Early Human Development 103 (2016) 37–41

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Group B streptococcus infections in neonates admitted to a German NICU: Emphasis on screening and adherence to pre-analytical recommendations

Claudia Reinheimer [a], Volkhard A.J. Kempf [a], Boris E. Wittekindt [b], Antje Allendorf [b], Thomas A. Wichelhaus [a], Michael Hogardt [a], Rolf L. Schlößer [b], Doris Fischer [b,*]

[a] Institute for Medical Microbiology and Infection Control, University Hospital Frankfurt, Germany
[b] Department of Pediatrics, Division of Neonatology, University Hospital Frankfurt, Germany

ARTICLE INFO

Article history:
Received 26 May 2016
Received in revised form 19 July 2016
Accepted 19 July 2016
Available online xxxx

Keywords:
Neonatology
Group B *streptococcus*
Intrapartum antibiotic prophylaxis
Screening adherence
Early onset disease
Late onset disease

ABSTRACT

Background: Infections by group B *streptococci* (GBS), *e.g. Streptococcus agalactiae*, presenting as early-onset disease (EOD) or late-onset disease (LOD), are leading causes of severe infections in newborn and premature patients. Although screening and *intra partum* antibiotic prophylaxis are frequently performed, vertically transmitted GBS remain a challenge for pediatrics.
Aims: In order to prevent or reduce potential life-threatening events, this study retrospectively investigated epidemiological, microbiological and clinical aspects of infants admitted to the Division of Neonatology at the Department of Pediatrics at the University Hospital Frankfurt, Germany (UHF).
Study design and subjects: Between January 2010 and January 2016, perinatal GBS screening status, clinical presentation of EOD or LOD and therapeutic management of neonates admitted to UHF were retrospective analysed. Infants tested positive for GBS within their first three months of life were included; patient data were obtained from the chart report. Severity of neonatal disease was analysed by using the *NEOMOD* and CRIB score.
Results: 108 GBS infected infants born to 105 mothers were observed. N = 101 of them (93.5%) presented with EOD, whereof n = 9 (10%) primarily presented with pneumonia or pneumothorax. In 82 (78%) mothers of infected infants GBS status was unknown prior to hospitalization of the neonate. 3/108 (2.8%) infants died from GBS septicemia.
Conclusion: Avoidance of GBS transmission *sub partu* is the key issue in preventing neonatal GBS infection and should be the focus of preventive strategies. Our results highlight the impact of perinatal screening.

1. Introduction

Group B *streptococci* (GBS), *e.g. Streptococcus agalactiae*, are leading cause of severe infections in newborn and preterm patients [1], commonly presenting as sepsis, pneumonia and/or meningitis [2–4], with an incidence of 0.5/1000 births in Germany [5].

Invasive GBS infections have been categorized as early-onset disease (EOD; occurring within the first seven days of life) or late-onset (LOD; after the first week of life and within the first three months of life) [3], mostly caused by capsular GBS serotypes Ia, Ib, II, III, and V [6].

Since several routes of transmission are known [7], an estimated 50% or more of newborns exposed to GBS *sub partu* will become colonized [8]. Thus, preventing potentially life-threatening events and severe cerebrovascular complications [9] caused by GBS in neonates, considerations need to be targeted on prevention of materno-fetal GBS transmission. Therefore, culture-based screening methods using vaginal and ano-rectal swabs of all pregnant women at 35–37 weeks of gestation is recommended to identify those who should receive *intra partum* antibiotic prophylaxis (IAP) [10].

Since the early 1990s, when IAP to prevent GBS disease was implemented, incidence of EOD has declined by approximately 80% [11], with an estimated incidence of GBS related sepsis in newborns and prematures of 0.5/1,000 live births in Germany [5]. Moreover, the relation between EOD and LOD shifted from 80:20 towards 60:40 in Germany [11], with an estimated amount of 20% of mothers being positive for GBS in vaginal swabs [12].

Despite the encouraging achievements of GBS screening and IAP, infections with GBS remain one of the leading cause for infection-associated admittance to neonatal intensive care units (NICU).

In order to improve prevention of GBS infection in pre-/term neonates, this study retrospectively elucidates perinatal GBS diagnostic and therapeutic management of GBS infection and outcome of GBS

* Corresponding author at: Dept. Pediatrics, Div. Neonatology, Goethe University Hospital, Theodor Stern Kai 7, 65090 Frankfurt/Main, Germany.
E-mail address: doris.fischer@kgu.de (D. Fischer).

http://dx.doi.org/10.1016/j.earlhumdev.2016.07.007
0378-3782/

infected preterm and term neonates admitted to the NICU of University Hospital Frankfurt (high level perinatal center) between January 2010 and January 2016.

2. Material and methods

2.1. Case definition

While "colonized with GBS" might be valid for asymptomatic adults, it however seems not to be proper in neonates. This might wrongly lead to an underestimation of the health threat linked to GBS, especially if detected in non-invasive materials, *e.g.* ear or throat swab, in contrast to invasive materials, *e.g.* blood or cerebrospinal fluid (CSF). We therefore prefer the terminus "infected with GBS" for all infants within their first three months of life, as also suggested by Malik et al. [13]. For note, this approach is furthermore backed up by fact that all infants tested positive for GBS at any location receive antibiotic therapy at University Hospital Frankfurt, Germany (UHF). Neonatal GBS infection therefore is defined as GBS detection from *any* material +/− clinical impairment +/− elevated blood infection parameters (*e.g.* elevated CRP, increased or decreased leucocyte count). If GBS was detected in non-invasive *and* invasive material, case was accounted to sepsis or meningitis in case of positive blood or CSF culture, respectively.

2.2. Patients and patients' data

We retrospectively evaluated data from preterm and newborn patients (in- or outborn) treated at the Division of Neonatology at the Department of Pediatrics at UHF between January 2010 and January 2016 and tested positive for GBS.

As defined by the World Health Organization, preterm birth is defined as birth <37 weeks of gestational age [1].

Patient data were obtained from the chart report. Newborns tested positive for GBS in any material within their first week of life and beyond the first week of life up to the third month of life are classified as EOD and LOD, respectively, following the definition by CDC [3]. Patients beyond their first three months of life were excluded. Severity of the neonatal GBS infection was scored by *NEOMOD* and *CRIB* [14–16].

2.3. Detection of GBS and antibiotic susceptibility testing

Vaginal swabs were collected by clinicians using Amies collection and transport medium (Hain Lifescience, Nehren, Germany) and streaked onto a selective 5% sheep blood agar supplemented with colistin 10 μg per ml and aztreonam 2 μg per ml (CAP agar; Oxoid, Wesel, Germany), incubated in 5% CO_2 atmosphere at 35 °C and examined after 18–24 h. Identification of presumed GBS was done by matrix-assisted-laser desorption ionization-time of flight analysis (VITEK MS, bioMérieux, Nürtingen, Germany). In individual cases, identification of presumed β-haemolysing *streptococci* was performed by detection of the Lancefield group B antigen by a rapid latex agglutination test (StrepPRO™ Streptococcal Grouping Kit (Hardy Diagnostics, Santa Maria, CA USA). Antibiotic susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines by agar diffusion testing and antibiotic gradient tests (bioMérieux) where necessary.

All laboratory testing was performed under strict quality-controlled criteria (laboratory accreditation according to ISO 15189:2007 standards; certificate number D–ML–13102–01–00, valid through January 25th, 2021).

2.4. Statistical analysis

Chi squared test for statistical calculation. Confidence intervals were calculated based on binomial distribution. p–Values of $p \leq 0.05$ were considered statistically significant.

2.5. Ethics

Based on the utilization of retrospective data and with regard to §15 Hessian Medical Association's Professional Code of Conduct (*Berufsordnung für in Hessen tätige Ärzte/innen*), this study was approved by the Ethics Board of the Goethe University Hospital on November 30th, 2015.

3. Results

3.1. General findings

Within the observational period, 3374 neonates were admitted to NICU at UHF. In 27 preterms and 81 terms (108 totally, including three twins) born from 105 mothers, GBS was detected as causative for the infection they were treated for. Three neonates died from GBS associated multi-organ failure (Table 1), the other survived without any long-term GBS-related sequelae, *e.g.* seizures following meningitis.

GBS status of 83/105 mothers was unknown (Table 1), which was due to preterm delivery (n = 13; 15.6%; 8.6–25.3), un-monitored pregnancy (n = 2; 2.4%; 0.3–8.4) or unknown reasons.

Within mothers tested positive for GBS, ten received IAP. Except for one case with erythromycin treatment due to allergy to penicillin, all mothers received single shot ampicillin (2 g once i.v.) or penicillin G (5,000,000 units once) *sub partu,* as recommended by CDC [10]. Within mothers tested negative for GBS (n = 8) or with unknown status (n = 83), 4 and 9 mothers, respectively, received IAP due to amnionitis; in one case erythromycin was administered due to allergy to penicillin. Consecutively, 23 mothers received an IAP, with 21 and two received ampicillin i.v. and erythromycin i.v. *sub partu,* respectively. All infants of mothers with IAP were tested positive for GBS. Maternal GBS status was not examined prior to delivery in any of the fatal cases.

Table 1
General demographic description of the cohort at NICU at UHF Abbreviations and symbols: OBPE = observational period; ♣ = 95% confidence interval; * non-invasive materials are: swabs taken from ear, nose, throat or umbilicus.

Demographic data of the UHF cohort		
		♣
Total number of infants admitted to NICU at UHF in the OBPE	3374	
Number of infants suffering from GBS related disease in the OBPE	108	
Birth weight (range; g)	710–4910	
Median (g)	3115	
Duration of hospital stay (range; d)	2–156	
Median (d)	8	
Incidence of GBS related disease in infants at NICU at UHF (%)	3.2	2.6–3.8
Early onset disease (n;%)	101 (93.5)	87.1–97.4
Thereof GBS positive in non-invasive materials* only (n; %)	5 (4.9)	1.6–11.2
Late onset disease (n;%)	7 (6.5)	2.6–12.9
Thereof GBS positive in non-invasive materials* only (n; %)	–	–
Number of GBS infected infants' mothers	105	
Number of gemini in the cohort (pairs)	3	
Female (n; %)	60 (55.6)	45.7–65.1
Median gestational age at birth (completed weeks + days)	40 + 0	
Median birth weight (g)	3115	
Maternal GBS status (n; %)		
GBS screening performed	22 (21.0)	13.6–29.9
Positive	14 (63.6)	40.7–82.8
Negative	8 (36.4)	17.2–59.3
GBS screening not performed/status unknown	83 (79.0)	70.0–86.3