



Antibiotic Prophylaxis in the Delivery Room – A Slippery Slope

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The topic of a meeting of the Israel Society of Perinatal Medicine held last year was current antibiotic prophylactic treatment for certain conditions, in the light of recent guidelines from the Centers for Disease Control and the Cochrane Review conclusions [1–3]. These diagnostic entities include preterm premature rupture of membranes, preterm labor with intact membranes, and early-onset group B streptococcal disease. While various (minor) aspects of the recommendations were addressed, there was no discussion on whether these guidelines are appropriate for Israeli circumstances. One of them (guideline no. 1) was based on epidemiologic data that do not necessarily correlate with local data, thereby rendering their relevance to Israel questionable, and the others (nos. 2 and 3) were outdated by newer evidence-based data. We were left with the impression that the guidelines are beyond debate. These guidelines are rapidly becoming the basis for clinical decision-making in Israel, and a referendum among the audience revealed that many had already implemented them in their clinical practice. The rapid and indiscriminate implementation of these foreign guidelines is in accordance with belief systems among physicians, namely – “I believe, therefore I practise” [4].

Current practice

According to current guidelines and medical practice, as many as 55–65% of all parturients receive antibiotic treatment in the delivery ward, *for prophylactic purposes only*.

- Prevention of early-onset GBS disease according to CDC guidelines, by using risk factors as a determinant since screening is not practiced in Israel. This means antibiotic treatment for every fourth parturient (18.3–26.7%) according to CDC estimates [1].
- Two recent Cochrane Reviews using meta-analysis of antibiotic trials for spontaneous preterm labor with intact membranes and those with pPROM suggested some health benefits for the neonate [2,3]. Although the conclusions of these Reviews hold many uncertainties, many institutions currently use antibiotic prophylaxis to treat women presenting with these problems,

adding another 15–20% to those receiving antibiotics. This group of women partially overlaps the women with risk factors for GBS.

- It is current practice to administer antibiotic prophylaxis in every case of cesarean section [5,6], even in patients at low risk for post-cesarean febrile morbidity [6–8]. According to the cesarean section rate in different obstetric departments, this adds another 10–20% to those given antibiotics prophylactically.
- Some 3–5% of patients are given antibiotic prophylaxis in the delivery ward either for prevention of bacterial endocarditis because of mitral valve prolapse, or for suspected urinary tract infection while waiting for culture results. A further 3–5% of hospitalized patients receive antibiotics for the treatment of established febrile intrapartum or postpartum disease (e.g., pyelonephritis, chorioamnionitis, post-cesarean or postpartum fever).

There is no doubt that providing antibiotics to as many as two-thirds of hospitalized patients in any obstetric department is conducive to the emergence of resistant nosocomial infections. It is therefore not surprising that a recent survey of urinary pathogens in the delivery ward at Rambam Medical Center found a high proportion to be unusual and multi-resistant uropathogens. This occurred in a department that had not implemented the CDC guidelines and where antibiotics are used in a restrictive manner [9].

Rationale

What lies behind the enthusiasm of local obstetrics authorities to so quickly adopt foreign guidelines on infectious conditions? We believe the answer is multi-faceted:

- The type of infection is common, irrespective of local circumstances. Therefore, we can use experience accumulated in other parts of the world (e.g., rubella, see further comments on mitral valve prolapse).
- The local incidence of the disease is too small to perform ample-sized local studies (e.g., pPROM). Again, we need to rely on the experience gained in other places, but with possible local adaptations as is the case for acquired immunodeficiency [10,11].
- Local authorities tend to adopt the practice guidelines published by prestigious professional societies, without exam-

GBS = group B *Streptococcus*

CDC = Centers for Disease Control

pPROM = preterm premature rupture of membranes

ining in depth the facts and logic behind their conclusions and whether or not they apply to our local situation (see further comments on GBS).

- In the absence of local guidelines, foreign guidelines serve as the only basis for standards of care – for doctors as well as for lawyers. Because we are perturbed by the high financial risk of lawsuits in obstetrics in Israel (31% of all financial risks in medical lawsuits are obstetrics-related) [12], these guidelines are implemented as quickly as possible. The dictum of a 1996 editorial states: “There will be many trial lawyers waiting to see whether you followed these recommendations... It will be just a matter of where they place the decimal point in the out-of-court settlement” [13]. In our legal system judges place greater importance on the opinions of local experts, who base their recommendations on local data, than on guidelines formulated in other countries and circumstances. The argument is even stronger if these opinions are published in *local* medical journals or are expressed in official statements of *local* professional organizations.

Evidence for a change in policy

The above indicates the need to critically examine the current practice of providing antibiotic prophylaxis in the delivery ward for the following diagnostic entities:

- *Group B Streptococcus*. We have published several updates of our ongoing experience and rationale for not implementing the CDC guidelines at Rambam Medical Center [14–16]. The background for the CDC recommendations is summarized in length in the official publication [1]. These guidelines are based on the epidemiology of the disease in the USA, which has an attack rate of about 3/1,000 liveborns and 40/1,000 carriers with risk factors. In other geographic regions, with a different epidemiology, these guidelines may be totally irrelevant. Because of the high rate of antibiotic use recommended by this protocol, the CDC also recommends establishing surveillance to monitor both the occurrence of adverse reactions to antimicrobial prophylaxis and the emergence of perinatal infections caused by penicillin-resistant organisms [1]. The U.S. experience with the implementation of these guidelines shows a reduction in the attack rate of early-onset GBS disease to 0.8/1,000 in some places [17] and to even lower levels in others, but with a concomitant increase in ampicillin-resistant gram-negative sepsis resulting in an overall unchanged incidence of neonatal sepsis [18]. The attack rates reported in Israel – 0.27/1,000 at Rambam Medical Center in Haifa, 0.39/1,000 at Soroka Medical Center in Beer Sheva [15], and 0.56/1,000 in Jerusalem [19], in a cohort of approximately 160,000 neonates, without the implementation of CDC guidelines – are substantially lower than those in the USA, even following proposed intervention [17,18]. Thus, according to local data, we do not meet the U.S. criteria for adopting the CDC guidelines. Instead, we need continuing surveillance of the attack rate in our region. The Rambam protocol, based on 10 years of ongoing experience, is to wait for culture results and to administer intrapartum antibiotic

prophylaxis only to women who are documented GBS carriers [15]. Thus, antibiotics are given to only 2–3% of parturients, a tenfold reduction compared with the CDC guidelines. The disturbing medico-legal point can be met by the formulation of local guidelines, by local experts, based on available local data and published in local medical journals. This is certainly preferable to importing foreign recommendations aimed at solving problems in other parts of the world and irrelevant to our country.

- *Spontaneous preterm labor and pPROM*. The Cochrane Reviews, meta-analysis and conclusions were based on relatively small clinical trials bearing many uncertainties [2,3]. In contrast, the two recently published ORACLE trials designed by the Cochrane database team [20,21], a superbly conducted multi-center randomized trial involving more than 11,000 women and specifically aimed at resolving the uncertainties of these Reviews, together with the accompanying editorial [22], provide sound evidence that antibiotics should not be used in women with spontaneous preterm labor. As for pPROM, these trials suggest some benefit in a small subgroup of women only [20], an interpretation challenged by the accompanying editorial which deduced that the results of the ORACLE trials do not support the use of antibiotics in women with pPROM [22]. Therefore, according to evidence-based medicine and the lack of local data, antibiotics should not be given routinely in pPROM, but only in individual cases when benefits outweigh risks [22].
- *Cesarean section*. The value of antibiotic prophylaxis in reducing postoperative febrile morbidity after cesarean section by 66–75% is well documented [5,6], even in low risk patients [6–8]. However, the efficacy of this practice in elective cesarean sections was recently challenged [23]. Since roughly 40% of cesarean sections are elective, a change in current prophylaxis policy may prevent antibiotic use in 4–8% of all parturients. The decision of whether to change existing protocols must be made according to the prevalence of postoperative febrile morbidity in each institution.
- *Mitral valve prolapse and suspected urinary tract infection*. While mitral valve prolapse is common, according to the guidelines of the American Heart Association only a minority of these patients – those with significant mitral regurgitation and/or thickened leaflets – requires antibiotic prophylaxis during labor [24]. Unfortunately, and probably for ‘medico-legal’ reasons, most of these women in our delivery wards do receive antibiotics, without medical justification. As for suspected urinary tract infection without fever, treatment can be delayed until culture results are available in 24–48 hours, thus preventing unnecessary treatment in many women and inappropriate empiric treatment in others [9].

Conclusions

The antibiotic prophylaxis practices in the major diagnostic categories have contributed to the rapidly increasing use of antibiotics in delivery wards in Israel. Using local and foreign evidence-based data, a critical assessment of these practices indicates unequivocally that they should be restricted in the

departments where they are already in use. Secondly, they should not be introduced into departments that do not use them routinely but are considering their implementation as a result of 'benchmarking' following professional meetings. However, even with such restrictions, the prevalence of antibiotic usage in the delivery wards will be as high as 25–30%, albeit far lower than the rapidly reached peak of 60%. This rate of antibiotic usage will still necessitate surveillance of nosocomial infections and the emergence of resistant bacteria. A slippery slope indeed.

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