Invasive group B streptococcal infections in adults, France (2007–2010)

A. Tazi[1,2,3,4], P. C. Morand[1,2,3,4], H. Réglier-Poupet[1,3,4], N. Dmytruk[1,5], A. Billoët[1], D. Antona[6], P. Trieu-Cuot[5,7] and C. Poyart[1,2,3,4]

1) *Centre National de Référence des Streptocoques (CNR-Strep), Groupe Hospitalier Cochin-Hôtel Dieu-Broca Assistance Publique Hôpitaux de Paris,* 2) *Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine,* 3) *INSERM 1016, Institut Cochin,* 4) *CNRS, UMR8104,* 5) *Laboratoire associé au CNR-Strep, Institut Pasteur,* 6) *Département des maladies infectieuses, Institut de Veille Sanitaire, St Maurice and* 7) *Unité de Biologie des Bactéries Pathogènes à Gram-positif-URA CNRS 2172, Institut Pasteur, Paris, France*

Abstract

Group B streptococcus (GBS) has emerged as an important cause of invasive infection in adults. Here, we report the clinical and microbiological characteristics of 401 non-redundant GBS strains causing adult invasive infections collected during a 4-year period (2007–2010). Bacteraemia without focus (43.4%) and bone and joint infections (18.7%) were the main clinical manifestations. The distribution of capsular polysaccharide (CPS) type showed that types Ia, III, and V accounted for 71.8% of all strains. Resistance to erythromycin increased from 20.2% in 2007 to 35.3% in 2010, and was mainly associated with CPS type V harbouring the *erm*(B) resistant determinant.

Keywords: Antibiotic resistance, capsular serotype, GBS, invasive infections, *Streptococcus agalactiae*

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Corresponding author: C. Poyart, Service de Bactériologie, Centre National de Référence des Streptocoques, Groupe Hospitalier Cochin-Hôtel Dieu-Broca, Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, 27 rue du Faubourg Saint Jacques, 75014 Paris, France
E-mail: claire.poyart@cch.aphp.fr

Group B streptococcus (GBS) has emerged as an important cause of invasive infection in adults [1–6]. We report here the clinical and microbiological characteristics of 401 non-redundant GBS strains causing adult invasive infections collected during a 4-year period (2007–2010). GBS strains were sent to the CNR-Strep, and epidemiological and clinical information was abstracted from questionnaires sent with the strain. A case of invasive disease was defined as the isolation of GBS in any sample obtained from a normally sterile site (e.g. blood, cerebrospinal fluid, joint, bone, synovial fluid, or pleural fluid) in a patient aged ≥18 years. Bacteraemia was considered to be without focus when no source of infection could be identified. All strains were identified as GBS on the basis of colony morphology, β-haemolysis on horse blood agar plates (bioMérieux, Marcy l'Etoile, France), Gram staining, and Lancefield grouping with type B antisera (Oxoid, Basingstoke, UK). Molecular capsular polysaccharide (CPS) typing was performed with a multiplex PCR assay, as previously described [7]. Susceptibility testing of antibiotics was performed according to CLSI recommendations. Detection of antibiotic resistance genes was performed with a multiplex PCR assay [8]. Statistical analysis was performed according to two-tailed Fischer's exact and χ^2-tests. A p-value of <0.05 was considered to be statistically significant.

A total of 401 cases of GBS adult invasive infections were analysed. The median age of the patients was 61 years (range, 18–103 years), and 51.9% were male (Table 1). GBS strains were isolated primarily from blood (81.5%), but also from joint or bone (15.9%), cerebrospinal fluid (4.9%), or other specimens (4.2%). The clinical characteristics of adult invasive GBS infections are shown in Table 1. Disease primarily presented as bacteraemia without focus, corresponding to 43.4% of the cases, but was significantly more frequent among the 18–39-year age group (65.6%; p <0.0001), among which 23 (54.8%) GBS diseases were pregnancy-related. Bone and joint infections constituted the second most common GBS infection (75/401, 18.7%); the median age of the patients was 57.7 years (range, 21–87 years), and 57.3% (43/75) were male. Skin and soft tissue infections occurred in 48 cases (12%), with a higher incidence in patients aged ≥65 years (14.1%) than in patients aged 18–39 years (4.6%; p 0.003). Erysipelas accounted for 31% of these infections; the median age of the patients was 71 years (range, 43–88 years), and 51.7% were males. Endocarditis was diagnosed in 42 (10.5%) patients according to Duke's modified criteria [9]. The median age of the patients with endocarditis was 68.4 years (range, 34–87 years), and 52.4% were male. Meningitis accounted for 5.2% of the cases; the median age of the patients was 51 years (range, 26–82 years), and 43% were male (data not shown). Respiratory

TABLE 1. Characteristics of adults with invasive group B streptococcal infections (2007–2010)

Variable	No. of cases (%)			
	All, *n* = 401 (100)	18–39 years, *n* = 64 (16)	40–64 years, *n* = 125 (31.2)	≥65 years, *n* = 212 (52.8)
Male gender	208 (51.9)	22 (34.4)	75 (60)	111 (53.4)
Female gender	193 (48.1)	42 (65.6)	50 (40)	101 (47.6)
Age, median years	61	31	53	79
Clinical syndrome				
Bacteraemia without focus	174 (43.4)	42 (65.6)	39 (31.2)	93 (43.9)
Bone and joint infection	75 (18.7)	11 (17.2)	32 (25.6)	32 (15)
Skin and/or soft tissue infection	48 (12)	3 (4.6)	15 (12)	30 (14.1)
Endocarditis	42 (10.5)	1 (1.6)	15 (12)	26 (12.3)
Meningitis	21 (5.2)	6 (9.4)	10 (8)	5 (2.4)
Respiratory tract infection	16 (4)	1 (1.6)	4 (3.2)	11 (5.2)
Peritonitis	13 (3.2)	0 (0.0)	6 (4.8)	7 (3.3)
Urinary tract infection	12 (3)	0 (0.0)	4 (3.2)	8 (3.8)

tract infections (4%), peritonitis (3.2%) and urinary tract infections (3%) accounted for the remaining GBS diseases.

A CPS type was assigned to all strains except one, owing to a deletion in the *cps* locus, as previously described [7] (Table 2). The most prevalent CPS types were types III (25.7%), V (23.4%), and Ia (22.7%), which together accounted for 71.8% of cases (Table 2). CPS types Ib (10.5%), II (11.2%), IV (4.7%), VII (1%) and VI (0.5%) accounted for the remaining 27.9% of cases. Stratified by age, CPS type V was predominant in the 40–64-year and >65-year age groups, whereas CPS type III was predominant in the 18–39-year age group, most of these cases (23/64; 36%) being related to pregnancy (Table 2).

All strains were susceptible to penicillin, amoxycillin, cefotaxime, imipenem, rifampicin, and vancomycin, and displayed low-level resistance to gentamicin. Resistance to erythromycin increased during the study period, from 20% in 2007 to 35.3% in 2010 (p 0.0099). Globally, erythromycin resistance was detected in 31% (124/401) of all strains (Table 2), and was 4.6 times more likely to occur (p <0.0001) in CPS type V strains (48.4%) than in other CPS types (median, 11%; range, 5.6–13.7%). Clindamycin resistance was detected in 23% of the strains and, as observed for erythromycin resistance, CPS type V accounted for 53.7% of clindamycin-resistant strains (p <0.0001). A significant association of erythromycin resistance and skin and soft tissue infection (p 0.0009) or bone and join infection (p 0.027) was also observed(not shown).

Among the 124 erythromycin-resistant strains, 64.5% (80/124) were constitutively resistant to clindamycin [constitutive macrolide, lincosamide and streptogramin B resistance (cMLS)], 18.5% (23/124) showed an inducible clindamycin resistance phenotype [inducible macrolide, lincosamide and streptogramin B resistance (iMLS)], and 16.7% (21/124) showed a macrolide-resistant but clindamycin-susceptible and streptogramin B-susceptible (M) phenotype.

Genetic analysis of erythromycin and clindamycin resistance genes showed that all strains with the M phenotype contained *mef* only (21/124). Among the 80 strains with the cMLS phenotype, 67.5% (54/80) harboured *erm*(B) and 32.5% (26/80) *erm*(A). Among the 23 strains with the iMLS phenotype, *erm*(B) and *erm*(A) were detected in 4.3% (1/23) and 87% (20/23) of strains, respectively, and 8.7% (2/23) of strains tested negative for both erythromycin resistance genes (not shown). The *mef* gene was significantly associated

TABLE 2. Characterization of macrolide-resistant group B streptococcal strains according to capsular polysaccharide (CPS) type

CPS type	No. of strains (%)					
	Phenotypic pattern			Resistance gene		
		Ery^R	Ery^R Cli^R	*erm*(A)	*erm*(B)	*mef*(A)
Total	401 (100)	124 (31)	80 (23)	46 (37)	57 (46)	21 (17)
Ia	91 (22.7)	17 (13.7)	1 (1.2)	1 (2.1)	2 (3.5)	16 (76.2)
Ib	42 (10.5)	12 (9.6)	9 (11.2)	9 (19.6)	3 (5.3)	0 (0)
II	45 (11.2)	14 (11.3)	12 (15)	3 (6.5)	11 (19.3)	0 (0)
III	103 (25.7)	14 (11.3)	9 (11.2)	5 (10.8)	7 (12.3)	2 (9.5)
IV	19 (4.7)	7 (5.6)	6 (7.5)	5 (71.4)	1 (1.75)	1 (4.8)
V	94 (23.4)	60 (48.4)	43 (53.7)	23 (39.6)	33 (57.9)	2 (9.5)
VI	2 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
VII	4 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
NT	1 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

NT, non-typable.

with CPS type Ia (76.2%, 16/21) as compared with all other CPS types ($p < 0.0001$).

Seventy-nine per cent of the strains (320/401) were phenotypically resistant to tetracycline (MIC >8 mg/L). Among these strains, *tet*(M), *tet*(O) and tet(L) accounted for 93.75% (300/320), 5% (16/300), and 0.3% (1/320), respectively, and the search for *tet*(M), *tet*(O) *tet*(K) and *tet*(L) gave negative results for three strains (not shown). Interestingly, 14 strains that were phenotypically susceptible to tetracycline (MIC <8 mg/L) were *tet*(M)-positive.

In conclusion, this study provides the clinical and microbiological characteristics of GBS strains isolated from adult invasive infections in France. From these data, we show that: (i) GBS invasive infections in adults are more frequent among people ≥65 years of age, as described in other European and US surveys [1–6]; (ii) CPS types Ia, III and V accounted for 72% of all strains, a distribution similar to those observed in other countries [1–6]; (iii) resistance to erythromycin increased from 2007, reaching 35.24% in 2010, and was strongly associated with CPS type V; and (iv) the *mef* genotype was associated with CPS type Ia GBS. Continued surveillance of invasive GBS disease in adults and genetic characterization of isolated strains are necessary, as this might impact on strategies related to antibiotic use and vaccine design.

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Transparency Declaration

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Lactobacillus rhamnosus administration causes sepsis in a cardiosurgical patient—is the time right to revise probiotic safety guidelines?

P. Kochan[1,2], A. Chmielarczyk[1], L. Szymaniak[3], M. Brykczynski[4], K. Galant[3], A. Zych[4], K. Pakosz[1], S. Giedrys-Kalemba[3], E. Lenouvel[5] and P. B. Heczko[1,2]

1) Chair of Microbiology, Jagiellonian University Medical College in Cracow, 2) Polish Society for Probiotics and Prebiotics, Cracow, 3) Chair and Department of Microbiology and Immunology, 4) Department of Cardiac Surgery, Pomeranian Medical University in Szczecin, Szczecin and 5) School of Medicine, Jagiellonian University Medical College in Cracow, Cracow, Poland

Abstract

A 24-year-old female patient developed sepsis resulting from preoperative administration of probiotics following an aortic valve replacement. Blood cultures revealed the causative agent to be the probiotic *Lactobacillus rhamnosus*, which has recently been implicated as an emerging aetiology of infection in those taking probiotics. In the past few years, probiotic use in hospitals has increased greatly. However, there is growing global evidence that the use of probiotics in patients with organ failure, immunocompromised status and dysfunctional gut barrier mechanisms can cause infections. This and other reports show the importance of establishing generally recognized safety guidelines.