IN VITRO ACTIVITY OF TEDIZOLID AND OMADACYCLINE IN NONTUBERCULOUS MYCOBACTERIA

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Background: Nontuberculous mycobacteria (NTM) are opportunistic pathogens found everywhere, especially in soil and water sources. Several challenges are encountered when establishing a treatment regimen for NTMs. These include the fact that they are often environmental contaminants and therefore not considered as true infectious agents, long treatment durations involving multiple drug regimens and side effects of existing drugs. In addition, the lack of a defined drug combination, dosage and duration of treatment basically limits the establishment of an appropriate treatment regimen from the outset. Antibiotic susceptibility testing is necessary to establish appropriate drug regimens against NTM infections. Our study aimed to investigate the effect of tedizolid and omadacycline on nontuberculous mycobacterial strains isolated from samples sent for routine examination to the Istanbul University Istanbul Faculty of Medicine Mycobacteriology laboratory and Istanbul Duzen Laboratory.

Methods: A total of 105 NTM isolates from various clinical specimens were analyzed in this study. MALDI-TOF MS analysis was performed with the NTM colonies being inactivated by heating and then zirconia / silica beads were used for mechanical disruption. Formic acid and acetonitrile were used for protein extraction. The NTM isolates included 60 rapid and 45 slow strains from 15 different species. In this study, we aimed to investigate the in vitro antimicrobial susceptibility of Omadacycline and Tedizolide in NTM strains by colorimetric microdilution method in accordance with CLSI M24 and M62 guidelines. The MIC range of 0.015-32 µg/ml was used for tedizolid and 0.003-64 µg/ml was used for omadacycline.

Table. MIC values of nontuberculous mycobacteria against tedizolid and omadacycline.

	Strains	N	MIC values against tedizolid (µg/mL)										
			≥32	16	8	4	2	1	0.5	0.25	0.125	0.06	0.03	≤0.015
RAPID GROWING NTM (60)	*M. fortuitum*	29		1		2	1	2	10	6	3	3	1	
	M. abscessus	21						1	5	7	4	2		2
	M. chelonae	3					1			2				
	M. peregrinium	3						1	1	1				
	M. elephantis	1								1				
	M. neoaurum	1									1			
	M. farcinogenes	1									1			
	M. tokaiense	1								1				
SLOW GROWING NTM (45)	*M. lentiflavum*	15						3	4	1	2	1	3	1
	M. gordonae	9								1	2	4	1	1
	M. avium	6	1					1		2		1		1
	M.intracellulare	4					1	2			1			
	M. chimera	4				1			1	2				
	M. simiae	4					2			2				
	M. kansasii	3							2	1				

	Strains	N	MIC values against omadacycline (µg/mL)										
			≥64	32	16	8	4	2	1	0.5	0.25	0.125	0.06	≤0.03
RAPID GROWING NTM (60)	*M. fortuitum*	29		3	1	1	3	1	5	2	5	7	1	
	M. abscessus	21		1			6	1	1	5	3	2	1	1
	M. chelonae	3		2	1									
	M. peregrinium	3									2	1		
	M. elephantis	1							1					
	M. neoaurum	1											1	
	M. farcinogenes	1							1					
	M. tokaiense	1						1						
SLOW GROWING NTM (45)	*M. lentiflavum*	15	3			1	1	4		2	1		1		2
	M. gordonae	9				1	1	1	2	1	2			1	
	M. avium	6	2										2		2
	M.intracellulare	4	2							1				1	
	M. chimera	4			1		1	1	1						
	M. simiae	4	2					1		1					
	M. kansasii	3	2						1						

Results: In this study, the antimicrobial susceptibilities of a total of 105 NTM strains, including 60 rapid-growing and 45 slow-growing strains, to tedizolid and omadacycline were investigated using the colorimetric microdilution method according to CLSI M24 and M62 guidelines. The MIC range of 0.015-32 µg/ml was used for tedizolid and 0.003-64 µg/ml for omadacycline. Based on literature information, the critical concentration values recommended for linezolid in CLSI M62 (≤8 µg/ml susceptible; 16 µg/ml intermediate; ≥32 µg/ml resistant) were used to evaluate the susceptibility of tedizolid. Only one rapid-growing strain, *M. fortuitum*, was found to be intermediate (1/29; 16 µg/ml) to tedizolid, and one slow-growing strain, *M. avium*, was found to be resistant (1/6; ≥32 µg/ml), while all other NTM strains were susceptible (103/105; ≤8 µg/ml). As there is no recommended critical concentration value for omadacycline, only the MIC values obtained were reported for this antibiotic. The obtained MIC values are shown in the attached table.

In conclusion, this study shows that tedizolid maight have a potent in vitro effect on NTM, but omadacycline may give variable results on NTM strains, suggesting that species-specific antimicrobial susceptibility testing is necessary to establish NTM treatment regimens.

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