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Mini Review

A One Health Perspective on the Human-Pets *Pseudomonas aeruginosa* Transmission

Płókarz D*, Rypuła K

Department of Epizootiology and Clinic of Birds and Division of Infectious Diseases of Animals and Veterinary Administration, Exotic Animals, Wroclaw University of Environmental and Life Sciences, Wroclaw, Poland

ABSTRACT

In this review we considered the importance of *Pseudomonas aeruginosa* within the context of One Health Perspective. This pathogen is one of the most popular causative agents of opportunistic and nosocomial infections both in humans and animals. This bacterium poses problem in immunodeficiency humans and animals. Abundance of virulence factors, particular antibiotic resistance mechanisms and biofilm formation ability situates *Pseudomonas aeruginosa* in the number of the most clinically and epidemiologically important bacteria in the world. We explore the possibilities of human-pet transmission, the prevalence of *Pseudomonas aeruginosa* in dogs and cats, and the challenges facing veterinary medicine in terms of pathogen control.

Keywords: *Pseudomonas aeruginosa*; Antimicrobial resistance; Virulence genes; One health idea

INTRODUCTION

Pseudomonas aeruginosa is an opportunistic microorganism widely distributed in the environment of human and animal populations. Difficulties to treat this pathogen arise from intrinsic resistance to many classes of antimicrobials, a broad spectrum of resistance for anti-pseudomonal antibiotics and pathogenic factors, especially biofilm forming ability. Moreover, there is a well-defined non-clonal epidemic structure among the different animal strains or ecological niches. Dogs and cats are important reservoirs for *Pseudomonas aeruginosa* and can transmit bacteria to humans directly by saliva, aerosols, urine or feces, and close contact. Several case reports suggest household transmission of resistant strains between pets and their owners [1]. Despite considerable progress in antibiotic monitoring in recent years, animals still are an underestimated source of multidrug resistance strains. Increasing attention is now paid to antibiotic resistance genes. Presence of defined in literature genes can be markers for epidemiology of multidrug resistance strains. Exposure to *Pseudomonas aeruginosa* has the potential to lead to selection for resistance. *P. aeruginosa* is able to acquire resistance gene plasmids and transfer these genes by transduction and conjugation [2]. The genome of *P. aeruginosa* contains two elements: a core genome and an accessory genome. It should be noted that this genome has one of the highest percentages of predicted regulatory genes (8.4%) of all bacteria. Parts of the *P. aeruginosa* accessory genome are involved with changed virulence in *P. aeruginosa* clinical isolates [3]. It is not surprising that belongs to the Multi-Drug Resistant (MDR) ESKAPE pathogens, including *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Enterobacter spp*. [4]. Unfortunately, relationships among the determinants of virulence of *P. aeruginosa* have not yet been well evaluated in the population of animal isolates [5]. We must consider the exchange of genetic information between humans and animal strains of *Pseudomonas aeruginosa* and focus on implications.

LITERATURE REVIEW

Paz Zarza, et al. showed *Pseudomonas aeruginosa* as an important part of the natural oral cavity microbiota in canine [6]. In their research, *Pseudomonas aeruginosa* was found in 10.7% of the samples by saliva can occur during direct contact with their owners or others, which are obviously contact on the animal-human line. Furthermore, owners often neglect the hygiene of their animal's teeth, which can cause periodontal infection. It is significant not only because of the veterinary aspect, but also has

Correspondence to: Płókarz D, Division of Infectious Diseases of Animals and Veterinary Administration, Department of Epizootiology and Clinic of Birds and Exotic Animals, Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, Wroclaw, Poland, E-mail: daria.plokarz@upwr.edu.pl

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zoonotic importance [7]. Knowledge of the distribution of pathogens and their antibiotic resistance profile in pets is very important, especially for pets in close contact with people, which offers favorable conditions for the transmission between species of Multidrug Resistance Bacteria (MDR) [8].

Frequent recombination of chromosomal genes between different isolates of *P. aeruginosa* allows for genetic variability of these bacteria. The mechanisms of genetic exchange, incorporates transformation, transduction and conjugation. In this way, *P. aeruginosa* adapts to changing conditions by acquiring new genetic information. In genome sequences can be absent or rearranged from isolate to isolate [9] or the gene may not be found in these isolates [10]. So antibiotics genes may be exchanging too. Fluoroquinolones such as enrofloxacin, marbofloxacin, and pradofloxacin are routinely used in *Pseudomonas spp*. infection in veterinary medicine. The widespread use of enrofloxacin in small animal clinical practice has led to a continuous increase in resistant isolates of P. aeruginosa associated with dog infections. Alarming resistance of *P.aeruginosa* to enrofloxacin is described for many years in Europe, for example, in Greece (44%) [11], France (67%) [12] and Italy (43%) [13]. While there are available data and recommendations, we still commonly use fluoroquinolones in veterinary practice. Molecular background of antimicrobial resistance is confirmed in the dog population. Point mutations in the Quinolone Resistance-Determining Region (QRDR) are related to the increased fluoroquinolone resistance of *Pseudomonas aeruginosa*. Park, et al. showed antimicrobial susceptibility and fluoroquinolone resistance in strains of *P. aeruginosa* isolated from sick and healthy dogs [13]. Interestingly, a similar prevalence of *P. aeruginosa* occurs in the healthy population (16.7%) and in the infected population (17.7%). This situation realizes the presence of *P.aeruginosa* as a natural microbiome in dogs' population similar to human carriage. The authors not only analyzed phenotypic antibiotic susceptibility but also argued for a change in the genome. Point mutations in QRDR were confirmed by the gyrA and parC polymerase chain reaction and nucleotide sequencing analysis [13]. Particularly interesting are the results of studies based on carbapenem resistance analysis in dogs and cats. Indeed, in veterinary medicine routine bacteriology diagnosis in this field is usually not used. Despite lack of use, this group of antibiotics in veterinary medicine Gentilini, et al. [14]. showed a prevalence of carbapenem-resistant bacteria estimated at 6.3%. Six strains from this group (46% all resistance strains) were isolates of *Pseudomonas aeruginosa*. Interestingly, carbapenemase resistance genes were detected in all isolates except *P. aeruginosa*. But all of *P.aeruginosa* isolates possess mutations in OprD. Changes were situated in the gene causing a premature stop codon as an outgrowth of an insertion, a frame shift or a nonsense mutation [13]. Noteworthy are studies from Spain. Samples came from different counties of the Iberian Peninsula during 2016-2018 and they investigated large sampling of dogs (5086) and cats (789). In dogs, clinical samples were most commonly from otitis, and in cats, from wounds, respiratory tract infections, and conjunctivitis. The prevalence of *Pseudomonas spp*. in this study was 16% of dogs and 10% of cats. Dogs presented higher frequencies of *Pseudomonas aeruginosa* (92%) than cats (72%). *Pseudomonas spp*. presented the highest levels of antimicrobial resistance in both dogs and cats [15]. The results obtained from the pets in this study were compared with those reported in the same period of time in human hospitals in Spain. The prevalence of *P.aeruginosa* was even lower (8%) than in cases of dogs and cats [14]. The next remarkable data comes from Spain too; Darwich et al. [15] investigated 1368 dogs' urine samples and 457 cats urine samples. *P.aeruginosa* has been isolated from 3.2% dogs and 5.2% cats. *Pseudomonas aeruginosa* confirmed 3.4% MDR in dog's cases and 4.6% in cat's cases in large statistical sampling and PDR 0.2% in cats cases. The percentage of MDR and PDR was higher in cats than in dogs [16]. Understanding the prevalence of AMR among pets, mainly dogs and cats, is demanded from both veterinary and human medicine perspectives. However, due to the fact that clinical cases are not always entirely recorded and monitored, the available data on pet-related AMR is very minimal. Although existing programs reporting antimicrobial resistance of pathogens are implemented only in few countries. An example of monitoring *Pseudomonas aeruginosa* in populations of dogs and cats and simultaneously good practice can be the ComPath program. In this project, twelve countries: Belgium, Czech Republic, France, Germany, Hungary, Italy, The Netherlands, Poland, Spain, Sweden, Switzerland, and the UK [17]. The next problem in monitoring antimicrobial profiles of *Pseudomonas aeruginosa* isolates is that they are difficult to compare between different studies, due to many variables that represent a challenge for the harmonization of global data.

DISCUSSION

Despite recognize *P. aeruginosa* in different niches, studies mainly focus on clinical *P. aeruginosa* strains from humans. Only a small number of scientists examine bacteria from pets such as dogs and cats or environmental strains. Most often, small statistical sampling is not enough. The low prevalence of *Pseudomonas aeruginosa* in animals is related to the necessary investigation of large statistical sampling. In my opinion, it is the main problem in veterinary study. Therefore, the risk of transmission from humans to animals is still not enough known. Generally, more studies include date dogs than cats. Although the first report of interspecies transmission of the LES strains of *P.aeruginosa* from an adult patient with CF to a pet cat [18]. The natural microbiome is still an underestimated source of multidrug resistance bacteria in both humans and animals. Both antimicrobial susceptibility and virulence factors are involved in mortality and morbidity in *Pseudomonas aeruginosa* infection. Therefore, not only antibiotic resistance is important to analyze, but biofilm forming ability and virulence genes occur too. The creation of a control system for public health risks of *Pseudomonas aeruginosa* needs new easy-to-use and fast tools. In our previous study [19] we showed the possibility of action in a new direction [20-22].

CONCLUSION

We need more studies to find species differences in *Pseudomonas aeruginosa* infection and their implications for public health risk. Surveillance should include concrete follow-up of corrective

actions against antimicrobial resistance. We should not ignore possible but unknown sources of diversity in the genetic pool. The fusion of the phenotype and genotype approach is needed. We leave open the question: why in the One Health Idea era do we still depreciate the impact of animals on public health protection?

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