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Understanding staphylococcal pathogenesis and evolution

Low proportion of mupirocin resistance in *S. aureus* isolates collected from four Belgian nation-wide surveillances between 2005 and 2014

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OBJECTIVES:

Mupirocin is a topical antimicrobial that has been widely used for decolonisation strategies of *Staphylococcus aureus*. Resistance to mupirocin were rapidly reported reducing the effectiveness of eradication regimens. Two categories of resistance to mupirocin are described; low level resistance (MLLR) (MIC 2-128 mg/l), resulting of independent spontaneous mutation events in the gene encoding isoleucyl-tRNA synthetase (*ileS*), and high level resistance (MHLR) (MIC ≥ 256 mg/l) acquired by a plasmid-encoded *mupA* gene or by a novelty described *mupB* gene. The aim of the study was to determine the prevalence of mupirocin resistance and to explore resistance mechanisms among a large collection of *S. aureus* isolates (n = 1669).

METHODS:

A total of 1136 MRSA isolates and 533 MSSA isolates, collected from four nationwide surveillances conducted between 2005 and 2014 (n=100-116 Belgian hospitals), were analysed for their resistance to mupirocin. Identification and oxacillin resistance were confirmed by PCR. Antimicrobial susceptibility testing was realised by broth microdilution or agar dilution method. MHLR was confirmed by E-Test. A new multiplex PCR was performed for the detection of the *mupA*/*mupB* genes involved in MHLR. MLLR was further analysed by sequencing a fragment of the *ileS* gene. The genetic relatedness of the strains was determined by *Spa*-typing.

RESULTS:

A total of 59 MRSA isolates (5.2 %) were resistant to mupirocin as characterised by a MIC > 1 mg/L. Among these, 37 isolates (3.3 %) presented a high level resistance and harboured the *mupA* gene. The *mupB* gene was not detected in any of the strains. Twenty-two (1.9 %) MRSA isolates were classified as low-level resistant. The majority of the MLLR isolates harboured the V588F point mutation in the isoleucyl-tRNA synthetase (n=21, 1.8 %); only one strain (0.1 %) presented the V631F point mutation. Resistance to mupirocin in MSSA strains was 0.9 % (n=5), with 4 strains (0.8%) classified as MHLR and harbouring the *mupA* gene. The V588F point mutation was detected in the MLLR MSSA strain. All but two mupirocin resistant *S. aureus* strains belonged to three major *spa* types or closely related t008 (n = 25), t038 (n = 24), t002 (n = 9) corresponding to major epidemic MRSA genotypes found in Belgian hospitals.

CONCLUSION:

This first Belgian nationwide 10-year surveillance shows a low prevalence of mupirocin resistance among MRSA and MSSA circulating in hospitals. Resistance in *S. aureus* was mainly mediated by the presence of *mupA* gene (64.1%) and the V588F point mutation in *ileS* gene (35.9%). Mupirocin resistant strains belonged to major epidemic clones found in Belgium, highlighting the importance of monitoring resistance to topical agents used in decolonisation programs.