



Influence of Different Families of Commercial Antibiotics on Controlling Nosocomial Infections

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MAR and MMZ designed the study. Authors MAR and DM wrote the protocol. Authors MSA and HMA performed the statistical analysis, wrote the manuscript and managed the analyses of the study. Authors HMA and AEA managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/SAJRM/2019/v4i230103

Editor(s):

(1) Dr. Eliton da Silva Vasconcelos, Department of Physiological Sciences, Federal University of Sao Carlos – UFSCar, Rod. Washington Luiz, Sao Carlos, Brazil.

Reviewers:

(1) Hideharu Shintani, Chuo University, Japan.

(2) Maria Antonietta Toscano, University of Catania, Italy.

Complete Peer review History: <http://www.sdiarticle3.com/review-history/50392>

Received 16 May 2019

Accepted 26 July 2019

Published 06 August 2019

Original Research Article

ABSTRACT

Aims: Nosocomial infection (NI) is one of the most important problems facing the world. This work is dedicated to investigating the prevalence rates of NI in addition to estimating the minimum inhibition concentration (MIC) of commercial antibiotics on isolated bacteria in order to determine the most diluted antibiotic that performed well with more efficiency and minimal toxicity.

Place and Duration of Study: Gastroenterology Surgical Center, Mansoura University, Mansoura, Egypt, between July 2017 and July 2018.

Methodology: This study included 368 different samples (urine, stool, sputum and surgical wounds) from 100 patients. A total of 15 commercial antibiotics selected from seven families having different mode of action were used.

Results: Our findings demonstrated that the highest prevalence rate of NI was detected in *K. pneumoniae* (40%, n=56) followed by MRSA (22.85%, n=32), *E. coli* (20%, n=28), *P. mirabilis*

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(7.85%, n=11), *P. putida* (5%, n=7) and finally *P. aeruginosa* (4.3%, n=6). In addition, the results showed variable MICs of various antibiotics on isolated bacteria associated with NI.

Conclusion: Interestingly, our findings showed that quinolones family had the highest impact on all types of isolated bacteria associated with nosocomial infections.

Keywords: Nosocomial infections; antibiotics; *K. pneumoniae*; MRSA; *E. coli*; *P. mirabilis*; *P. putida*; *P. aeruginosa*.

1. INTRODUCTION

Nosocomial infection (NI) is considered to be the most difficult problems confronting clinicians who deal with severely ill patients. The incidence of NI is estimated at 5-10% in tertiary care hospitals reaching up to 28% in intensive care unit and 90% of these are caused by bacteria [1]. Generally, NIs can be defined as infection that were acquired during hospitalization by patients in whom the infection was not present or incubating at the time of admission [2,3], or any infections that were occurred within two days of hospital admission, three days of discharge or thirty days of an operation [4]. Indeed, NI could spread in the hospital and nursing home environments as well as clinic or other clinical settings. Interestingly, different routes for spreading NI to the susceptible patients in the clinical setting were reported. These routes include health care staff, contaminated equipment, bed linens and air droplets, etc [5]. NIs could also be originated from the outside environment, another infected patient, or the patient's own skin microbiota, becoming opportunistic after surgery or other procedures that compromise the protective skin barrier [6]. On the other hand, antibiotic treatment is more effective when started early, as well as when it is adapted to the sensitivity of the pathogens [7]. In this work, we are concerning with assessing the influence of different families of commercial antibiotics, that were diluted serially, on the isolated bacteria obtained from cultured patients' samples who have NIs in order to determine the extent to which the isolated bacteria could be affected. This in turn may give a clue to determine the most diluted antibiotic that performed well with more efficiency and minimal toxicity.

2. MATERIALS AND METHODS

One hundred consecutive patients staying three days or more were randomly recruited from the Gastroenterology Surgical Center (GEC), Mansoura University, Egypt. Different samples of urine, stool, sputum and surgical wound swabs were collected from patients for microbiological

studies in order to identify nosocomial infection. Next, the obtained samples were cultured using nutrient agar in addition to MacConkey agar. The isolated bacteria were then morphologically and biochemically identified by VITEK 2 compact 15 (Biomerieux, France) and in turn kept for subsequent analysis for assessing the influence of different commercial antibiotics on them. Interestingly, different families of commercial antibiotics (Table 1) were diluted serially from 10^1 to 10^{-5} . Next, a variety of cultured nutrient agar plates were then inoculated with 120 μ L of each diluted antibiotic according to agar well-diffusion method [8].

3. RESULTS AND DISCUSSION

No doubt, nosocomial infections are considered to be a serious public health issue. Of note, prevalence reports that were conducted in some developing countries have showed hospital-wide nosocomial infection rates mostly higher than 15% with a range from 6% to 27% [9].

The first part of this work was concerned with identifying different bacterial isolates related to nosocomial infections and estimating their prevalence rates in different samples. Three-hundred and sixty-eight samples were incorporated in this work. These samples were categorized into four different groups. They are urine (n=100), stool (n=100) and sputum (n=100) samples in addition to surgical wounds (n=68). These samples were further classified based on nosocomial infections into positive and negative groups as depicted in Fig. 1A. Overall, one hundred and forty (38%) samples were tested positive for the presence of nosocomial infections bacteria.

On the contrary, sputum samples were accompanied with the lowest positivity rate of 27% for nosocomial infections as shown in Fig. 1A lower than that reported previously by Custivic et al. [10] who showed that the nosocomial infections were detected in 60% in respiratory tract. On the contrary, our findings showed that 73.5% of surgical wounds, 28% of stool and 35% of urine samples were tested

positive for the presence of nosocomial infections higher than that produced previously by Custivic et al. [10] who demonstrated that nosocomial infections were found in only 7%, 9% and 16% of surgical wounds, stool and urine samples, respectively.

It is noteworthy that nosocomial infections are caused by many microbes. However, bacteria are responsible for approximately 90% of nosocomial infections [11]. In this study, the agents that have been isolated from the included samples were *K. pneumoniae*, MRSA, *E. coli*, *P. mirabilis*, *P. putida* in addition to *P. aeruginosa*. Out of these bacteria, *K. pneumoniae* and MRSA were found to have the highest detection rates. The results showed that *K. pneumoniae* had a prevalence rate in urine, stool and surgical wounds accounting for 40%, 46.43% and 42%, respectively. On the other hand, MRSA infection displayed the highest detection rate in sputum samples (51.9%).

Custivic et al. [10] reported that most MRSA infections occurred in the respiratory tract whereas MRSA accounted for 18.4% of all respiratory tract isolates. He also showed that *K. pneumoniae* was the most common, associated with more than half of surgical wound infections. On the other hand, Shaikh et al. [12] reported *E. coli* as the most frequent pathogen (26.3%) while *Klebsiella* spp. was responsible for only 5.2% of all urinary tract infections.

Overall, our results indicate that 25%, 20%, 19.3% and 35.7% of total positive samples of NIs was detected in urine, stool, sputum and surgical

wound swabs samples, respectively. Based on the appearance of isolated bacteria in different samples, samples of urine and surgical wounds swabs were found to be the best samples that could identify the bacterial nosocomial infections quickly. The positive samples were identified by VITEK 2 compact 15 (Biomerieux, France). As a consequence, different pathogenic bacteria were appeared with variable prevalence rates in different samples.

Overall, the present study showed that *K. pneumoniae* was found to have the highest detection rate of 40% (n=56) followed by MRSA (22.85%, n=32), *E. coli* (20%, n=28), *P. mirabilis* (7.85%, n=11), *P. putida* (5%, n=7) and finally *P. aeruginosa* (4.3%, n=6) as depicted in Fig. 1B. However, Borg et al. [13] reported that the highest levels of MRSA were observed in Jordan, Egypt and Malta, which were all above 50% higher than that provided in this study. Custivic et al. [10] reported that *K. pneumoniae* was the most frequently isolated gram negative pathogen (51% of all positive samples), followed by *P. aeruginosa* (10%), *P. mirabilis* (7%) and *E. coli* (4%), respectively; while MRSA was the most common among gram positive bacteria (15%).

The second part of this work was dedicated to investigating the influence of seven different families of commercial antibiotics on nosocomial infections. Thus, the efficiency of different families of commercial antibiotics in terms of minimum inhibition concentration (MIC) was then measured against the aforementioned bacteria associated with nosocomial infections and the results were summarized in Table 2 and Fig. 2.

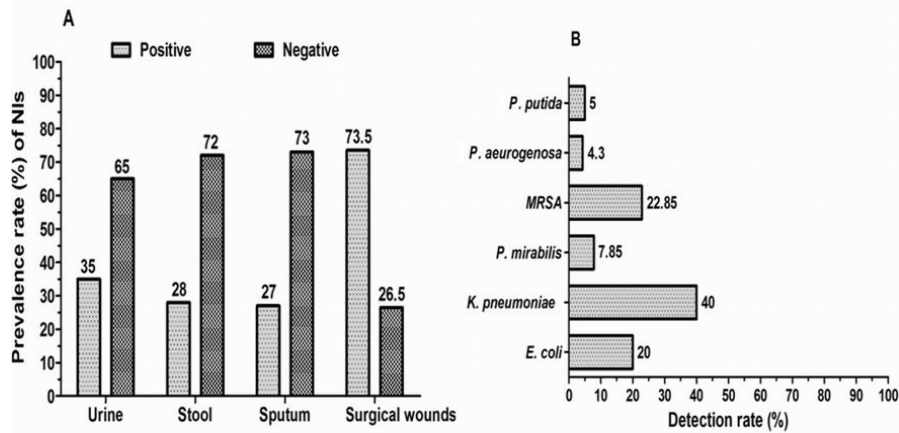


Fig. 1. Different bacterial isolates associated with nosocomial infections (A) Prevalence rate of bacterial isolates in different patient samples, and (B) Types of isolated bacteria and their detection rate in different samples

Table 1. The mode of action of common antibiotics

Antibiotic family	Scientific name	Abbreviation	Commercial name	Conc. (mg)	Mode of action
Quinolones	Ciprofloxacin	CIP	Ciprofloxacin	250	DNA Inhibitors
Quinolones	Norfloxacin	NOR	Noracin	400	DNA Inhibitors
Quinolones	Ofloxacin	OFX	Tarivid	200	DNA Inhibitors
Quinolones	Levofloxacin	LEV	Lee-Flox	250	DNA Inhibitors
Quinolones	Nitrofurantoin	F	Macrofuran	50	DNA Inhibitors
β -lactam	Meropenem	MEM	Meronem	1000	Cell wall Inhibitors
β -lactam	Cefotaxime	CTX	Cefotax	250	Cell wall Inhibitors
β -lactam	Amoxicillin	AX	E-Mox	1000	Cell wall Inhibitors
β -lactam	Ampicillin	AM	Epicocillin	500	Cell wall Inhibitors
Aminoglycosides	Amikacin	AK	Emijectacin	500	Protein Inhibitors
Aminoglycosides	Neomycin	N	Neomycin	500	Protein Inhibitors
Macrolides	Erythromycin/Trimethoprim	E	Erythroprim	400/100	Protein Inhibitors
Tetracyclines	Tetracycline	TET	Cefaxone	250	Protein Inhibitors
Cephalosporines	Ceftriaxone	CRO	Doxymycin	100	Cell wall Inhibitors
Glycopeptides	Vancomycin	V	Vancomycin	500	Cell wall Inhibitors

Table 2. Minimum Inhibition Concentration (MIC) of different families of antibiotics on bacterial isolates associated with nosocomial infections

Family ^a	Abbreviation ^b	MIC					
		<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. mirabilis</i>	MRSA	<i>P. aeruginosa</i>	<i>P. putida</i>
F1	CIP	1x10 ⁻⁴	1x10 ⁻¹	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻³
	NOR	1x10 ⁻⁴	1x10 ⁻¹	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻³	1x10 ⁻²
	OFX	1x10 ⁻⁴	1x10 ⁻¹	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻²	1x10 ⁻²
	LEV	1x10 ⁻⁴	1x10 ⁻²	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻⁴	1x10 ⁻³
	F	1x10 ⁻²	1	1	1	1	1
F2	MEM	1x10 ⁻⁴	1x10 ⁻¹	1x10 ⁻⁴	1x10 ⁻²	1x10 ⁻⁴	1x10 ⁻⁴
	CTX	1x10 ⁻⁴	1	1	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻²
	AX	1x10 ⁻⁴	1	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻¹	1x10 ⁻¹
	AM	1x10 ⁻⁴	1	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻¹	1x10 ⁻¹
F3	AK	1x10 ⁻⁵	1x10 ⁻²	1x10 ⁻²	1x10 ⁻³	1x10 ⁻⁴	1x10 ⁻³
	N	1x10 ⁻²	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻²	1x10 ⁻³	1x10 ⁻³
F4	E	1x10 ⁻⁴	1	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻¹	1
F5	TET	1x10 ⁻¹	1x10 ⁻¹	1x10 ⁻²	1x10 ⁻⁴	1x10 ⁻²	1x10 ⁻¹
F6	CRO	1x10 ⁻⁴	1	1	1	1x10 ⁻²	1x10 ⁻³
F7	V	1x10 ⁻¹	1	1	1x10 ⁻³	1x10 ⁻¹	1x10 ⁻¹

^a F1: Quinolones; F2: β -lactams; F3: Aminoglycosides; F4: Macrolides; F5: Tetracyclines; F6: Cephalosporines and F7: Glycopeptides. ^b Show Table 1

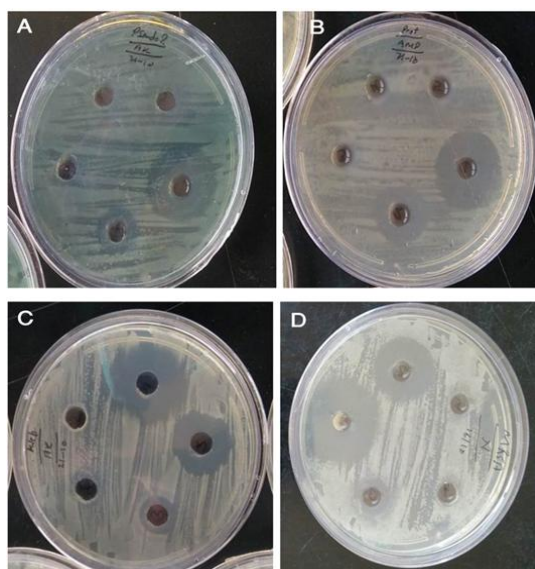


Fig. 2. Influence of some commercial antibiotics with different concentration on isolated bacteria associated with nosocomial infections (a) Amoxicillin on *P. Aeruginosa*, (b) Ampicillin on *P. Mirabilis*, (c) Amikacin on *K. Pneumoniae*, and (d) Neomycin on MRSA

The obtained MIC for quinolones were found to be the same (10^{-4}) in case of *E. coli*, MRSA, *P. aeruginosa* and *P. mirabilis* and the maximum antibiotic activity was found in levofloxacin followed by ciprofloxacin. The same goes for β -lactam (MIC= 10^{-4}) in case of *E. coli*, *P. mirabilis*, *P. aeruginosa* and *P. mirabilis* followed by MRSA (MIC= 10^{-2}) and the maximum antibiotic activity was found in meropenem. The obtained MIC for aminoglycosides was found to be 10^{-5} and 10^{-4} in case of *E. coli* and *P. aeruginosa*, respectively, and the maximum antibiotic activity was found in amikacin (MIC= 10^{-5}) with *E. coli* compared to other antibiotics. The obtained MIC for macrolides was found to be 10^{-4} and 10^{-2} in case of *E. coli* and MRSA, respectively. The obtained MIC for tetracycline was found to be 10^{-4} in case of MRSA and 10^{-2} in case of *P. mirabilis* and *P. aeruginosa*. Surprisingly, cephalosporin family showed no activity upon dilutions while its antibiotic activity was shown in case of its original form in *K. pneumoniae*, MRSA and *P. mirabilis*. Finally, the obtained MIC for glycopeptides was found to be 10^{-3} in case of MRSA and 10^{-1} in case of *E. coli*, *P. aeruginosa* and *P. putida*. Based on the aforementioned results, that quinolones family had the highest impact on all types of isolated bacteria associated with nosocomial infections.

Among these, the study that was reported by Lombardi et al. [14] who showed that *P. putida*

was resistant to quinolones but it was susceptible to aminoglycosides except for amikacin. As well, Kim et al. [15] reported that *P. Putida* was susceptible to ciprofloxacin, levofloxacin, amikacin and meropenem. Another study was reported by Ayub et al. [16] showed that *S. aureus* and *P. mirabilis* were resistant to amoxicillin but susceptible to tetracycline. In addition, Mustafa et al. [17] reported that MRSA was resistant only to β -lactams while *S. aureus* was resistant to penicillin and susceptible to nitrofurantoin, vancomycin, levofloxacin, tetracycline, and erythromycin. Mustafa et al. [17] also reported that the most potent antimicrobials on *E. coli* were meropenem, levofloxacin and amikacin. It was also reported that *K. Pneumoniae* was susceptible to amikacin and moderately sensitive to ceftriaxone, ciprofloxacin and tetracycline. Additionally, Mustafa et al. [17] reported that the most potent antimicrobials on *P. Aeruginosa* were meropenem and levofloxacin while *P. Aeruginosa* was resistant to tetracycline, erythromycin and vancomycin. This is comparable with the rates reported by various authors Maehara et al. [18], Aga et al. [19] and Baker et al [20].

4. CONCLUSION

Our findings showed that quinolones family had the highest impact on all types of isolated bacteria associated with nosocomial infections.

CONSENT AND ETHICAL APPROVAL

Informed consents were obtained from all participants and they were fully informed concerning the diagnostic procedures involved and disease nature. The study protocol conformed to ethical guide-lines of 1975 Helsinki Declaration.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
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