EDITORIAL

Early-onset group B streptococcus neonatal disease: a target for prevention?

Group B streptococcus (GBS), or *Streptococcus agalactiae*, is a coloniser of the gastro-intestinal and urogenital tracts of humans and animals such as cattle. It has a worldwide distribution. Occasionally, it is implicated in human disease, such as urinary tract and soft tissue infections, and invasive disease especially in immunocompromised hosts.[1] In pregnancy, the organism can lead to maternal chorioamnionitis, puerperal endometritis, and neonatal sepsis.[2] Early-onset (EO) neonatal disease, occurring within the first 7 days of life, is the most significant disease entity amenable to preventive measures. Late-onset disease occurs in infants 7 days or older. Determinants of late-onset disease are not well documented, although evidence suggests that it could be acquired through either vertical or nosocomial transmission, and that acquisition from community sources was also possible.[3] Neonatal disease usually occurs as bacteraemia, pneumonia, or meningitis. Among the risk factors increasing the likelihood of EOGBS disease, the most important is GBS colonisation of the maternal urogenital or gastro-intestinal tract. Other risk factors include prolonged membrane rupture, intrapartum fever, less than 37 weeks' gestation, GBS bacteriuria during pregnancy, and previous delivery of an infant who had GBS disease.[3] Affected neonates usually acquire the bacteria during delivery via the ascending route. Early-onset GBS disease was previously associated with high mortality rates (up to 50%), but more recent estimates yield figures of less than 10%, probably due to improvements in neonatal care.[3] Survivors may nevertheless suffer permanent disabilities, such as hearing or visual loss or mental retardation.

Female GBS colonisation rates differ depending on geographic area, but are similar for pregnant and non-pregnant women. In most populations that have been studied, 10 to 30% of pregnant women were colonised with GBS in the vaginal and/or rectal area.[3] A European study on data collected between 1996 and 2006 yielded GBS vaginal colonisation rates from 6.5 to 36%.[4] An article in the current issue of the *Hong Kong Medical Journal* reported a vagino-rectal colonisation rate in an obstetrics unit of a local hospital to be 10.4% in 2002.[5] Of all infants born to colonised parturients, approximately 1 to 2% would develop EO invasive disease. The disease burden varies in different countries. In the US, the EOGBS disease attack rate was approximately 2 per 1000 live births in the 1970s, with around 12 000 neonates affected annually out of a birth cohort of over 4 million.[2] With the introduction of national guidelines for maternal GBS screening and intervention by the Centers for Disease Control and Prevention (CDC) in 1996, the EOGBS disease incidence in the US has decreased from 1.7 per 1000 live births in 1993 to 0.6 per 1000 in 1998.[3,6] Other countries that have adopted perinatal GBS disease prevention guidelines similar to those of the US have seen comparable declines in the incidence of EOGBS disease. For example Australia reported a reduction from 2.0 per 1000 live births in 1991-1993 to 0.5 in 1995-1997.[7]

The most effective method for EOGBS disease prevention available currently is intrapartum antibiotic prophylaxis (IAP). The challenge is to adopt the most appropriate method for selecting pregnant women for IAP. In the 1996 CDC guidelines,[3] two options for IAP were proposed. The first depended on screening, with the goal of detecting the maximal number of GBS carriers for IAP administration. As the large bowel is believed to be the reservoir for GBS from which sporadic recolonisation of the vagina occurs intermittently, it was recommended that screening for GBS be performed using a combined low vaginal and rectal swab. The intermittent colonisation theory also led to the recommendation to perform GBS screening culture at 35 to 37 weeks of gestation.[2] As it was shown that direct agar plating, instead of selective enrichment broth, led to false-negative culture results in as many as 50% of women GBS carriers, the latter method was recommended to maximise sensitivity.[8] Any positive results from screening would prompt IAP. The second option was the risk-factor approach, taking into consideration different risk factors such as preterm labour, prolonged rupture of membranes, maternal fever during labour, previous delivery of an infant with GBS disease, and GBS bacteriuria during the current pregnancy. Patients with any such risk factor would receive IAP.

Subsequent to the adoption of the 1996 guidelines in the US, it was shown that the risk of EOGBS disease was significantly lower among the infants of screened women than among those in the risk-factor group.[9] The CDC thus further revised its guidelines on prevention of perinatal GBS disease in 2002, to recommend a universal screening approach to decide on IAP.[10] The US EOGBS disease incidence rate showed a continued downward trend from 2000 to 2003 (0.52 to 0.31 cases per 1000 live births), followed by an increase from 2003 to 2006 (0.31 to 0.40 cases per 1000 live births). This increase was evidently driven by an increasing incidence among black term infants, but

the underlying cause is still not apparent.[11]

The adoption of prevention strategies for neonatal GBS infection varies with different countries and requires cost-effectiveness considerations, which in turn depend on the disease burden. In addition, the potential downside of IAP also needs to be taken into account, including adverse consequences which may be serious such as anaphylaxis, and the emergence of antimicrobial-resistant infections. In fact, GBS with reduced susceptibility to penicillin has also been reported locally.[12]

In Hong Kong, as EOGBS disease is not notifiable, there are no formal data on the disease burden. In the article published in the current issue of the Journal,[5] the institution recorded four cases of EOGBS disease per 5000 deliveries per year, translating to an annual incidence of 0.8 per 1000 live births. Significantly, of the 96 GBS maternal carriers who would have received IAP according to the study protocol, none of the neonates had EOGBS disease. On the other hand, four who had early sepsis attributed to GBS in the non-GBS carrier group were not offered IAP. As the screening was undertaken at the booking visit to the antenatal clinic, the sensitivity for determining the carrier status during labour would be expected to be compromised, as also pointed out by the authors. Findings from this study thus support the recommendation to screen for GBS later into gestation (at about 35-37 weeks) to maximise sensitivity for IAP and disease prevention. In particular, in the current study one of the neonates with GBS sepsis and meningitis was delivered preterm. A protocol to administer IAP in the setting of preterm labour, when the GBS screening result is not yet available, could potentially prevent such cases. An interesting finding in the current study was the association of GBS carriage among professionals. The definition of professionals was however not given, and those attaining tertiary education levels did not show significantly higher GBS carriage rates than the groups with lower education levels. Further studies are necessary to elucidate the association.

In the consideration to administer prevention programmes for EOGBS disease, a concerted effort from different specialties appears necessary. These have to address a variety of aspects, including public health policy based on local disease patterns, provision of prenatal, obstetric and paediatric care, and supporting microbiology laboratory services.

Janice YC Lo, FRCPA, FHKCPath
E-mail: janicelo@dh.gov.hk
Microbiology Division
Public Health Laboratory Centre
382 Nam Cheong Street
Shek Kip Mei
Hong Kong

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