Abstract

Glycopeptides are the so-called last-resort antibiotics in clinical practice used to treat heavier, predominantly nosocomial infections caused by multi-resistant coagulase-negative staphylococci. The origin and genetic basis of resistance to glycopeptide antibiotics has not yet been elucidated within coagulase-negative staphylococci. Research on *Staphylococcus aureus* has shown, that intermediate resistance to glycopeptide antibiotics is associated with the presence of one or more mutations, rather than being conditioned by the support of a particular genetic element, such as in enterococci.

By using various types of *in vitro* resistant mutant selection, we were able to obtain isogenic pairs of glycopeptide sensitive and resistant strains of *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*. By sequencing the genomes of these pairs, one nucleotide polymorphisms were identified and predominantly found in metabolic and cell wall control systems. Phenotypic analysis did not reveal a direct association of glycopeptide resistance with increased biofilm formation.

In clinical practice, the cross-resistance of glycopeptides and other antibiotics is problematic. For the non-glycopeptide antibiotics imipenem and rifampicin, the incidence of cross-resistance with glycopeptide antibiotics in *S. aureus* has previously been described. Selection of resistant mutants by incubation in increasing concentrations of imipenem did not show cross-resistance to glycopeptides in coagulase-negative staphylococci. Conversely, in the development of glycopeptide resistance, the selection of cross-resistance to imipenem in *S. haemolyticus* has been confirmed. Incubation of coagulase-negative staphylococci strains with increasing concentrations of rifampicin resulted in selection of cross-resistance to teicoplanin, more than vancomycin.

Key words: coagulase-negative staphylococci, selection of resistant mutants, *S. epidermidis*, *S. haemolyticus*, glycopeptide antibiotics, resistance, imipenem, rifampicin, susceptibility testing, population analysis profile