Objectives

Aminoglycosides (i.e. amikacin and kanamycin) are considered highly important classes of drugs in the treatment of multidrug resistant tuberculosis. Amikacin and kanamycin are both administered in the same dose and show a similar pharmacokinetic profile. However, in vitro drug susceptibility testing suggests a difference in mean inhibitory concentration (MIC) between amikacin and kanamycin. There are however limited studies comparing the MIC distribution of amikacin and kanamycin in both normally sensitive and multidrug resistant strains. Therefore, the objective of this study is to assess the possible difference in MIC between these drugs.

Methods

Using the 7H10 absolute concentration method, a concentration range of amikacin and kanamycin (0.25, 0.50, 1.00, 5.00 and 10.00 mg/L) was tested against 75 isolates of Mycobacterium tuberculosis that were either drug susceptible or (multi-)drug resistant. The plates were examined for mycobacterial growth after 6, 12 and 19 days. After this initial experiment we exposed a subset of the strains sensitive to 1 mg/L amikacin (n = 22), to kanamycin in the range of 1.25 – 2.5 – 5 mg/L. MICs were considered ‘different’ if strains differed in MIC by at least one dilution step. Differences in MIC between amikacin and kanamycin were assessed using a Wilcoxon Signed-Rank test. Differences in MIC distribution between normally sensitive- and multidrug resistant strains were tested using Mann-Whitney U-tests.

Results

At 1 mg/L, 65 strains (86.7%) were inhibited by amikacin and only 22 strains (29.3%) were inhibited by kanamycin (Z = -4.417, p = 0.000), as displayed in figure 1. Furthermore, no difference was observed between multidrug resistant and full susceptible strains in the MIC-distribution of both amikacin (Z = -0.399, p = 0.704) and kanamycin (Z = -0.703, p = 0.472). When comparing the strains individually there were only two strains with a higher MIC for amikacin. The majority had equal MICs (n = 56) and 17 strains were more susceptible to amikacin.

The majority of the 22 strains in the tested subset were susceptible to 2.5 mg/L kanamycin (n = 16). The MIC of amikacin was equal (n = 8) or lower than kanamycin (n = 14) in all cases.

Conclusion

The results of our study indicate that the MIC of amikacin is generally lower than that of kanamycin, using the absolute concentration method. As the efficacy of aminoglycosides is correlated with the $C_{\text{max}}$/MIC-ratio, this finding indicates the need for a further pharmacokinetic and pharmacodynamic evaluation.