≤ 32 weeks gestation with negative blood cultures[8]:
A) It is common to complete the antibiotic course, even if blood cultures are negative due to a lack of confidence in them.
B) It is uncommon to continue antibiotics with negative blood cultures, only in highly symptomatic patients or in conditions such as enterocolitis.
C) All premature infants at a predetermined gestational age (< 30, < 28, or < 26 weeks gestation) receive antibiotic regimens of 7, 10, 14, or 21 days regardless of symptoms or laboratory tests.
Use of antibiotics in your unit:
12. In your unit, do you think that:
A) Antibiotics are used excessively.
B) Antibiotics are used sparingly.

Results

Figure 1 illustrates the units compared to Unit 2, which serves as the baseline due to having the lowest number of antibiotic days per 1000 patient-days and enough cases. The light blue color on the graph indicates the number of cases in each unit. The two numbers next to each dot represents the number of antibiotic days per 1000 patient-days next to the adjusted IRR and its 95% confidence interval (CI) adjusted with the mentioned variables.

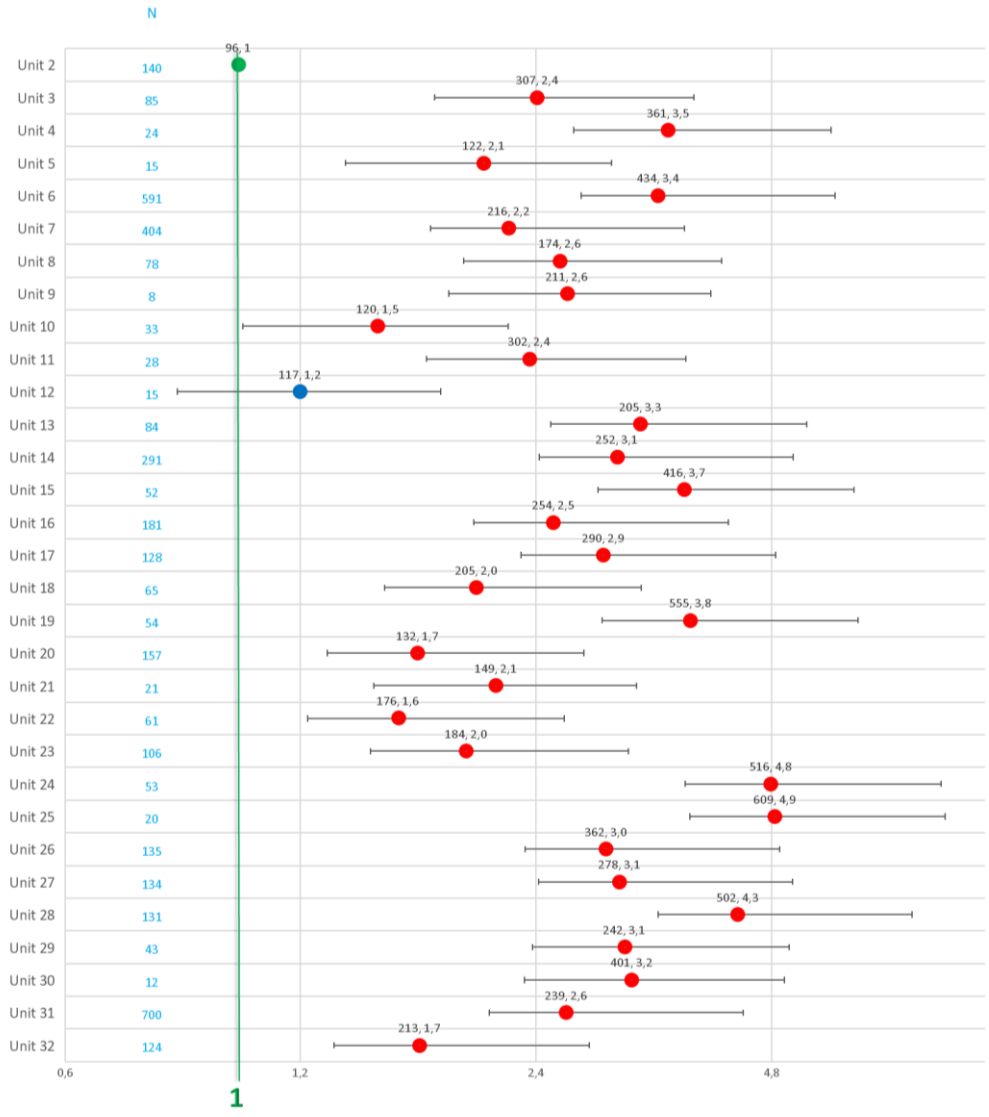

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Figure 1. Statistics of EpicLatino units, numbered for confidentiality. The number of cases is indicated in light blue. Unit 2 (highlighted in green) was used as the base due to its lowest statistic value in DA/P and an adequate number of cases. Units with a significant difference, indicated in red and confidence intervals for the incidence-rate ratio (IRR) (see text). NEC: Necrotizing Enterocolitis, CSF: cerebrospinal fluid. Unit 1 was excluded due to only 1 case of infants of ≤ 32 Weeks GA

Table 3 presents the parameters used by unit 2 to reduce the use of antibiotics. All units that responded the questionnaire (representing 99.5% of records) showed 1-6 differences compared to the baseline unit. There was no clear relationship between the responses and the IRR of each unit. Notably, among units that perceived themselves as using few antibiotics (as indicated in the last question), the average IRR for these units was 2.4, and three of them had an IRR above 3.

Table 3. The base unit (Unit 2 for statistical calculation) uses the following criteria to minimize antibiotic use, which served as the basis for the comparison:.

1. Premature infants ≤ 32 weeks gestation who will receive antibiotics are selected based on risk factors and/or laboratory tests.
2. Antibiotics are not used solely based on being born outside the institution or maternal antibiotic use.
3. Antibiotics are only administered if clinical symptoms are present and confirmed by laboratory data (complete blood count and C-reactive protein).
4. If the premature infant is stable and blood cultures are negative, antibiotics are discontinued within 24 to 72 hours, provided that the clinical picture and laboratory results allow it.
5. If the premature infant deteriorates during their stay, tests are conducted, and a collective decision is made whether to initiate antibiotics or not.
6. Antibiotics are discontinued when symptoms disappear or 2-3 days later, regardless of the treatment duration. Continuation of antibiotics with negative cultures is very rare.
7. In reality, this unit genuinely uses a minimal amount of antibiotics.

Discussion

To understand the practices leading to this marked difference, the questionnaire on antibiotic use practices showed some differences, but there was no clear association with the IRR. Units that believed they used few antibiotics may not be fully aware of their higher antibiotic usage.

It is noteworthy that a significant number of units claim to comply with most internationally recognized concepts of good antibiotic usage practices. However, it is possible that some units may report what they would like to happen in their facilities rather than the actual practices. Based on international literature, there is always some variables that were not considered. Each EpicLatino unit should review its statistics to explore possibilities for reducing antibiotic usage.

Acknowledgment is given to the units in EpicLatino for their efforts in maintaining this database, which allows us to improve quality and to Pablo Vasquez-Hoyos for the help in statistics.

EpicLatino Database 2015-2022, Premature Infants ≤ 32 Weeks GA, Actual Value (days of antibiotics per 1000 patient-days [DA/P]) and Adjusted Incidence Rate Ratio (IRR) (95% CI) on Logarithmic Scale Adjusted for Gestational Age, Positive Blood/CSF cultures, Length of Stay, NEC, time period and Death

References

1. Z. Willis and A. de St Maurice, "Strategies to improve antibiotic use in the neonatal ICU," (in eng), Curr Opin Pediatr, vol. 31, no. 1, pp. 127-134, Feb 2019, doi: 10.1097/MOP.0000000000000716.
2. EpicLatino, "Epiclatino Repport 2021," https://www.epiclatino.co/reports-2021, 2021. [Online]. Available: https://www.epiclatino.co/reports 2021
3. M. Ibáñez-Pinilla, S. Villalba-Niño, and N. N. Olaya-Galán, "Negative log-binomial model with optimal robust variance to estimate the prevalence ratio, in cross-sectional population studies," (in eng), BMC Med Res Methodol, vol. 23, no. 1, p. 219, Oct 04 2023, doi: 10.1186/s12874-023-01999-1.

 doi:10.20944/preprints202404.1381.v1

4. J. A. Grembi and E. T. Rogawski McQuade, "Introducing riskCommunicator: An R package to obtain interpretable effect estimates for public health," (in eng), PLoS One, vol. 17, no. 7, p. e0265368, 2022, doi: 10.1371/journal.pone.0265368.
5. S. Mukhopadhyay, S. Sengupta, and K. M. Puopolo, "Challenges and opportunities for antibiotic stewardship among preterm infants," (in eng), Arch Dis Child Fetal Neonatal Ed, vol. 104, no. 3, pp. F327-F332, May 2019, doi: 10.1136/archdischild-2018-315412.
6. I. Viel-Thériault, A. Agarwal, E. Bariciak, N. Le Saux, and N. Thampi, "Antimicrobial Prophylaxis Use in the Neonatal Intensive Care Unit: An Antimicrobial Stewardship Target That Deserves Attention!," (in eng), Am J Perinatol, vol. 39, no. 12, pp. 1288-1291, Sep 2022, doi: 10.1055/s-0040-1722600.
7. Katz S, Banerjee R, Schwenk H. Antibiotic Stewardship for the Neonatologist and Perinatologist. Clin Perinatol. 2021 Jun;48(2):379-391. doi: 10.1016/j.clp.2021.03.009. PMID: 34030820.
8. Morowitz MJ, Katheria AC, Polin RA, Pace E, Huang DT, Chang CH, Yabes JG. The NICU Antibiotics and Outcomes (NANO) trial: a randomized multicenter clinical trial assessing empiric antibiotics and clinical outcomes in newborn preterm infants. Trials. 2022 May 23;23(1):428. doi: 10.1186/s13063-022-06352-3. PMID: 35606829; PMCID: PMC9125935.