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Characterization of the adherence to hemoculture-guided monotherapy for the treatment of neonatal infections in a teaching maternity hospital

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Abstract

Objective: To characterize positive blood cultures and medical adherence to blood culture-guided antimicrobial monotherapy, as well as factors associated with this practice, in a neonatal intensive care unit (NICU). **Methods:** A cross-sectional retrospective study carried out using notification forms of infections related to healthcare in newborns hospitalized with positive blood cultures from January to December 2019, in the NICU of a teaching maternity hospital from Fortaleza, Brazil. Demographic and clinical data of the newborns were collected, as well as antimicrobials used and blood culture result. Adherence to monotherapy was considered when there was prescription of only one antimicrobial agent sensitive to the isolated microorganism. Data analysis was performed using Excel® and GraphPad Prism softwares. **Results:** 62 positive blood cultures from 48 newborns were included. Of these, the majority were female (54,2%), extremely preterm (29,2%) and had extremely low birth weight (35,4%). Gram-positive bacteria (59,7%) were the most isolated, mainly *Staphylococcus epidermidis* (54,1%) and *Staphylococcus haemolyticus* (18,9%). Vancomycin (21%) was the most prescribed antimicrobial, followed by oxacillin (19,4%). Regarding adherence, it was observed that 53.2% of prescriptions did not adhere to monotherapy. On the other hand, adherence to monotherapy was observed in 53.3% of hospital discharge cases. Adherence to monotherapy was more frequent after detection of fungi (75%) and Gram-negative bacteria (66,7%) than after detection of Gram-positive bacteria (32,4%). Furthermore, infections with Gram-negative bacteria were significantly associated with adherence to monotherapy (p = 0.03, relative risk = 1.82), while infections with Gram-positive bacteria were significantly associated with non-adherence to monotherapy (p = 0.01, relative risk = 0.48). No statistically significant associations were found between the other analyzed variants. **Conclusion:** Adherence to antimicrobial monotherapy guided by blood culture occurred in less than half of the therapies in preterm and low birth weight newborns. Gram positive bacteria are related to non-adherence to monotherapy. There were also high prevalence rates of vancomycin prescription and of Staphylococcus spp (mostly resistant to oxacillin).

Keywords: Sepsis; Antimicrobials; Newborn; Blood culture; Intensive care units, Neonatal.

Caracterização da adesão à monoterapia guiada por hemocultura no tratamento de infecções neonatais em uma maternidade escola

Resumo

Objetivo: Caracterizar as hemoculturas positivas e a adesão médica à monoterapia antimicrobiana guiada por hemocultura, assim como os fatores associados a esta prática, em unidade de terapia intensiva neonatal (UTIN). **Métodos:** Estudo transversal e retrospectivo realizado por meio das fichas de notificações de infecções relacionada à assistência à saúde em recém-nascidos internados com hemocultura positiva de janeiro a dezembro 2019, na UTIN de uma maternidade escola em Fortaleza, Brasil. Coletou-se dados demográficos e clínicos dos recém-nascidos, assim como antimicrobianos utilizados e resultados de hemoculturas. A adesão à monoterapia foi considerada quando houve prescrição de apenas um antimicrobiano sensível ao microrganismo isolado. A análise dos dados foi feita através dos Softwares Excel® e GraphPad Prism. **Resultados:** Foram incluídas 62 hemoculturas positivas provenientes de 48 recém-nascidos. Destes, a maioria era do sexo feminino (54,2%), pré-termo extremo (29,2%) e de extremo baixo peso ao nascer (35,4%). As bactérias Gram-positivas (59,7%) foram as mais isoladas, principalmente o Staphylococcus epidermidis (54,1%) e Staphylococcus haemolyticus (18,9%). A vancomicina (21%) foi o antimicrobiano mais prescrito, seguido da oxacilina (19,4%). Com relação à adesão, observou-se que 53,2% das prescrições não aderiram à monoterapia. Por outro lado, a adesão à monoterapia foi observada em 53,3% dos casos de alta hospitalar. A adesão à monoterapia foi mais frequente após o isolamento de fungos (75%) e bactérias Gram negativas (66,7%), do que após o isolamento de bactérias Gram-positivas (32,4%). Ademais, as infecções por bactérias Gram-negativas foram significativamente associadas com a adesão à monoterapia (p = 0,03, risco relativo = 1,82), enquanto as infecções por bactérias Gram-positivas foram significativamente associadas com a não adesão à monoterapia (p = 0,01, risco relativo = 0,48). Não foram encontradas associações estatisticamente significativa entre as outras variantes analisadas. **Conclusão:** Adesão à monoterapia antimicrobiana guiada por hemocultura ocorreu em menos da metade dos tratamentos em recém-nascidos prematuros e de baixo peso. As bactérias Gram positivas estão relacionadas a não adesão à monoterapia. Observou-se, também, uma maior prevalência de prescrição de vancomicina e presença de Staphylococcus spp (em maioria resistente à oxacilina).

Palavras-chave: Sepse; Antibacterianos; Recém-nascido; Hemocultura; Unidades de terapia intensiva neonatal.

Introduction

The neonatal period, which comprises the first 28 days of life, is considered the most vulnerable time for the survival of an individual, mainly due to the high susceptibility to infections. The immature immune system, low birth weight and the need for invasive procedures can explain this greater predisposition to infections, especially those related to healthcare, and limit the survival of these newborns.[1]

Healthcare-Associated Infections (HAIs) in Neonatology are those acquired during the assistance provided in a hospital or other health unit in the processes of prevention, diagnosis and/or treatment of diseases. They are classified as early when they manifest in the first 48 hours of life, and as late when they emerge after 48 hours of life.[2,3] Late neonatal sepsis is one of the main causes of mortality and affects approximately 60% of the newborns in Brazil.[4]

The treatment of HAIs is performed by using antimicrobials, with the use of combined therapy being common in empirical treatments. This consists of administering two or more antimicrobials with different action spectra, considering the probable microorganisms and the infection site, until the results of the cultures are released. Knowledge of the microbial sensitivity and resistance profile of the institution can assist in the selection of the most appropriate empirical antimicrobials and enable a faster and safer recovery for the newborn.[5]

Immediately after a diagnostic/laboratory confirmation of the microorganism involved in the infection, it is recommended to adapt the treatment to the sensitivity profile observed and it is preferable to prescribe antimicrobial monotherapy, in case of isolation of a single pathogen.[6,7] Culture-guided antimicrobial monotherapy reduces treatment toxicity and selection of multidrug-resistant pathogens, which in turn increase morbidity, mortality, costs and hospitalization time. However, in the clinical practice, non-adherence to monotherapy is frequent and can be related to uncertainties in diagnosis, neglect of the severity of bacterial resistance and/or insecurity on the part of the medical team.[8,9,10]

In the hospital environment, the presence of a Hospital Infection Control Service (*Serviço de Controle de Infecção Hospitalar*, SCIH) is of fundamental importance to increase awareness about the infection control and prevention practices, reduce the emergence of multidrug-resistant in-hospital pathogens and supervise compliance with antimicrobial prescription protocols. Follow-up of the culture results released is a fundamental tool of the SCIH in the evaluation of the antibiotic therapies prescribed, in the follow-up of patients, and in the elaboration of indicators of adherence to protocols at the institutional level, especially in intensive care units.[6]

In this context, and considering the importance of the rational and hemoculture-guided use of antimicrobials, the current study was conducted with the objective of characterizing the results of positive hemocultures and medical adherence to hemoculture-guided antimicrobial monotherapy, as well as the factors associated with this practice in a neonatal intensive care unit in northeastern Brazil.

Methods

This is a cross-sectional and retrospective study carried out through the analysis of the HAI notification forms of newborns admitted to the Neonatal Intensive Care (NICU) in a teaching maternity hospital from Fortaleza, Ceará. The study was approved by the Ethics Committee of the Assis Chateaubriand Teaching Maternity Hospital (*Maternidade Escola Assis Chateaubriand*, MEAC), which is part of the hospital complex of the Federal University of Ceará (*Universidade Federal do Ceará*, UFC) under opinion number: 4,246,797 and C.A.A.E.: 36722120.8.0000.5050.

The study data were taken from the HAI notification forms, completed by the Hospital Infection Control Service (SCIH) from January to December 2019. The forms analyzed were filled in by physicians and nurses who work in the SCIH team of the institution under study. The study sample was for convenience.

The study locus is a reference institution for high-risk pregnancies and Neonatology, which is linked to the public health system. It has 204 hospitalization beds: 68 for pediatric and neonatal cases and 21 NICU beds. In the neonatal units there is a multiprofessional team consisting of a physician, nurse, physiotherapist, occupational therapist, speech therapist, pharmacist, nutritionist, psychologist, social worker, Nursing technicians and laboratory and radiology technicians, as well as other support professionals and a team of multiprofessional residents.[11,12]

The population consisted of newborns admitted to the NICU, whose records for monitoring the infections indicated prescription of antimicrobials, with results of positive hemocultures and antibiogram, identifying the species of the microorganism isolated. It is noted that a single newborn might have more than one positive hemoculture during the hospitalization period. The data were collected in a form prepared by the authors and included gender, gestational age at birth, weight, diagnosis at birth, antimicrobials prescribed, hemoculture results, hospitalization time in the NICU and hospital outcome. The newborns excluded from the study were those who died or were transferred to another hospital up to four days after hemoculture collection, with incomplete HAI notification forms, and whose antimicrobial was suspended before the hemoculture result was verified.

A newborn can have its gestational age at birth classified as term (>37 weeks), moderate preterm (from 32 to <37 weeks), very preterm (from 28 to <32 weeks), and extremely preterm (<28 weeks). In relation to birth weight, it is classified as extremely low weight (<1,000 g), very low weight (1,000 g – 1,449 g), low weight (1,500 g – 2,500 g), and adequate weight (>2,500 g).[13] The previously described classification was the same used in this study.

The hemocultures were evaluated as for the type of microorganism isolated and regarding the sensitivity profile of the antibiogram. The vancomycin-resistant microorganisms, such as *Enterococcus faecium* and *Enterococcus faecalis*, were classified as Vancomycin-Resistant *Enterococcus* (VRE); those resistant to ceftriaxone and/or ceftazidime and/or cefepime were categorized as *Enterobacteriaceae* producing Extended-Spectrum Beta-Lactamase (ESBL); the meropenem- and imipenem-resistant microorganisms, as *Klebsiella pneumoniae* producing Carbapenems (KPC); and those resistant to oxacillin, as methicillin-resistant *Staphylococcus aureus* (MRSA).[14] The evaluation of adherence to monotherapy was carried out 24 to 48 hours after the hemoculture results were released, being considered as adherent when only one antimicrobial to which the isolated microorganism was sensitive was prescribed.

The data were introduced and analyzed in *Excel*® (version 2016). The numerical variables were presented as mean values, standard deviations, and absolute and relative frequencies. The categorical variables were presented as frequencies, in order to investigate adherence to monotherapy. A 5% significance level was adopted and, when investigating the association between the variables, Fisher's Exact Test was performed in the *GraphPad Prism* 6 statistical program, version 6.07.

Results

During the study period, data from 48 newborns were collected, identifying 68 positive hemocultures. Five (7.3%) hemocultures were excluded due to death of the newborn before the hemoculture result was released and one (1.5%) due to treatment discontinuation before the hemoculture result was released. Therefore, only 62 hemocultures were analyzed (Figure 1).

Most of the newborns were female (54.2%, n=26) and extremely preterm (29.2%, n=14), with a mean gestational age of 30.75 ± 4.19 weeks. The mean birth weight was 1,512.8 ± 801.32 g, and most of the newborns were extremely low weight (35.4%, n=17). Acute respiratory distress syndrome was the most prevalent diagnosis (54.2%, n=26), followed by risk for Neonatal Infection (NNI) (31.3%, n=15) and presumed NNI (10.4%, n=5). The most prevalent types of late infection in the study were related to bloodstream (64%, n=32), necrotizing enterocolitis (18%, n=18) and mechanical ventilation-associated pneumonia (8%, n=4). In addition, it was noticed that the hospitalization outcome was discharge for 54.2% (n=26) and that 18.7% (n=9) evolved to death. In most of the newborns (66.7%, n=32), the hospitalization time was over 30 days (Table 1).

In relation to the hemocultures, most of them were isolated Gram-positive microorganisms (59.7%, n=37), mainly *Staphylococcus epidermidis* (54.1%, n=20) and *Staphylococcus haemolyticus* (18.9%, n=7). Among the Gram-negative (33.9%, n=21) there was prevalence of *Escherichia coli* (19%, n=4). *Candida albicans* (75%, n=3) and *Candida parapsilosis* (25%, n=1) were also isolated. Presence of oxacillin-resistant microorganisms (n=32) and positive ESBL (n=5) was identified in the results of hemocultures and antibiograms. VRE and KPC were not identified. After the hemoculture results, the most prescribed antimicrobial was vancomycin (21.0%, n=13), followed by oxacillin (19.4%, n=12), cefepime (17.7%, n=11) and amikacin (14.5%, n=9), as indicated in Table 1.

Of the antimicrobial therapies of the newborns analyzed, 53.2% (n=33) indicated non-adherence to monotherapy, of which 43.5% (n=27) were in cases of late infections and 9.7% (n=6) in cases of early infections. Among the late infections, adherence to monotherapy was observed in 50% (n=16) of the primary bloodstream infections, in 22.2% (n=2) of the necrotizing enterocolitis, and in 25% (n=1) of the mechanical ventilation-associated pneumonia cases. No type of infection had a statistically significant association with adherence to hemoculture-guided monotherapy. In relation to the hospital outcome, adherence to monotherapy was observed in 55.6% (n=5) of the deaths, in 50% (n=13) of the hospital discharge cases, and in 38.5% (n=5) of the hospital transfers, although no significant association among the events was observed.

Figure 1. Flowchart corresponding to the analysis of the HAI notification forms of the newborns in the Neonatal ICU of a teaching maternity hospital located in Fortaleza-CE, Brazil (2019).

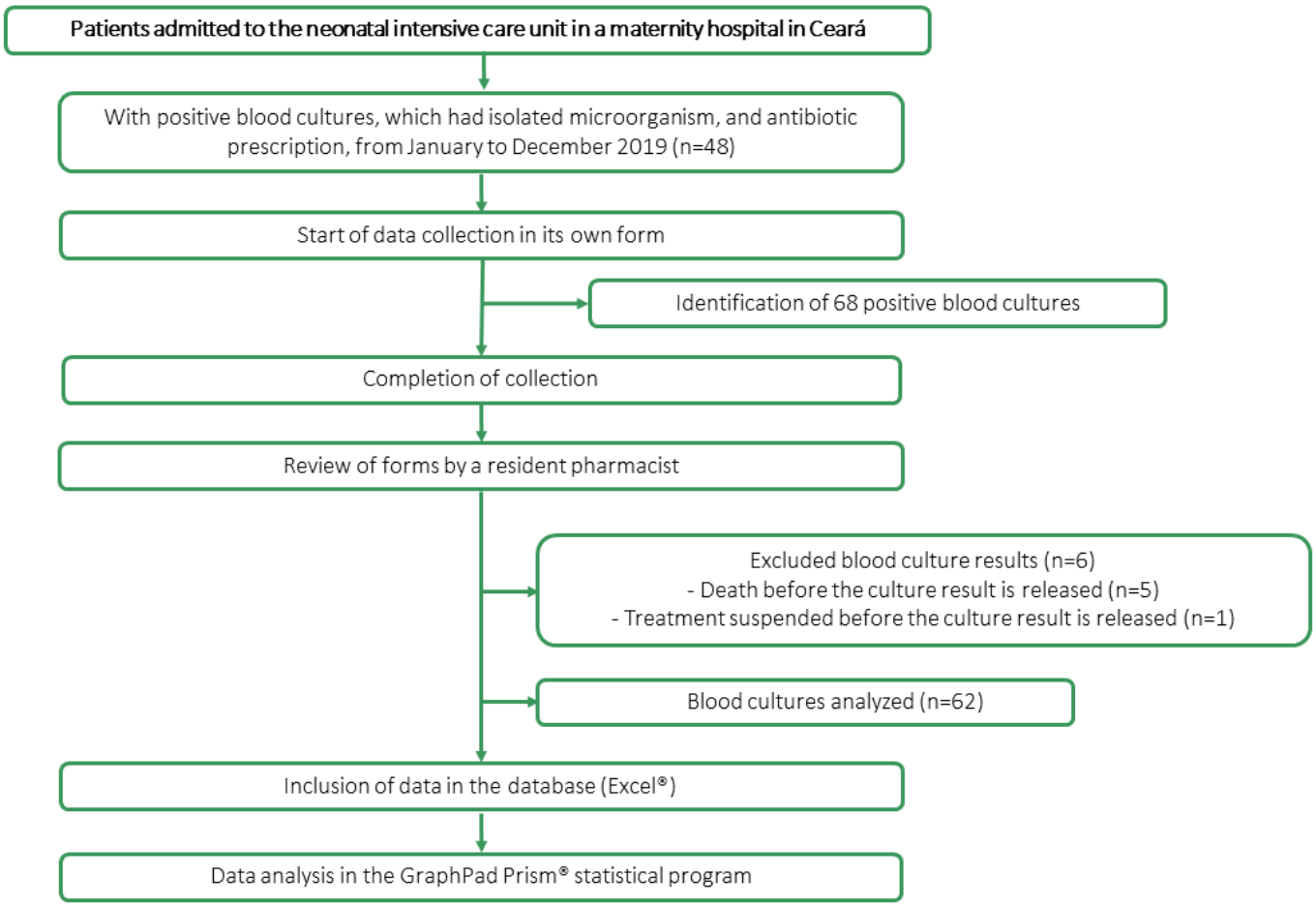

Table 1. Demographic and clinical profile of the newborns with positive hemocultures hospitalized in a Neonatal ICU of a teaching maternity hospital located in Fortaleza-CE, Brazil (2019). (Continued)

Information	All N (%)
Profile of the newborn	
Gender	
Female	26 (54.2)
Male	21 (43.8)
Undetermined[1]	1 (2.0)
Total	48 (100.0)
Gestational age at birth	
Term (>37 weeks)	6 (12.5)
Moderately preterm (From 32 to <37 weeks)	16 (33.3)
Very preterm (From 28 and <32 weeks)	12 (25.0)
Extremely preterm (<28 weeks)	14 (29.2)
Total	48 (100.0)
Birth weight	
Extremely low weight (<1,000 g)	17 (35.4)
Very low weight (1,000 g – 1,449 g)	11 (22.9)
Low weight (1,500 g – 2,500 g)	13 (27.1)
Adequate weight (>2,500 g)	7 (14.6)
Total	48 (100)
Diagnosis at birth[2]	
Respiratory distress syndrome/Early respiratory distress	26 (54.2)
Risk for neonatal infection	15 (31.3)
Congenital malformations	9 (18.7)
Presumed neonatal infection	5 (10.4)
Others[3]	17 (35.4)
Classification of the infection	
Late	50 (80.6)
Early	12 (19.4)
Total	62 (100)
Hospitalization time in the NICU	
≥30 days	32 (66.7)
<30 days	16 (33.3)
Total	48 (100)
Microorganisms	
Gram-positive bacteria	
Staphylococcus epidermidis	20 (54.1)
Staphylococcus haemolyticus	7 (18.9)
Staphylococcus hominis	3 (8.1)
Staphylococcus aureus	3 (8.1)
Others[4]	4 (10.8)
Total	37 (100.0)
Gram-negative bacteria	
Escherichia coli	4 (19.0)
Enterococcus faecalis	3 (14.3)
Pseudomonas aeruginosas	3 (14.3)
Serratia marcescens	3 (14.3)
Sphingomonas paucimobilis	3 (14.3)
Klebsiella pneumonie	2 (9.5)
Others[5]	3 (14.3)
Total	21 (100)
Fungi	
Candida albicans	3 (75.0)
Candida parapsilosis	1 (25.0)
Total	4 (100)

Table 1. Demographic and clinical profile of the newborns with positive hemocultures hospitalized in a Neonatal ICU of a teaching maternity hospital located in Fortaleza-CE, Brazil (2019). (Concluded)

Information	All N (%)
Resistance pattern	
Resistance to oxacillin	
Staphylococcus epidermidis	20 (62.5)
Staphylococcus haemolyticus	7 (21.9)
Staphylococcus hominis	3 (9.4)
Staphylococcus warneri	1 (3.1)
Staphylococcus aureus	1 (3.1)
Total	32 (100.0)
Expanded resistance to beta-lactams	
Pseudomonas aeruginosas	3 (60.0)
Klebsiella pneumonie	1 (20.0)
Acinetobacter baumannii	1 (20.0)
Total	5 (100.0)
Antibiotics prescribed[6]	
Vancomycin	13 (21.0)
Oxacillin	12 (19.4)
Cefepime	11 (17.7)
Amikacin	9 (14.5)
Meropenem	7 (11.3)
Metronidazole	6 (9.7)
Gentamicin	5 (8.1)
Teicoplanin	5 (8.1)
Ampicillin	4 (6.4)
Piperacillin/Tazobactam	4 (6.4)
Micafungin	4 (6.4)
Fluconazole	4 (6.4)
Amphotericin	2 (3.2)
Others[7]	4 (6.4)

[1]Gender was considered as undetermined due to the absence of a defined genital organ and of genetic typing result when the study was conducted. [2]The calculation corresponding to each item was made on the total of study patients (n=48); however, each NB can have more than one diagnosis. [3]Others: It includes different types of diagnoses that obtained an occurrence frequency of 1. [4,5]Others: It includes different types of microorganisms that obtained an occurrence frequency of 1. [6]Antibiotics prescribed: The calculation was made by number of forms/NB and more than one antibiotic per form was accepted, reason why the sum exceeds 100%. [7]Others: It includes different types of antibiotics that obtained an occurrence frequency of 1.

Adherence to monotherapy was observed in 32.4% (n=12) of the infections by Gram-positive bacteria, 66.7% (n=14) of the infections by Gram-negative bacteria and 75% (n=3) of the fungal infections. In addition, the infections by Gram-negative bacteria were significantly associated with adherence to monotherapy (p = 0.03, Relative Risk = 1.82), while the infections by Gram-positive bacteria were significantly associated with non-adherence to monotherapy (p = 0.01, Relative Risk = 0.48) (Table 2). No statistically significant associations were found between the other variables analyzed.

Discussion

In this study, most of the newborns were moderately preterm, with extremely low weight and an extended hospitalization time in the NICU, being considered patients with a high severity profile. This profile supports literature data pointing out that almost half of the admissions to the NICU correspond to premature newborns.[15] According to Sossolote et al. (2017), 37% of the newborns with laboratory-confirmed bloodstream infection, had a weight between 751 g and 999 g.[16]

Tabela 2. Caracterização da adesão à monoterapia de antimicrobianos em uma UTI neonatal de uma maternidade escola, em Fortaleza-CE, Brasil (2019).

Information	All n (%)	Adherence to monotherapy n (%)	Non-adherence to monotherapy n (%)	*p*-value[1]	RR[2]	CI[3]
Early infection	12 (100.0)	6 (50.0)	6 (50.0)	1.0000	1.09	0.57-2.06
Late infection	50 (100.0)	23 (46.0)	27 (54.0)			
Classification						
Primary bloodstream infection	32 (64.0)	16 (50.0)	16 (50.0)	0.5601	1.29	0.65-2.52
Necrotizing enterocolitis	9 (18.0)	2 (22.2)	7 (77.8)	0.1522	0.43	0.12-1.52
Mechanical ventilation-associated pneumonia	4 (8.0)	1 (25.0)	3 (75.0)	0.6140	0.52	0.09-2.93
Meningitis	2 (4.0)	2 (100.0)	-	0.2033	2.29	1.66-3.15
Bloodstream infection	1 (2.0)	-	1 (100.0)	1.0243	-	-
Skin infection	1 (2.0)	1 (100.0)	-	0.4612	2.23	1.63-3.04
Fungal abscess	1 (2.0)	1 (100.0)	-	0.4612	2.23	1.63-3.04
Hospital outcome						
Death	9 (18.7)	5 (55.6)	4 (44.4)	1.0453	1.11	0.55-2.24
High	26 (54.2)	13 (50.0)	13 (50.0)	1.0398	1.08	0.51-2.19
Transfer	13 (27.1)	5 (38.5)	8 (61.5)	1.0462	1.12	0.57-2.35
Types of microorganisms						
Gram-positive	37 (59.7)	12 (32.4)	25 (67.6)	0.0090	0.48	0.28-0.82
Gram-negative	21 (33.9)	14 (66.7)	7 (33.3)	0.0320	1.82	1.10-3.02
Fungi	4 (6.4)	3 (75.0)	1 (25.0)	0.3330	1.67	0.89-3.15

[1]Teste de Fischer. [2]Risco relativo. [3]Intervalo de confiança 95%.

In relation to the microorganisms isolated, prevalence of Gram-positive bacteria was observed, especially coagulase-negative *Staphylococcus*. In fact, a number of studies point out that most of the neonatal infections are associated with Gram-positive bacteria, whose cases in the literature are significantly increasing.[17,18] Additionally, it was found that most of them are oxacillin-resistant, but sensitive to vancomycin. This finding also supports the results in the literature pointing out that Negative-coagulase negative *Staphylococcus* present higher resistance to oxacillin (80%), but good susceptibility to vancomycin (100%).[19] Additionally, in this study, the profile of isolated negative microorganisms was similar to that reported in the literature in hospital environments, with presence of positive and carbapenem-producing ESBL.[20,21,22] In general, our data support a microbiological profile of another hospital that assists neonates of the region.[5]

In this study, vancomycin, oxacillin and cefepime were the most prescribed antimicrobials, while antifungals amphotericin, fluconazole and micafugin were the least prescribed ones. In fact, in the teaching maternity hospital under study, the empirical therapy is initiated for late sepsis with oxacillin and amikacin, added to lumbar puncture to discard the presence of meningitis, and antibiogram to evaluate the sensitivity profile of the microorganism involved and the need to scale the antimicrobial therapy. It is highlighted that, in the study institution, it is recommended to remain with the prescription of oxacillin despite the isolation of oxacillin-resistant Gram-positive bacteria, provided that there is a good clinical response. This recommendation was not applied in the case of oxacillin-resistant *Staphylococcus aureus* isolation.

The prevalence of the vancomycin prescription can be directly related to the fact that most of the isolated microorganisms were oxacillin-resistant Gram-positive and that most of the infections were late. In fact, according to the recommendation by the Brazilian Society of Pediatrics, treatment of early infections should be carried out with ampicillin or crystalline penicillin and amikacin and gentamicin; vancomycin is the second treatment option in case of resistance and the first option in empirical therapy in late HAIs in neonates.[23,24] On the other hand, cefepime is used as a second option for the treatment of late HAIs. For being a fourth-generation cephalosporin, it acts on Gram-negative bacteria and has anti-pseudomona activity and against Gram-positive cocci.[16,23] In the study institution, cefepime represents the treatment of choice in neonatal meningitis.

In relation to compliance, the study results show that there was adherence to monotherapy in less than half (46.8%) of the prescriptions evaluated. It was observed that infections caused by Gram-positive bacteria are mostly resistant to oxacillin, and that they were associated with non-adherence to monotherapy, while those by Gram-negative microorganisms were more associated with adherence. This result can be related to the fact that some antimicrobials against Gram-negative bacteria can also be effective to treat infections by Gram-positive bacteria, such as piperacillin-tazobactam and cefepime, which can justify maintenance of the prescription of more than one antimicrobial.[26] On the other hand, non-adherence to the hemoculture-guided monotherapy can be related to lack of knowledge about the institutional protocol and the antimicrobial prescription protocols, to non-observance of the SCIH guidelines, to insecurity to meet the institutional protocol, and to the newborn's severity.[25]

The diagnostic challenges are many and the absence of clear findings in the physical and laboratory examination does not exclude the presence of an infection in its initial or remission stages. Errors may occur in the hemoculture exam such as one pathogen growing more than another; therefore, it may not be possible to identify two different microorganisms in the same culture.[27] This difficulty can make the ideal medical course of action difficult to be performed. On the other hand, prematurity by itself is already a major risk factor for the development of infections. However, it is necessary to prefer a monotherapy treatment guided by the results of hemocultures and antibiogram, as polytherapy predisposes for the development of microbial resistance and increases the risk for necrotizing enterocolitis and death.[23,28]

The findings of this study provide valuable information about the prescribers' adherence to antibiotic monotherapy, which enables an evaluative and comparative process between the reality of the institution under study and other national and international neonatology services. Through the study, a brief microbiological profile of the neonatal unit where the study was conducted was made available, as well as a warning for local antimicrobial high resistance. However, the research presents some limitations. In the first place, this is a single-center study, conducted during a short period of time and with a small sample. Secondly, the study resorted to a secondary information source, namely: the SCIH monitoring forms. Additionally, the study did not evaluate the consequences of non-adherence to monotherapy, as the later emergence of other infections, such as enterocolitis and late sepsis. Thus, it is suggested that further studies are necessary to evaluate the impact of non-adherence to monotherapy in newborns, having a foundation to devise measures in order to prevent neonatal morbidity and mortality.

Conclusion

There was adherence to hemoculture-guided monotherapy in less than half of the treatments with antibiotics prescribed to preterm low-weight newborns. In addition, a statistically significant association was found between infections by Gram-positive bacteria and non-adherence to antimicrobial monotherapy, as well as between infections by Gram-negative bacteria and adherence to monotherapy. Higher prevalence of vancomycin prescriptions and presence of *Staphylococcus spp* were also observed, the latter mostly oxacillin-resistant. Consequently, the study results warn about the problem of microbial resistance in the institution and about non-adherence to monotherapy, pointing out the need to elaborate infection control protocols, as well as the application of policies and programs for the rational use of antimicrobials.

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Collaborators

Conception and design or data analysis and interpretation: JMP, EFC, KSN. Writing of the article or relevant critical review of the intellectual content: JMP, EFC, KSN, HID, NSC, JSA, FJT, FCS.

Conflicts of interest statement

Authors declare no conflicts of interest in relation to this article.

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