Serotypes and Genotypes of Erythromycin-Resistant Group B Streptococci in Korea

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Among 78 erythromycin-resistant group B streptococcus (GBS) isolates from Korea, *ermB* was detected in 58 (74.4%), *mefA* was detected in 14 (17.9%), and *ermTR* was detected in 6 (7.7%). The most prevalent serotypes of erythromycin-resistant GBS were V (detected in 34 isolates [43.6%]) and III (detected in 33 isolates [42.3%]). All serotype V erythromycin-resistant GBS harbored the *ermB* gene.

Streptococcus agalactiae (group B streptococcus [GBS]) is a well-known cause of invasive infections in neonates and pregnant women. It has increasingly been recognized as a significant pathogen in nonpregnant adults, particularly in elderly persons and persons with significant underlying diseases (9, 19). For treatment or prevention of GBS infections, erythromycin and clindamycin therapy are recommended alternatives for patients who are allergic to β -lactam agents (3). In the past, GBS was reported to be susceptible to erythromycin and clindamycin (2). However, recent studies have shown that changes in the susceptibility of GBS to erythromycin and clindamycin have been substantial, although rates of resistance to these agents have differed according to geographical variation and different investigators (1, 3, 5, 15, 18, 22). Serotyping has been used as an epidemiological tool to explain GBS infections because the distribution of GBS serotypes is associated with patient type and the site of infection and the prevalent serotype may also change with time (4, 13, 14, 20). Over the past decade, several investigators have reported that an increasing proportion of GBS disease is due to serotype V (1, 4, 8, 21). In addition, several reports have documented an association between macrolide resistance and GBS serotype V (4, 7, 10, 20). The aim of this study was to elucidate the relationship between genotypes and serotypes of macrolide-resistant GBS isolates in a Korean population.

The GBS isolates used in this study were collected between January 1990 and December 2000 at Wonju Christian Hospital, a 1,000-bed teaching hospital in South Korea. Multiple isolates from the same patient were avoided. The isolates were identified by conventional methods and by latex agglutination assay (Streptex; Murex Biotech Ltd., Dartford, England). The strains were stored in brain heart infusion broth plus 20% glycerol at -70°C until they were studied. The frozen isolates of GBS were thawed, inoculated onto a 5% sheep blood agar plate, and incubated at 35°C overnight. Three hundred eight pure isolates of GBS obtained from three consecutive subcultures were subjected to susceptibility testing, serotyping, and PCR. Susceptibility to penicillin G, erythromycin, clindamycin, tetracycline, ceftriaxone (Sigma Chemical Co., St Louis, Mo.), vancomycin (Daewoong Lilly, Seoul, Korea), and chloramphenicol (Chongkundang, Seoul, Korea) was tested by the agar dilution method (16). Serotyping was done with hemolytic streptococcus group B typing sera (Denka Seiken Co., Ltd., Tokyo, Japan). The typing sera used in this study were Ia, Ib, II, III, IV, and V. The presence of *ermA*, *ermB*, *ermC*, *ermTR*, and *mefA* resistance genes were determined as previously described (12, 17).

During the study period, neither the clindamycin-resistant GBS nor the erythromycin-resistant GBS existed until 1993 or 1995, respectively. Of the 78 erythromycin-resistant (intermediate or resistant) isolates of GBS, 65 (83.3%) were resistant to clindamycin. Of the 87 clindamycin-resistant (intermediate or resistant) isolates, 65 (74.7%) were also resistant to erythro-

TABLE 1. Rates of antimicrobial resistance among different serotypes of 308 isolates of GBS

Anti-microbial	No. of resistant isolates (% of total isolates) of serotype ^a :						
	Ia (n = 27)	Ib (n = 81)	II (n = 5)	III (n = 120)	IV (n = 4)	V (n = 45)	NT (n = 26)
Erythromycin	1 (4)	2 (2)	1 (20)	33 (28)	2 (50)	34 (76)	5 (19)
Clindamycin	3 (11)	10 (12)	1 (20)	32 (27)	2 (50)	34 (76)	5 (19)
Tetracycline	23 (85)	81 (100)	5 (100)	118 (98)	3 (75)	44 (98)	21 (81)
Chloramphenicol	3 (11)	5 (6)	0 (0)	33 (28)	1 (25)	19 (42)	11 (42)

^a n, number of isolates; NT, nontypeable.

TABLE 2. Erythromycin resistance phenotypes and genotypes of GBS according to serotype^a

Pheno-type	Geno-type	No. of isolates of serotype:							Total no. (%) of isolates
		Ia	Ib	II	III	IV	V	NT	
ERY-I/R	<i>ermB</i>	0	1	0	19	2	34	2	58 (18.8)
	<i>ermTR</i>	0	1	1	3	0	0	1	6 (1.9)
	<i>mefA</i>	1	0	0	11	0	0	2	14 (4.6)
ERY-S		26	79	4	87	2	11	21	230 (74.7)
Total		27	81	5	120	4	45	26	308 (100)

^a NT, nontypeable; ERY-I/R, erythromycin intermediate or resistant; ERY-S, erythromycin susceptible.

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TABLE 3. Isolation frequency of macrolide resistance genes of GBS by year

Genotype	No. of isolates with erythromycin resistance ^a										Total no. (%) of isolates	
	1990 (n = 6)	1991 (n = 5)	1992 (n = 12)	1993 (n = 3)	1994 (n = 13)	1995 (n = 7)	1996 (n = 50)	1997 (n = 48)	1998 (n = 40)	1999 (n = 57)		2000 (n = 67)
<i>ermB</i>	0	0	0	0	0	0	9	9	8	14	18	58 (74.4)
<i>ermTR</i>	0	0	0	0	0	0	1	0	4	1	0	6 (7.7)
<i>mefA</i>	0	0	0	0	0	0	3	0	4	2	5	14 (17.9)

^a n, number of isolates examined.

mycin. In the most recent studies performed in Western countries, the rate of resistance to erythromycin ranged from 4 to 25% and the rate of resistance to clindamycin was close to or less than that of resistance to erythromycin (1, 3, 5, 10, 15, 18, 19). Our results show resistance to clindamycin to be more common than resistance to erythromycin, and similar results were described in southern Taiwan (13). Although the reasons for such a discrepancy between different continents are not clear, the distribution of macrolide-lincosamide-streptogramin B (MLS_B) resistance genes and the frequency of the isolation of serotypes of GBS may be major contributing factors.

The GBS serotypes, in order of decreasing frequency, were III (39.0%), Ib (26.3%), V (14.6%), Ia (8.8%), II (1.6%), and IV (1.3%). Of the 308 GBS isolates, 91.6% were typeable (Table 1). Serotypes V and IV did not exist before 1996 and 1999, respectively. The distribution of GBS serotypes has changed over time. The results of this study showed that the proportions of serotype IV, serotype V, and nontypeable (NT) strains were increasing, that the proportion of serotype Ib isolates was decreasing, and that the proportion of serotype III isolates remained unchanged. The rates of resistance to erythromycin found among our serotypes, in decreasing order, were 76% (V), 50% (IV), 28% (III), 20% (II), 19% (NT), 4% (Ia), and 2% (Ib). These results were consistent with those of other reports (11, 15, 21), suggesting a relationship between erythromycin resistance and serotype. In contrast, Ko et al. (13) reported that serotype Ib isolates had a lower rate of susceptibility to erythromycin than did serotype Ia, III, or V isolates. The clindamycin resistance rates of our serotype Ia and Ib isolates were higher than erythromycin resistance rates for these isolates, while erythromycin and clindamycin resistance rates were nearly equal for isolates of the other serotypes. The high rates of resistance to erythromycin, clindamycin, and tetracycline among GBS strains in this study has limited the value of these antibiotics as prophylaxes for high-risk populations or in treatment of GBS infections in Korea.

The distribution of MLS_B resistance genes of GBS is influenced by geographical variation and serotypes (3, 6, 11, 21). The predominant MLS_B resistance gene of GBS was *ermB* in Spain (3), France (11), and Germany (21), whereas *ermTR* was prevalent in Canada (6). In United States, the *mefA* and *ermB* genes were detected with equal frequencies (7). Among the 78 erythromycin-resistant strains examined in this study (Table 2), *ermB* was detected in 58 (74.4%), *mefA* was detected in 14 (17.9%), and *ermTR* was detected in 6 (7.7%). The most prevalent serotypes of erythromycin-resistant GBS isolates were V (detected in 34 isolates [43.6%]) and III (detected in 33 isolates [42.3%]). Of special note, all serotype V erythromycin-resistant isolates harbored the *ermB* gene. There was no sig-

nificant change in genotype frequency during the study period (Table 3).

Further molecular epidemiological studies are needed to determine whether the increase in numbers of *ermB*-positive isolates is due to clonal spread or to an increased number of patients with GBS or is the result of the introduction of polyclonal resistant strains.

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