The Journal of Maternal-Fetal & Neonatal Medicine

ISSN: 1476-7058 (Print) 1476-4954 (Online) Journal homepage: http://www.tandfonline.com/loi/ijmf20

Intrapartum test for detection of Group B Streptococcus colonization during labor

Elena Picchiassi, Giuliana Coata, Giulia Babucci, Irene Giardina, Valentina Summa, Federica Tarquini, Michela Centra, Vittorio Bini, Benito Cappuccini & Gian Carlo Di Renzo

To cite this article: Elena Picchiassi, Giuliana Coata, Giulia Babucci, Irene Giardina, Valentina Summa, Federica Tarquini, Michela Centra, Vittorio Bini, Benito Cappuccini & Gian Carlo Di Renzo (2017): Intrapartum test for detection of Group B Streptococcus colonization during labor, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2017.1369041

To link to this article: http://dx.doi.org/10.1080/14767058.2017.1369041

Accepted author version posted online: 17 Aug 2017.
Published online: 31 Aug 2017.

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE, 2017
https://doi.org/10.1080/14767058.2017.1369041

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Intrapartum test for detection of Group B Streptococcus colonization during labor

Elena Picchiassi[a], Giuliana Coata[a], Giulia Babucci[a], Irene Giardina[a], Valentina Summa[a], Federica Tarquini[a], Michela Centra[a], Vittorio Bini[b], Benito Cappuccini[c] and Gian Carlo Di Renzo[a]

[a]Department of Obstetrics and Gynecology, University Hospital of Perugia, Perugia, Italy; [b]Department of Internal Medicine, University Hospital of Perugia, Perugia, Italy; [c]Department of Neonatology, University Hospital of Perugia, Perugia, Italy

ABSTRACT

Purpose: The purpose of this study was to evaluate the potential improvement of introducing an intrapartum test for the detection of Group B Streptococcus (GBS) during labor and to estimate its cost-effectiveness versus antepartum GBS screening culture.

Materials and methods: Three hundred and thirteen women at beginning of labor, with unknown GBS status or with antepartum GBS screening culture were enrolled. A vaginal–rectal specimen was collected from each woman for GBS detection by real-time PCR. Results of intrapartum test and antepartum GBS screening culture were compared.

Results: Antepartum culture results did not always reflect the intrapartum maternal GBS colonization status since in 15.1% of the cases it was not concordant with intrapartum test. However, selecting only women, who underwent antepartum culture and intrapartum test at the same time, the percentage of concordance was 96.6%. Based on intrapartum test results, 74.9% of the total number of intrapartum antibiotic prophylaxis (IAP) was administered uselessly, while 1.9% of women did not receive IAP although they were positive to intrapartum test. Intrapartum test resulted less cost-effective than antepartum culture but it became more cost-effective at a cost threshold of about 16.00 €.

Conclusions: The clinical introduction of intrapartum test could be a valuable mean for identification of GBS colonization during labor, allowing an appropriate management of mothers and neonates with consequent benefit for their health and with limited costs for Healthcare System.

ARTICLE HISTORY
Received 8 May 2017
Revised 4 August 2017
Accepted 15 August 2017

KEYWORDS
Antepartum Group B Streptococcus (GBS) screening culture; GBS; GBS Early Onset Disease (EOD); intrapartum antibiotic prophylaxis (IAP); nucleic acid amplification test (NAAT)

Introduction

Maternal colonization with Group B Streptococcus (GBS) remains a leading cause of neonatal morbidity and mortality in the world [1].

Many countries have adopted screening strategies [2], such as the antepartum GBS screening culture at 35–37 weeks of pregnancy (antepartum culture), to identify women who need intrapartum antibiotic prophylaxis (IAP) in order to avoid the GBS peripartum transmission to the fetus. IAP has reduced, but not eliminated the incidence of GBS early onset disease (EOD) in neonates [3,4]. The remaining cases of GBS EOD are mainly due to the intermittent/transient vaginal colonization characteristic of GBS [5–8].

The screening strategy of antepartum culture has two limitations: first, it has led to a widespread use of antibiotics not always targeted since the variability of GBS colonization and, second, the impossibility to know the maternal GBS status during labor due to the time consuming detection of bacterial growth [9].

In order to improve GBS-colonized pregnancy management during delivery, recently, the European consensus conference recommended [10] IAP based on a GBS intrapartum test. This opportunity has been opened with the development of molecular tests, based on nucleic acid amplification (NAAT). Among these tests, GeneXpert GBS test (Cepheid, Maurens-Scopont, France) (intrapartum test) is very promising because it allows a rapid GBS detection with high diagnostic accuracy [11–14].

The objective of the study was to investigate on the potential improvement derived from the clinical introduction of this intrapartum test for the detection of GBS during labor and to estimate its cost-effectiveness versus antepartum GBS screening culture.

Materials and methods

Strengths and weaknesses of intrapartum test were evaluated both in pregnant women with unknown

CONTACT Elena Picchiassi elena.picchiassi@pec.enpab.it Department of Obstetrics and Gynecology, S. Maria della Misericordia University Hospital, 06132 S. Andrea delle Fratte, Perugia, Italy

GBS status at the time of the delivery and in those with antepartum culture.

We considered the antepartum culture as our reference test because it is currently used for GBS screening strategy in our Hospital. All pregnant women enrolled in the study attended the obstetrics and gynecology outpatient Clinic of the Perugia University, Italy between 2014 and 2016. Obstetric data of pregnant women were collected either at the time of the enrollment by a direct interview or after delivery by searching in the medical records.

All women provided written informed consent after they were aware of the purpose and experimental nature of the study. The study was approved by the local Ethics Committee (Register no. 2048/12).

Three hundred and thirteen women were enrolled at beginning of labor either-term or preterm. Exclusion criteria were the following: planned caesarean section, use of systemic, or topical antibiotics in the 10 d before admission.

The sample collection was performed with a vaginal and rectal swab by Copan – Cepheid collection device (Copan, Italia, Brescia, Italy) without the use of speculum. The swab obtained from each woman was inserted in the Xpert GBS cartridge (Cepheid) containing all the reagents for lysis of the sample, DNA extraction, amplification and control reagents.

The cartridge was then placed on the GeneXpert System (Cepheid) for GBS detection. DNA extraction, amplification, and detection were executed in a one-step process and in an automated fashion.

GBS primers and probe detect a target within a 3′DNA region adjacent to the *cfb* gene (encoding the extracellular protein CAMP factor) of *Streptococcus agalactiae*.

The kit was used in according to the instructions from the manufacturer; DNA extraction and PCR analysis were performed directly on the specimens sampled without culture enrichment prior to PCR.

The results were interpolated by the GeneXpert System (Cepheid) from measured fluorescent signals and specific calculation algorithms. Results were neither provided to personnel in charge of the patients nor used for clinical decisions.

We compared the results of antepartum culture and intrapartum test in order to evidence the intermittent and transient nature of GBS infection. We used the term "concordant" when antepartum and intrapartum tests gave the same result, while "discordant" when antepartum and intrapartum tests gave the opposite result. In our study, the terms "concordant" and "discordant" were not referred to the diagnostic accuracy of the antepartum and intrapartum GBS tests because they were performed in different times during pregnancy.

Statistical analysis

The results of the numerical variables were expressed as median and interquartile range. For cost-effectiveness analysis (CEA), the costs considered were: microbiological test used for antepartum culture, antepartum antibiotic therapy, IAP, and intrapartum test. All the costs were obtained from the pharmacy department of our hospital apart from intrapartum test, which were provided from Cepheid. Unlike the others, the cost of IAP is variable according to the duration of labor; therefore, we considered the mean value obtained from all women included in the study. The economic aspect was evaluated considering the costs sustained by our Regional Healthcare System. The costs, related to clinical and technician staff involved in the execution of the tests and in the management of pregnant women and newborns, were considered fixed and therefore they were not evaluated in the analysis. In this study, the number of appropriate treatments and appropriate no treatments were considered as clinical effectiveness outcome.

The incremental cost–effectiveness ratio (ICER) was used in our analysis to evidence the cost-effectiveness of intrapartum test versus antepartum culture. It is defined by the difference in cost (*C*) between the two tests, divided by the difference in their effectiveness (*E*):

$$\mathrm{ICER} = (C_{\mathrm{IntrapartumTest}} - C_{\mathrm{AntepartumCulture}})/(E_{\mathrm{IntrapartumTest}} - E_{\mathrm{AntepartumCulture}})$$

It provides an estimation of the average incremental cost required to have one additional adequate treatment or adequate no treatment [9].

In order to carry out cost-effectiveness analysis, a decision tree model was built by putting in branches the results of antepartum culture and intrapartum test and for each result of the tests, the percent of wrong treatments, appropriate treatments, wrong no treatments, and appropriate no treatments were indicated together with costs.

Almost all methods of cost-effectiveness analysis revolve around ICER, but one limitation of those methods involves the determination and presentation of statistical uncertainty. Addressing this problem, a variety of solutions have been proposed involving the delta method, Feiller's method, and bootstrapping [15], we preferred to use the so-called cost-effectiveness acceptability curve (CEAC). The CEAC provides the probability that the new treatment is cost-effective, at

different values of the outcome of interest (or levels of willingness to pay). The policy maker might have varying degrees of tolerance for different treatment decisions and the CEAC provides the necessary information for an informed decision under uncertainty [16].

Then, to construct CEAC, a scatter plot was produced on the basis of the results of 10,000 Monte Carlo simulations, to show the probability that a treatment is less or more cost effective than the other, according to different thresholds of willingness to pay. Furthermore, to investigate robustness of the model to different scenarios, we used a sensitivity analysis, calculating cost effectiveness using a range of estimates of unit cost of intrapartum test, which was the only variable we hypothesized might change in future.

Decision tree construction and acceptability curves were performed using Tree-Age Pro version 2011 (TreeAge Software, Inc, Williamstown, MA).

Results

Among 313 enrolled women, 299 were included in the study. We excluded 14 women since the collection of obstetric data was not complete or incorrect. The obstetric data of the included women are shown in Table 1. The studied population was mainly nulliparous and with singleton pregnancy. Among women, there were two groups at high risk of GBS transmission to the newborn, 42 women with premature rupture of membrane (PROM) at term pregnancy (37–41 weeks of gestation) and 24 with preterm birth (PTB) with or without PROM. No women reported to have had previous neonates affected by GBS EOD.

We compared the results of antepartum culture and intrapartum test in order to evidence the intermittent and transient nature of GBS infection. This comparison was performed with the results of 280 out of 299 included women since intrapartum test gave no result for 19 women.

Table 1. Obstetric data of the pregnant women included in the study.

Variable	Value
Maternal age (years)	32 (27–36)
Gestational age at sampling (weeks)	39 (38–40)
Time from ROM to delivery (h)	1 (0–4)
Duration of labor (h)	5 (2–5)
Twin pregnancy (%)	1.3
PROM (%)	14.0
PTB (%)	8.0
Parity (%)	
Nulliparous	52.2
Primiparous	27.4
Multiparous	20.4

Data are reported as median (first quartile-third quartile) or percentage (%). ROM: rupture of membranes; PROM: premature rupture of membranes; PTB: preterm birth.

Among 280 women, 53 (18.9%) had a positive intrapartum test while 227 (81.1%) resulted negative. Two hundred and five out of 280 women underwent to antepartum culture: 164 were negative (80.0%) and 41 positive (20.0%).

Negative antepartum culture group

In the group of 164 women resulted negative to antepartum culture, 151 (92.1%) were still negative to intrapartum test, while 13 (7.9%) were positive.

The 45.7% of women with negative antepartum culture received IAP, as suggested by current guidelines, because the antepartum culture test was performed more than 30 d before giving birth. On one hand, the 89.3% of these performed IAP were useless since the intrapartum test was negative. On the other hand, the 38.5% of women with negative antepartum culture but with positive intrapartum test did not receive IAP because they delivered before than 30 d.

Positive antepartum culture group

In the group of 41 women resulted positive to antepartum culture, 18 (43.9%) were negative while 23 (56.1%) were still positive to intrapartum test.

Before intrapartum test, the 85.4% of women with positive antepartum culture, underwent to antepartum antibiotic therapy due to positive GBS culture, as suggested by current guidelines. However, all the 41 women received IAP because the efficacy of antepartum antibiotic treatment was not known at the time of delivery and the 18 women with positive antepartum but negative intrapartum test received uselessly IAP.

No antepartum culture group

Seventy-five women did not undergo to antepartum culture and 58 (77.3%) of them resulted negative to intrapartum test while 17 (22.7%) were positive.

All 75 women received IAP, as suggested by current guidelines, but it was useless in 77.3% of cases since they had negative intrapartum test.

PROM group: antepartum culture versus intrapartum test

In the group of 42 women with PROM at term pregnancy, 11 (26.2%) did not perform antepartum culture while in the remaining women, 23 (74.2%) had negative antepartum culture and 8 (25.8%) positive.

Considering those PROM women without antepartum culture, 8 (72.7%) were negative and 3 (27.3%) were positive to intrapartum test. Among PROM women with negative antepartum culture, 19 (82.6%) remained negative at intrapartum test, while 4 (17.4%) converted to positive. Among PROM women with positive antepartum culture, 3 (37.5%) converted to negative at intrapartum test, while 5 (62.5%) remained positive.

On one hand, IAP was administered, as suggested by current guidelines, to 100% of PROM women without antepartum culture (unknown GBS status), 43.5% of women with negative antepartum culture (performed more than 30 d before delivery), and 100% of women with positive antepartum culture. The 65.5% of these performed IAP were useless since the intrapartum test was negative. On the other hand, the 6.9% of PROM women with negative antepartum culture but with positive intrapartum test did not receive IAP because they delivered before than 30 d.

PTB group: antepartum culture versus intrapartum test

In the group of 24 pregnancies delivering preterm with or without PROM, 10 (41.7%) did not perform antepartum culture while among the remaining women, 9 (64.3%) had negative antepartum culture and 5 positive.

All PTB women without antepartum culture were negative to intrapartum test, all PTB women with negative antepartum culture remained negative at intrapartum test and all PTB women with positive antepartum culture converted to negative at intrapartum test.

IAP was administered, as suggested by current guidelines, to 100% of PTB women without antepartum culture (unknown GBS status), 44.4% of PTB women with negative antepartum culture (performed more than 30 d before delivery), and 100% of those with positive antepartum culture. The 100% of these performed IAP were useless since the intrapartum test was negative. No PTB woman had positive intrapartum test and, therefore, there was no missed IAP.

Diagnostic accuracy and technical performance of intrapartum test

Overall, the percentage of discordant results between antepartum culture and intrapartum test was 15.1%. However, when we selected 29 women with antepartum culture and intrapartum test performed in the same day or in close proximity (not allowing in any case any therapy of the positive results), the percentage of concordance was 96.6%, with only one test resulting positive to intrapartum test and negative to antepartum culture. Therefore, considering these 29 results and comparing the intrapartum test with the antepartum culture (our gold standard), the sensitivity and the specificity of the new test were 100% (CI 95%: 100–100) and 95.8% (CI 95%: 87.8–100), respectively.

Finally, based on intrapartum test results, 74.9% of the total number of IAP was administered uselessly, while 1.9% of the included women did not receive IAP (because negative antepartum culture), although they were positive to intrapartum test.

Regarding the technical performance of intrapartum test, 13.42% of the performed tests did not yield result at the first attempt, giving 7.35% of error, 4.47% of invalid and 1.60% of no result. Sixty seven percent of these cases were repeated and after the second attempt, the percentage of missing results was 1.43% (0.77% error, 0.33% invalid, and 0.33% no result).

The interval between the availability of intrapartum test result and delivery was evaluated since the effectiveness of a GBS test depends on timely administration of IAP. In 79% of positive intrapartum tests, the results were available 4 h before delivery, in time to perform an efficacious IAP. It was possible because we obtained the results in about 50 min when the GBS was absent and in about 30 min when it was present in the sample.

Table 2. Characteristics of the newborns at birth.

Variable	Value
Weight at birth (g)	3325 (2940–3600)
Length (cm)	50 (49–51)
Apgar 1° min	9 (9–10)
Apgar 5° min	10 (10–10)
Gender (%)	
Male	46.2
Female	53.8

Data are reported as median (first quartile-third quartile) or percentage (%).

Neonatal outcome

Considering neonatal outcome, the data of neonates are reported in Table 2. Among the 299 included women, four had twin pregnancies and 83.3% of newborns had no health problems. The neonatal problems more frequently observed were prematurity (8.0%) and jaundice (2.7%). Only seven newborns (2.3%) showed infection but blood culture did not evidence any type of GBS presence. Two newborns were positive to *Staphylococcus haemolyticus* and epidermidis.

Cost-effectiveness analysis

In the cost-effectiveness analysis, the results of intrapartum test were considered as the real status of

maternal GBS colonization at the time of delivery because intrapartum test was executed during labor and it showed high diagnostic accuracy on the 29 cases analyzed in respect to antepartum culture.

Figure 1 represents the decision tree model in which all the probabilities of appropriate treatment and appropriate no treatment observed in both test groups, were used.

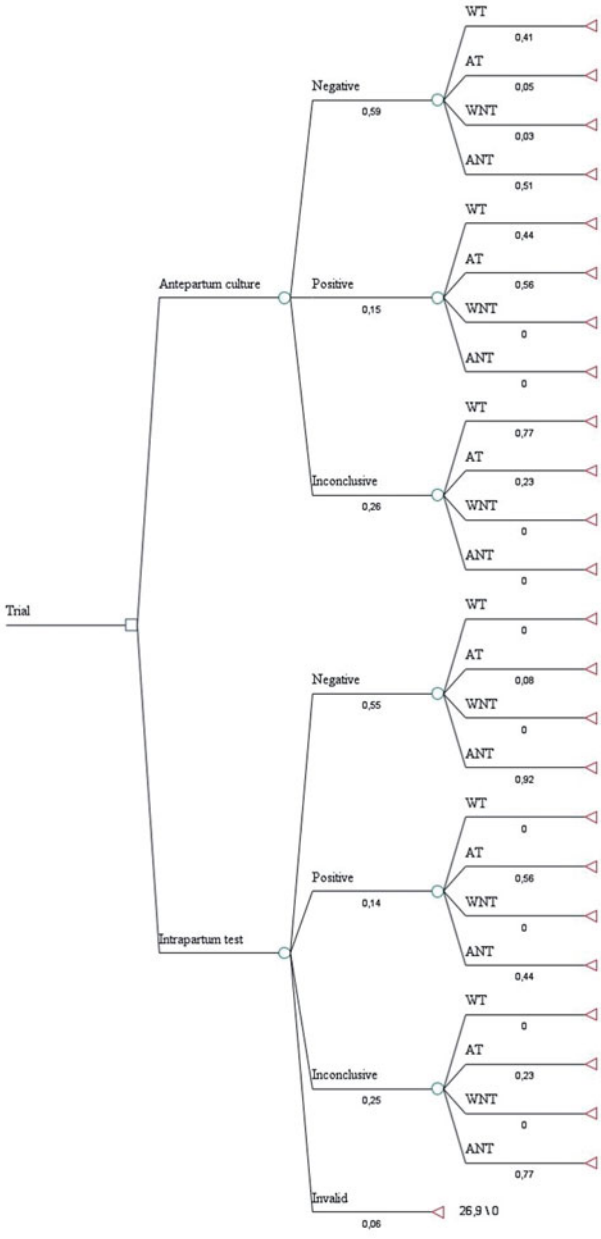

Figure 1. Decision tree model comparing intrapartum test versus antepartum culture. WT: wrong treatment; AT: appropriate treatment; WNT: wrong no treatment; ANT: appropriate no treatment.

From cost-effectiveness analysis, intrapartum test resulted more expensive than antepartum culture, but its effectiveness increased of about 50%. Therefore, the ICER to avoid an inadequate clinical management of GBS was 30.28 € (Table 3).

The measure of the uncertainty of cost-effectiveness to adopt the new test was evaluated by the acceptability curve (CEAC), obtained with 10,000 Monte Carlo simulations (Figure 2). The CEAC showed that the antepartum culture was cost-effective in 53% of the samples and the intrapartum test in 47% if there was no availability to pay (level of 0 € of willingness to pay), while at the ICER value of 30.28 € of willingness to pay, the cost-effectiveness was the same.

Sensitivity analysis showed that when the cost of intrapartum test decreased until to a cost threshold of about 16.00 €, it became more cost-effective than antepartum culture.

Discussion

Main findings

In the present study, we showed the improvement of GBS management during pregnancy derived from clinical introduction of intrapartum test for rapid GBS detection at delivery.

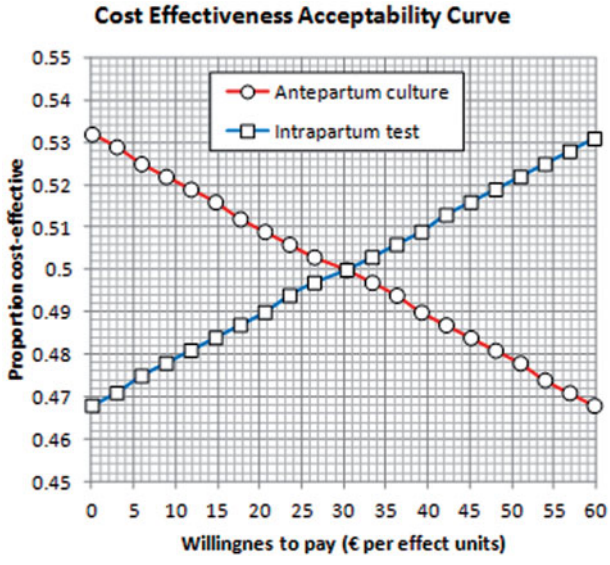

Figure 2. CEAC.

Table 3. Costs and effectiveness of intrapartum test versus antepartum culture.

Strategy	Cost (€)	Incremental cost (€)	Effectiveness	Incremental effectiveness	C/E	ICER (€)
Antepartum culture	7.55		0.47		15.92	
Intrapartum test	21.67	14.10	0.94	0.47	23.04	30.28

Comparing antepartum and intrapartum tests, we evidenced some discordant results confirming the intermittent and transient nature of GBS infection. However, selecting only results of women who underwent antepartum culture and intrapartum test at the same time, the concordance was very high. Intrapartum test showed elevated diagnostic accuracy with only one discordant result out of 29.

The advantage of intrapartum test is the possibility to evaluate the GBS colonization status of women during labor. It could have avoided the inadequate antimicrobial management, mainly among PTB or PROM cases, observed in our study, where 75% of all IAP resulted unnecessary and 9.4% of GBS-colonized women did not receive IAP during labor.

By the cost-effectiveness analysis, the intrapartum test resulted more effective and expensive that antepartum culture; however, if in the next years intrapartum test is introduced in clinical practice and its cost decreases to 16.00 €, it will be more cost-effective than antepartum culture.

Regarding neonatal outcome, no neonates developed GBS EOD. Although five women, not treated with IAP, were GBS colonized at the time of delivery, neonates did not develop GBS sepsis.

Strengths and limitations

A limit of this study could be that intrapartum test and antepartum culture were performed in two different times of pregnancy. However, our purpose was not to evaluate the diagnostic accuracy of intrapartum test, since it is well known from the literature [11–14], but it was to point out the positive or negative effects of intrapartum test on pregnancy management and on neonatal outcome and its cost-effectiveness versus antepartum culture.

We had no case of GBS EOD and no information about colonized asymptomatic newborns, so we cannot demonstrate whether the clinical introduction of intrapartum test could reduce GBS EOD rate. For this reason, our cost-effectiveness analysis was related only to pregnancy management. Other studies are required to verify whether the ICER could be reduced considering also the reduction of neonatal GBS infection as effectiveness and the management of infected neonates and their related long-term disabilities as costs.

Interpretation

The discordant results between antepartum and intrapartum tests are attributed to different times of sample collection or to antibiotic therapy administration after positive antepartum culture. These discrepancies were observed by other Authors [11,17] when they compared antepartum and intrapartum cultures, suggesting that it could be due to the intervals between cultures or the intermittent nature of GBS colonization. On the contrary, when the two tests were performed at the same time, intrapartum test was concordant with antepartum culture showing a high diagnostic accuracy, comparable to other studies [11,12,14,17–19]. The only one result positive to intrapartum test and negative to antepartum culture probably was due to poor selectivity of the enrichment broth against other bacteria with consequent hamper of GBS isolation [18,20].

Our cost-effectiveness analysis showed that additional resources are requested for an improvement in the pregnancy management. In fact, intrapartum test gave an ICER of 30.28 €, comparable with that obtained by Poncelet-Jasserand et al. [9]. This ICER could be acceptable if we consider clinical advantages of intrapartum test in the management of pregnant women and newborns, such as the avoidance of antibiotic overuse with consequent antibiotic resistance in mother and neonate. Many studies showed that IAP could have long-term implications as the alteration of gut microbiota, improper maturation of immune system with possible health problems in adult life [21,22]. So far, only the study of El Helali et al. [23] evaluated the cost-effectiveness of intrapartum test at level of pregnancy and neonatal management, showing that this test was cost-neutral when compared to antepartum culture.

A weakness of intrapartum test was the percentage of missing results, as previously reported by other authors [14,17,24]. The main causes of invalid results are PCR inhibition or air bubbles, while for error results, the reason is the achievement of maximum syringe pressure, a system component failed or the probe check failed. Therefore, to reduce unavailable results rate, it is important to collect adequate specimens avoiding excess of mucus and feces [24].

The strength of intrapartum test is a short turnaround time. In our population, this characteristic could have been useful to perform a valid IAP (4 h of exposure, as suggested by the latest CDC guidelines [2]) in 79% of pregnant women with positive intrapartum test. However, if we considered that IAP exposure of 2-h could decrease GBS neonatal colonization [19,25], intrapartum test could have been useful for the management of 87% of our positive women.

By recovering neonatal data, we could know whether the newborn had clinical symptoms of general infection or sepsis status but not the number of

colonized asymptomatic newborns since the auricular/nasal swabs were not executed. The lack of GBS EOD cases, in our population of neonates, could be due to the fact that GBS transmission from mother to newborns occurs in 40–60% of cases and GBS EOD follows in 1–2% of colonized neonates while the remaining cases are asymptomatic [26–28].

Conclusion

In accordance to the recent recommendations of the European consensus conference [10], our study evidence the need of clinical introduction of intrapartum GBS testing since it could be a valuable mean for more accurate identification of intrapartum GBS colonization. It allows an appropriate management of mothers and neonates with consequent benefit for their health with limited spending for Health System.

Acknowledgements

The authors are very grateful to Cepheid (Maurens-Scopont, France) for supplying the swabs for sample collection and the reagents for the GBS analysis. The authors are also grateful to all the midwives of the Department of Obstetrics and Gynecology for swab collection and to administrative, nursing, and medical staff of Department of Neonatology for the help in data collection.

Disclosure statement

The authors report no conflict of interest.

References

[1] Melin P. Neonatal group B streptococcal disease: from pathogenesis to preventive strategies. Clin Microbiol Infect. 2011;17(9):1294–1303.
[2] Verani JR, McGee L, Schrag SJ. Division of bacterial diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and prevention (CDC). Prevention of perinatal group B streptococcal disease–revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010;59:1–36.
[3] Centers for Disease Control and Prevention. Early-onset and late-onset neonatal group B streptococcal disease. MMWR Morb Mortal Wkly Rep. 2005;54(47):1205–1208.
[4] Schrag SJ, Zell ER, Lynfield R, et al. Active Bacterial Core Surveillance Team. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. N Engl J Med. 2002;347(4):233–239.
[5] Goins WP, Talbot TR, Schaffner W, et al. Adherence to perinatal group B streptococcal prevention guidelines. Obstet Gynecol. 2010;115(6):1217–1224.
[6] Van Dyke MK, Phares CR, Lynfield R, et al. Evaluation of universal antenatal screening for group B streptococcus. N Engl J Med. 2009;360(25):2626–2636.
[7] Pulver LS, Hopfenbeck MM, Young PC, et al. Continued early onset group B streptococcal infections in the era of intrapartum prophylaxis. J Perinatol. 2009;29(1):20–25.
[8] Puopolo KM, Madoff LC, Eichenwald EC. Early-onset group B streptococcal disease in the era of maternal screening. Pediatrics. 2005;115(5):1240–1246.
[9] Poncelet-Jasserand E, Forges F, Varlet MN, et al. Reduction of the use of antimicrobial drugs following the rapid detection of *Streptococcus agalactiae* in the vagina at delivery by real-time PCR assay. BJOG. 2013;120(9):1098–1108.
[10] Di Renzo GC, Melin P, Berardi A, et al. Intrapartum GBS screening and antibiotic prophylaxis: a European consensus conference. J Matern Fetal Neonatal Med. 2015;28(7):766–782.
[11] Abdelazim IA. Intrapartum polymerase chain reaction for detection of group B streptococcus colonisation. J Obstet Gynaecol. 2013;53(3):236–242.
[12] Church DL, Baxter H, Lloyd T, et al. Evaluation of the Xpert® group B streptococcus real-time polymerase chain reaction assay compared to StrepB Carrot Broth™ for the rapid intrapartum detection of group B streptococcus colonization. Diagn Microbiol Infect Dis. 2011;69(4):460–462.
[13] De Tejada BM, Pfister RE, Renzi G, et al. Intrapartum Group B. Clin Microbiol Infect. 2011;17(12):1786–1791.
[14] El Helali N, Nguyen JC, Ly A, et al. Diagnostic accuracy of a rapid real-time polymerase chain reaction assay for universal intrapartum group B streptococcus screening. Clin Infect Dis. 2009;49(3):417–423.
[15] Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. Health Econ. 1997;6(4):327–340.
[16] Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. J Health Econ. 1999;18(3):341–364.
[17] Young BC, Dodge LE, Gupta M, et al. Evaluation of a rapid, real-time intrapartum group B streptococcus assay. Am J Obstet Gynecol. 2011;205(4):372.e1–372.e6.
[18] Park JS, Cho DH, Yang JH, et al. Usefulness of a rapid real-time PCR assay in prenatal screening for group B streptococcus colonization. Ann Lab Med. 2013;33(1):39–44.
[19] Håkansson S, Källén K, Bullarbo M, et al. Real-time PCR-assay in the delivery suite for determination of group B streptococcal colonization in a setting with risk-based antibiotic prophylaxis. J Matern Fetal Neonatal Med. 2014;27(4):328–332.
[20] Dunne WM, Holland-Staley CA. Comparison of NNA agar culture and selective broth culture for detection of group B streptococcal colonization in women. J Clin Microbiol. 1998;36(8):2298–2300.
[21] Bedford Russell AR, Murch SH. Could peripartum antibiotics have delayed health consequences for the infant? BJOG. 2006;113(7):758–765.

[22] Conroy ME, Shi HN, Walker WA. The long-term health effects of neonatal microbial flora. Curr Opin Allergy Clin Immunol. 2009;9(3):197–201.
[23] El Helali N, Giovangrandi Y, Guyot K, et al. Cost and effectiveness of intrapartum group B streptococcus polymerase chain reaction screening for term deliveries. Obstet Gynecol. 2012;119(4):822–829.
[24] Cepheid. Xpert GBS. (Updated on Sep 2011). Available from: http://www.diagnostictechnology.com.au/persistent/catalogue_files/products/xpert-gbspi.pdf.
[25] Lin FY, Brenner RA, Johnson YR, et al. The effectiveness of risk-based intrapartum chemoprophylaxis for the prevention of early-onset neonatal group B streptococcal disease. Am J Obstet Gynecol. 2001;184(6):1204–1210.
[26] Centers for Disease Controland Prevention. Prevention of perinatal Group B streptococcal disease. MMWR Morb Mortal Wkly Rep. 2002;51(1):1–22.
[27] Baker C. Group B streptococcal infections. New York (NY): Oxford University Press; 2000. p. 222–237.
[28] Bidgani S, Navidifar T, Najafian M, et al. Comparison of group B streptococci colonization in vaginal and rectal specimens by culture method and polymerase chain reaction technique. J Chin Med Assoc. 2016;79(3):141–145.