

TITLE: CRISPR ELEMENTS AND THEIR ASSOCIATION WITH RESISTANCE AND VIRULENCE AMONG VRE (VANCOMYCIN-RESISTANT ENTROCOCCI) AND VSE (VANCOMYCIN-SUSCEPTIBLE ENTROCOCCI)

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ABSTRACT:

CRISPR (Clustered regularly interspaced short palindromic repeats) and Cas (CRISPR-associated) genes provide a prokaryotic acquired immune system against foreign genetic elements, such as phages and plasmids. Previous studies have suggested that the loss or absence of CRISPR may be related to increased virulence and resistance among enterococci. In the past few decades, enterococci have emerged as a pathogen involved in Healthcare-Associated Infections due to the indiscriminate use of antimicrobial agents along with their ability to acquire resistance and, to a less extent, virulence genes. Currently, VRE (vancomycin-resistant *Enterococcus*) constitutes a major healthcare problem around the world. Therefore, the aim of this study was to determine the virulence potential and resistance among 91 VRE and 89 VSE (vancomycin-susceptible *Enterococcus*) strains recovered from different origins to correlate with the presence/absence of CRISPR regions. The isolates were identified by PCR or MALDI-TOF: 95 *E. faecalis*, 77 *E. faecium*, 5 *E. gallinarum*, 1 *E. casseliflavus*, 1 *E. avium* and 1 *E. durans*. By disk-diffusion test, all VRE isolates were multidrug resistant (MDR) and 55 (62%) VSE were MDR. The highest resistance prevalences were observed for erythromycin (n=131; 72.8%) and fluoroquinolones (n=111; 61.6%). Among the 152 erythromycin-non susceptible isolates, 92 (60.3 %) had the *ermB* gene. All VRE isolates presented the *vanA* gene. The *gelE* gene was the most common virulence gene, detected in 79 (37.2%) isolates, followed by *esp* (n=77; 42.8%) and *asa1* (n=68; 37.8%) genes. There was no significant difference in the prevalence of virulence genes between VRE and VSE. The CRISPR3-Cas system was the most frequent (n=63; 35%), followed by CRISPR2 (n=44; 24.4%) and CRISPR1 (43; 23.9%). CRISPR regions were much more common in *E. faecalis* than in *E. faecium* and in VSE isolates than in VRE (p <0.01). Sixty (95%) of the 63 VSE. *faecalis*, but 11 (34.4%) of the 32 VRE. *faecalis* presented at least one CRISPR region (p<0.01); no difference was observed for *E. faecium*. Vancomycin (*vanA*) and aminoglycoside [*aph* (2'')-Ib and *aph*(2'')-Ic] resistance genes as well as the *esp* and *hyl* virulence genes were more frequently detected in isolates without CRISPR elements (p<0.05), suggesting that isolates with their compromised genomic defense may be more permissive to the entry of mobile genetic elements containing such genes.

Keywords: CRISPR, *Enterococcus* spp., VRE, antimicrobial resistance, virulence

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