Identification of newborns at risk of early-onset neonatal infection: New French guidelines and practices at Nantes University Hospital

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Short title: Early onset neonatal infection and new French guidelines

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Abstract

New French guidelines in 2017 aimed to improve the identification of newborns at risk of early-onset neonatal infection (EONI). Identification is based on perinatal risk factors, management of perinatal antibiotic prophylaxis, and standardized clinical assessment. We conducted a retrospective cross-study at the University Hospital of Nantes. The main objective was to assess implementation of the French guidelines. Of 1240 births included, 40% (501) required perinatal antibiotic prophylaxis (adequate in 67.3%) and 306 (24.7%)

needed a standardized clinical assessment (performed in 69.2%). Only two newborns (0.16%) included in the study received neonatal antibiotic therapy. On the basis of the assessment conducted in our maternity ward, implementation of the recommendations seems to be effective.

Keywords: newborn; early-onset neonatal infection; French guidelines

1. Introduction

Bacterial early-onset neonatal infection (EONI) occurs in the first 3 days of life. EONI is still one of the leading causes of neonatal mortality and morbidity despite antibiotic peripartum prophylaxis [1]. Therefore, EONI remains a daily problem for maternity hospital teams [2].

Before 2017, identification of groups at risk of EONI was based on non-sensible risk factors (carriage of group B streptococcus (GBS), prolonged rupture of membranes, etc.). Then, diagnostic tests performed, such as gastric aspirates for bacterial culture, led to excessive blood tests (25% of newborns) and antibiotic therapies (4% of newborns) [3]. Moreover, it is now well known that antibiotics have potentially deleterious effects on neonatal digestive microbiota implantation, on immune system maturation, and antibiotic-resistant bacteria selection [4,5].

New French recommendations were published in 2017 to improve the strategy to identify newborns at risk of EONI and to limit antibiotic therapy [6]. Identification of newborns according to their risk for EONI is based on perinatal risk factors. The following criteria defined the risk of EONI and indicate maternal antibiotic peripartum prophylaxis: maternal GBS carriage, antecedent of GBS EONI, prolonged rupture of membranes (>12 h), perinatal maternal fever of >38°C, and unexpected preterm birth at <37 gestational weeks. Presence of perinatal maternal fever or inadequate antibiotic prophylaxis defined the EONI at-risk group

and monitoring is now based on clinical standardized evaluation on the maternity ward. This standardized clinical monitoring consists of 10 monitoring rounds with five clinical parameters at each assessment (body temperature, heart rate, respiratory rate, respiratory distress, and cutaneous coloration) during 48 h. Blood samples can be taken analyzed depending on the clinical examination findings.

These new French recommendations are no longer based on complementary examinations, but focus on a clinical evaluation. Assessment of potential team difficulty in managing adequate antibiotic prophylaxis in the delivery room and practicing a standard clinical evaluation in the maternity ward is key for application of the recommendations. The main aim of this study was to assess the implementation of the French Health Authority recommendations when applied in a university maternity ward.

2. Methodology

We conducted a single-center, descriptive, and retrospective study in the University Hospital of Nantes, France. All infants born alive at ≥ 36 gestational weeks in the University Hospital of Nantes were included in the study. According to French Health Authority recommendations, an EONI at-risk group was defined according to the presence of at least one of the following criteria: maternal GBS carriage, GBS EONI antecedent, prolonged rupture of membranes (>12 h), and unexpected preterm birth at <37 gestational weeks. Peripartum antibiotic prophylaxis is recommended in this EONI at-risk group. Intravenous penicillin G, ampicillin or amoxicillin, or cefazolin antibiotic administration, at least 4 h before birth, was considered adequate.

The presence of perinatal maternal fever or inadequate antibiotic prophylaxis defined newborns at high risk. Midwives in the delivery room screen for these factors and recorded the information in the computerized file. The monitoring of these newborns was based on

standardized clinical evaluation in the maternity ward. The standardized clinical monitoring grid is presented in **Appendix 1** (10 monitoring rounds with five clinical parameters at each assessment during 48 h). Midwives had to call the pediatrician if clinical symptoms appear.

When both peripartum risk factors were present (maternal fever and inadequate antibiotic prophylaxis), the newborns were considered to be at the highest risk. Standardized clinical monitoring was then applied and a systematic pediatric clinical examination was performed between 6 h and 12 h. Blood samples were taken in the case of abnormal clinical examination results only.

All data were extracted retrospectively from the patients' medical records, recorded by midwives in the delivery room for EONI risk factors and by midwives in the maternity ward for standardized clinical monitoring.

The main objective of this study was to assess the implementation of the new French recommendations in a university maternity ward. Applying these recommendations depends on the identification of newborns in the delivery room, on transmission to the maternity ward, and on the quality of monitoring. The judgment criterion was the percentage of newborns who underwent a standardized clinical assessment among those who actually needed this assessment.

3. Results

Between September 1 and December 31, 2018, there were 1418 births at the University Hospital of Nantes, and 1240 were included in the study (**Figure 1**). According to the new French recommendations, 40.4% (501) of newborns included were subjected to maternal antibiotic prophylaxis and considered as newborns at risk of EONI. Maternal and neonatal

characteristics as well as the management of maternal antibiotic prophylaxis are presented in **Table 1**.

The classification and monitoring of newborns are presented in **Figure 2**. Among the 501 newborns who presented with EONI risk factors, 61.1% were newborns at high risk for EONI (because of maternal fever or inadequate antibiotic prophylaxis) and should had have a standardized clinical assessment in maternity ward (*n*=306; 24.7% of the included population). Among the EONI at-risk newborns requiring a standardized clinical assessment, 21% (*n*=64) also needed a pediatric clinical examination (**Figure 2**). Among the 306 EONI at-risk newborns, no data were available for 18 (6%), while 212 (69.2%) had a standardized clinical assessment and 76 (24.8%) had no standardized clinical assessment.

Concerning the 212 standardized clinical assessments, clinical information was respectively 100% completed in 39% of cases, ≥ 90% completed in 37% of cases, ≥ 80% completed in 16% of cases, and <80% completed in 8% of cases. The most frequent missing information was on the respiratory rate (36%) and then cutaneous coloration (28%).

Among the 212 at-risk newborns who were monitored, 53 (25%) had clinical symptoms at the standardized assessment, most of them related to respiratory rate (21 respiratory rate > 60/min). Among them, the pediatrician had been called in 16 (30%) cases, and two (0.9%) EONI at-risk newborns had been hospitalized and antibiotics had been prescribed. One of the newborns was treated for 7 days. The blood culture was negative and the outcome was satisfactory for both patients.

4. Discussion

We report on the implementation of the new French recommendations to identify newborns at risk of EONI. Whereas a clinical standardized assessment was recommended in 24.7% of the newborns, 24.8% of them were not monitored. When monitoring was actually performed, 6%

of the data from the monitoring rounds were missing. The main items not recorded during monitoring were respiratory rate and cutaneous coloration.

Nearly 25% of newborns did not have adequate monitoring, either they were not identified or the information was not transmitted from the birth room (no monitoring) or some monitoring was not done in the maternity ward due to workload. Our results underline the importance of communication between the delivery room and the maternity ward. Indeed, in the presence of EONI risk factors, antibiotic prophylaxis was started in 86.4% of cases (**Table 1**) and newborns were therefore identified in the delivery room. In this case, the maternity team should set up a system for tracking information on risk situations such as inserting a red flag in a computer file as soon as antibiotic prophylaxis is indicated.

The second important point of our results concerns the quality of monitoring. The respiratory rate was the clinical item that was most often missing, yet polypnea is the earliest clinical sign of neonatal infection [7]. This is an important point to be underlined in applying the French recommendations.

Our study has several limitations, including the lack of an analysis on the causes and the consequences of the non-implementation of monitoring rounds. There is no description of the fluctuation of workload in the maternity ward. Nevertheless, teams have to integrate this clinical monitoring into their daily work, which makes it possible to limit additional blood tests by venous punctures and intravenous antibiotic treatment. Indeed, only 0.16% of our population received antibiotics (2/1240) versus 4% previously reported in French practices.

5. Conclusion

The new French recommendations for the management of newborns suspected of early neonatal bacterial infection are therefore applicable and can help limit neonatal antibiotic

therapy. We emphasize the importance of communication between the delivery room and the maternity ward in order not to miss any newborns at risk.

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Table 1. Maternal and neonatal characteristics

Maternal characteristics	Population *n* (%)
	1240
Parity	
0	502 (40.5)
1	402 (32.4)
≥2	336 (27.1)
Labor mode	
Spontaneous labor	905 (73)
Cesarean section before labor	101 (8.1)
Induced labor	234 (18.9)
Delivery mode	
Cesarean section	241 (19.4)
Vaginal delivery	999 (80.6)
Occurrence of perinatal infection risk factors	
PROM ≥12 h	317 (25.6)
Maternal GBS carriage	155 (12.6)
Antecedent of GBS EONI	5 (0.4)
Unexpected preterm birth <37 GA (and >36 GA)	21 (1.7)
Perinatal maternal fever>38°C	133 10.7)
Maternal antibiotic prophylaxis indicated	501 (40.4)
Antibiotic therapy administered	433 (86.4)
No antibiotic therapy administered	68 (13.6)
Adequate antibiotic prophylaxis	276 (63.7)
Inadequate antibiotic prophylaxis	157 (36.3)
Inadequate antibiotic prophylaxis	157
<4 h	122 (77.7)
Inadequate antibiotic	22 (14)
Oral administration	12 (7.6)
Inappropriate dosage	1 (0.6)

PROM: premature rupture of membranes; GBS: group B streptococcus; EONI: early-onset neonatal infection; GA: gestational age

Figures:

Figure 1: Flowchart

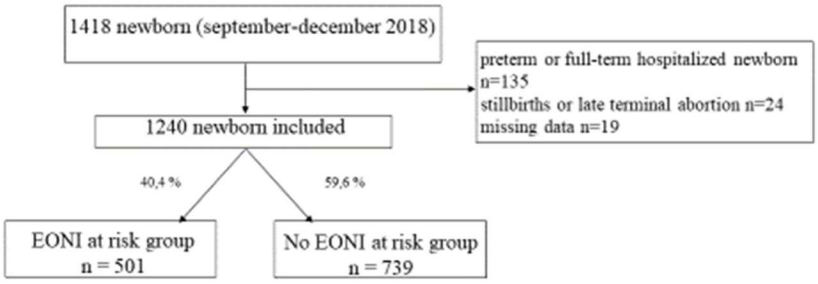
EONI: early-onset neonatal infection

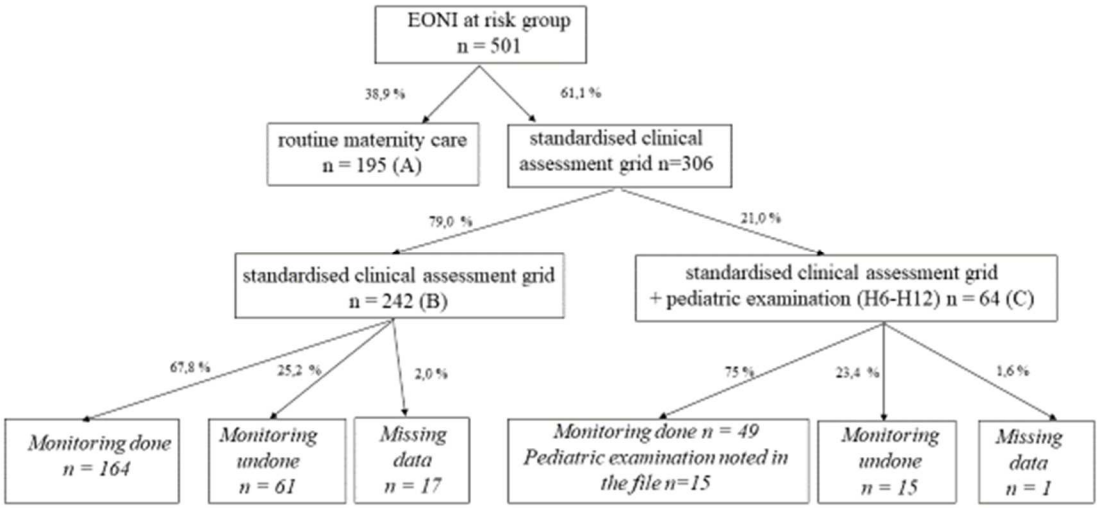
Figure 2: Classification and monitoring of newborn

A. Perinatal risk factors (maternal GBS carriage, antecedent of GBS EONI, prolonged rupture of membranes (>12 h), unexpected preterm birth (>37 gestational weeks), and adequate antibiotic prophylaxis.
B. Inadequate antibiotic, prophylaxis or maternal fever
C. Inadequate antibiotic, prophylaxis and maternal fever

GBS: group B streptococcus; EONI: early-onset neonatal infection

Appendix 1: Standardized clinical assessment grid


1418 newborn (september-december 2018)
preterm or full-term hospitalized newborn n=135
stillbirths or late terminal abortion n=24
missing data n=19
1240 newborn included
40,4 %
59,6 %
EONI at risk group n = 501
No EONI at risk group n = 739


EONI at risk group
n = 501
38,9 %
61,1 %
routine maternity care
n = 195 (A)
standardised clinical
assessment grid n=306
79,0 %
21,0 %
standardised clinical assessment grid
n = 242 (B)
standardised clinical assessment grid
+ pediatric examination (H6-H12) n = 64 (C)
67,8 %
25,2 %
2,0 %
75 %
23,4 %
1,6 %
Monitoring done
n = 164
Monitoring
undone
n = 61
Missing
data
n = 17
Monitoring done n = 49
Pediatric examination noted in
the file n=15
Monitoring
undone
n = 15
Missing
data
n = 1