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Analysis of Antibiotic Use in Premature Infants with Gestational Age less than 34 Weeks

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Abstract: *This paper analyzes the use of antibiotics and recent clinical outcomes in premature infants with gestational age<34 weeks. This paper collects clinical data of 129 premature infants with gestational age<34 weeks admitted to the neonatal intensive care unit (NICU) of Texas City Hospital from January 1, 2017 to December 31, 2023. The research results found that there were a total of 129 premature infants with gestational age<34 weeks. The antibiotic use rate of premature infants with gestational age<34 weeks was 80.6%, and the median antibiotic use rate (AUR) per 100 days of hospital stay was 44. The incidence of infectious pneumonia in premature infants with gestational age less than 34 weeks is 59.7%, the incidence of bronchopulmonary dysplasia (BPD) is 7.8%, the incidence of neonatal pulmonary hemorrhage is 3.1%, the incidence of intraventricular hemorrhage (IVH) is 2.3%, the incidence of necrotizing enterocolitis (NEC) is 0.8%, the incidence of early onset sepsis (EOS) is 6.2%, the incidence of late onset sepsis (LOS) is 1.6%, and the mortality rate is 1.6%. The study suggests that premature infants with gestational age<34 weeks in our NICU have a longer duration of antibiotic use and a higher rate of antibiotic use, and further measures need to be taken to reduce the AUR of premature infants.*

Keywords: *antibiotics, premature infant, Late-onset sepsis, prognosis*

1. Introduction

Antibiotics are one of the most widely used drugs in neonatal intensive care units (NICUs). There are many complex factors involved in the use of antibiotics in the treatment of newborns, especially premature infants.

A series of risk factors for perinatal mothers are closely related to the use of antibiotics when premature infants are suspected of sepsis. For example, premature birth itself is a key factor. Premature babies have underdeveloped organ systems and extremely low immune systems, resulting in insufficient resistance to infections [1]. Therefore, once there are signs of suspected sepsis, the possibility of using antibiotics for intervention increases significantly. Premature rupture of membranes and prolonged rupture of membranes can make it easier for external bacteria to invade the fetus and cause infections, which is also an important reason for clinical doctors to consider using antibiotics. As a common pregnancy infection, chorioamnionitis also increases the risk of fetal infection, leading to the use of antibiotics. In addition, the colonization of Group B Streptococcus (GBS) in mothers cannot be ignored. GBS may be transmitted to newborns during delivery, causing serious diseases such as neonatal sepsis[2]. Therefore, when faced with such situations, doctors often choose to use antibiotics for prevention or treatment. At the same time, the severity of neonatal diseases can also affect the decision to use antibiotics. If a newborn's condition is severe, antibiotics often become a necessary treatment to prevent further deterioration of infection.

However, the diagnosis and treatment of neonatal sepsis face many challenges. The clinical symptoms of neonatal sepsis are usually very subtle and non-specific, and may only manifest as unstable body temperature, poor breastfeeding, and mental fatigue. These symptoms are difficult to distinguish from other common neonatal diseases such as neonatal pneumonia and neonatal jaundice. In addition, the use of antibiotics during the perinatal period or errors in blood culture collection may lead to false negative blood cultures in newborns, making it difficult for clinical doctors to diagnose neonatal sepsis solely based on blood culture results [3-5]. Without positive blood cultures, many clinical doctors have to rely on inflammatory markers such as C-reactive protein, procalcitonin, etc. to determine the presence of infection and treat "clinical sepsis" in premature infants. However, the

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evidence base for determining the timing of antibiotic treatment for clinical sepsis in premature infants is currently quite weak, and there is a lack of clear and unified standards to guide clinical practice.

Neonatal sepsis has a insidious onset, rapid progression, and extremely high mortality rate. Once treatment is delayed, the consequences can be unimaginable. Therefore, in order to protect the life and health of premature infants, clinical physicians often begin empirical antibiotic treatment immediately after birth. However, it is worth noting that a large amount of research has shown that long-term use of antibiotics is not without risks. Long term use of antibiotics can alter the gut microbiota and disrupt the balance of gut microbiota. The gut microbiota is crucial for the digestive and immune functions of the human body, and its imbalance increases the risk of necrotizing enterocolitis (NEC), late onset sepsis (LOS), bronchopulmonary dysplasia (BPD), and mortality in premature infants.

Based on the above situation, this study aims to retrospectively analyze the current status of single center antibiotic use. By collecting relevant data on the use of antibiotics in newborns in the NICU of our center, including the types, doses, treatment courses, indications for use, etc., a detailed analysis and summary will be conducted. I hope that through such research, the problems existing in the current use of antibiotics can be discovered, providing scientific reference for the standardized use of antibiotics, so as to effectively treat neonatal diseases while minimizing the adverse effects of irrational use of antibiotics and ensuring the healthy growth of newborns.

2. Data and methods

Retrospective collection of clinical data of premature infants admitted to the NICU of Texas City Hospital from January 1, 2017 to December 31, 2023. Inclusion criteria: (1) gestational age<34 weeks; (2) Born in Texas City Hospital and transferred to NICU for hospitalization, receiving systematic treatment with complete medical records. Exclusion criteria: (1) Patients with significant deformities requiring surgical treatment; (2) Suspected or diagnosed individuals with genetic metabolic disorders; (3) Those with incomplete medical records.

3. Antibiotic use strategy

(1) Conduct early onset sepsis (EOS) risk assessment for premature infants with gestational age<34 weeks. For premature infants with high risk of neonatal sepsis, blood samples are collected immediately upon admission for blood culture and empirical antibiotic treatment is initiated. Non specific infection indicators such as blood routine and CRP are checked within 12-24 hours after birth; 36-48 hours to rule out infection and stop empirical treatment; (2) Stop medication after a 5-day course evaluation for pneumonia; (3) Clinical sepsis 5-day course evaluation and discontinuation of medication; (4) According to the clinical diagnosis and treatment guidelines for infectious diseases, standardize the application of antibiotics, standardize the diagnosis of EOS and LOS, reduce the course of antibiotics for different infected people, and standardize the diagnosis of "neonatal pneumonia".

4. Relevant definitions and diagnostic criteria for diseases

The median antibiotic use rate (AUR) refers to the ratio of the duration of use of one or more antibiotics to the length of hospital stay, normalized to every 100 days of hospital stay. Neonatal infectious pneumonia BPD、 The diagnostic criteria for neonatal pulmonary hemorrhage, intraventricular hemorrhage (IVH), NEC, EOS, LOS, and other diseases are referenced in the literature [6-7].

5. Results

There were a total of 129 premature infants with gestational age less than 34 weeks, including 75 males (58.1%) and 54 females (41.9%).

The general situation and antibiotic use of premature infants with gestational age<34 weeks are detailed in Table 1. The antibiotic usage rate was 80.6%, and the median AUR/100 hospitalization days was 44. As shown in Table 1.

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Table 1. General information and antibiotic use of pediatric patients

Gestational age M(P25,P75),w	Birth weight M(P25,P75),g	Number of antibiotic users n(%)	Antibiotic usage time M(P25,P75),d	Length of hospital stay M(P25,P75),d	AUR/100 hospitalization days M(P25,P75),d
32 (31,33)	1800(1345,2040)	104 (80.6)	7 (2,14)	17 (10,28)	44 (23,84)

The recent outcomes of premature infants with gestational age<34 weeks are detailed in Table 2. The incidence of neonatal infectious pneumonia is 59.7%, the incidence of BPD is 7.8%, the incidence of neonatal pulmonary hemorrhage is 3.1%, the incidence of IVH is 2.3%, the incidence of NEC is 0.8%, the incidence of early-onset sepsis is 6.2%, the incidence of late-onset sepsis is 1.6%, and the mortality rate is 1.6%. As shown in Table 2.

Table 2. Incidence and outcome of complications in pediatric patients

Neonatal infectious pneumonia n(%)	BPD n(%)	Neonatal pulmonary hemorrhage n(%)	IVH n(%)	NEC n(%)	Early onset sepsis n(%)	Late-onset sepsis n(%)	Death n(%)
77 (59.7%)	10 (7.8%)	4 (3.1%)	3 (2.3)	1 (0.8)	8 (6.2)	2 (1.6)	2 (1.6)

6. Discussion

Due to concerns among clinical doctors about the occurrence of early-onset sepsis, premature infants admitted to the NICU often begin antibiotic treatment early after birth. However, this often leads to many premature infants continuing antibiotic treatment for a long time or even until discharge despite negative blood culture results. Early and long-term exposure to antibiotics can affect the developing gut microbiota of premature infants, increasing their risk of developing various diseases [8-9].

In this study, the proportion of premature infants with gestational age less than 34 weeks who used antibiotics was 80.6%, which is comparable or slightly higher than other related studies at home and abroad, such as 84.9% in Canada [5], 69.1% in Hunan Province [11], and 88.4% reported by Jiang et al. [10] nationwide. The median AUR of this study was 44/100 hospital days, higher than the 25-29/100 hospital days reported in a multicenter study in Canada [5], and similar to the 53/100 hospital days in Hunan Province [11] and the 44/100 hospital days nationwide [10]. In this study, the proportion of premature infants with gestational age less than 34 weeks and large gestational age was relatively high, but the AUR was still significantly higher than relevant studies in advanced countries, indicating that there were cases of non-standard use of antibiotics by primary hospital physicians in the diagnosis and treatment of premature infants. This is related to the concern of primary hospital physicians about serious consequences caused by delayed diagnosis and treatment, so they began empirical antibiotic treatment early and dared not stop using antibiotics.

Related studies both domestically and internationally have confirmed that taking relevant measures can reduce the use of antibiotics in NICU without increasing or improving the outcomes of premature infants. Meyers et al. [12] By adopting empirical treatment methods such as "48 hour hard stop antibiotic treatment" to exclude suspected infections, and implementing a 5-day antibiotic course for neonatal infectious pneumonia and non culture confirmed sepsis, the use of antibiotics was reduced by 27% within 9 months [13]. American Ying et al. [14] implemented quality improvement interventions through multiple PDSA cycles (plan do study act cycles), reducing the percentage of antibiotic use time to hospital stay in NICU very low birth weight (VLBW) preterm infants from 49% to 32%. According to the 12 step action plan for preventing antibiotic resistance initiated by the Centers for Disease Control and Prevention in the United States, Chu Meiyan et al. [2] found that the use of antibiotics during hospitalization in premature infants with gestational age<35 weeks significantly decreased, and the hospitalization time of premature infants with gestational age<35 weeks was significantly shortened after reducing the use of antibiotics. The incidence of intraventricular hemorrhage and late-onset sepsis also showed a decreasing trend. This study showed that the incidence and mortality rates of complications such as BPD, NEC, IVH, LOS, etc. in premature infants with gestational age<34 weeks were lower than those in relevant domestic studies [2], which may be related to the high proportion of premature infants with older gestational age in this study. In addition, this study found that the incidence of neonatal pneumonia is relatively high, which may be related to the overly broad diagnosis.

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7. Conclusion

The survey results on the use of antibiotics in the neonatal intensive care unit (NICU) of our unit show that there are currently prominent issues. In NICU, the duration of antibiotic use in pediatric patients is generally longer, and statistical analysis has found that many children's antibiotic use exceeds the reasonable range recommended by general clinical guidelines. At the same time, the use of antibiotics is also at a high level, and a large number of children receive antibiotic treatment during hospitalization.

Particular concern is the group of premature infants born in our unit with gestational age<34 weeks. These premature infants often rely more on antibiotics in clinical treatment due to their immature organ development, incomplete immune system function, and weaker resistance to infections. However, the current usage status indicates that there is still significant room for improvement in the rational use of antibiotics for premature infants. Inappropriate use of antibiotics may not only lead to the development of bacterial resistance, increase the difficulty of subsequent treatment, but also trigger a series of adverse reactions, posing a potential threat to the health of premature infants.

In order to improve this situation, our unit will continue to conduct in-depth clinical research on the quality improvement of antibiotic management measures in the next step. We will strictly follow the scientific method of planning, execution, research, and re execution. Firstly, we will develop a detailed antibiotic management plan, clarify the usage norms and course restrictions of antibiotics under different conditions; Then strictly implement these plans in clinical practice and closely monitor the treatment response and various physiological indicators of the children; Subsequently, conduct in-depth research and analysis on the data collected during the execution process to identify existing problems and shortcomings; Finally, based on the research results, adjust the execution plan again and continuously optimize the antibiotic management measures. Through this iterative process, the aim is to reduce the antibiotic use rate (AUR) of hospitalized children in the NICU, achieve rational and precise use of antibiotics while ensuring the safety of the children, improve medical quality, and better care for the health of newborns.

Author Contribution Statement

Qinghe Song and Yingna Shi made equal contributions in this study.

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