Invasiivsed enterokokid ja vankomütsiin

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KM sektsiooni koosolek
Terviseamet

LQ kontrolltöö 2020, Blood Culture

- Kahjuks ei ole kultuur säilitatud laborites
- A Silenced vanA Gene Cluster on a Transferable Plasmid Caused an Outbreak of Vancomycin-Variable Enterococci (VVE)
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Unit for Infection Control, St. Olavs University Hospital, Trondheim, Norra

- We report an outbreak of vancomycin-variable vanA enterococci (VVE) able to escape phenotypic detection by current guidelines
- and demonstrate the molecular mechanisms for in vivo switching into vancomycin resistance and horizontal spread of the
- vanA cluster. Forty-eight vanA Enterococcus faecium isolates and one Enterococcus faecalis isolate were analyzed for clonality
- with pulsed-field gel electrophoresis (PFGE), and their vanA gene cluster compositions were assessed by PCR and whole-genome
- sequencing of six isolates. The susceptible VVE strains were cultivated in brain heart infusion broth containing vancomycin at 8
- g/ml for in vitro development of resistant VVE. The transcription profiles of susceptible VVE and their resistant revertants
- were assessed using quantitative reverse transcription-PCR. Plasmid content was analyzed with S1 nuclease PFGE and hybridizations.
- Conjugative transfer of vanA was assessed by filter mating. The only genetic difference between the vanA clusters of
- susceptible and resistant VVE was an ISL3-family element upstream of vanHAX, which silenced vanHAX gene transcription in
- susceptible VVE. Furthermore, the VVE had an insertion of IS1542 between orf2 and vanR that attenuated the expression of
- vanHAX. Growth of susceptible VVE occurred after 24 to 72 h of exposure to vancomycin due to excision of the ISL3-family element.
- The vanA gene cluster was located on a transferable broad-host-range plasmid also detected in outbreak isolates with different
- pulsotypes, including one E. faecalis isolate. Horizontally transferable silenced vanA able to escape detection and revert
- into resistance during vancomycin therapy represents a new challenge in the clinic. Genotypic testing of invasive vancomycinsusceptible
- enterococci by vanA-PCR is advise

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- The susceptible VVE strains were cultivated in brain heart infusion broth containing vancomycin at 8 mkg/ml for *in vitro* development of resistant VVE.
- The transcription profiles of susceptible VVE and their resistant revertants were assessed using quantitative reverse transcription-PCR. Plasmid content was analyzed with S1 nuclease PFGE and hybridizations.
- Conjugative transfer of vanA was assessed by filter mating. The only genetic difference between the vanA clusters of susceptible and resistant VVE was an **ISL3-family element** upstream of vanHAX, which silenced vanHAX gene transcription in susceptible VVE. Furthermore, the VVE had an **insertion of IS1542 between orf2 and vanR** that attenuated the expression of vanHAX.

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- **Genotypic testing of invasive vancomycin susceptible enterococci by vanA-PCR is advised**

EARS-Net 2020 Eesti andmed

- *Enterococcus faecalis* 93 tüve
- *Enterococcus faecium* 74 tüve
- VRE 4,1% *E. faecium* (3 tüve, arvatavasti fenotüüpiline resistentsus)

- Kas TA labor saaks testida mingi perioodi vältel invasiivseid enterokokke VRE geenide suhtes?
- Kas ainult *E. faecium*? Kas ainult vanA?

Vancomycin susceptibility testing in *E. faecalis* and *E. faecium,* EUCAST warning

- Several studies (Norwegian Reference Laboratory, Tromsö, Norway; The EUCAST Development Laboratory, Växjö, Sweden; Robert Koch Institute, Wernigerode, Germany) show that the use of MIC gradient tests with standard inoculum and incubation fail to detect glycopeptide resistance in low-level resistant enterococci (see posters 1754 and 1764, ECCMID 2019).
- Confirmation of suspected vancomycin resistance with gradient tests, can be significantly improved by the use of a **macro method (BHI-medium, McF 2.0 and 48 hours incubation**; see poster 1764, ECCMID 2019).
- Uncertain results should be confirmed with a molecular test for vanA and vanB

VRE algoritm

- Kas täiendame algoritmi?
- Nt: * Invasiivsete *E. faecium/E. faecalis?* tüvede isoleerimisel kaaluda genotüübi (vanA) määramist sõltumata *in vitro* vankomütsiini tundlikkusest, eriti kui raviks kasutatakse vankomütsiini
- Kas TA ref. laborina on valmist sellist teenust osutama ja millise perioodi vältel? Milline peaks olema saatekiri?

Infektsionistide arvamus

- Kas enterokokk-sepsise ravis on tagasilööke vankomütsiiniga ravides?
- Kas on kliiniline huvi sellise töö suhtes?
- Kui pikalt või kui mitme tüve testimist tasuks ette võtta?