

Profile of *Pseudomonas aeruginosa* Antibiotic Sensitivity from Corneal Scrapings Specimens of Keratitis Patients with Contact Lens and without Contact Lens at Dr. Soetomo Hospital Surabaya

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Abstract

Background: *Pseudomonas aeruginosa* have a significant proportion of the causes of bacterial keratitis. Corneal ulcers infected with *P. aeruginosa* are more severe than other bacterial corneal ulcers. *P. aeruginosa* is often associated with keratitis that results from wearing contact lenses, which eventually leads to corneal ulcers. This study aims to determine the differences in the results of the antibiotic sensitivity test of *P. aeruginosa* from corneal scraping specimens of keratitis patients using contact lenses and non-contact lens users at RSUD dr. Soetomo.

Methods: This study is an observational analytic study of secondary data from corneal scraping cultures of patients with keratitis infected with *P. aeruginosa* at Dr. Soetomo Hospital period January 2017-December 2020.

Results: The total number of samples included in the inclusion criteria was 46 samples. Of the total sample, 8 (17.40%) were contact lens users and 38 (82.60%) were non-contact lenses. The male sex and female sex each as much as 50%. The distribution of sample age categories for 0-20 years was 21.74%, 21-40 years was 13.04%, 41-60 years was 41.30%, and >60 years was 23.91%. Based on samples from 8 contact lens patients, antibiotics were found to be 100% sensitive, namely Amikacin, Cefepime, Ciprofloxacin, Imipenem, Levofloxacin, Meropenem, and Piperacillin tazobactam, Aztreonam and Gentamicin 87.5%, Ceftazidime 75%, Tobramycin 37.5% and Piperacillin 25%. Meanwhile, from a sample of 38 patients who did not wear contact lenses, the sensitive antibiotics were Cefepime 100%, Meropenem 94.8%, Amikacin 92.1% Imipenem 86.9%, Piperacillin-tazobactam 76.3%, Ciprofloxacin 73.8%, Gentamicin 73.8%, Aztreonam 68.4%, Levofloxacin 68.4%, Piperacillin 50%, Ceftazidime 44.7%, and Tobramycin 28.9%.

Conclusion: The results of the antibiotic sensitivity test against *P. aeruginosa* from keratitis patients with a history of contact lens use showed that 8/8 (100%) of the active antibiotics were Amikacin, Cefepime, Ciprofloxacin, Imipenem, Levofloxacin, Meropenem, and Piperacillin tazobactam. Then followed by Aztreonam and Gentamicin (7/8).

The results of the antibiotic sensitivity test against *P. aeruginosa* from keratitis patients who had no history of using contact lenses showed that the active antibiotics were above 50%, namely Cefepime 38/38 (100%), Meropenem 36/38 (94.8%), Amikacin 35 /38 (92.1%), Imipenem 33/38 (86.9%), Piperacillin-tazobactam 29/38 (76.3%), Ciprofloxacin 28/38 (73.8%), Gentamicin 28/38 (73.8%), Aztreonam 26/38 (68.4%), and Levofloxacin 26/38 (68.4%).

Keywords: Antibiotic sensitivity, *Pseudomonas aeruginosa*, keratitis, contact lenses

1. Introduction

Microbial keratitis is an important cause of eye pathology and, along with trauma, contributes to 1.52 million new cases of corneal blindness each year. Almost 50% of cases of microbial keratitis are caused by bacteria (Fernandes et al., 2016). Bacteria commonly associated with keratitis, or bacterial corneal ulcers, include staphylococci, epidermal staphylococci, pneumonia streptococci, purulent streptococci, moracicella, glaucoma, proteus, clebsiera pneumonia, 2016). Among the causative agents of bacterial keratitis, *Pseudomonas aeruginosa* is of particular interest for several reasons. *P. aeruginosa* accounts for a significant portion of bacterial keratitis, causing 6% to 39% of cases in the United States and 8% to 21% in southern India. In addition, *Pseudomonas aeruginosa* corneal ulcers have been described as being more severe than other

bacterial corneal ulcers. *Pseudomonas aeruginosa* is also known to be extremely toxic, *Pseudomonas aeruginosa* ulcers are generally difficult and difficult to handle, and cause annoying visual results than other bacterial yellow ulcers (SY et al., 2012). The use of inappropriate antibiotics and long-term treatments resulted in a global increase in the onset of drug resistance between mitasets. Regardless of the natural chromosome code mechanism, *Pseudomonas aeruginosa* has the ability to acquire resistance genes from the same or different species (Thirumalmuthu et al., 2019). *Pseudomonas aeruginosa* also causes corneal inflammation when wearing contact lenses and also cause corneal ulcers (Suwal et al., 2016).

Consumption of contact lenses is becoming more common and it is an advantageous industry. The global contact lens market is estimated to be US \$ 1247.63 million in 2020 with a growth rate of 6.7% (Alipour et al., 2017). There are increasing indications for its use, including cosmetology, refraction, myopia control, and therapeutic reasons. Based on sales growth, it is estimated that there are 140 million contact lens wearers worldwide, an increase over the previous year. Different types of lenses and uses are available to correct vision. These lenses interact with the surface of the eye and are associated with many properties and risk profiles. This requires contact lens prescribers and ophthalmologists to be aware of complications associated with wearing contact lenses (Lim et al., 2018).

One study estimates that 6% of contact lens wearers experience complications each year. Complications associated with contact lenses are an important part of ophthalmology. Diseases range from benign allergic conjunctivitis to severe microbial keratitis (Li et al., 2018). Improper use of lens cleaning solutions, such as the addition of antibiotics and the reuse of solutions in lens cases, can expose bacteria to non-lethal levels of disinfectants and further develop resistance (Subedi et al., 2018).). Studies have shown that *Pseudomonas aeruginosa* collected from corneal swabs in patients with microbial keratitis is also contained in storage vessels (Dantam et al., 2016). Increased use of contact lenses followed by increased prevalence of bacterial keratitis caused by *Pseudomonas aeruginosa*.

2. Methods

This type of study describes the secondary data found in the dr. Soetomo General Hospital Surabaya. The design of this study is cross-cutting. The population of this study is Dr. It was consistent with the data of *Pseudomonas aeruginosa* isolated from the corneal swab of the patient is enrolled in Department of Clinical Microbiology from January 2017 to December 2020. Determination of samples for this study by continuous sampling. Patients with keratitis or corneal ulcer eyes who submitted a microbiological test sample in the form of a corneal swab to Department of Clinical Microbiology. As a result of this identification, *Pseudomonas aeruginosa* contained in the study sample was found.

Inclusion criteria:

Data from microbiological examination of corneal scraping specimens from keratitis patients identified *Pseudomonas aeruginosa* which was examined at dr. Soetomo Surabaya during January 2017 – December 2020.

Exclusion criteria:

Data on antibiotic sensitivity test results are missing, error or invalid.

3. Result

The total number of samples included in the inclusion criteria was 46 samples. Of the total sample, 8 (17.40%) were contact lens users and 38 (82.60%) were non-contact lenses. The male sex and female sex each as much as 50%. The distribution of sample age categories for 0-20 years was 21.74%, 21-40 years was 13.04%,

41-60 years was 41.30%, and >60 years was 23.91%. Based on samples from 8 contact lens patients, antibiotics were found to be 100% sensitive, namely Amikacin, Cefepime, Ciprofloxacin, Imipenem, Levofloxacin, Meropenem, and Piperacillin tazobactam, Aztreonam and Gentamicin 87.5%, Ceftazidime 75%, Tobramycin 37.5% and Piperacillin 25%. Meanwhile, from a sample of 38 patients who did not wear contact lenses, the sensitive antibiotics were Cefepime 100%, Meropenem 94.8%, Amikacin 92.1% Imipenem 86.9%, Piperacillin-tazobactam 76.3%, Ciprofloxacin 73.8%, Gentamicin 73.8%, Aztreonam 68.4%, Levofloxacin 68.4%, Piperacillin 50%, Ceftazidime 44.7%, and Tobramycin 28.9%.

Table 1 Distribution of samples by age

Age	Contact lens	Non contact lens	N (%)
0-20 year	2	8	10 (21.74%)
21-40 year	4	2	6 (13.04%)
41-60 year	2	17	19 (41.30%)
>60 year	0	11	11 (23.91%)
Total	8	38	46 (100.00%)

Table 2 Distribution by gender

Gender	Contact lens	Non Contact Lenses	N(%)
Man	1	22	50%
Woman	7	16	50%
Total	8	38	100%

Table 3 Distribution by room

Room	Contact lens	Non contact lens	N(%)
Jasmine	2	13	32.61%
NICU	0	1	2.17%
IRD	6	18	52.17%
BONA 2	0	2	4.35%
ROI 2	0	1	2.17%
Palm	0	1	2.17%
Out patient clinic	0	1	2.17%
HCU GRAHA	0	1	2.17%
Total	8	38	100.00%

Table 1 Distribution of antibiotic sensitivity of Pseudomonas aeruginosa-infected keratitis patients using contact lenses

ANTIBIOTICS	SENSITIVITY		
	S (%)	I (%)	R(%)
Amikacin	8 (100)	0	0

ANTIBIOTICS	SENSITIVITY		
	S (%)	I (%)	R(%)
Cefepime	8 (100)	0	0
Ciprofloxacin	8 (100)	0	0
Imipenem	8 (100)	0	0
Levofloxacin	8 (100)	0	0
Meropenem	8 (100)	0	0
piperacillin-tazobactam	8 (100)	0	0
Aztreonam	7 (87.5)	0	1 (12.5)
Gentamicin	7 (87.5)	0	1 (12.5)
Ceftazidime*	6 (75)	0	0
Tobramycin*	3 (37.5)	0	0
piperacillin*	2 (25)	0	2 (25)
Amoxicillin clavulanic acid	0	0	8 (100)
Ampicillin	0	0	8 (100)
Ampicillin-sulbactam	0	0	8 (100)
Cefazolin	0	0	8 (100)
Cefotaxime	0	0	8 (100)
Cefoxitin	0	0	8 (100)
Ceftriaxone	0	0	8 (100)
Cloramphenicol	0	0	8 (100)
Ertapenem	0	0	8 (100)
Tetracycline	0	0	8 (100)
Cotrimoxazole	0	0	8 (100)

*some samples failed to produce sensitivity test results to certain antibiotics

Table 5 Distribution of antibiotic sensitivity of patients with keratitis infected with *Pseudomonas aeruginosa* who do not use contact lenses

ANTIBIOTICS	SENSITIVITY		
	S (%)	I (%)	R(%)
Cefepime	38 (100)	0	0
Meropenem	36 (94.8)	1 (2.6)	1 (2.6)
Amikacin	35 (92.1)	0	3 (7.9)
Imipenem	33 (86.9)	2 (5.2)	3 (7.9)
Piperacillin-tazobactam*	29 (76.3)	5 (13.1)	2 (5.2)
Ciprofloxacin	28 (73.8)	5 (13.15)	5 (13.15)
Gentamicin	28 (73.8)	2 (5.2)	8 (21)
Aztreonam	26 (68.4)	3 (7.9)	9 (23.7)
Levofloxacin	26 (68.4)	2 (5.2)	10 (26.4)
piperacillin*	19 (50)	0	2 (5.2)
Ceftazidime*	17 (44.7)	1 (2.6)	2 (5.2)
Tobramycin*	11 (28.9)	0	3 (37.5)
Amoxicillin clavulanic acid	0	0	38 (100)
Ampicillin	0	0	38 (100)
Ampicillin-sulbactam	0	0	38 (100)

ANTIBIOTICS	SENSITIVITY		
	S (%)	I (%)	R(%)
Cefazolin	0	0	38 (100)
Cefotaxime	0	0	38 (100)
Cefoxitin	0	0	38 (100)
Ceftriaxone	0	0	38 (100)
Cloramphenicol	0	0	38 (100)
Ertapenem	0	0	38 (100)
Tetracycline	0	0	38 (100)
Cotrimoxazole	0	0	38 (100)

*some samples failed to produce sensitivity test results to certain antibiotics

4. Discussion

Pseudomonas aeruginosa infection of the eye can be visually threatening, has a rapid onset and progressively causes inflammation of the corneal stroma. Keratitis caused by *Pseudomonas aeruginosa* causes a rapid suppurative infiltration, subsequent discoloration and perforation of the cornea which eventually leads to blindness. Contact lens wearers are particularly susceptible to the development of *P. aeruginosa* keratitis.(Oka et al., 2015).

In the field of eye care, contact lenses have a great impact on improving vision, but their use can be limited by eye infections. The use of contact lenses is the most important risk factor for microbial infection. Wearing contact lenses is associated with changes in the ocular microbiota where the ocular conjunctival microbiota is found to be similar to the skin under the eyes. Gram-negative bacteria are the main cause of contact lens-associated microbial keratitis with *Pseudomonas* spp. the most frequently isolated organisms, while *Staphylococcus* spp. and *Serratia* spp. in the next order(Di Onofrio et al., 2019).

In this study, from a total of 46 patients, 23 (50%) male patients and 23 (50%) female patients were found. This data is almost similar to a study in Taiwan in 2015 which examined microbial keratitis in general, namely 171 (47.1%) men and 192 (52.9%) women.(Oka et al., 2015).

The age of the individuals in this study was mostly 41-60 years, namely 19 people (41.3%). Then followed by age >60 years as many as 11 people (23.91%), aged 0-20 years 10 people (21.74%) and age 21-40 years as many as 6 people (13.04%). From a study in Taiwan in 2019, it was found that the average age of the microbial keratitis population was getting older. There is a growing trend for the percentage of patients over 60 years in the microbial keratitis population (Liu et al., 2019).

Out of a total of the 46 samples obtained, the most samples were from IRD room 24 (52.17%) and Melati 15 (32.61%). This is probably because more keratitis patients go to the IRD for eye complaints, especially when outside working hours or holidays. Meanwhile, the Melati room is an inpatient room for eye patients. Next is Bona Room 2 (4.35%), NICU 1 (2.17%), ROI-2 1 (2.17%), Palem 1 (2.17%), Out patient clinic 1 (2.17%) , and HCU Grha 1 (2.17%).

Based on samples from 8 patients with a history of contact lens use, 100% sensitive antibiotics were obtained, namely Amikacin, Cefepime, Ciprofloxacin, Imipenem, Levofloxacin, Meropenem, and Piperacillin tazobactam. Then followed by Aztreonam 87.5%, Gentamicin 87.5%, Ceftazidime 75%, Tobramycin 37.5% and Piperacillin 25%. These results are slightly different from those found in studies in the Middle East where the antibiogram results showed 100% of *P. aeruginosa* cases were sensitive to ceftazidime and ciprofloxacin, whereas amikacin, imipenem, and gentamicin were the second most effective antibiotics.(Naduvilath et al., 2016). The equation obtained is that Ciprofloxacin is 100% sensitive to contact lens wearers.

Meanwhile in 38 patients who had no history of using contact lenses, sensitive antibiotics were found, namely Cefepime 100%, Meropenem 94.8%, Amikacin 92.1%, Imipenem 86.9%, Piperacillin-tazobactam 76.3%, Ciprofloxacin 73.8 %, Gentamicin 73.8%, Aztreonam 68.4%, Levofloxacin 68.4%, Piperacillin 50%, Ceftazidime 44.7%, and Tobramycin 28.9%.

The weakness of this study is that the number of samples from keratitis patients who wear contact lenses is still very small when compared to the number of samples that do not wear contact lenses, which is 8 versus 38, making it a less proportional comparison.

Meanwhile, when compared with research in India and Australia, it will appear a different pattern. Among Australian isolates (n = 14), the sensitivity was 100% to gentamicin or polymyxin, 93% to tobramycin, 86% to levofloxacin, 79% to piperacillin, 50% to ciprofloxacin, 43% to ceftazidime and 22% to imipenem. In contrast, the sensitivity of Indian isolates (n=12) was 75% for polymyxin, 60% for gentamicin, 59% for piperacillin, 50% for levofloxacin, tobramycin, and ceftazidime, 42% for imipenem and 25% for ciprofloxacin. This difference may occur because in Australia, there are strict regulations on prescribing antibiotics, and antibiotics can only be obtained legally with a prescription from a qualified healthcare professional under the Therapeutic Goods Act 1989. While in India, apart from brand-name antibiotics, there are also substandard antibiotics, and 'fake' antibiotics that make monitoring and regulation difficult. While the consumption of antibiotics per person in Australia and India in 2010 was almost the same, there was a more rapid increase between 2000 and 2010 in India. These differences may influence the development of antibiotic resistance (Khan et al., 2020).

5. Conclusion

The results of the antibiotic sensitivity test against *P. aeruginosa* from keratitis patients with a history of contact lens use showed that 8/8 (100%) of the active antibiotics were Amikacin, Cefepime, Ciprofloxacin, Imipenem, Levofloxacin, Meropenem, and Piperacillin tazobactam. Then followed by Aztreonam and Gentamicin (7/8).

The results of the antibiotic sensitivity test against *P. aeruginosa* from keratitis patients who had no history of using contact lenses showed that the active antibiotics were above 50%, namely Cefepime 38/38 (100%), Meropenem 36/38 (94.8%), Amikacin 35 /38 (92.1%), Imipenem 33/38 (86.9%), Piperacillin-tazobactam 29/38 (76.3%), Ciprofloxacin 28/38 (73.8%), Gentamicin 28/38 (73 .8%), Aztreonam 26/38 (68.4%), and Levofloxacin 26/38 (68.4%).

Conflict of interest

None.

Acknowledgement

None.

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