

EVOLUTION OF ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF CLINICAL GROUP B STREPTOCOCCI ISOLATED IN BELGIUM

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BACKGROUND:

Group B streptococcus (GBS) continue to be a major cause of life-threatening infections, sepsis, pneumonia and meningitis in neonates. Pregnant women and non-pregnant adults are also affected by severe GBS diseases. Either for therapy or for intrapartum chemoprophylaxis, penicillin G for its bactericidal activity and narrow spectrum, remains the agent of choice. In the penicillin allergic patients, clindamycin or erythromycin have been recommended as alternative drugs. However, probably as a consequence of the important use of macrolides, related drug resistance among streptococcal isolates is currently recognized in many countries. Among clinical GBS isolated in Belgium, erythromycin-resistance rate increased from 3% in the early 1990s to 10% in 1999-2000. Therefore, to recommend empiric therapy or chemoprophylaxis, accurate susceptibility surveillance data are needed.

OBJECTIVE

To analyze susceptibility profiles to penicillin, erythromycin and clindamycin of GBS isolated from severe infections among different patients' age-groups, in Belgium.

To determine macrolide-lincosamide (MLS) resistance phenotypes among erythromycin resistant isolates.

METHODS

Bacterial isolates

From January 2001 to December 2007, a total of 481 clinically significant isolates of GBS recovered by laboratories belonging to the Belgian surveillance network were included in the study. These GBS were isolated from neonates' blood, cerebrospinal fluid or any deep site, from adults and pregnant women with severe infections.

The distribution of serotypes of these isolates of GBS was: 16.1% Ia, 9.3% Ib, 9.3% II, 31.9% III, 5% IV, 20.7% V and 7.2% belonged to serotypes VI, VII or VIII or were non typable.

Determination of MICs

- Etest® method (ABBioDisk, Sweden) with benzylpenicillin (PEN), erythromycin (ERY) and clindamycin (CLI) strips.
- Inoculum 0.5 McFarland on Mueller-Hinton agar + 5% sheep blood
- Incubation 18 to 24 h at 35°C
- MIC interpretative criteria according to CLSI

Determination of MLS resistance phenotypes

- ERY and CLI double-disk and double-Etest® diffusion assays
- ERY (15 µg) and CLI (2 µg) paper disks (Becton Dickinson, USA) or Etest® strips placed 15-20 mm apart on inoculated Mueller-Hinton agar with sheep blood, incubation 18 to 24 h at 35°C.

Interpretation for ERY-resistant isolates

MLS_B phenotypes:

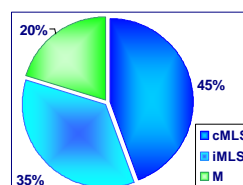
- Inducible resistance (IR):** blunting of the CLI zone of inhibition proximal to the ERY disk or Etest strip, or "D shape".
- Constitutive resistance (CR):** resistance to CLI with no blunting of the CLI zone of inhibition.
- M phenotype:** R to ERY but not to CLI with no blunting of the CLI zone of inhibition.

RESULTS

Resistance of GBS isolated in Belgium from different groups of patients, newborns and adults with severe infections. Trend from 1999 till 2007.

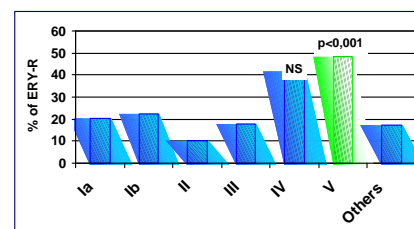
Antimicrobial agent	1999-2000 N= 326	2001-2002 N= 125	2005 N= 133	2006 N= 104	2007 N= 58	2001-2007 N= 420
Penicillin	0 %	0 %	0 %	0 %	0 %	0 %
Erythromycin	10.4 %	19.2 %	30.8 %	27.9 %	27.6 %	26.2 %
Clindamycin		15.2 %	24.8 %	25.0 %	20.7 %	21.4 %
Clindamycin R						
CR		12.8 %	20.3 %	16.3 %	13.8 %	16.2 %
IR		2.4 %	4.5 %	8.6 %	6.9 %	5.2 %

MLS-R phenotypes and MICs for ERY of 119 isolates of GBS resistant to erythromycin.



Phenotypes	Number isolates	MIC ₅₀ (mg/L)	MIC ₉₀ (mg/L)
MLS _B			
Constitutive	53	> 256	> 256
Inducible	42	4	> 256
M	24	4	12

Rate of resistance to erythromycin per serotype of 481 GBS



Rate of resistance to ERY is significantly higher among serotype V isolates of GBS (p < 0.001).

CONCLUSION

- ◆ Penicillin remains active against all isolates
- ◆ Prevalence of macrolides R has increased since the 1990s but seems stabilized.
- ◆ Erythromycin resistance is higher among serotype V isolates of GBS, as already reported in Belgium and in other countries.
- ◆ Erythromycin resistance mechanisms are mainly target site modification, MLS_B phenotypes: constitutive and inducible. The M phenotype, efflux R mechanism, is also prevalent.