

Are We Using the Optimal Strategy for GBS Management in Pregnancy?

Mark H. Yudin, MD, MSc, FRCSC,¹ Vibhuti Shah, MD, FRCPC,²
Arne Ohlsson, MD, MSc, FRCPC, FAAP,^{2,3} Dan Farine, MD, FRCSC³

¹Department of Obstetrics and Gynaecology, St. Michael's Hospital, University of Toronto, Toronto ON

²Department of Paediatrics, Mount Sinai Hospital, University of Toronto, Toronto ON

³Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto, Toronto ON

Infection with group B streptococci (GBS) is a significant cause of neonatal morbidity and mortality, and maternal infection. Mortality rates for early onset neonatal GBS infection range from 5% to 20%.¹ Currently recommended screening and treatment approaches in Canada and the United States have been associated with a decrease in the incidence of early onset disease from 2–3 per 1000 to 0.5 per 1000 over the last two decades.^{2,3} With the implementation of these strategies, a large proportion of women and their offspring are exposed to antibiotics, and there has been no decrease in late onset infection, leading to the question, are we using the optimal strategy for GBS management in pregnancy?

Over the past 20 years, researchers have examined several strategies to decrease morbidity and mortality from GBS infection. This research shows that antibiotic therapy must be given intrapartum rather than antenatally to be most effective.⁴ The next questions to be addressed are which women should be screened and treated, and when should screening occur? As GBS colonization status changes throughout pregnancy, the initial approach of screening women at 26 to 28 weeks' gestation was criticized. Guidelines published in 1996 by the Centers for Disease Control and Prevention (CDC) in the United States,⁵ and guidelines published in 1997 by the Society of Obstetricians and Gynaecologists of Canada (SOGC),⁶ recommended two acceptable approaches to screening: universal screening of all pregnant women at 35 to 37 weeks' gestation and treatment in labour of those who tested positive; or no screening, and treatment only of women in labour who developed certain risk factors (rupture of membranes greater than 18 hours or fever).

These guidelines were updated in 2002 by the CDC and in 2004 by the SOGC to state that the preferred approach was universal screening, with the risk factor approach reserved for women who had not been screened.^{7,8} In general, however, the quality of research has been poor, leading to many different guidelines based on different interpretations of the data.⁹

The SOGC guideline uses relative risk as the outcome statistic.⁸ With few outcomes in these studies, there are impressive relative risk or odds ratio results, but the absolute risk differences in outcomes between treatment and control groups are small, and the number needed to treat to avoid one early onset infection is very large.¹⁰ In 2003, the Royal College of Obstetricians and Gynaecologists had a different interpretation of the same evidence: "Until it is clear that antenatal screening for GBS carriage does more good than harm and that benefits are cost effective, there seems little justification at present for recommending routine screening in the UK."¹¹ Many would argue that the dramatic drop in rates of neonatal disease and maternal infection is a success story, and surely any strategy that has decreased the incidence of this devastating infection is to be commended. However, has this great success come at a price? Maternal colonization rates range from 10% to 30%. Therefore, up to almost one third of all women and their offspring are being exposed to antibiotics as part of prevention efforts. It is important to examine the costs, both health and financial, associated with these management approaches.

Maternal side effects caused by a short course of antibiotics given during labour are uncommon, and life-threatening reactions are rare. A greater concern, however, is the long-term effect of large increases in antibiotic use on maternal and newborn bacterial flora. A decrease in the number of neonatal GBS cases could be accompanied by

rising infections due to other, more virulent, organisms, such as *E coli*, *Enterococcus*, or other gram-negative and penicillin- or ampicillin-resistant bacteria. Neonatal sepsis caused by gram-negative organisms such as *E coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Enterobacter* carries a higher mortality rate than sepsis caused by GBS and other gram-positive organisms.¹²

There have been conflicting reports in the literature with regard to intrapartum antibiotic use: some studies show an increase in neonatal gram-negative sepsis, and others show no difference. An important distinction may be made by antibiotic, as penicillin may be safer than ampicillin because of its narrower spectrum of coverage. Nonetheless, if we continue to administer intrapartum antibiotics to such a large proportion of labouring women, further surveillance studies for neonatal infection rates will be crucial.

Another concern with respect to high rates of intrapartum chemoprophylaxis is antibiotic resistance of the organism itself. Although GBS remains universally sensitive to penicillin, there are increasing rates of resistance to other antibiotics. In North America, resistance rates to erythromycin are 7% to 25%, and to clindamycin, 3% to 15%.^{13–15} With maternal colonization rates and antibiotic usage high, resistance rates could rise even further, limiting the choice of effective medications.

Financial costs are also an issue. Millions of dollars are spent to provide thousands of women in labour with prophylactic antibiotics. The economic benefits of preventing neonatal infection and the care it requires must be balanced against the costs of maternal prophylaxis.

To fight against GBS infections, we need a strategy to decrease antibiotic exposure, while maintaining the low rates of neonatal infections that have been achieved in recent years. Large databases, such as the Atlee database in Halifax, the Canadian Neonatal Network database, or the database of women enrolled in the term PROM (Premature Rupture of Membranes) trial, could be examined to look at neonatal GBS infection rates in different cohorts.

Women with fast labours and multiparous women may not need intrapartum chemoprophylaxis or screening because of the short time the fetus is exposed to the maternal genital tract. At the same time, GBS-positive women often are not managed actively in order to give enough time to administer antibiotics; perhaps it would be better to expedite labour and delivery rather than to prolong labour in order to give medications. In the term PROM trial, induction of labour actually lowered the rate of neonatal GBS infection.¹⁶ These are important issues that need further study.

In conclusion, the decrease in the incidence of early-onset GBS infection over the past two decades is considerable and commendable. We should keep in mind that colonization and infection rates due to GBS change over time, and the results we have seen following many different guidelines may be only temporary associations without causal relationships. However, we must not rest on our laurels; we need further evaluation and study. Although we cannot prevent all GBS infections, with reliable information we may be able to refine our approach to the prevention of neonatal GBS disease, thereby keeping infection rates low without increasing antibiotic resistance and neonatal infections due to organisms other than GBS.

REFERENCES

1. Franciosi RA, Larsen JW, Zimmerman RA. Group B streptococcal neonatal and infant infections. *J Pediatr* 1973;82:707–18.
2. Davies HD, Adair C, Schuchat A, Low DE, Suave RS. The Alberta Neonatal Group B Streptococcal Network. *CMAJ* 2001;164:479–85.
3. Schrag SJ, Zywicki S, Farley MM, Reingold AL, Harrison LH, Lefkowitz LB, et al. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. *N Engl J Med* 2000;342(1):15–20.
4. Boyer KM, Gotoff SP. Strategies for chemoprophylaxis of GBS early-onset infections. *Antibiot Chemother* 1985;35:267–80.
5. Centers for Disease Control and Prevention. Prevention of group B streptococcal disease: a public health perspective. *Mor Mortal Wkly Rep* 1996;45(RR-7):1–24.
6. Society of Obstetricians and Gynaecologists of Canada. Statement on the prevention of early-onset group B streptococcal infections in the newborn. *J Soc Obstet Gynaecol Can* 1997;19:751–8.
7. Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. *Mor Mortal Wkly Rep* 2002;51(RR-11):1–22.
8. Society of Obstetricians and Gynaecologists of Canada. The prevention of early-onset neonatal group B streptococcal disease. *J Obstet Gynaecol Can* 2004;26(9):826–32.
9. Ohlsson A, Myhr TL. Intrapartum chemoprophylaxis of perinatal group B streptococcal infections: a critical review of randomized controlled trials. *Am J Obstet Gynecol* 1995;172:1326–7.
10. Shah V, Ohlsson A with the Canadian Task Force on Preventive Health Care. Prevention of early-onset group B streptococcal (GBS) infection in the newborn. Systematic review and recommendations. CTFPHC Technical report. #01–6. May 2001. London, ON: Canadian Task Force. Available at URL <http://www.ctfphc.org>.
11. Royal College of Obstetricians and Gynaecologists. Guideline No. 36 available at URL http://www.rcog.org.uk/resources/Public/pdf/GroupB_strep_no36.pdf.
12. Kaushik SL, Parmar VR, Grover N, Grover PS, Kaushik R. Neonatal sepsis in hospital born babies. *J Commun Dis* 1998;30:147–52.
13. De Azavedo JCS, McGavin M, Duncan C, et al. Prevalence and mechanisms of macrolide resistance in invasive and noninvasive group B streptococcus isolates from Ontario, Canada. *Antimicrob Agents Chemother* 2001;45:3504–8.
14. Andrews JI, Diekema DJ, Hunter SK, et al. Group B streptococci causing neonatal bloodstream infection: Antimicrobial susceptibility and serotyping results from SENTRY centers in the Western hemisphere. *Am J Obstet Gynecol* 2000;183:859–62.
15. Rouse DJ, Andrews WW, Lin FC, et al. Antibiotic susceptibility profile of group B streptococcus acquired vertically. *Obstet Gynecol* 1998;92:931–4.
16. Hannah ME, Ohlsson A, Wang EEL, et al for the TermPROM Study Group. Maternal colonization with group B streptococcus and prelabor rupture of the membranes at term: the role of induction of labor. *Am J Obstet Gynecol* 1997;177:780–5.