European Journal of Obstetrics & Gynecology and Reproductive Biology 240 (2019) 178–181

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

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

Full length article

Prevalence and treatment of group B streptococcus colonization based on risk factors versus intrapartum culture screening

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ARTICLE INFO

Article history:
Received 13 March 2019
Received in revised form 20 June 2019
Accepted 30 June 2019

Keywords:
Group B streptococcus
Prevalence
Intrapartum antibiotic prophylaxis
Risk based strategy
Intrapartum screening

ABSTRACT

Objectives: To estimate the prevalence of group B streptococcus at onset of labor and to compare the accuracy of intrapartum antibiotic prophylaxis based on a risk factor strategy versus an intrapartum screening.

Study design: In this cross-sectional study, 700 women referred for intended vaginal delivery were tested for group B streptococcus at onset of labor by gold standard culture in vaginal and rectal swabs. The results were blinded, and intrapartum antibiotic prophylaxis was given to women with risk factors for group B streptococcus infection: previous neonatal group B streptococcus infection, group B streptococcus in urine and/or vagina in current pregnancy, gestational age <36 + 0 weeks, temperature ≥38.0 °C or rupture of membranes ≥18 h.

Results: Of 642 women, who delivered within three days of specimen collection, 170 (26.5%) received benzylpenicillin as intrapartum antibiotic prophylaxis based on risk factors. The prevalence of group B streptococcus at onset of labor was 17.8% (114/642), with 62 women positive for group B streptococcus in both the vagina and rectum, 12 in the vagina only and 40 in rectum only.

Intrapartum antibiotic prophylaxis was administered correctly in 31.6% (36/114) of GBS positive women at time of delivery and 78.8% (134/170) of women who received antibiotics were actually GBS negative. The positive predictive value of intrapartum antibiotic prophylaxis based on risk factors was 21.2%. The sensitivity was 31.6% and the specificity was 74.6%.

Conclusion: The accuracy of predicting maternal group B streptococcus infection from risk factors is low. Intrapartum group B streptococcus diagnostics is more precise and will not increase the overall use of intrapartum antibiotic prophylaxis.

Introduction

Group B streptococcus (GBS), also known as *Streptococcus agalactiae*, is the most common beta-hemolytic streptococcus species found rectovaginally in pregnant women [1], and colonization is often asymptomatic. GBS is a part of the normal intestinal flora, and the gastrointestinal tract is considered the primary reservoir, and the source of secondary vaginal colonization [2].

The prevalence of GBS in the vagina and/or rectum during the pregnancy has in Denmark been reported between 8 and 36% [3–5] and is of the same magnitude as in other European countries [6].

Transmission of GBS from mother to child can take place through the birth canal during delivery, and colonized newborns are at risk of early-onset GBS infection (EOGBS) during their first week of life. EOGBS can have serious neonatal outcomes such as sepsis, pneumonia and meningitis, which are conditions with a high morbidity and mortality [7]. The incidence of EOGBS has decreased over the years in many countries, and in Denmark the national incidence decreased from 0,6/1000 live birth in 1995 to 0,2/1000 in 2002 [8].

Intrapartum antibiotic prophylaxis (IAP) can prevent transmission of GBS and neonatal GBS infection. Mainly two different strategies are used: one based on risk factors for GBS colonization and one based on antenatal universal culture-based screening [9]. In Denmark, a risk-based strategy is used including GBS in urine and/or vagina in current pregnancy, preterm delivery, fever, prolonged rupture of membranes during delivery or previous neonatal GBS infection [10]. In other countries such as the USA, a

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https://doi.org/10.1016/j.ejogrb.2019.06.037
0301-2115/

culture-based universal screening with vaginal and rectal swabs of all women between gestational ages 35–37 weeks is recommended. The universal screening strategy is more effective than the risk-based strategy in identifying women at risk of transmitting GBS and reducing EOGBS [11], but it is also more resource intensive.

The aim of this study was to estimate the prevalence of GBS at onset of labor and to compare the diagnostic accuracy of IAP based on a risk factor strategy with an intrapartum GBS culture screening of all women in labor. Furthermore, we evaluated the need for improving antibiotic stewardship.

Material and methods

In this cross-sectional study we addressed women presenting at Hvidovre Hospital between February and July 2017 at onset of labor (contractions, rupture of membranes or planned inductions of labor) and who fulfilled the following criteria: intended vaginal delivery, age over 18 years, gestational age more than 24 + 0, no antibiotic treatment within the last seven days and expected delivery within three days. Totally, 3012 women were eligible and 700 women were included, based on a sample size calculation expecting a GBS prevalence of 20% and 296% uncertainty at 95% confidence interval.

In those accepting participation, vaginal and rectal swabs were tested for GBS, but the results were blinded. Benzylpenicillin was given as IAP to women with risk factors for GBS: GBS in urine or vagina during the pregnancy, a previous newborn with invasive GBS infection, gestational age < 36 weeks, rupture of membranes for ≥18 h, or temperature ≥380 °C.

The vaginal sample was collected by rotating a cotton swab in the lower part of the vagina, and the rectal sample was obtained two centimeters inside the external anal sphincter by rotating a separate swab carefully. A detailed sampling guide was attached to the sample kit to ensure uniformity in the sample collection performed by either midwives or the research fellow.

The swabs were collected using Eswab (Copan, Italy) and transported to the Department of Clinical Microbiology without delay. Samples were cultured on a 5% blood agar and a bi-plate chromogenic agar that identified hemolytic streptococci group B (CHROMagarTM StrepB, CSB, France). Both plates were incubated in CO_2 for 18 h and the CSB plate was compared with the blood agar to identify growth of GBS. Hemolytic colonies were finally confirmed as GBS using MALDI-TOF. Swabs were registered as either GBS positive or GBS negative.

The participating women were registered by their unique 10-digit personal identification number, which is used in Denmark making it possible to collect data from the local obstetric database and from the medical files. Data regarding the study population on maternal age, date and time of delivery, gestational age, parity, body mass index, smoking and previous preterm delivery were obtained from the local obstetric database at Hvidovre Hospital. The medical files were reviewed to find information on previous culture of urine or vaginal swabs at any time in this pregnancy and antibiotics during delivery.

Statistical analyses

Baseline data on our study population was compared to the women with intended vaginal delivery at Hvidovre Hospital in the same period not included in the study (n = 2312) by calculating frequencies, mean values, chi square test for groups and independent *t*-test of the means. To compare GBS status according to the medical file with our GBS swabs (gold standard) cross-tabulation was used and sensitivity, specificity, positive predictive and negative predictive values were calculated. The same statistical methods were used to compare the use of IAP with our GBS swabs. For the statistical analysis IBM SPSS Statistics for Windows version 22 (IBM Corp. Released 2013. Armonk, NY: IBM Corp.) was used.

Ethical approval

The study was approved by the Danish Ethical Committee (protocol number: H-16047697) and the Danish Data Protection Agency (j.nr: 2012-58-0004). All participants received written and oral information about the study and gave written consent before entering the study.

Table 1
Comparison of the study population and all other women with intended vaginal delivery who gave birth at Hvidovre Hospital, Denmark during the study period.

	Study population n = 642	All other women n = 2312	P-value
Maternal age, years, mean (SD)	31.4 (4.65)	31.1 (4.80)	**0.178**
Gestational age at delivery, weeks, n (%)			<**0.001**
<37 + 0	13 (2.0)	140 (6.1)	
37 + 0-40 + 6	366 (57.0)	1676 (72.5)	
≥ 41 + 0	263 (41.0)	496 (21.5)	
Parity, no. of previous births, n (%)			<**0.001**
0	366 (57.0)	1121 (48.5)	
1	205 (31.9)	851 (36.8)	
≥2	71 (11.1)	340 (14.7)	
Body mass index, kg/m^2, mean (SD)	24.1 (4.53)	23.8 (4.52)	**0.077**
Smoking during pregnancy, n (%)			**0.116**
Yes	36 (6.6)	174 (8.6)	
No	512 (93.4)	1838 (91.4)	
Previous preterm delivery[a], n (%)			**0.114**
Yes	10 (3.6)	72 (6.0)	
No	266 (96.4)	1119 (94.0)	

SD, standard deviation.
[a] Nulliparous is not included in data of previous preterm delivery.

Results

Of the 700 included women, 642 were qualified for analysis, and 58 were excluded due to more than three days between GBS sampling and delivery (n = 37), delivery at another hospital (n = 18), no Danish identification number (n = 2), and in one the result of the rectal swab was missing.

The study population was compared to the background population of 2312 women with intended vaginal delivery at Hvidovre Hospital in the same period. The study population had a lower parity ($p < 0.001$) and a higher gestational age ($p < 0.001$), but the same maternal age ($p = 0.178$), body mass index ($p = 0.077$), smoking status ($p = 0.116$) and history of preterm delivery ($p = 0.114$) as the background population (Table 1).

The prevalence of GBS at onset of labor was 17.8% (114/642) in the study population, as 62 (9.7%) had GBS in both the vagina and rectum, 12 (1.9%) in the vagina only and 40 (6.2%) in the rectum only.

Only 2.8% (18/642) were identified as GBS positive according to the medical file based on urine cultures and/or vaginal swabs during the pregnancy (Table 2). The sensitivity and specificity of the current testing in pregnancy was 11.4% and 99.1% respectively.

Prophylactic antibiotic treatment was in total given to 26.5% (170/642). Among these, 788% (134/170) was actually GBS negative at time of delivery. Furthermore only 316% (36/114) of GBS positive women at time of delivery had IAP (Table 3). The positive predictive value of the risk-based strategy for IAP was 21.2% and the negative predictive value was 83.5%. The sensitivity and specificity were 31.6% and 74.6% respectively.

The indications for IAP are given in Table 4. Overall 36 (5.6%) women received IAP due to fever during labor, and of these 32 were GBS negative with no information about other bacteria present and 27 had an epidural during labor (data not shown).

Table 3
Cross-tabulation of intrapartum antibiotic prophylaxis (IAP) during labor and the intrapartum Group B Streptococcus (GBS) screening.

		Intrapartum GBS screening		
		Positive	Negative	Total
IAP during labor[a]	Yes	36	134	170
	No	78	394	472
Total		114	528	642

[a] Indications for IAP were rupture of membranes ≥18 h, temperature ≥38.0 °C, previous Group B Streptococcus (GBS) colonization in this pregnancy or gestational age <36 + 0.

Discussion

We found a prevalence of GBS at onset of labor of 17.8% in either the vagina or the rectum. The sensitivity and specificity of the current GBS algorithm during pregnancy was 11.4% and 99.1% respectively, and this testing strategy based on risk factors is insufficient to predict the intrapartal GBS positive women. The current risk-based strategy for IAP had a positive predictive value of 21.2% and a negative predictive value of 83.5% and leads to both unnecessary treatment and lack of treatment with IAP.

The prevalence of GBS in our study is within the range of the 8–36% earlier reported in Denmark [3–5] and of the same magnitude as in other European studies [6]. Inclusion of rectal sampling will increase the prevalence [12] and can along with varying sampling technics explain the variations in frequency. The identified prevalence is about six times higher when using intrapartum culture screening compared to the current more random GBS culturing during pregnancy. This indicates that the current testing of pregnant women only reveals a minor fraction of all GBS colonized women at onset of labor potentially capable of transmitting GBS to their newborn. This is also reflected by the very low sensitivity of the testing method. GBS colonization can vary through pregnancy [3], so detection or rejection of colonization at one point of the pregnancy cannot predict the GBS status at labor. In addition, GBS colonization is often asymptomatic and there are no specific criteria for performing a GBS culture, which leads to variation in the examination rate [13].

The overall use of IAP could be reduced about one-thirds (26.5% to 17.8%) when comparing the number of women who received IAP during labor (those with risk factors) with the number of GBS positive at labor. The use of IAP in the risk factor group could be reduced from 100% (170/170) to 21.2% (36/170). A reduction in the use of IAP with intrapartum screening is also found in other Danish studies. One study – screening high-risk women only - found that IAP could have been avoided in 67% of the women with preterm deliveries (gestational age 35 + 0 to 36 + 6) or prolonged rupture of membranes [14]. Another study – screening all women in the vagina only - found a possible reduction in IAP from 12% to 4% when the risk factor based strategy and intrapartum polymerase chain reaction (PCR) test were combined, and IAP only were given to those with both one or more risk factors and a positive GBS-PCR sample [15]. The difference between the possible reduction of IAP in those two studies and in ours might be explained by the inclusion of all women, and not only high-risk women, as well as both vaginal and rectal sampling in our study.

However, the introduction of IAP based on risk factors decreased the incidence of EOGBS at Rigshospitalet, Denmark from 227 cases per 1000 live birth in 2002 to 130 cases per 1000 live birth in 2010 [13]. The national guideline recommends IAP at gestational age < 37 + 0 (optionally < 35 + 0), and at Hvidovre Hospital IAP is only used routinely at GA < 36 + 0. For this reason, we used the gestational age <36 + 0 as a risk factor in our calculations. The sensitivity and specificity of IAP administration based on risk factors is low. In our population it led to unnecessary use of antibiotic in some cases (134/642) and lack of antibiotic prophylaxis in others (78/642).

Unnecessary use of antibiotics may contribute to the development of resistant bacteria [16], may have a negative effect on the microbiome of the newborn [17], and is associated with prolonged hospitalization [10]. Conversely, lack of relevant

Table 2
Cross-tabulation of Group B Streptococcus (GBS) status according to the medical file based on urine cultures and vaginal swabs during the pregnancy and intrapartum GBS culture screening.

		Intrapartum GBS screening		
		Positive	Negative	Total
GBS status in medical file	Positive	13	5	18
	Negative/not tested[a]	101	523	624
Total		114	528	642

[a] 163 women had no results from urine or vaginal culture in the medical file.

Table 4
Cross-tabulation of the indications for intrapartum antibiotic prophylaxis (IAP) and the intrapartum Group B Streptococcus (GBS) screening.

		Intrapartum GBS screening		
		Positive, n (%)	Negative, n (%)	Total
Indications for IAP	Rupture of membranes ≥18 hours	20 (17.4)	95 (82.6)	115 (100)
	Temperature ≥380 °C	4 (11.1)	32 (88.9)	36 (100)
	Previous GBS colonization in this pregnancy	11 (68.8)	5 (31.3)	16 (100)
	Gestational age <36 + 0	1 (33.3)	2 (66.7)	3 (100)
Total		36	134	170

antibiotics in GBS positive woman increases the risk of transmission of GBS to the newborn. Further, IAP with benzylpenicillin to women with fever during delivery might be an insufficient treatment as 32 women with fever were actually GBS negative. Optimal treatment could be a more broad-spectrum antibiotic, or maybe no antibiotics at all if there is no infection, as 27 of the 32 women had an epidural during labor, which is associated with fever [18].

The strength of this study is the large number of participants and the prospective study design. Culture sampling was possible concurrently with the standard treatment. Another strength is the use of gold standard cultures and the inclusion of both vaginal and rectal swab, which makes the GBS results reliable. Furthermore, the study population was comparable to the overall population regarding maternal age, body mass index, smoking status and history of preterm delivery. More nulliparous women and women with higher gestational age were included in the study, however, this difference is not crucial, as GBS colonization is independent of the gestational age [4] and probably parity.

A limitation of this study is that even though a detailed sampling guide was attached to the sample kit, variations in sampling technique can theoretically have occurred and affected the identified prevalence of GBS. Further, a period of up to three days between swab and delivery was accepted for this trial. An ideal time frame between swab and delivery should have been shorter to identify the actual intrapartum GBS status. The term intrapartum screening is still used even though some of the women were not in active labor when the swabs were taken. The colonization of GBS is previously shown to vary during the pregnancy [3], but the maximal time between sampling and delivery of three days, is not expected to change the GBS status significantly.

The risk-based strategy is insufficient to detect the true GBS positive women at delivery, but so is the universal culture screening in week 35–37 [19,20]. Sampling at delivery gives the most accurate prevalence, but the result of the test is often too late for IAP indication, as culturing takes 24–48 hours. The use of a rapid PCR test has been investigated in several studies finding relatively high sensitivities (85.7–100 %) and specificities (95.9–97.5 %) [14,19,21]. The PCR method may be challenged by a high number of invalid tests, and therefore thorough training of the hospital ward staff is required [21]. This is supported by a recent Danish study by Helmig et al. [14], where the low number of invalid test results (< 1%) was attributed to the fact that skilled laboratory staff performed swab processing and analysis.

We found that the current risk-based IAP strategy was inadequate for identification of women at risk of transmitting GBS to their newborn. It results in both unnecessary antibiotic treatment and lack of treatment with IAP. To provide the best prevention of GBS and only use the necessary amount of antibiotics, intrapartum GBS testing is optimal. A PCR test, preferably as a point of care test with short turnaround time, would be the best option. Further studies – including health economical perspective are needed.

Acknowledgments

Thanks to all the midwives at the Department of Obstetrics and Gynecology, Hvidovre Hospital, Denmark for helping with the samples. This study was financial supported by The Independent Research Fund Denmark.

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