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LETTER TO THE EDITOR

High Prevalence of Heterogeneously Glycopeptide-Intermediate Coagulase-Negative Staphylococci in Sternal Wounds

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The emergence of heterogeneously glycopeptide-intermediate staphylococci (hGIS) has been linked to increasing therapeutic difficulties in sternal wound infections caused by methicillin-resistant *Staphylococcus aureus* (1, 2). Staphylococci with the hGIS phenotype appear susceptible to vancomycin in routine susceptibility testing, but a small subset of the population has decreased susceptibility. This has been proposed to be a precursor state to intermediate vancomycin resistance (3). In Sweden, coagulase-negative staphylococci (CoNS) are the staphylococci most commonly causing sternal wound infections after cardiac surgery (4). The hGIS phenotype is not well studied for CoNS, although a few studies have indicated their relevance (5, 6). High rates (77.9%) of *Staphylococcus epidermidis* isolates displaying the hGIS phenotype have been reported for isolates from patients with prosthetic joint infections at Swedish hospitals (7), and there is a need to investigate the prevalence and clinical significance of hGIS among CoNS in other types of infections.

CoNS were isolated from 60 out of 97 patients with revision surgery at the thoracic surgery unit at the University Hospital in Linköping, Sweden, between 2011 and 2014. Twenty-nine unique isolates from 20 patients were randomly selected and retrospectively evaluated. The isolates were tested for antimicrobial susceptibility with disc diffusion or Etest, *mecA* or *mecC* genotype with real-time PCR, species with matrix-assisted laser desorption–ionization time of flight (MALDI-TOF) mass spectrometry, and hGIS status with the population analysis profile-area under the curve (PAP-AUC) method. Associations between investigated parameters were tested using Fisher's exact test.

Phenotype and genotype prevalence data are presented in Table 1. No isolate was linezolid or daptomycin resistant, suggesting their potential therapeutic usefulness, although daptomycin resistance in *S. aureus* has been observed to emerge *in vivo* without drug exposure (8). The hGIS phenotype was detected in 21 (72%) isolates and among 15 (75%) of the patients. Although the hGIS phenotype among CoNS has been associated with a higher prevalence of multidrug resistance (MDR) and methicillin resistance (7), neither MDR, methicillin resistance, nor *mecA* was significantly associated with hGIS in the data collected in this study (Table 1). The isolates were *S. epidermidis* ($n = 26$), *Staphylococcus capitis* ($n = 2$), and *Staphylococcus hominis* ($n = 1$). None of the *S. capitis* or *S. hominis* isolates were determined to be hGIS. The vancomycin MIC for 93% of the isolates was 2.0 mg/liter, and none of the isolates were determined to be vancomycin resistant; however, single colonies among nine hGIS isolates were observed to grow on agar with a vancomycin concentration of 32 mg/liter or higher (up to 128 mg/liter). After isolation and reculturing of bacteria from these colonies, the MIC values for four isolates were higher (up to 8 mg/liter) than those for the main population.

TABLE 1 Prevalence of resistance phenotypes and genotypes among coagulase-negative staphylococci[a]

Antibiotic or gene	No. (%) of resistant isolates		
	hGIS ($n = 21$)[b]	Non-hGIS ($n = 8$)	Total (%) ($n = 29$)
Cefoxitin	15 (71)	6 (75)	21 (72)
Erythromycin	12 (57)	5 (63)	17 (59)
Clindamycin	11 (52)	5 (63)	16 (55)
Fusidic acid	10 (48)	1 (13)	11 (38)
Tobramycin	13 (62)	6 (75)	19 (66)
Gentamicin	13 (62)	4 (50)	17 (59)
Norfloxacin	16 (76)	5 (63)	21 (72)
Moxifloxacin	5 (24)	2 (25)	7 (24)
Rifampin	2 (10)	3 (38)	5 (17)
Linezolid	0	0	0
Daptomycin	0	0	0
MDR[c]	16 (76)	6 (75)	22 (76)
mecA	16 (76)	5 (63)	21 (72)
mecC	0	0	0

[a] Resistance breakpoints were used as defined by the European Committee for Antimicrobial Susceptibility Testing (EUCAST).
[b] hGIS, heterogeneously glycopeptide-intermediate staphylococci.
[c] MDR, multidrug resistant. Isolates were considered multidrug resistant if they were resistant to at least three different classes of antibiotics.

In this study, we observed a high prevalence of hGIS and MDR among CoNS isolates from sternal wounds together with a tentative increase in MICs for colonies exposed to growth media containing vancomycin for a subset of isolates. This emphasizes the need to further investigate the prevalence of hGIS among CoNS and the risk for selection of these organisms with suboptimal dosing. To avoid the overuse of vancomycin and thus the potential of promoting vancomycin resistance, the possibility of using other antimicrobials for treatment of sternal wound infections caused by staphylococci should be considered.

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