IS PROPHYLAXIS OF EARLY-ONSET GROUP B STREPTOCOCCAL DISEASE APPROPRIATE FOR SOUTH AFRICA?

H N Bomela, D E Ballot, P A Cooper

Background. Early-onset group B streptococcal (GBS) disease in neonates can be prevented by the use of intrapartum chemoprophylaxis. There are two prevention strategies, one based on risk factors and the other on culture screening for GBS. This study sought to establish whether GBS chemoprophylaxis is appropriate in a developing country such as South Africa.

Methods. All neonates with early-onset GBS disease born at Johannesburg Hospital between 1 January 1995 and 21 December 1997 were reviewed. Data were collected prospectively between 1 January and 31 October 1998. Data included demographic information, obstetric information, disease characteristics, admission details and mortality. The approximate cost of implementing both strategies was determined.

Results. The overal incidence of early-onset GBS was 1.16 per 1 000 live births. The rate was significantly greater in 1998 compared with the previous years. Most of the babies were born preterm (70%), and 60% required admission to the neonatal intensive care unit (ICU) (a total of 81 ICU days). Twelve of the babies died. Assuming that chemoprophylaxis would reduce the number of ICU days by half, this would save an amount of R52 000. Culture-based chemoprophylaxis would cost R10 million, whereas an approach based on risk factors would cost R31 140.

Conclusion. In conclusion, we feel that early-onset GBS disease is sufficiently prevalent in our unit to justify the implementation of a chemoprophylaxis strategy based on risk factors. Whether other units should adopt a similar approach would depend on the local incidence of early-onset GBS.

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Group B streptococcus (GBS) is a common commensal of the maternal genito-urinary tract and colonises 15 - 40% of pregnant women. Early-onset GBS disease is associated with 1 - 2 % of colonised mothers.[1] In infants, GBS disease is characterised as early-onset (i.e. occurring in infants < 7 days old) or late-onset (i.e. occurring in infants ≥ 7 days old). Disease in infants usually occurs as bacteraemia, pneumonia or meningitis.[1] Between 50% and 70% of the cases of neonatal GBS disease occur in preterm infants. In 1990, GBS infection caused 7 600 serious illnesses (incidence rate of 1.7/1 000 live births) and 310 deaths among US infants aged < 90 days; early-onset disease accounted for 80% of these illnesses.[2] The incidence of early-onset GBS disease in Oxford, England, between 1985 and 1996, was reported as being 0.5/1 000 live births for definite early-onset infection and 0.4/1 000 for probable early-onset infection, giving a total of 0.9/1 000 live births.[3]

Because a vaccine is not yet available, many neonatal infections can be prevented through the use of intrapartum antibiotic prophylaxis in women who are at risk of transmitting the infection to their newborns.[2] However, despite clinical trials that demonstrate the effectiveness of intrapartum antibiotic prophylaxis, prevention strategies have not been implemented widely or consistently, and the incidence of neonatal GBS disease has not declined.[2]

In South Africa GBS is a significant cause of early-onset disease. The incidence of early-onset infections at Baragwanath Hospital during 1989 and 1990 was 1.9/1 000 live births, which was higher than the incidence quoted for the USA.[4] In a more recent survey, 21% of early-onset infections at Baragwanath Hospital from January 1997 to June 1998 were caused by GBS (H Saloojee — personal communication).

The aim of this study was to evaluate the incidence and mortality associated with early-onset GBS disease at Johannesburg Hospital and to determine whether the American Academy of Pediatrics (AAP) and American College of Obstetricians and Gynecologists (ACOG) recommendations for prophylaxis of GBS[5,6] are appropriate for the local situation.

SUBJECTS AND METHODS

This was a descriptive study done at Johannesburg Hospital. Approximately 7 800 pregnant women deliver each year at this hospital. Subjects were all neonates with a positive blood or cerebrospinal fluid (CSF) culture for GBS. Infants were identified from laboratory records. The hospital files of both neonates and mothers were reviewed retrospectively from January 1995 to December 1997 and collected prospectively from January 1998 to October 1998. Demographic data, admission to the neonatal intensive care unit (NICU), mode of delivery, symptoms and signs of illness and short-term outcome were collected for all subjects. Maternal data included age and risk factors for GBS, viz. fever, prolonged rupture of membranes (PROM), urinary tract infections (UTI), preterm delivery and previous GBS history.[3] Babies born outside Johannesburg Hospital were excluded from the study.

Data were captured on the Epi-Info version 6.0 program. Standard statistical tests were used to analyse the data. Continuous variables were described using means and

Department of Paediatrics, University of the Witwatersrand, Johannesburg
H N Bomela, FCPaed (SA)
D E Ballot, FCPaed (SA), PhD
P A Cooper, FCPaed (SA), PhD

tandard deviations (SDs), while categorical variables were escribed using percentages and frequencies.

RESULTS

here was a total of 33 neonates with GBS infection during the tudy period. The mean birth weight was 2 100 g (SD 763.7 g, inge 1 005 - 3 600 g), with 24 of the 33 subjects (72%) having a rth weight less than 2 500 g. The mean gestational age was 35 eeks (SD 4.02, range 25 - 42 weeks) and 23 of the 33 subjects 0%) were born prematurely. The mean Apgar scores were 58 at 1 minute, 7.17 at 5 minutes and 7.9 at 10 minutes.

The incidence of early-onset GBS disease showed a gnificant increase in 1998 compared with the 3 preceding ears (Table I). The clinical presentation was pneumonia 3/33), septicaemia (6/33) and meningitis (4/33). A number of fants had GBS infection in more than one site. A total of 2/33 of the subjects had positive blood cultures; of these, 7 resented with septicaemia and pneumonia, while 4 presented ith meningitis and septicaemia. Twenty subjects (60%) quired admission to the NICU. The initial clinical diagnoses n admission to the NICU are given in Table II. The mortality te was 12 of all NICU admissions (60%), and the causes of eath are shown in Table III.

Mean maternal age was 24.4 years (range 18 - 33 years). leven of the 33 women had not received antenatal care. There ere maternal risk factors (as listed above) for GBS in 24 of the 3 pregnancies. Risk factors included prematurity (23), PROM "), maternal UTI (2) and maternal pyrexia (1). A number of regnancies had more than one risk factor. A history of early-nset GBS disease in a previous infant was not recorded in any of the cases. There were no risk factors in 9 of 33 pregnancies (27%).

Table I. Incidence of GBS infection by year

Year	Incidence (/total no. of live births)	Incidence (/1 000 live births)
1995	5/7 195	0.69/1 000
1996	5/7 979	0.62/1 000
1997	7/7 897	0.89/1 000
1998	16/ 5353	*2.90/1 000

*Chi-square statistic 19.2505, 3 degrees of freedom, P-value 0.00024 compared with previous years. Log linear model shows that cases in 1999 were significantly higher than in previous years.

Table II. Primary clinical presentation of neonates with GBS admitted to the NICU

Clinical presentation	Number (%)
Pneumonia	13 (40)
Meningitis	7 (20)
Septic shock	5 (15)
Septicaemia	3 (10)
Hyaline membrane disease	3 (10)
Persistent fetal circulation	2 (5)

Table III. Causes of death

Cause	Number (%)
Pneumonia	4/12 (33)
Meningitis	4/12 (33)
Septicaemia	2/12 (16)
Intraventricular haemorrhage	1/12 (8)
Necrotising enterocolitis	1/12 (8)

DISCUSSION AND CONCLUSION

Early-onset GBS is an ongoing problem at the Johannesburg Hospital as shown in the above study, the overall incidence being 1.1/1 000 live births. There was an increase in the incidence of early-onset GBS at Johannesburg Hospital during 1998 (2.9/1 000 live births) compared with previous years (0.63 - 0.88/1 000 live births). This may reflect the fact that data were collected retrospectively during the previous years and some cases may have been missed. However, an independent prospective survey of bacterial infection in 1997 confirmed the same incidence of GBS disease.[7] There were no obvious reasons for this increase in incidence during 1998 and it may merely reflect natural fluctuation in annual figures. A fluctuating incidence of GBS was also noted in the Oxford study.[3]

Early-onset GBS can be prevented by intrapartum chemoprophylaxis to the mother. The AAP and ACOG have made recommendations based on combining two strategies: culture screening for GBS carriage at 35 - 37 weeks' gestation, or the presence on admission for delivery of one or more risk factors for neonatal GBS disease (i.e. previous infant with invasive GBS disease, GBS bacteriuria during this pregnancy, gestation < 37 weeks, duration of membrane rupture > 18 hours, or intrapartum fever >38°C).[3] A modified algorithm for prevention of early-onset GBS disease using culture-based screening is reproduced in Fig. 1. The Center for Disease Control (CDC) recommends either a culture-based approach or one based only on risk factors.[8] The CDC recommends that cultures be performed at 35 - 37 weeks' gestation, which has better predictive value for the presence of GBS at term than the cultures performed earlier in gestation (26 - 28 weeks).[9] It has been estimated that this strategy results in intrapartum treatment of 27% of women and prevents up to 86% of early-onset GBS disease. The strategy based on risk factors only results in intrapartum treatment of 18% of women and prevents 69% of early-onset GBS disease.[3] It is clear, however, that any scheme for prophylaxis will fail to prevent all cases of GBS. Approximately 25% of infants with early-onset GBS disease have no identifiable risk factors for infection (27% in this study).[9] In addition, for intrapartum therapy to be successful, antibiotics need to be administered to the mother at

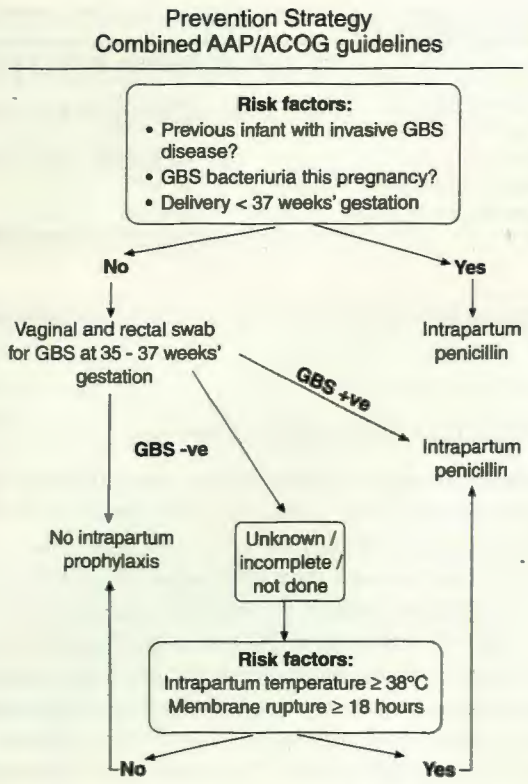

Fig. 1. Guidelines for prevention strategy (combined AAP/ACOG).

least 4 hours before delivery. Known GBS cases are often delivered too quickly for chemoprophylaxis to be effective. Also there is concern about penicillin allergy and anaphylaxis; however, erythromycin is a suitable alternative.[10]

The present survey showed a high mortality rate (60%) and frequent number of ICU admissions in comparison with other data,[11,12] which would appear to justify the need for intrapartum GBS prophylaxis. It has been suggested that prevention strategies would not be warranted if the incidence of early-onset GBS disease is below 0.6/1 000 live births.[12] All prevention strategies have been shown to be cost effective compared with no strategy, but the cheapest is the one based on risk factors alone without culture screening.[13]

Health care in a developing country with limited resources is a question of priorities. The AIDS epidemic and the issue of vertical transmission of HIV over shadows other health problems such as GBS infection that are far less prevalent. We feel, however, that the incidence of GBS infection is sufficiently high to be cause for concern and that a programme of intrapartum prophylaxis based on risk factors would be cost beneficial. From a neonatal perspective, any simple measure that avoids ICU admission and prevents neonatal death and handicap is worthwhile. We agree that routine culture-based screening of all pregnant women for GBS at 28 weeks is too costly to be implemented. A culture-based programme would cost the Johannesburg Hospital approximately R10 million per annum, based on R132 per patient for rectal, vaginal and urine cultures on all antenatal patients. A programme based on risk factors would be affordable. Most of the pregnant women with GBS risk factors such as PROM or maternal pyrexia are treated with antibiotics in our obstetric unit and hence would not require additional chemoprophylaxis and would not add to the cost. The cost of a GBS prophylaxis programme would therefore be determined by the additional use of intrapartum penicillin in women with uncomplicated preterm delivery. During the study period there were a total of 3 460 preterm deliveries — assuming that most women would have received three doses of penicillin (i.e. delivered within 24 hours), at R3 per dose the cost of the GBS prophylaxis would have been R31 140. Previous prophylactic programmes have prevented 69% of ICU admissions. It is possible that some of the infants may have required NICU on the basis of prematurity and not GBS. It is therefore assumed that our GBS prophylaxis would prevent 50% of ICU admissions or 40 NICU days at R1 300 per day (total R52 000). The overall saving would have been R20 860. The cost of level 2 neonatal care is not considered as these babies were delivered preterm and would have been hospitalised for prematurity, even in the absence of GBS. The prematurity would not have been prevented by the GBS prophylaxis. The cost of neonatal care in the public sector is not well established; the above figure of R1 300 per day is derived from a recent cost analysis of the neonatal unit at the Johannesburg Hospital (J Flett — unpublished data). Another important issue is that 12 of these babies died and some of these deaths may have been prevented by GBS prophylaxis.

In conclusion, we feel that a programme of GBS prophylaxis based on risk factors would be beneficial in our hospital. Whether all units should adopt a similar approach would depend on their own rates of GBS infection.

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