

TITLE: PHENOTYPIC AND MOLECULAR CHARACTERIZATION OF CARBAPENEM-RESISTANT *PSEUDOMONAS AERUGINOSA* ISOLATED FROM PATIENTS WITH CYSTIC FIBROSIS

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ABSTRACT:

Chronic airway infection with *Pseudomonas aeruginosa* is a major cause of increased morbidity and mortality in patients with cystic fibrosis (CF). Multidrug-resistant (MDR) and carbapenem-resistant (CR) *P. aeruginosa* are significant threats globally but in CF patients MDR strains was reported only by 2013. Using phenotypic and molecular methods, the present study analyzed the antimicrobial resistance profile and molecular mechanisms of resistance to CR in *P. aeruginosa* recovered from CF patients assisted in two reference centers in Rio de Janeiro. The inclusion criterion adopted was CF patients chronically colonized with *P. aeruginosa* isolates showing resistance to at least one carbapenems (imipenem, meropenem and / or doripenem). All isolates from eight patients were included. A total of 179 *P. aeruginosa* obtained from 2010 to 2014 were analyzed by Disk Diffusion Test (DDT) for 12 antimicrobials. The highest resistance rates were 45.8%, 44.6%, 44.1%, 37.9% and 31.2% for imipenem (IPM), amikacin (AMI), gentamycin (GEN), aztreonam (ATM) and tobramycin (TOB), respectively. 51.9 % of isolates was classified as MDR and many of these isolates were obtained from adult patients. We highlighted the presence of 67 non-susceptible profiles. Resistance to GEN-AMI-TOB and resistance only to IMP were the most resistance profiles in adults and pediatric patients, respectively. The minimum inhibitory concentration (MIC) for imipenem, meropenem and doripenem was determined in 79 (44.1%) isolates resistant to at least one CR in DDT. Phenotypic tests to detect the presence of carbapenemases, such as, method of inhibition of carbapenemases (CIM), classic Hodge test (HT) and modified (MHT) were performed. In the MIC determination, the rates of non-susceptible isolates showed percentages of 92.4%, 54.4% and 48.1% for the IPM, MEN and DOR, respectively. Of the 79 isolates no-susceptible to at least one carbapenem, 10 were positive for MIC, 9 for MHT and only 4 for HT. This shows a good correlation between MIC and MHT. Using polymerase chain reaction (PCR) to detection of genes *blaIMP*, *blaVIM*, *blaKPC*, *blaSPM* and *blaNDM*, that encoding enzymes with carbapenemase activity most commonly found in our country, none isolate showed positive test. Epidemiological and resistance studies of *P. aeruginosa*, not-sensitive to carbapenems, are important for the success of chronic CF patients therapy.

KEYWORDS: *Pseudomonas aeruginosa*. Antimicrobial resistance. Cystic fibrosis. Carbapenemases.

DEVELOPMENT AGENCY: FAPERJ, CNPQ.