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Trend of Isolation and Serotypes of Group B Streptococci in Korea

Yunsop Chong, Kyungwon Lee, Oh Hun Kwon, Chung Hyun Nahm
Teiko Murai[1] and Yoshiko Inazumi[1]

Group B streptococci (GBS) neonatal infection, a prevalent disease in western countries, is considered rare in Korea. GBS neonatal infection is known to be often due to serotype III organisms, but the serotypes in Korea have not been reported. In this study, GBS were frequently isolated from specimens of genitalia, urine and various pus. Among the 186 isolates 14 (7.5%) were from neonates, two with concomitant bacteremia and meningitis and one with pneumonia. Frequently isolated GBS serotypes were Ib (9.2%), Ib/c (26.6%) and III/R (23.9%). Change of frequently isolated serotypes during the study was noted, but JM9 which became increasingly isolated in Japan was not found. It is concluded that less prevalence of severe neonatal GBS infection in Korea is not due to the absence of serotype III, but possibly due to low genital carriage rate of GBS by pregnant women.

Key Words: Group B streptococci, neonatal infection, serotype

It is now well recognized that *Streptococcus agalactiae* (group B *Streptococcus*, GBS) can cause serious infections in neonates (Wenger *et al.* 1990). To prevent the high morbidity and mortality, preventive measures such as antibiotic treatment of colonized or high risk pregnant women (Tuppurainen and Hallman, 1989; Wanger, 1992) and immunoprophylaxis of pregnant women with deficient anti-GBS capsular antibody (Baker *et al.* 1988), have been considered in America.

Increased GBS infections in adults with underlying diseases were reported (Eykyn, 1991). Such a tendency was also noted in Korea, but neonatal infection was reported to remain very rare (Nahm, 1992). One of the risk factors for early onset neonatal infection is the GBS carriage of pregnant women (Dillon *et al.* 1987). Serotyping has been used as an epidemiological tool to explain GBS infections (Wilkinson, 1978). It was reported that neonatal meningitis or bacteremia were more often caused by serotype III. Not only the carriage rates of the pregnant women, but also the regional differences of prevalent serotypes were reported. The prevalent serotype may also change in time (Murai *et al.* 1990). In Korea, we do not know the maternal carriage rate nor the serotypes distribution of GBS.

In this study, the recent trend of GBS isolation was analyzed and the serotypes were tested as these may reveal part of the reasons for the rarity of the GBS neonatal infections in Korea.

MATERIALS AND METHODS

GBS were isolated from various clinical

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Department of Clinical Pathology, Yonsei University College of Medicine, Seoul, Korea
[1]Department of Public Health, Toho University School of Medicine, 5-21-16, Omori-Nishi, Otaku, Tokyo, Japan
Address reprint requests to Dr. Y Chong, Department of Clinical Pathology, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul, Korea, 120-752

materials of patients at the Severance Hospital, Seoul. Species of the isolates were identified by the conventional method. Catalase negative gram-positive cocci with characteristic hemolysis, no growth in SF broth (Difco) and on bile esculin azide agar (Difco), and positive coagglutination test with Phadebact group B Streptococcus reagent (Karo Biodiagnostics AB, Huddinge, Sweden) were identified as GBS. The trend of GBS isolation during the years 1986 to 1990 was analyzed retrospectively by reviewing laboratory records.

Part of the strains which were isolated during 1979 to 1992 and kept frozen at −35℃ in skim milk were tested for the serotype. Serotyping was carried out at the Toho University School of Medicine, Tokyo, Japan. The antisera against reference strains were prepared by the Jelinkova's method (1976) using reference strains provided by the WHO Collaborating Center for Reference and Research on Streptococcus, Prague, Czechoslovakia. The typing sera use in this study were Ia, Ib, II, III, IV, V, type cand. NT6, type cand. 7271, JM9, c, R and X. Extracts of the isolates were prepared by the modified Lancefield's method (Sugiyama *et al.* 1990), using 0.2 N hydrochloric acid and incubating the suspension at 52℃ for 2 hours. Capillary precipitation method was used for the typing (Lancefield, 1934).

RESULTS

During the 1986 to 1990 period, 799 isolates of β-hemolytic *Streptococcus* were identified as group A, B, C or G (Table 1). Among the β-hemolytic streptococcal isolates, 326 (41%) were from respiratory specimens, 249 (31%) from various pus, 164 (21%) from genitourinary specimens, 42 (5%) from blood and 18 (2%) from other body fluid. The genitourinary specimens were mostly from female patients. Among the isolates, 45% were group A, 23% B, 10% C and 22% G. Over 50% of the β-hemolytic streptococci isolated from specimens of respiratory, blood and pus were group A. However, over 60% of the isolates from specimens of genitalia and urine were group B. From body fluids such as spinal and pleural fluid, GBS were more frequently isolated than A, C or G group streptococci, and 4 of the 8 GBS isolates were from spinal fluid. Among the 17 isolates of group B, C and G streptococci, from patients less than one month of age, 14 (82%) were GBS.

The serotype of 109 isolates of GBS were determined (Table 2). Among them, 26 were strains isolated in 1979~1986 (period 1) and the remaining 83 in 1991~1992 (period 2). More frequently encountered serotypes were: 29 isolates of Ib/c, 26 of III/R, 9 each of Ia, II/c, and III, and 7 of Ia/c. Serotype JM9 was not found. Serotype Ib and Ib/c did not exist in the first period, but became isolated during the second period and the latter was the most prevalently isolated one.

Serotype II/c, which was the predominant type in the first period, was not isolated in the second period. The proportion of serotype III/R markedly increased during the second

Table 1. β-hemolytic *Streptococcus* group A, B, C and G isolated during 1986 to 1990

Specimen	No. (%) of isolates with				Total
	Group A	Group B	Group C	Group G	
Respiratory	169 (52)	21 (6)	38 (12)	98 (30)	326
Pus	140 (56)	29 (12)	19 (8)	61 (24)	249
Genitalia	12 (13)	60 (67)	13 (15)	4 (4)	89[a]
Urine	7 (9)	56 (75)	7 (9)	5 (7)	75
Blood	25 (60)	12 (29)	1 (2)	4 (10)	42
Body fluid	6 (33)	8 (44)[b]	1 (6)	3 (17)	18
Total	359 (45)	186 (23)	79 (10)	175 (22)	799

[a] All except 2 were from female patients.
[b] 4 from spinal fluid, 3 pleural fluid and 1 peritoneal fluid.

Table 2. Serotypes of group B *Streptococcus* by source of isolation

Source	Period[a]	No. of isolates with serotype													Total
		Ia	Ia/c	Ib	Ib/c	II	II/c	III	III/c	III/R	V	NT/c	NT/R	NT	
Blood	1	1	0	0	0	0	1	0	0	0	0	0	0	0	2
	2	0	0	1	5	0	0	0	0	2	0	0	0	0	8
Spinal	1	0	0	0	0	0	0	1	0	0	0	0	0	0	1
fluid	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ear	1	0	0	0	0	0	1	0	0	0	0	0	0	0	1
	2	0	0	0	1	0	0	0	0	1	0	0	0	0	2
Throat	1	0	0	0	0	0	5	0	1	0	0	0	0	0	6
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sputum	1	0	0	0	0	0	1	0	0	0	0	0	0	1	2
	2	1	1	1	5	0	0	0	0	2	0	0	0	0	10
Urine	1	1	1	0	0	0	1	1	0	3	0	0	0	0	7
	2	1	2	6	9	1	0	5	0	10	2	1	1	0	38
Cervix	1	2	2	0	0	0	0	1	0	1[b]	0	0	0	0	6
	2	2	1	1	8	0	0	0	0	4	0	0	0	2	18
Others[c]	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	2	1	0	1	1	0	0	1	0	3	0	0	0	0	7
Total	1	4	3	0	0[d]	1	9[d]	3	1	4	0	0	0	1	26
	2	5	4	10	29[d]	1	0[d]	6	0	22	2	1	1	2	83
	All	9	7	10	29	2	9	9	1	26	2	1	1	3	109

[a] Period: 1, 1979–1986; 2, 1991–1992.
[b] Isolate from inguinal area.
[c] Umbilical, peritoneal and wound specimens.
[d] χ^2 test: $p<0.05$.

Table 3. Comparison of serotypes of group B *Streptococcus* isolated in Korea and in other countries

Country and source		% of isolates with serotype					Total (No.)	Reference
		I	II	III	V	NT[a]		
Korea	All sources (1979–86)	27	38	31	0	4	26	Present study
	All sources (1991–92)	58	1	34	2	5	83	
Japan	All sources	40	0	49	0	11	45	Iimura, 1979
	All sources	46	8	17	4	25	238	Takazawa and Tomizawa, 1991
USA	Meningitis (≥10 d)	9	1	91			155	Wilkinson, 1978
	Meningitis (<10 d)	18	0	83			83	
	Bacteremia, adult	35	34	27			45	
	Pregnant women	25	38	35			455	
	Hospital personnel	20	38	41			94	
	GU-GI sites	27	34	34			475	
Italy	Mothers and neonates	44	36	17		4	108	Visconti *et al.* 1985
Israel	Mothers and neonates	64	0	27			11[b]	Weintraub *et al.* 1983

[a] NT, nontypable.
[b] One isolate (9%) was type IV.

period (Table 3).

DISCUSSION

In America, neonatal meningitis and septicemia due to GBS are so prevalent that prophylactic chemotherapy or immunization is being considered (Baker, 1988; Tuppurainen and Hallman, 1989; Wanger, 1992). GBS was the 5th most frequently isolated etiologic agent of bacterial meningitis in 1986 and was the most frequent in the age group of less than one month (Wenger *et al.* 1990). The rates of early onset disease per 1000 live births were 1.09 in a cohort study in Atlanta and even 1.9−5.4 in hospital series (Schuchat *et al.* 1990). The National Institute of Allergy and Infectious Disease reported rates of 2−3/1000 live births (1983).

In Korea, an accurate rate of GBS neonatal infection is not known, but laboratory data (Nahm, 1992) suggest much lesser prevalence. A much lower incidence of neonatal infections was reported in Israel (Weintraub *et al.* 1983), United Kingdom (Mayon-White, 1985), Italy (Visconti *et al.* 1985) and Sweden (Sjoeberg *et al.* 1990). In Japan, the rate was also reported to be low (Iimura, 1979). Takazawa and Tomizawa (1991) reported that only 5 of the 238 GBS strains were isolated from blood and spinal fluid during 1985 to 1989.

GBS carried by pregnant women has been proven to be the source of infection of early onset neonatal disease (Ferrieri *et al.* 1977; Dillon *et al.* 1987). The carriage rates of American women were reported from 18% to 41% depending on races (Anthony *et al.* 1978). In Sweden, an increased annual incidence from 0.1 to around 0.5/1000 live births and increased colonization, from 16% in the late 1970s to 30% in the later period, were reported (Sjoeberg *et al.* 1990). In this study, an increase of proportion of GBS among the hemolytic streptococci was noted compared to the previous one (Choi *et al.* 1981). It is more difficult to detect GBS than other β-hemolytic streptococci, because of its characteristic incomplete hemolysis. But the recent increase can not be explained by the improved detection alone. For example, GBS became more often isolated from blood cultures at this hospital. Although the increased isolation from blood was mostly from adult patients with various underlying diseases, some were from neonates.

In Israel, neonatal sepsis was estimated at 1 in 12,500 newborns during the period of 1977 to 1982 (Weintraub *et al.* 1983). The mother to infant transmission rate of 66% and nosocomial infection rate of 6.6% were similar to those in western countries. Therefore, the low incidence of GBS neonatal sepsis in Israel was explained by the low vaginal colonization rate of 2.8% compared with 4.6% to 36% in western countries. We consider the GBS carriage rate of pregnant Korean women to be very low (unpublished data) and this may partly explain the rarity of neonatal GBS infections. Other factor(s) may also influence the incidence of neonatal infection. The carriage rate of Chinese women in Hong Kong was 19.0% and the neonatal colonization rate was 19.6%, but the neonatal infection was rare, 0.58/1000 live births (Liang *et al.* 1986). Greater prevalence of GBS neonatal infection among infants born from black young mothers was considered to be due to socioeconomic factors, as could be seen in *Haemophilus influenzae* type b infection (Schuchat *et al.* 1990). Interestingly, *H. influenzae* neonatal infection is also less prevalent in Korea.

It was reported that 70% of strains isolated from blood and spinal fluid were serotype III, whereas overall proportion of this type was 32% (Wilkinson, 1973). Infants born from mothers carrying type III became carriers more often than those born from mothers carrying other types (Ancona *et al.* 1980). In our study, although a definite conclusion could not be drawn as the number of GBS isolates was not large, it was apparent that the proportion of type III was not significantly different from those of pregnant women and hospital personnel in America (Table 3). Therefore, the rarity of neonatal infection can not be due to the rarity of type III. In Japan, Murai *et al.* (1990) and Sugiyama *et al.* (1990) reported a gradual increase of serotype JM9 (M9) isolates, but this serotype was not found among our isolates, possibly indicating a regional difference of the distribution.

GBS may spread nosocomially (Paredes *et*

al. 1977; Liang *et al.* 1986), and some of the late onset neonatal infection may be due to nosocomially acquired strains (Schuchat *et al.* 1990). GBS also causes various infections in adults. GBS is a significant urinary pathogen in nonpregnant women and it was reported that its presence signals a need for screening for urinary tract abnormalities (Munoz *et al.* 1992). It also causes meningitis and other infections (Aharoni *et al.* 1990; Bernatchez and Tourangeau, 1992). In our study, GBS were most often isolated from genital and urine specimens of women, but it was also isolated from other infections. Most of the patients had various underlying diseases. It is unclear whether the infections were caused by GBS carried by the patients or transmitted from other sources. The appearance of a large number of type Ib/c and the disappearance of II/c, during the second period of our study is statistically significant and may suggest a nosocomial spread of GBS. GBS were reported more resistant to antimicrobial agents than other β-hemolytic streptococci (Berkowitz *et al.* 1990; Buu-Hoi *et al.* 1990). This factor may play some role for the nosocomial spread of the organism.

In conclusion, less prevalence of the early onset neonatal GBS infection in Korea is not due to the rarity of more virulent serotype III, but is probably due to the low carriage rate of GBS by the pregnant women. The recent increase of GBS isolation from various clinical materials may suggest a possible increase of neonatal infection in the future.

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