TITLE: PRELIMINARY EVALUATION OF THE NEW ANTIMICROBIAL TEDIZOLID AGAINST A COLLECTION OF CLINICAL *S. aureus* AND *E. faecalis* STRAINS FROM BRAZIL

AUTHORS: DABUL, A. N. G. [1]; CAMARGO, I. L. B. C. [1].

INSTITUTION: 1. UNIVERSIDADE DE SÃO PAULO – IFSC, SÃO CARLOS – SP (Avenida João Dagnone, 1100. Jardim Santa Angelina. São Carlos – SP. CEP: 13563-120)

ABSTRACT

Tedizolid is an oxazolidinone antimicrobial recently approved by the Food and Drug Administration (FDA). It emerged as an alternative for the treatment of skin infections caused by *Staphylococcus aureus*, *Streptococcus* sp. and *Enterococcus faecalis.* The drug is administered orally or intravenously as tedizolid phosphate, a prodrug that turns into the active form after the action of endogenous phosphatases. It was reported as eight times more active *in vitro* than linezolid against *S. aureus*, two to four times against *E. faecalis* and 4 times against streptococci. The drug acts by inhibiting the protein synthesis, as it interacts to the 50 S ribosomal subunit and avoids the ligation of aminoacyl-tRNAs. It is supposed that the advantage of tedizolid over linezolid is due to extra binding sites on the 23 S ribosomal subunit. Also, because of that, the frequency of mutations is lower than that observed in the presence of linezolid. Some mutations were already found on lineages with reduced susceptibility to tedizolid, but the resistance mechanism is still to be solved.

Even though tedizolid is not approved for use in Brazil, we aimed to screen a collection of Brazilian clinical strains of *S. aureus* and *E. faecalis* determining their minimal inhibitory concentration (MIC) for this new drug. As it is water-insoluble, the broth microdilution experiment was performed as recommended by the manufacturer using 2% DMSO. The breakpoints for *S. aureus* are ≤ 0.5 mg/L for susceptibility, 1 mg/L for intermediate-resistance, and ≥ 2 mg/L for resistance. For *E. faecalis*, a strain is considered susceptible if the MIC is ≤ 0.5 mg/L. Following FDA recommendations, the quality control strains used were *S. aureus* ATCC29213 and *E. faecalis* ATCC29212, with acceptable MIC between 0.25 and 1 mg/L.

Only five out of 29 *S. aureus* tested were susceptible to tedizolid with MIC = 0.5 mg/L, near the limit to intermediate-resistance. The other 24 *S. aureus* strains had MIC = 1 mg/L, putting them on the status of intermediate-resistant. Regarding the *E. faecalis* strains tested, only one was susceptible to tedizolid (MIC = 0.5 mg/L), and the other 6 were resistant (MIC = 1 mg/L). This is a very preliminary study; however, it brings attention to a potential dissemination of resistance to tedizolid in the Brazilian scenario. This is an important fact to be known even before the introduction of the drug into clinical use, as it may not be so effective as expected.

Keywords: Tedizolid; *S. aureus*; *E. faecalis*

Development Agency: FAPESP