TITLE: MINIMUM BACTERICIDAL CONCENTRATION OF LINEZOLID AND LEVOFLOXACIN WITH ANTITUBERCULOSIS DRUGS COMBINATIONS AGAINST *Mycobacterium tuberculosis*

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ABSTRACT: Tuberculosis (TB) is an infectious disease that mainly affects the lungs and can spread to other organs and tissues of the body. The anti-TB therapy requires a drugs combination for at least six months. However, with the emergence of resistant strains to the classical anti-TB drugs as multidrug resistant (MDR) and extensively resistant (XDR), new drugs or combinations are required for the treatment. In these sense, other drugs have been studied, in recent years, to treat patients with resistant form of the disease. These drugs include levofloxacin (LVX), moxifloxacin, linezolid (LNZ), amoxicillin-clavulanate, clarithromycin, thioridazine, clofazimine and others. In this study it was evaluated the *in vitro* Minimum Bactericidal Concentration (MBC) of the combinations LNZ or LVX with rifampicina (RIF) plus isoniazida (INH) in *Mycobacterium tuberculosis* $H_{37}Rv$ (ATCC 27294) reference strain and four MDR *M. tuberculosis* clinical isolates, in which the three-dimensional checkerboard showed synergism by the drugs combinations. Initially, the inoculum count verification was prepared by using the same previously standardized three-dimensional checkerboard inoculum (1.5 X 10^6 CFU/mL) and carried out 1:500 dilution in sterile water. After, 100 µL of those inoculums were seeded on Middlebrook 7H11 supplemented with OADC enrichment. The plates were incubated for 21 days at 37 ºC for determining the antimicrobial agents-free growth control. For detecting the MBC, 100 µL of each drug alone and in combination dilutions, before MIC values in REDCA microplates were seeded on Middlebrook 7H11 supplemented with OADC enrichment. The colonies counting were visually performed for each dilution after 21 days at 37 ºC. Then, the number of colonies allowable for a 99.9 % MBC endpoint was determined for INH/RIF/LVX and INH/RIF/LNZ combinations. In the assays in which the combination showed bactericidal effect was observed the individual bactericidal effect of isoniazid (100%), rifampicin (66.6%), LNZ (100 %) and LVX (100 %). The INH/RIF/LVX and INH/RIF/LNZ combinations showed bactericidal effect in *M. tuberculosis* $H_{37}Rv$ and in 50% of the MDR isolates in both combinations. LNZ and LVX showed relevant potential use, mainly in resistant TB treatment as they were highly bactericidal in some MDR isolates, which MBC were very close to the MICs of drugs alone.

KEYWORDS: Tuberculosis, multidrug-resistant, bactericidal effect.