Correlation of Aminoglycoside Consumption and Amikacin- or Gentamicin-Resistant *Pseudomonas aeruginosa* in Long-Term Nationwide Analysis: Is Antibiotic Cycling an Effective Policy for Reducing Antimicrobial Resistance?

Young Ah Kim, M.D.¹, Yoon Soo Park, M.D.², Taemi Youk, M.D.³, Hyukmin Lee, M.D.⁴, and Kyungwon Lee, M.D.⁴

Department of Laboratory Medicine¹, National Health Insurance Service Ilsan Hospital, Goyang; Department of Internal Medicine², National Health Insurance Service Ilsan Hospital, Goyang; Department of Statistics³, Korea University, Seoul; Department of Laboratory Medicine and Research Institute of Bacterial Resistance⁴, Yonsei University College of Medicine, Seoul, Korea

Dear Editor,

Bacteria continuously develop, acquire, and spread numerous resistance patterns shortly after new antibiotics reach the market. Recently, carbapenem-resistant Enterobacteriaceae (CRE) and colistin-resistant *Acinetobacter baumannii* are emerging, which may lead us into the pre-antibiotic era. Pipelines of new antibiotics are becoming thinner and thinner across all therapeutic areas due to difficulties in innovation and challenges of regulatory hurdles. Under such a situation, maintaining antibiotic effectiveness in the long term requires not only innovation to develop new antibiotics, but also conservation of the effectiveness of existing antibiotics.

Antibiotic cycling or rotation consists of the sequential use of antibiotics not sharing a common mechanism of resistance, which could be considered as a strategy for conservation. Aminoglycoside consumption has continuously decreased during the recent five years [1]. The rates of amikacin or gentamicin-resistant *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter* spp. also showed declining trends according to data from the Korean Nationwide Surveillance of Antimicrobial Resistance (KON-NSAR) program [2]. The decreasing prevalence of amikacin and tobramycin resistance in some Gram-negative bacteria was associated with decreased consumption levels of these antimicrobial agents in a single-center study [3]. Aminoglycosides, except amikacin, can be considered as old drugs; however, they remain key roles in the treatment of infections. They also possess potent bactericidal activity against some CRE [4].

We investigated the correlation of aminoglycoside consumption and its resistance in *P. aeruginosa* using a nationwide surveillance and antibiotic prescription database to provide background data on the effectiveness of antibiotic cycling at the national level. Data on antibiotic usage in Korea from 2002 to 2013 were acquired from the database of the National Health Insurance Service-National Sample Cohort (NHIS-NSC), a population-based cohort established to provide public health researchers and policy makers with representative information regarding the utilization of health insurance and health examinations among citizens [5]. We also included prescription data for systemic an-
tobramycin decreased the resistance rate to both antimicrobials especially in *P. aeruginosa* in the 1980s [8, 9]. The study was performed during the period of introduction of amikacin and emergence of plasmid-mediated resistance to gentamicin. In Korea, Ku *et al* [3] reported that decreasing prevalence of amikacin and tobramycin resistance in *P. aeruginosa* isolates were associated with decreased consumption levels of these antimicrobials; but this correlation was not observed with gentamicin. This was discordant with our study and that of Lai *et al* [10], which showed good correlation with gentamicin and amikacin. The study by Ku *et al* [3] was a single center analysis from 2001 to 2011, and could be affected by patients’ characteristics, infection control policy, and microbiological factors.

The strength of this study is that it is based on nationwide surveillance and antibiotic prescription database spanning an extended period; thus the findings are representative of the population. This study suggests that less aminoglycoside consumption correlates with less resistance levels, hence the need for an antibiotic cycling strategy at the national level.

**Authors’ Disclosure of Potential Conflicts of Interest**

We have nothing to declare.

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