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Antimicrobial Susceptibilities and Clinical Sources of *Facklamia* Species

L. LACLAIRE AND R. FACKLAM*

Centers for Disease Control and Prevention, Atlanta, Georgia 30333

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***Facklamia* spp. are gram-positive cocci, arranged in short chains or diplos, and resemble viridans streptococci on 5% sheep blood agar. Eighteen strains representing four species of *Facklamia* were isolated from blood cultures, an abscess, bone, cerebrospinal fluid, gall bladder, vaginal swab, and one unknown source. Cultures were tested against 15 antimicrobial agents by using the broth microdilution MIC method. Reduced susceptibilities to the beta lactams, erythromycin, clindamycin, trimethoprim-sulfamethoxazole, and tetracycline were found. These results indicate that the susceptibilities of the *Facklamia* species are varied and that some strains have resistance patterns which may present difficulty in managing systemic infections in patients.**

Since the first description of a *Facklamia* species in 1997, four additional species of this genus have been described (2–5, 11). These species, *Facklamia hominis*, *Facklamia ignava*, *Facklamia sourekii*, and *Facklamia tabaciasalis*, are most often arranged in chains, whereas *Facklamia languida* is most often arranged in clusters with very little chaining. The identification of these bacteria is problematic since none of the rapid testing systems currently include them in their databases. In a previous study examining 120 strains of unidentified gram-positive cocci with phenotypic characteristics that eliminated them from the known genera of bacteria, such as *Aerococcus*, *Streptococcus*, *Enterococcus*, and *Lactococcus*, we identified 18 strains (21.6%) of bacteria as *Facklamia* species. These carbon dioxide-enhanced bacteria were included in a group of previously unidentified gram-positive cocci since they had an unusual combination of positive reactions that included only leucine aminopeptidase, L-pyrrolidonyl-B-naphthylamide, and growth in 6.5% sodium chloride for genus identification (8). The purpose of this study was to further the knowledge of the clinical syndromes caused by *Facklamia* species and to report on the antimicrobial susceptibility of these strains.

MATERIALS AND METHODS

The strains tested were taken from the culture collection of the *Streptococcus* laboratory at the Centers for Disease Control and Prevention. The majority of cultures were submitted to the *Streptococcus* laboratory for identification from various state health departments throughout the United States (Table 1). Strains were identified according to procedures previously described (10). Based on 10 tests used to identify catalase-negative, gram-positive coccal genera, four genera have similar phenotypic profiles for genus identification by conventional tests: *Alloiococcus otiditis*, *Ignavigranum ruoffiae*, *Dolosigranulum pigrum*, and *Facklamia* species (8, 10). Members of genus *Alloiococcus* differ from the *Ignavigranum*, *Dolosigranulum*, and *Facklamia* species by their aerobic nature (12). The majority of *Dolosigranulum* cultures are positive for esculin hydrolysis, while *Ignavigranum* and *Facklamia* species do not hydrolyze esculin. Specific identification has been published previously (10).

MICs were determined by using the methods described by the National Committee for Clinical Laboratory Standards (NCCLS) (13). The following 15 antimicrobial agents and concentration ranges were tested in customized panels (PML Microbiologicals, Wilsonville, Oreg.) by using the microdilution method in Mueller-Hinton broth supplemented with 3% lysed horse blood: penicillin, 0.03 to 16.0 μg/ml; amoxicillin, 0.03 to 8.0 μg/ml; cefotaxime, 0.06 to 16.0 μg/ml; cefuroxime, 0.12 to 32 μg/ml; erythromycin, 0.06 to 16 μg/ml; trimethoprim-sulfamethoxazole, 0.12/2.38 to 8/152 μg/ml; clindamycin, 0.06 to 2.0 μg/ml; chloramphenicol, 2.0 to 16.0 μg/ml; levofloxacin, 0.5 to 16 μg/ml; trovafloxcin, 0.25 to 8.0 μg/ml; meropenem, 0.06 to 2.0 μg/ml; vancomycin, 0.12 to 2.0 μg/ml; tetracycline, 1.0 to 8.0 μg/ml; and quinupristin-dalfopristin and rifampin only at dilutions 1.0 μg/ml and 4.0 μg/ml, respectively. The panels were incubated under 5% carbon dioxide for 22 to 24 h. The *Facklamia* species are facultatively anaerobic and grow best in an atmosphere of increased carbon dioxide. In most cases, the growth from a single 15- by 100-mm Trypticase soy-5% sheep blood agar plate was required to prepare a 0.5 McFarland density of the bacteria. Panels were read visually with the aid of a mirror panel viewer.

RESULTS AND DISCUSSION

Since it is likely that *Facklamia* species were previously identified as viridans streptococci, and were therefore probably included in previous studies of infections and antimicrobial susceptibility of viridans streptococci, it is of interest to note whether the clinical sources and antimicrobial susceptibility patterns of the *Facklamia* species differ from those of the viridans streptococci. Our studies seem to indicate that the types of infections caused by *Facklamia* species are similar to those caused by viridans streptococci and that the antimicrobial susceptibilities may also be similar; however, some differences are noted.

Of the 18 human isolates of the *Facklamia* species, 12 of the strains were isolated from blood cultures. The sources and age of the patients indicate that the *Facklamia* species are opportunistic pathogens, similar to the viridans streptococci. Only one nonsterile-source isolate from a vaginal swab was examined. The other five isolates were from an abscess, bone, cerebrospinal fluid, gall bladder, and an unknown source. In the original description of *F. hominis*, the authors described the identification of six isolates of this bacterium (2). Four of the six isolates were identified from female patients; the gender of the patients from whom the other two strains were isolated was not given (1). Of the 18 *Facklamia* cultures, the gender of 14 of the patients from whom these cultures were taken was provided: 13 of the 14 cultures were from female patients (Table 1). The fact that three of the six original strains were isolated from vaginal swabs may indicate that the female genitourinary tract is the natural habitat of the *Facklamia* species. This speculation demonstrates a difference between *Facklamia* and viridans streptococci: the natural habitat of the majority of viridans streptococci is the oropharynx (9).

The interpretation of resistant, intermediate, and susceptible was determined by using the NCCLS guidelines for *Streptococcus* species other than *Streptococcus pneumoniae* (13) for

* Corresponding author. Mailing address: Centers for Disease Control and Prevention, Mailstop C-02, Atlanta, GA 30333. Phone: (404) 639-1379. Fax: (404) 639-3123. E-mail: rrf2ecdc.gov.

TABLE 1. Source, clinical diagnosis, and demographic information on 19 strains of *Facklamia* species

Species	CDC no. of strain	Source	Clinical diagnosis	Sex	Age (years)	Locale
F. hominis	ss-1463	Boil	Boil	NA[a]	NA	France
	1811-77	Vagina	Vaginitis	F	8	Rhode Island
	660-79	Blood	Leukemia	M	7	Pennsylvania
	2063-80	Blood	Wound infection	F	37	California
F. ignava	164-97	Blood	NA	F	83	Canada
	1440-97	Blood	Sepsis	F	87	North Carolina
	3493-97	Blood	NA	F	1	Canada
	2160-97	Bone	NA	F	76	Canada
	246-98	Blood	NA	F	48	Canada
F. languida	1664-95	Blood	NA	F	74	Canada
	1144-97	Blood	NA	F	6	Ohio
	1502-86	Blood	Cardiac arrest	F	62	Missouri
	763-92	Blood	NA	F	86	Canada
	5940-99	Gall bladder	NA	F	NA	Ohio
	ss-1530	CSF[b]	NA	F	40	Sweden
F. sourekii	ss-1533	Blood	NA	NA	NA	Sweden
	1665-95	Blood	NA	NA	NA	Canada
	ss-1019	Unknown	NA	NA	NA	France
F. tabacinasalis	ss-1566	Tobacco	NA	NA	NA	Sweden

[a] NA, not available.
[b] CSF, cerebrospinal fluid.

penicillin, amoxicillin, cefotaxime, erythromycin, clindamycin, chloramphenicol, levofloxacin, trovofloxacin, and tetracyline. The interpretive standards for *S. pneumoniae* were used for presumptive susceptibility values for cefuroxime, trimethoprim-sulfamethoxazole, vancomycin, and rifampin. No interpretive standards are available for meropenem and quinupristin-dalfopristin.

The cumulative MIC data for all the *Facklamia* species are listed in Table 2. Seventeen percent of the strains are intermediate to penicillin, 44% are resistant to cefotaxime, and 33% are presumptively resistant to cefuroxime. There are no breakpoints for meropenem at this time. Twenty-two percent of the strains are resistant to erythromycin, and 33% are resistant to clindamycin. Twenty-eight percent of the strains are presumptively resistant to trimethoprim-sulfamethoxazole, and 17% of the strains are presumptively resistant to rifampin. These numbers are not appreciably different from those of more recent studies of viridans streptococci (1, 6, 7).

There are differences in susceptibilities among the *Facklamia* species to various antimicrobials. Two of five *F. ignava* and one of four *F. hominis* isolates were intermediate to penicillin while all of the *F. sourekii* and *F. languida* isolates were susceptible. While none of the strains were resistant to amoxicillin, several strains were resistant to cefotaxime and were presumptively resistant to cefuroxime. One *F. ignava*, one *F. sourekii*, and all six *F. languida* isolates were resistant to cefotaxime while one *F. hominis* and five of the six *F. languida* isolates were presumptively resistant to cefuroxime. More strains of *F. ignava* (three of five) than *F. languida* (two of six) were resistant to erythromycin. Strains of the other two species were susceptible to erythromycin. However, this was not true for the susceptibilities of *F. ignava* (one of five) and *F. languida* (five of six strains), which were resistant to clindamycin. Presumptive resistance, either full or intermediate, to trimethoprim-sulfamethoxazole was present in most strains. None of the isolates were resistant to chloramphenicol, levofloxacin, trovafloxacin, or vancomycin. Three of the four strains of *F. hominis* were presumptively resistant to rifampin while all strains of the other three species were susceptible. Resistance to tetracycline was present in three of the four species (Table 2).

Although the number of strains of the *Facklamia* species tested are limited, there appear to be appreciable differences in antimicrobial susceptibility between species. This finding does not differ much from that among the viridans streptococci. However, *Streptococcus mitis* is more likely to be resistant to penicillin (6, 14), and *Streptococcus oralis* and *S. mitis* are more resistant to the macrolides (15). It is noteworthy that the majority of isolates are from female patients. This observation merits additional attention. There is a need for the manufacturers of commercial rapid identification kits for gram-positive cocci to include *Facklamia* species in their databases in order for additional studies to proceed.

TABLE 2. MICs of 15 antimicrobial agents against all *Facklamia* species

Drug (range)	No. of strains for which MIC of antimicrobial agent is (μg/ml):										
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	≥32
Penicillin (0.03–16.0)	6	6	3	*1*	*2*	0	0	0	0	0	
Amoxicillin (0.03–8.0)	13	4	0	1	0	0	0	0	0		
Cefotaxime (0.06–8.0)		3	1	1	3	*2*	**3**	**5**	0		
Cefuoxime (0.12–32.0)			3	3	0	*6*	**3**	**2**	**1**	0	0
Meropenem (0.06–2.0)		6	0	0	1	6	5				
Erythromycin (0.06–16.0)		7	5	1	**1**	0	0	**1**	0	**3**	
Clindamycin (0.06–2.0)		5	1	5	1	2	4				
Trimethoprim-sulfamethoxazole (0.12–8.0)			4	3	1	*4*	*1*	**1**	**4**		
Chloramphenicol (2.0–16.0)							9	8	**1**	0	
Levofloxacin (0.5–16.0)					12	4	1	**1**	0	0	
Trovafloxacin (0.25–8.0)				17	1	0	0	0	0		
Vancomycin (0.12–2.0)			6	7	4	1	0				
Rifampin (1.0–4.0)						15	0	**3**			
Tetracycline (1.0–8.0)						15	0	*3*	0		
Quinupristin-dalfopristin (1.0–4.0)						16	0	**2**			

[a] Italic values, intermediate or presumptive intermediate; boldface values, resistant or presumptive resistant according to the NCCLS interpretive values for streptococci other than *S. pneumoniae* or interpretive values for *S. pneumoniae* (presumptive).

REFERENCES

1. **Alcaide, F., J. Linares, R. Pallares, J. Carratala, M. A. Benitez, F. Gudiol, and R. Martin.** 1995. In vitro activities of 22 β-lactam antibiotics against penicillin-resistant and penicillin-susceptible viridans group streptococci isolated from blood. Antimicrob. Agents Chemother. **39:**2243–2247.
2. **Collins, M. D., E. Falsen, J. Lemozy, E. Akervall, B. Sjoden, and P. A. Lawson.** 1997. Phenotypic and phylogenetic characterization of some *Globicatella*-like organisms from human sources: description of *Facklamia hominis* gen. nov., sp. nov. Int. J. Syst. Bacteriol. **43:**880–882.
3. **Collins, M. D., R. A. Hutson, E. Falsen, and B. Sjoden.** 1999. *Facklamia sourekii* sp. nov., isolated from human sources. Int. J. Syst. Bacteriol. **49:**635–638.
4. **Collins, M. D., R. A. Hutson, E. Falsen, and B. Sjoden.** 1999. *Facklamia tabacinasalis* sp. nov., from powdered tobacco. Int. J. Syst. Bacteriol. **49:** 1247–1250.
5. **Collins, M. D., P. A. Lawson, R. Monasterio, E. Falsen, B. Sjoden, and R. R. Facklam.** 1998. *Facklamia ignava* sp. nov., isolated from clinical specimens. J. Clin. Microbiol. **36:**2146–2148.
6. **De Azavedo, J. C. S., L. Trpeski, S. Pong-Porter, S. Matsumura, The Canadian Bacterial Surveillance Network, and D. E. Low.** 1999. In vitro activities of fluoroquinolones against antibiotic-resistant blood culture isolates of viridans group streptococci across Canada. Antimicrob. Agents Chemother. **43:**2299–2301.
7. **Doern, G. V. M., J. Ferraro, A. B. Brueggemann, and K. L. Ruoff.** 1996. Emergence of high rates of antimicrobial resistance among viridans group streptococci in the United States. Antimicrob. Agents Chemother. **40:**891–894.
8. **Facklam, R., and J. A. Elliott.** 1995. Identification, classification, and clinical relevance of catalase-negative, gram-positive cocci, excluding the streptococci and enterococci. Clin. Microbiol. Rev. **8:**479–495.
9. **Frandsen, E. V. G., V. Pedrazzoli, and M. Kilian.** 1991. Ecology of viridans streptococci in the oral cavity and pharynx. Oral Microbiol. Immunol. **6:**129–133.
10. **LaClaire, L., and R. Facklam.** 2000. Comparison of three commercial rapid identification systems for the unusual gram-positive cocci *Dolosigranulum pigrum*, *Ignavigranum ruoffiae*, and *Facklamia* species. J. Clin. Microbiol. **38:**2037–2042.
11. **Lawson, P. A., M. D. Collins, E. Falsen, B. Sjoden, and R. R. Facklam.** 1999. *Facklamia languida* sp. nov., isolated from clinical human specimens. J. Clin. Microbiol. **37:**1161–1164.
12. **Miller, P. H., R. R. Facklam, and J. M. Miller.** 1996. Atmospheric growth requirements for *Alloiococcus* species and related gram-positive cocci. J. Clin. Microbiol. **34:**1027–1028.
13. **National Committee for Clinical Laboratory Standards.** 1998. Performance standards for antimicrobial susceptibility testing, vol. 19. M100-S9. National Committee for Clinical Laboratory Standards, Wayne, Pa.
14. **Pottumarthy, S., and A. J. Morris.** 1998. Detection of decreased penicillin susceptibility in viridans group of streptococci. Pathology **30:**188–191.
15. **Teng, L. J., P. R. Hsueh, Y. C. Chen, S. W. Ho, and K. T. Luh.** 1998. Antimicrobial susceptibility of viridans group streptococci in Taiwan with an emphasis on the high rates of resistance to penicillin and macrolides in *Streptococcus oralis*. J. Antimicrob. Chemother. **41:**621–627.