

Intrapartum Prophylaxis of Group B Streptococcal Disease in Israel: Guidelines and Practice

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Abstract

Background: The incidence of perinatal, early-onset Group B streptococcal sepsis is very low in Israel and there are no local guidelines for prevention of the disease.

Objectives: To determine to what extent the current Centers for Disease Control guidelines are practiced in Israel, the reasons for their adoption or rejection, and the need for local official guidelines.

Methods: A telephone questionnaire was conducted of all 27 delivery units in Israel. Answers were obtained from 26, either from the clinical director or the senior obstetrician in charge at the time of the interview.

Results: Only in 2 of the 26 delivery units (8%) are the CDC guidelines adhered to exactly; in 6 units they are deliberately rejected, and in 8 units they are not practiced although they are allegedly implemented. Thus, the CDC guidelines are not practiced in 14 delivery units (54%). Medico-legal consideration is the sole or major reason for adopting these guidelines in 80% (16/20) of the delivery units where they are seemingly implemented. In the majority of these units (18/20) there is readiness to abandon current practice, should local guidelines differ from those of the CDC, provided that local guidelines are issued by an authoritative source.

Conclusion: CDC guidelines are either deliberately rejected or incorrectly practiced in most Israeli delivery units. The medico-legal argument is one of the main reasons for practicing these guidelines. Since the CDC guidelines probably do not apply in Israel, official local guidelines are urgently needed.

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Early-onset Group B Streptococcus sepsis was the leading cause of neonatal morbidity and mortality in the United States during the 1970s [1]. Preventive measures released in May 1996 by the Centers for Disease Control [2] led to a significant decline by 70% in the incidence of early-onset neonatal disease – from 1.5 cases per 1,000 live births to 0.5 cases per 1,000 live births [1]. The CDC guidelines were revised in 2002 [1] and currently recommend the screening of all pregnant women at 35–37 weeks of gestation and the administration of intrapartum antibiotics to all carriers. Alternatively, if the carrier status is unknown, a risk-based strategy is recommended and all women with risk factors should be treated. The CDC prefers the screening-based strategy because the risk of early-onset GBS disease was found to be significantly lower among infants in the group of mothers managed following the screening

results as compared to the group managed by the risk factors strategy [1]. However, the proportion of women receiving antibiotics managed by either strategy was similar, 24% (!) in each group [3].

Although universal screening is not practiced in Israel and there are no local guidelines for the prevention of GBS disease, the incidence of early-onset invasive GBS disease is as low as 0.08–1/1,000 live births [4–10] and is only a minor cause of neonatal morbidity and mortality. However, because of the escalating medico-legal climate, there is debate among local opinion leaders about adopting the current CDC guidelines, even though the benefit of these guidelines in Israel is questionable [4,11–13].

The aims of the present survey were threefold: a) to examine to what extent the recent CDC guidelines for early GBS disease prophylaxis are practiced in Israeli delivery units, b) to determine on what grounds these guidelines are implemented or rejected, and c) to assess whether there is a need for local guidelines.

Patients and Methods

During one week in December 2003 a telephone questionnaire was conducted in the 27 delivery units of Israel. Only one unit refused to cooperate, and our study therefore surveyed the GBS prophylactic practices in 26 (96%) of the delivery units in Israel. The questions were answered by the directors of the delivery units or, if they were unavailable, by the senior obstetricians in charge at the time of the interview. The questionnaire consisted of eight combined major questions: four questions aimed at investigating whether and to what extent the current CDC guidelines are practiced, and four aimed at determining the rationale and incentives behind the departmental practices in the institutions interviewed [Figure 1].

Results

Compliance with the current CDC risk-based guidelines is shown in Table 1. Women in active preterm labor receive antibiotic prophylaxis in only 16 (61%) of the delivery units in Israel. In 92% (24/26) of the units, prolonged rupture of membranes is a reason to give antibiotic prophylaxis. However, the definition of prolonged rupture of membranes varies: only in 15 units is antibiotic treatment started, in accordance with CDC guidelines, 18 hours after the membranes have ruptured. We also found variations in the definition of fever during labor prompting the initiation of antibiotic prophylaxis for GBS disease: 37.5°C, 37.7°C, 37.8°C and 38.0°C, and the distinction between GBS prophylaxis and the treatment for

CDC = Centers for Disease Control
GBS = Group B Streptococcus

Figure 1. The questionnaire

1. Do you give intrapartum antibiotic prophylaxis in all preterm deliveries (before 37 weeks gestation)? If yes, what antibiotic regimen do you use?
2. Do you administer intrapartum antibiotic prophylaxis to all women with rupture of the membranes? How many hours after the rupture of the membranes do you start the antibiotic treatment? What antibiotic regimen do you use?
3. Do you give intrapartum antibiotics to a woman who previously gave birth to an infant with GBS disease? If yes, what antibiotic regimen do you use?
4. Do you give antibiotic treatment during labor to women with fever only (without other signs of chorioamnionitis)? What is the cutoff temperature for starting such treatment? What antibiotic regimen do you use? Is the antibiotic regimen different if there are also signs of chorioamnionitis?
5. Do you practice the 2002 CDC guidelines in your delivery rooms?
6. Do you know the incidence of early GBS sepsis at your institution or in Israel?
7. Do you think that the CDC guidelines should be implemented in Israel? If your answer is positive, do you think that their implementation is justified for medical reasons, for medico-legal reasons, or for both reasons?
8. Do you think the Israel Ministry of Health should publish local guidelines on the issue of GBS prophylaxis? If yes, are you ready to change your current practice? If the local guidelines do not recommend intrapartum GBS prophylaxis, would you comply with such a recommendation?

Table 1. Compliance with the CDC risk-based strategy for GBS prophylaxis

Risk factor	Use of antibiotic prophylaxis	Compliance with CDC guidelines
Gestational age <37weeks	16/26, 61%	16/26, 61%
Premature rupture of membranes	24/26, 92%	15/26, 58%
	After 12 hr: 4 units	
	After 18 hr: 15 units	
	After 24 hr: 4 units	
	After 48 hr: 1 unit	
Fever during labor (without additional signs of chorioamnionitis)	21/26, 80%	17/26, 65%
	≥ 37.5°C: 4 units	
	≥ 37.7°C: 1 units	
	≥ 37.8°C: 2 units	
	≥ 38.0°C: 17 units	
Previous child with GBS disease	24/26, 92%	24/26, 92%

suspected chorioamnionitis from other etiologies is also not well defined. A previous child with GBS disease is an indication for antibiotic prophylaxis in 24/26 (92%) of the units.

With regard to the antibiotics used for prophylaxis, eight different protocols were found. In 23 delivery units, penicillin G or ampicillin is part of the antibiotic regimen. In nine units, penicillin or ampicillin is given alone, while penicillin or ampicillin is used in

Table 2. Should the CDC guidelines be implemented in Israel? Opinions stratified by the interviewed obstetricians' knowledge of the incidence of early GBS disease in Israel

Is the implementation of CDC guidelines in Israel:	Obstetricians unaware of the low incidence of GBS disease (n=14)	Obstetricians aware that the incidence of GBS disease is low (n=12)	Total (n=26)
Not justified?	1	2	3
Justified for medico-legal reasons?	0	4	4
Justified for medical reasons?	3	2	5
Justified for both medical and medico-legal reasons?	9	3	12
No definite opinion	1	1	2

combination with other drugs in 12 units. In one delivery unit, amoxicillin+clavulanic acid is used.

In six (23%) of the delivery units it was admitted that the CDC guidelines have been deliberately rejected. In the remaining 20 units it was acknowledged that the guidelines were adopted. However, in eight of these units (40%), the guidelines *are actually not practiced, although they are allegedly implemented*, as one or more risk factors for antibiotic prophylaxis are ignored. In 10 units the guidelines are practiced, although with variations. *Only in two* of the units are the CDC guidelines strictly adhered to. Overall, in 14 delivery units (54%) the CDC guidelines are not practiced, intentionally or unintentionally, and in another 10 units the treatment differs from that recommended by the guidelines.

Fourteen of the interviewed obstetricians admitted to not knowing the incidence of early GBS disease in their hospital or in Israel, while 12 knew that the incidence of the disease in Israel is very low. The opinions of the interviewed obstetricians on the reasons for implementation of the CDC guidelines, classified according to their knowledge of the incidence of GBS disease in Israel, are presented in Table 2. Medico-legal consideration is the sole or major reason for adopting these guidelines in 16 delivery units (80%, 16/20) where they are seemingly implemented.

The majority of the interviewed obstetricians (24/26, 92%) felt that there was a need for local guidelines on the GBS issue. Half of them (13/26) admitted that they would be ready to change their current practice according to future local guidelines, even if the local guidelines reject the current CDC guidelines, and nine obstetricians were willing to consider such a change in their policy. Only in 2 of 20 delivery units in which the CDC guidelines are "practiced" is there no desire to even consider a change in protocols. In these two institutions, the guidelines are practiced correctly according to risk factors, although antibiotic prophylaxis is begun even before the 18 hours of membrane rupture as recommended by the CDC. It is of interest that the interviewed obstetricians in these two institutions were convinced that the CDC guidelines should be adopted for medical reasons, although they admitted to not knowing the incidence of the disease in their institution or in Israel. In all four delivery units where the CDC guidelines are implemented solely for medico-legal reasons, there is readiness to discontinue their current practice if local guidelines reject the CDC guidelines.

Discussion

Our survey provides a fair picture of the current position of Group B Streptococcus prophylaxis in Israel. The weakness of our study might be the small number of obstetricians interviewed, but all the interviewed obstetricians were directors of the delivery units or senior obstetricians in charge at the time of the interview. We assumed that the interviewed obstetricians are among the opinion leaders in their institution; they should know their local protocols and are accountable for the execution of their own protocols.

Because there are no formal programs of antenatal screening for GBS in Israel, the risk-based approach should be practiced by those who follow CDC guidelines. In six delivery units the guidelines are intentionally not practiced, a rejection partially based on medical rationale and an approach justified in the medical literature [4,11–14]. Of the remaining 20 units where the guidelines are said to be adopted, they are not practiced in eight. Thus, in 14 (54%) of the Israeli delivery units the CDC guidelines are intentionally or unintentionally not implemented. In 10 units the guidelines are practiced but with discordance and variations of the recommended antibiotic treatment [15].

Our findings revealed that about half (14/26, 54%) of the interviewed obstetricians are unaware of the incidence of GBS disease in their hospital or in Israel. The knowledge or lack thereof of the local epidemiologic data has a paradoxical impact on the decision of whether to adopt or reject the CDC guidelines. In institutions where the obstetricians in charge were not familiar with the local incidence of the disease, the "medical justification" for adopting the guidelines and the reliance and dependence on them were more common than in institutions where the local incidence of the disease was known (12/14, 86% vs. 5/12, 42%) [Table 2]. Half of the 12 obstetricians who acknowledged that there is a low incidence of the disease in Israel felt that the implementation of the CDC guidelines is not justified at all, or it is justified only for medico-legal reasons. It is of interest that in all four units where the guidelines are implemented solely for medico-legal reasons, there is readiness to discontinue their current practice if official local recommendations reject the CDC guidelines.

The implementation of the 1996 CDC guidelines in the United States resulted in an impressive decline of early-onset disease, from as high as 1.5/1,000 live births to as low as 0.5/1,000 live births, a reduction of 70% [1,16]. The screening approach proved to be superior to the risk-based approach and is currently favored by the CDC [1]. On the other hand, implementation of the guidelines in various places in the USA resulted in the administration of antibiotics to as many as 15–24% of all women during labor by either strategy [1]. In a large multi-state cohort study it was found that the proportion of women receiving antibiotics managed by either strategy was similar – 24% (!) in each group [3]. Two recent studies demonstrated that as many as half of all pregnant women received antibiotic treatment for various prophylactic reasons at some point during their antenatal courses [17,18], which is very close to the theoretic estimate we predicted [14]. The administration of antibiotics to such a high proportion of delivering women can have serious effects on the emergence of resistant organisms, as reported by Stoll et al. [19] who found a reduction in the GBS

sepsis rate but a concomitant and dramatic increase in the ampicillin-resistant *Escherichia coli* sepsis rate – from 3.2/1,000 to 6.8/1,000. The overall rate of early-onset sepsis remained unchanged [19]. It seems that intrapartum antibiotic prophylaxis is the key factor increasing the probability that early-onset neonatal infection with gram-negative organisms will be caused by ampicillin-resistant organisms, regardless of the agent used [18].

In various parts of the world outside the U.S. there is an ongoing medical and economics debate, similar to that in Israel, about accepting or rejecting CDC guidelines [20–22]. For example, a national survey among all obstetric units in the UK on the screening and intrapartum management of GBS in 1999 and 2001 found that only 3% in 1999 and 2% in 2001 of all units used vaginal swab-based screening for GBS colonization in the antenatal period. Furthermore, appropriate dosage of a recommended antibiotic was prescribed in only 7% of the units in 1999 and in 20% of the units in 2001 [21]. In this respect, the situation in Israel is not very different.

The incidence of early-onset GBS sepsis in Israel has remained low during the last two decades: 0.08–0.37/1,000 in Haifa [4,6,11,12], 0.2–1/1,000 in Jerusalem [5,7,8], and 0.1/1,000 in southern Israel [10]. Since 1990, there has been an active and prospective reporting system for GBS disease to the Israeli Pediatric Bacteremia and Meningitis Group database. During 1990–1997, the reported incidence of early-onset neonatal GBS disease to this database (which included 72% of all live births) was 0.24/1,000 live births (Schimmel et al., presented at the Israel Neonatal Society, 1999). Therefore, it can be stated that the prevalence of the disease in Israel is similar or still below its prevalence in the USA (0.3/1,000), even following the preventive measures taken according to CDC guidelines [23]. Furthermore, the GBS attack rate in Israel is lower than the incidence of the disease in the USA that prompted the construction of the CDC guidelines! In 1992, it was specifically stated: "If GBS becomes a less frequent pathogen in the future, as it was before the 1970s, these recommendations would need to be revised" [24]. Therefore, in places like Israel, where the GBS attack rate is already low, as low as 0.24/1,000 live births, prophylactic antibiotic treatment cannot further reduce the prevalence of the disease clinically and significantly, while there is a threat of an even higher toll of emerging penicillin-resistant perinatal infections [17–19]. In these circumstances, the added number of cases of *E. coli* sepsis because of prophylaxis might be higher than the number of preventable cases of GBS sepsis. Hence, we feel that adopting the CDC guidelines in Israel is not justified medically and is even contraindicated [4,11–14].

Despite the low incidence of the disease in our region, in the current escalating medico-legal climate and the rise of medical law suits, and in the absence of local guidelines, the standard of care for doctors and particularly for trial lawyers in Israel is determined by existing and prestigious guidelines, such as those from the CDC. The medico-legal approach in Israel could follow the situation in the U.S., as described in an editorial [25]: "There will be many trial lawyers waiting to see whether you followed these recommendations.... Let's hope that you'll be able to *say that you did*.... It will be just a matter of where they place the decimal point in out-of-court

settlements." However, at present, in most delivery units, even in those where the CDC guidelines are allegedly adopted, there is no adherence to these guidelines. From a medico-legal point of view, it is probably safer to reject the implementation of the guidelines on the basis of medical arguments, arguments preferably discussed in the local and international medical literature, than seemingly to adopt the guidelines but not practice them exactly.

The majority (92%) of the interviewed obstetricians felt that there is a need for local guidelines on the issue of GBS prophylaxis. Moreover, half the obstetricians admitted that they would be willing to change their current practice, and nine others said that they are ready to consider such a change, should official local guidelines differ from those of the CDC.

In conclusion, because of the low incidence of early-onset GBS sepsis, there is no medical justification for implementing the current CDC guidelines in Israel. The implementation of these guidelines may cause more harm than benefit. In any event, in 54% of the delivery units in Israel the CDC guidelines are not practiced, either intentionally or unintentionally. Although the medico-legal argument is a major factor in adopting the CDC guidelines, delivery units where the guidelines are practiced incorrectly and with variations are liable for malpractice suits. It is probably better to state and justify the rejection of the guidelines than to adopt them officially but not adhere to them. In delivery units where the guidelines are deliberately rejected, especially when the reasons for non-practice are backed by arguments published in the medical literature, as at Rambam Medical Center [4,11–14], the defense of an accusation of malpractice might be easier. Most opinion leaders seek local instructions for medical and medico-legal backup and are ready to change their current practices should local guidelines reject implementation of the CDC guidelines. However, there is a need for continuous monitoring of the disease, reserving intervention to a situation if and when a significant epidemiologic change appears.

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