

Prevention of Neonatal Group B Streptococcal Disease

Su Eun Park

Department of Pediatrics, Pusan National University School of Medicine, Yangsan, Korea

Group B streptococci (GBS) are facultative anaerobic, gram-positive cocci that colonize the gastrointestinal and urogenital tracts of humans. GBS strains are serologically divided into 10 types (Ia, Ib, and II through IX) according to their capsular polysaccharides. Serotypes Ia, Ib, II, III, and V account for approximately 85% of global GBS disease cases in infants younger than 3 months [1]. Serotype III alone accounts for almost 50% of cases of infant GBS disease [1].

GBS are a major cause of neonatal sepsis. Early-onset (EO) neonatal disease is defined as that which occurs in the first 6 days of life, and results from vertical transmission from a colonized mother to an infant. In contrast to EO disease, the causes of late-onset (LO) disease (7-89 days old) are not well understood. LO disease can develop through vertical or horizontal transmission.

The incidence of neonatal GBS disease differs between countries. In the US, EO and LO disease rates were 1.4/1,000 live births and 0.4/1,000 live births, respectively, in the early 1990s [2]. The incidence of EO and LO disease in the UK during 2000–2001 was reported to be 0.47 and 0.25 per 1,000 live births, respectively [3]. Australia has reported an EO disease

rate of 2.0/1,000 live births [4]. The neonatal GBS disease burden in Korea has not been known, because GBS is not a notifiable disease in Korea and there have been no nationwide population-based surveillance studies. GBS has been considered to be a rare pathogen in neonatal sepsis in Korea, especially in EO disease, according to clinical experience. However, a recent study has revealed that GBS have become the most common cause of bacterial meningitis and LO sepsis in infants aged younger than 3 months in Korea [5].

Several clinical trials conducted in the mid-1980s demonstrated that intrapartum antibiotic prophylaxis (IAP) with ampicillin or penicillin in women at risk of transmitting GBS to their infants effectively prevented EO disease. After the introduction of the guidelines for preventing perinatal GBS disease in the US, the incidence of EO disease decreased by approximately 70% between 1996 and 1998 [6]. Australia also reported that the incidence of EO disease decreased from 1.43/1,000 live births in 1993 to 0.25/1,000 live births in 2001 as a result of the introduction of the guidelines [7]. Although maternal screening and IAP are the only available methods for preventing EO GBS disease, the choice to adopt this strategy for the

Corresponding Author : Su Eun Park, MD, PhD

Department of Pediatrics, Pusan National University Children's Hospital,
20 Geumo-ro, Yangsan 626-770, Korea

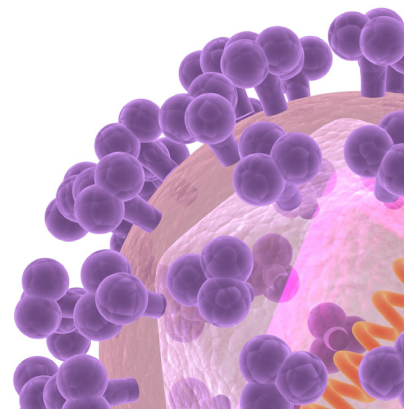
Tel: +82-55-360-3155 Fax: +82-55-360-2181

E-mail: psepse@naver.com

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prevention of EO disease usually depends on the local burden of disease. The rate of EO GBS disease in Korea has been considered to be much lower than that of other developed countries; it was estimated to be less than 0.1/1,000 live births in one retrospective, multicenter study [8]. The rate of maternal GBS colonization in Korea was reported to be 5-10% [9]. This relatively low rate of maternal colonization contributes to the low incidence of EO disease in Korea. IAP, however, has no effect on the incidence of LO GBS disease. The rate of LO disease has remained unchanged since the implementation of IAP in the US. For these reasons, the value of adopting universal maternal screening and IAP as preventive strategies for neonatal GBS disease is still a matter of debate in Korea.

The preventive strategies of universal maternal screening and IAP have some limitations. There are concerns about the emergence of antimicrobial-resistant organisms with implementing universal screening and IAP. Furthermore, IAP has no impact on the incidence of LO disease, stillbirth, and miscarriage caused by GBS. In addition, IAP cannot prevent all incidences of EO GBS disease. Providing protection to newborns against GBS by immunization is another conceivable strategy for preventing neonatal GBS disease. Theoretically, GBS vaccines could prevent almost all deleterious perinatal effects of GBS disease, including GBS-associated stillbirth and prematurity.

The capsular polysaccharide (CPS) and several surface-related proteins such as pillus and Sip have been assessed as candidate immunogens for the development of GBS vaccines. Although protein-based vaccines have shown immunogenicity in animal models [10], only CPS-based vaccines have been evaluated in human trials.

Lancefield already revealed that type-specific anti-CPS antibody can protect against GBS disease in mice [11]. Several studies have demonstrated that transfer of maternal type-specific anti-CPS antibodies can occur in newborns, and that these antibodies can protect against EO disease [12, 13]. As for other bacterial polysaccharides, the immunogenicity of the CPS of GBS is stronger when it is conjugated with an immunogenic protein. Several studies have shown that conjugated GBS vaccines are generally well tolerated and induce significant antibody responses in adults. When a serotype III conjugate vaccine was administered to pregnant women in their 3rd trimester, it was found to be safe, and the transfer of antibody from mothers to their newborns was demonstrated [14]. These maternally transferred antibodies persisted in the infants until 2 months of age [14]. To provide a wider range of protection, multivalent CPS-protein conjugate vaccines will

be needed.

Issues remain to be resolved, even if an effective vaccine is available. Optimal timing of vaccination is crucial. Vaccinating early in pregnancy is a safety concern. However, vaccinating too late in pregnancy will not provide immunity to infants born prematurely. Vaccinating adolescent girls before pregnancy is a possible approach, but the duration of immunity is uncertain. Theoretically, the optimal timing is early in the third trimester.

Although IAP is the only currently available preventive method against neonatal GBS infection, a safe and effective vaccine is expected to be available in the near future. Further studies are necessary to determine an effective strategy for preventing neonatal GBS disease in Korea, taking into account to the population-based GBS disease burden, local serotype distribution, and the antibiotic resistance status of GBS in Korea.

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