



EARLY-ONSET NEONATAL SEPSIS OR MENINGITIS IN BELGIUM, IN THE ERA OF PREVENTION FOR PERINATAL GROUP B STREPTOCOCCAL DISEASES



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ABSTRACT

Background: In the late 1990s, the era of "group B streptococcal (GBS) prevention" was set up. Progressively, prevention strategy has been implemented in the different hospitals. Important steps marked this period as national surveys related to GBS prevention, Belgian consensus meeting and launch of Belgian guidelines for prevention of GBS early onset diseases (EOD; ≤ 5 days). One unintended consequence of GBS prevention efforts may be an increase in the rate of sepsis/meningitis due to Gram negative bacteria (GNB).
Methods: Year based analysis of records from 2 databases: a) cases of neonatal bacteremia / meningitis notified by sentinel laboratories to the Belgian Surveillance Network (BSNet), data for EOD collected since 1991 and b) cases of GBS EOD and late onset diseases (LOD) reported voluntarily by some laboratories to the Belgian reference laboratory for GBS (BRLab).
Results: BSNet: an annual mean of 51 cases of EOD (24-104) were notified by 27 (16-35) laboratories. Overall GBS remained the leading cause and represented annually 34.8% (21.1-54.7%) of EOD but with a significant decrease ($p < 0.01$). It was followed by *E.coli* 12.5%, coagulase negative staphylococci (CNS) 16.4%, *S.aureus* 9.0%, *Listeria* sp 3.0%, *S.pneumoniae* 2.7%, *H.influenzae* 2.1% *S.pyogenes* 1.9%, and others. No significant trend was shown in the rates of *E.coli* and other GNB EOD. For CNS, we did not have data to differentiate definite infections from contaminations.
BRLab: From 1999 to 2005, for an annual mean of 29 cases (23-50), the ratio "LOD/EOD" increased from 0.16 to 0.71. The number of LOD remained stable but the number of EOD decreased ($p < 0.01$).
Conclusions: 1) Since 1991, GBS has remained the leading cause of neonatal EOD 2) But as expected with the implementation of a GBS prevention strategy, a significant decrease of GBS EOD has occurred 3) No significant trend of the annual rates of *E.coli* and other GNB infections was shown.

BACKGROUND

In Belgium, since the 1980s, group B streptococci (GBS) early onset (EO) sepsis is still an important cause of morbidity and mortality among newborns. After the release of CDC guidelines for the prevention of GBS perinatal disease in 1996, progressively hospitals (not all) have implemented the recommended intrapartum chemoprophylaxis. Their practice was not fully in agreement with CDC guidelines and was less effective.

In 1998-1999, two mail surveys covering the whole country performed to assess the Belgian GBS practices for prevention of GBS perinatal disease, demonstrated room for improvement! In 2000, several feed-back symposia related to the surveys and highlighting the major expected improvements were organized by different professional societies. In 2001, a consensus meeting was held and in 2003 the Belgian recommendations were issued by the Superior Health Council. The result of these recommendations is an increasing use of antibiotics during labor to decrease the risk of GBS perinatal infection. Therefore, there is concern that one unintended consequence of GBS prevention efforts might be a change in the spectrum of organisms involved in neonatal EOD, and particularly the risk of an increase in the rate of serious neonatal infections caused by Gram negative Bacilli (GNB).

OBJECTIVES

- ◆ To assess the distribution of pathogens involved in early onset sepsis +/- meningitis among neonates born in Belgium during 1991 - 2005.
- ◆ To correlate any trend in their distribution with key dates related to strategies for prevention of GBS perinatal disease.
- ◆ To monitor any change in the occurrence of GBS EOD and LOD in neonates through 1999 to 2005

METHODS

Population data bases

Belgian Surveillance network (BSNet)

- ◆ To monitor health problems, the Belgian Public Health Institute has developed a voluntary "passive" surveillance network.
- ◆ Sentinel laboratories report weekly the occurrence of defined infectious diseases including neonatal sepsis and meningitis occurring within 28 days after birth.
- ◆ Retrospective review of data reported by sentinel laboratories from 1991 to 2005 for EO sepsis and meningitis (excepted 2003-2004: computerized data not available).
- ◆ Information regarding clinical data or susceptibility patterns of the pathogen were not available, neither the total number of births per center during the related period.

National reference laboratory for GBS (BRLab)

- ◆ Any Belgian laboratory is invited to send to the BRLab all their GBS isolated from severe infection (from blood, CSF or any deep normally sterile site) for further characterization and epidemiological purposes.

Definition

- ◆ EO Disease (EOD) was defined by a positive culture of blood or cerebrospinal fluid drawn within 5 days after birth and LO Disease (LOD) for newborns aged >6 days.
- ◆ Reported case with coagulase negative staphylococci (CNS) are generally considered as contaminants except if clinical or other bacteriological data confirmed an infection.

RESULTS: Neonatal EOD

◆ Evolution of notifications to the BSNet

Between 1991 and 2005, 669 cases of EOD were reported. Each year, a mean of 27 laboratories (16-35) notified a number of cases fluctuating from 24 to 104 with an average of 51 cases (table1).

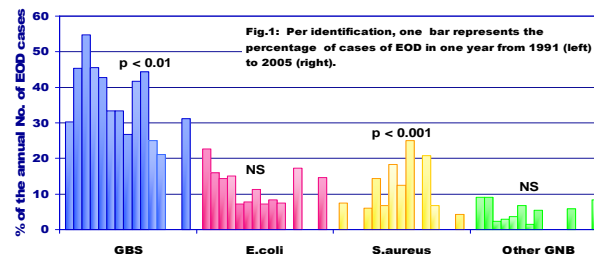
◆ Distribution of pathogens

Along this decade, GBS was always the most frequent cause of EOD representing on average 34.8% of them. Far behind came *E.coli* as the cause of 12.5% EOD, and *S.aureus*, 9.0%. The reported Gram negative bacilli (GNB) other than *E.coli* represented only 4.9% of the cases. Other neonatal pathogens as group A streptococci (GAS), *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Listeria monocytogenes* accounted respectively each for less than 3% of EOD. Meanwhile coagulase negative staphylococci (CNS) were reported as the agent recovered from 16.3% of infants with positive culture of blood or cerebrospinal fluid.

Table 1: Distribution of bacterial species causing 669 cases of EOD among infants born between 1991 and 2005, as reported by the BSNet.

Organism	Overall, No. With EOD (%)	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2005	Evolution
GBS	233 (34.8)	20	20	23	15	12	30	28	15	15	12	6	22	15	↓ ($p < 0.01$)
<i>E.coli</i>	84 (12.5)	15	7	6	5	2	7	8	4	3	2	0	18	7	NS
<i>S.aureus</i>	60 (9.0)	5	0	0	2	4	6	13	7	9	0	5	7	2	↔ ($p < 0.001$)
SCN	109 (16.3)	3	2	1	2	2	14	9	13	5	5	6	34	13	↔ ($p < 0.01$)
GAS	13 (1.9)	0	2	1	0	0	1	0	0	1	4	0	0	0	↔ ($p < 0.01$)
<i>S.pneumoniae</i>	18 (2.7)	3	0	1	0	1	4	1	2	1	1	0	3	1	NS
<i>H.influenzae</i>	14 (2.1)	2	4	1	1	1	2	0	0	0	2	1	0	0	↔ ($p < 0.05$)
<i>Listeria</i>	20 (3.0)	6	1	3	1	3	1	0	2	2	0	1	0	0	↔ ($p < 0.01$)
Other GNB	33 (4.9)	6	4	1	1	1	6	1	3	0	0	0	6	4	NS
Others	85 (12.7)	6	4	5	6	2	19	11	10	0	1	1	14	6	NS
Total	669	66	44	42	33	28	90	71	56	36	27	24	104	48	

◆ Evolution of some pathogens through the period



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RESULTS : GBS EOD and LOD

◆ Evolution

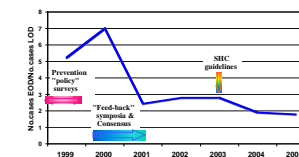
Through 1999 to 2005, 230 strains of GBS isolated from neonatal EO or LOD were sent to the NRLab with a mean of 33 cases per year (23-50) (Table 2)

Table 2: Annual distribution of GBS isolated from 230 neonates with EOD or LOD through 1999 to 2005, and referred to the NRLab.

	Overall No. (%)	1999	2000	2001	2002	2003	2004	2005	
EOD	172 (74.8)	42	28	22	28	17	17	18	↔ ($p < 0.01$)
LOD	58 (25.2)	8	4	9	10	6	9	12	
Total	230	50	32	31	38	23	26	30	

Cases of GBS LOD has remained stable through 1999-2005 but a significant decline of cases of EOD has been observed since 2001. It is well illustrated by the evolution of the annual balance between the numbers of EOD and LOD (fig.2).

Fig.2: Annual balance of cases of GBS EOD compared to cases of LOD, 1999 to 2005



DISCUSSION AND CONCLUSION

◆ This retrospective analysis gives probably a good overview of the Belgian distribution of pathogens causing neonatal EOD, but it has some important limitations: as the lack of information regarding the annual number of births, or as the knowledge regarding prevention or antibiotic policies in the different centers. Furthermore we ignore if all sentinel laboratories declared regularly all their cases. This emphasizes the need to improve the kind of data to collect through the surveillance network.

◆ Through the period covered by the surveillance, GBS has remained the leading cause of neonatal EOD, despite the significant decline observed since 2001.

◆ The major Belgian events related to this decline in neonatal GBS EOD are the different symposia organized, at the end of 2000 and in 2001, to feed-back the results of the surveys related to GBS prevention policy and to highlight the expected improvements.

◆ By the end of the period, the occurrence of *E.coli* cases has not significantly changed, neither the occurrence of cases caused by other GNB.

◆ An increase in *S.aureus* EOD occurred in the late 1990s before a return to its base line.

◆ EOD caused by *Listeria* and *H. influenzae* have become very scarce.

◆ CNS were more frequently reported. To attribute any signification to these notifications, it would have been mandatory to know a minimum of clinical data, of any change in the pediatric management of neonates or of any change in the used blood culture system.

◆ These changes in pathogens causing EOD require confirmation by ongoing improved surveillance as well as the evolution of the number of cases of GBS LOD. (Could not the intrapartum antibioprophyllaxis delay the onset of neonatal GBS disease?)