Prevention Effectiveness Case Study: Institutionalizing Prevention of Group B Streptococcal Infections

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Abstract: The value of cooperation between clinicians and laboratorians is scarcely controversial, yet failure to assure adequate laboratory participation in implementing new programs can have serious clinical consequences. The recent example of preventing group B streptococcal (GBS) disease in newborns is illustrative. Neonatal GBS infection can lead to death, long term disability, and substantial direct and indirect health care costs, while GBS prevention programs, when implemented appropriately, are cost-saving. Much perinatal GBS disease is potentially preventable through using prenatal screening cultures and administering antimicrobial prophylaxis intrapartum to mothers at increased risk of transmitting the infection to their newborns. Efforts by clinician groups to promote prevention strategies during 1992 appear to have had no measurable impact on disease incidence. GBS-related sepsis and meningitis continue to strike nearly 8,000 newborns each year in the United States. A series of investigations of the apparent failure of recent prevention efforts has identified potential pitfalls of implementing clinical programs without laboratory involvement and/or acceptance. For example, most clinicians reported collecting screening cultures, but few used appropriate culture sites. Most microbiology laboratories surveyed were using insensitive culture methods to process the specimens, limiting the validity of reported results. Results of late gestation screening cultures are needed by clinicians at the time and place of delivery. Thus, even when cultures are collected and processed appropriately, lapses in reporting can limit the ability of clinicians to optimally manage the mother-infant pair. Evaluating program effectiveness requires monitoring clinical outcomes of interest, many of which are best identified through laboratory-based surveillance systems (e.g., surveillance for invasive GBS disease and for infections due to antimicrobial resistant pathogens). As in this example, successful clinical management as well as disease prevention programs require a commitment from clinicians and laboratory personnel to coordinate practices and program evaluation.

Introduction

The value of cooperation between clinicians and laboratorians is scarcely controversial, yet failure to assure adequate laboratory participation in program implementation can have serious clinical consequences. In this session, we are concerned with patient outcomes. I will explore the evaluation of a prenatal screening program aimed at preventing perinatal infections as one example of how laboratory practice research can contribute to improving clinical outcomes.

The clinical outcome I will discuss is every family's nightmare: following a normal pregnancy, a few hours after delivery, a parent is faced with a critically ill newborn. The baby is infected with group B

Streptococcus, a leading cause of sepsis and meningitis in newborns in the United States. The parents have never heard of group B streptococcal (GBS) disease and are surprised to learn that many of these infections are preventable. To understand what might have gone wrong for these parents, I will focus on laboratory and clinical practices that may contribute to failed preventive measures. By reviewing the process by which the Centers for Disease Control and Prevention (CDC) has been evaluating the effectiveness of GBS disease prevention in the United States, I hope to highlight the interconnected nature of laboratory testing, clinical management, and patient outcomes.

The Disease

Group B *Streptococcus* first emerged as an important pathogen in the 1970s.[1] About 7500 cases of GBS sepsis and meningitis in newborns are reported each year. [2] The burden of perinatal group B streptococcal disease extends beyond neonatal illness and death, and includes long term disabilities such as hearing loss, impaired vision, and developmental problems.[3,4] Maternal morbidity from GBS includes sepsis, amnionitis, postpartum wound infections, and stillbirths.[5,6] The direct costs of neonatal disease alone in the U.S. have been estimated as $300 million annually.[7]

Most GBS disease among newborns results from maternal to infant transmission during labor and delivery. Many women are asymptomatically colonized by GBS in the genital and gastrointestinal tracts. About half the infants born to colonized mothers are themselves colonized on the skin and mucosal surfaces. Most of these infants, 98%, are asymptomatic. About 2%, however, will develop early onset disease, presenting with sepsis, pneumonia or meningitis in the first few days of life.

The Screening Test

To identify women with an increased risk of transmitting GBS to their newborns, clinicians would like to know which women are colonized with GBS in the genital or gastrointestinal tract. GBS colonization is not static, though, and women can acquire or lose carriage during the course of pregnancy.[8] Although clinicians would like to know maternal colonization status at the time that labor begins or membranes rupture, results of cultures collected at labor onset will not be ready before most women deliver, while the intervention--antibiotic prophylaxis--is ineffective in preventing transmission unless initiated before a woman delivers. Clinicians currently rely on prenatal cultures to predict intrapartum GBS colonization. The laboratory test, therefore, is at best an indirect measure of the intrapartum colonization status, but risk analysis in a large cohort study suggested that women with GBS identified by prenatal cultures had 29 times higher risk of delivering an infant with early onset GBS disease, compared with women whose prenatal cultures were negative.[9]

Prevention Strategies

Efforts to prevent perinatal GBS disease have focused on antimicrobial chemoprophylaxis. During the 1980s, investigators demonstrated that giving antibiotics to women early in pregnancy, or to infants after birth, was not effective in preventing GBS disease. Giving antibiotics during labor, however, proved to be extremely effective in reducing maternal infections and preventing early onset disease in newborns. During the 1990s, debate grew

over which women should receive antibiotics. Efforts to focus antibiotics on women who could benefit most but avoid exposing millions of low risk women to antibiotics led to several potential prevention strategies. Authorities have considered giving antibiotics to all maternal carriers,[10] to women with obstetric risk factors for GBS disease regardless of colonization status,[11] or to GBS carriers who also have obstetric risk factors.[12]

In 1992, clinical organizations began promoting prevention strategies. The American College of Obstetricians and Gynecologists (ACOG) published a technical bulletin on prevention in July 1992,[13] followed by two clarifications of their position in 1993.[11,14] ACOG recommended against prenatal screening cultures, and stressed that intrapartum prophylaxis should be given to all women with specific obstetric risk factors. The American Academy of Pediatrics (AAP) published guidelines for prevention in November of 1992,[12] recommending an approach that combined prenatal screening cultures with intrapartum treatment of GBS carriers who developed obstetric risk factors. Although the strategies differ, it was expected that consistent application of either approach would prevent from 60 to 75% of early onset cases. CDC undertook a series of investigations to assess whether effective prevention was occurring, and if not, why not.

Disease Detection

To collect population-based information on GBS disease, CDC has been collaborating with investigators in academic institutions and state health departments on active laboratory-based surveillance for invasive bacterial disease. Through regular contact between regional surveillance officers and microbiology and infection control personnel in all acute care hospitals in each surveillance area, simple clinical and demographic information is collected on all cases of illness where GBS is isolated from a usually sterile site, such as blood or cerebrospinal fluid. Surveillance in the multi-state population identified no reduction in incidence of early onset GBS disease between 1991 and 1993.

Prevention Effectiveness

To determine why the 1992 prevention statements had no discernible impact on disease occurrence, we conducted a series of surveys. The objective of these surveys was to identify potential barriers to effective GBS prevention. CDC first collaborated with the Georgia Department of Human Resources on a survey of obstetric caregivers in this state.[15] The survey of clinicians revealed that most respondents screened at least some of their prenatal patients for GBS. However, only 9% reported that they cultured the optimal sites -- vagina and rectum. Many clinicians were collecting cervical cultures for GBS, but cervical cultures are often negative when vaginal or rectal cultures are positive. Few clinicians knew what methods their laboratories used to process the clinical specimens, so in 1994 we queried the microbiology laboratories serving hospitals in our multi-state active surveillance system.[16] Results from a survey of over 200 clinical labs in five states suggested that very few labs used selective broth media, although use of this method can increase recovery of GBS by about 50%.

These surveys identified several problems with prevention practices. Results suggested that clinician and laboratory practices during 1993 and 1994 would not have been likely to reduce early onset cases, and thus explained

the trends identified in the CDC surveillance. These surveys also illustrate how tremendous resources may be invested in health services--diagnostic, preventive, or therapeutic--to influence clinical outcomes, but without careful coordination between laboratory practitioners and clinical providers, resources may be wasted and morbidity left unabated.

Economic Considerations

Today, cost considerations exert a strong influence on clinical and laboratory practices. In the Georgia survey, one of the most common reasons cited by clinicians who did not screen their patients was the belief that prenatal screening was not cost-effective. Laboratories considering the use of selective broth media over nonselective methods for GBS isolation may similarly question whether the more elaborate media are economically justifiable. Participants in specific components of the health care system are less likely to consider the societal perspective but focus instead on their own bottom line. To evaluate the economic impact of routine prenatal screening for GBS and antibiotic treatment of high risk mothers, CDC[7] and others have conducted economic analyses which assess the costs of a screening and prophylaxis program vs. the costs of treating cases that could otherwise be prevented. Consistently, these studies indicate that prevention programs--including those incorporating prenatal screening cultures--save money compared with treating GBS cases that would occur without these interventions. Because laboratory costs are often borne by the hospital, while costs of caring for the acute illness and chronic sequelae of neonatal infection are borne by numerous parties, assessing the economic impact of prevention programs ideally should incorporate the societal perspective.

Public Health Response

To address the specific problems identified in clinical practice and promote effective prevention programs, CDC prepared guidelines for prevention of GBS disease. To develop the guidelines, CDC solicited substantial input from outside experts and published a draft version of the guidelines for public comment in the Federal Register. The CDC guidelines addressed specific concerns identified by the practice surveys, including cost-effectiveness.[17] The guidelines also stressed the importance of appropriate culture methods. We received thousands of letters in response to the draft guidelines from families, clinicians, professional organizations, and others. The issue also has entered the political arena, since several state legislatures have considered bills that would mandate prenatal education or prenatal screening for GBS. In 1994, the California legislature, after reviewing one such proposal, passed a bill requiring the California health department to hold a consensus conference on the topic. CDC convened the meeting with the California Department of Health Services, and numerous organizations participated, including a community-based parent advocacy group, the Group B Strep Association. Revised recommendations are the product of this process, and the laboratory practice research on this issue played a major role in developing the new recommendations.

Conclusions

Specific recommendations for GBS prevention seek to enhance the effectiveness of prevention activities, a critical component of which is ensuring participation by supporting laboratories in designing and implementing prevention programs. As I

have tried to indicate, clinical outcomes depend on a mutual understanding by clinicians, laboratory personnel, and patient groups, of the goals of a testing program, interpretation of test results, the action plan necessitated by test results, and limitations of the program when optimally implemented. Communication between clinicians and laboratory personnel is critical even if clinicians collect the appropriate specimens and the laboratory processes specimens in the optimal fashion, clinical outcomes depend on information being available to providers at the time and place of delivery. As clinicians become more dependent on offsite laboratory services, perhaps in the context of expanding managed care, assuring communication systems for the prompt reporting of laboratory results to multiple facilities will be critical.

To monitor program performance, an ongoing commitment is needed to conduct surveillance for clinical outcomes of substantial importance (in this example, for cases of perinatal GBS disease). Because most hospitals are too small for meaningful trends in invasive GBS disease to be detected, surveillance will ideally involve larger populations. Managed care organizations and other groups of affiliated hospitals should provide ideal circumstances to monitor program effectiveness through laboratory-based surveillance systems.

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