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RESEARCH ARTICLE

CURRENT TREND OF RESISTANT FOR THE COMMONLY PRESCRIBED NEW FLUOROQUINOLONES AMONG HOSPITALISED PATIENTS IN SANA'A, YEMEN

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Abstract

Objective: The new fluoroquinolones have demonstrated enhanced activity against the most common bacteria involved in lower respiratory tract infection (LRTI). Moxifloxacin is the most commonly prescribed respiratory flouroquinolone drug in Yemen. Pneumonia is a major and an on-going public health problem globally. The aim of present study was to determine the trend of moxifloxacin resistant and the distribution of resistant for different sample types among hospitalised patients in Sana'a, Yemen.
Methods: The study was performed at a private hospital in Sana'a, Yemen. The records were taken from the microbiology department for hospitalised patients. Moxifloxacin susceptibility samples were collected from January, 2017 to December, 2017. The moxifloxacin susceptibility was studied ag *P*ainst several isolates. Full ethical clearance was obtained from the qualified authorities who approved the study design. All data were analyzed using SPSS Statistics version 21.
Results: Out of 927 sample isolates, 580 (62.6%) were moxifloxacin resistant isolates and only 30.1% were sensitive. The *Escherichia coli* was observed in 24.4% of total sample isolates, followed by *Pseudomonas aeruginosa* (12.1%). From the study findings, 44.8% of total sample was isolated from sputum cultures. There was a statistically significant difference between bacteria type and culture results ($p<0.001$). The study findings reported that 70.4% of *Escherichia coli* isolates were resistant for moxifloaxin, followed by methicillin resistant *Staphylococcus aureus* (64.7%), *Klebsiella pneumonia* (60.6%), and *Pseudomonas aeruginosa* (46.4%).
Conclusion: This study reveals that varieties of pathogens are responsible for LRTI and moxifloxacin resistance has become a great public health issue. This study may help the government's regulatory authority to develop a policy about rational prescription of antibiotics to minimize resistance of new antibiotics and also to ensure the maximum safety to the health of patients.
Keywords: Fluoroquinolones, Moxifloxacin, prevalence, resistance.

INTRODUCTION

The classic fluoroquinolones such as ciprofloxacin, norfloxacin, fleroxacin and ofloxacin have had strong activity against Gram-negative bacteria, but the effectiveness of these compounds against Gram-positive bacteria has been debated. The new fluoroquinolones developed during the 1990s, such as levofloxacin and moxifloxacin, have demonstrated enhanced activity against the most common bacteria involved in lower respiratory tract infection (LRTI). The mechanism of newer fluoroquinolone activity is the inhibition of essential bacterial type II topoisomerases (DNA gyrase) and topoisomerase IV[1]. All new fluoroquinolones have a bactericidal activity and a post-antibiotic effect. Compared with cipro-floxacin, all new fluoroquinolones have a longer elimination half-life that allows once daily dosing. In addition, these antibiotics have excellent penetration into respiratory tissues, with the highest concentrations found in the epithelial lining fluid and alveolar macrophages[2]. The newer fluoroquinolones such as levofloxacin and moxifloxacin are currently available in both IV and oral formulations. With regard to the pharmacodynamic characteristics, the new fluoro-quinolones cause concentration-dependent killing[3].

Moxifloxacin (Avelox; Bayer), a "fourth-generation" fluoroquinolone, is often used in the empirical treatment of severe community-acquired pneumonia (CAP), which is one of the most common infectious diseases and among the primary causes of death worldwide[4]. *Streptococcus pneumoniae* is the primary pathogen responsible for CAP, but many other microorganisms, including Gram-negative and atypical bacteria (e.g., *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*), may also be etiological agents[5]. The recommended dose of moxifloxacin is 400 mg/day (q.d.). No dosage adjustment is required in elderly patients, obese patients[6], or patients with renal or mild hepatic impairment[7].

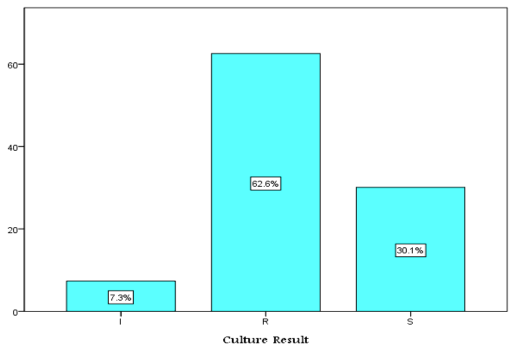

Figure 1: Distribution of Moxifloxacin susceptibility among study sample.

Furthermore, due to the risk of a prolonged QT interval (a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle), it is recommended that the daily dose of moxifloxacin should not exceed 400 mg[8]. The clinical efficacy of the newer fluoroquinolones in the treatment of LRTI has been demonstrated in several randomized, double-blind, prospective studies. In comparative community-acquired pneumonia (CAP) studies, newer fluoroquinolones almost have more activity than the cephalosporins (e.g. ceftriaxone, cefaclor or cefuroxime axetil) and the macrolides (e.g. erythromycin or roxithromycin)[1].
Niederman *et al*.,[9] compared hospitalization and mortality in patients with CAP being treated with moxifloxacin, amoxicillin or clarithromycin. The mortality rate for moxifloxacin-treated patients was significantly better (p=0.045) than for comparator-treated patients. Current treatment guidelines for the management of LRTI in adults recommend fluoroquinolones for empirical treatment in several patient groups. The new fluoroquinolones currently available offer major therapeutic advances compared with previous agents, and the incidence of adverse events is clearly outweighed by their clinically use[1]. As with other antimicrobial, the development of resistance is a potential problem associated with their increased use in RTIs. Rational prescribing and continous control of antibiotic resistance levels are needed to keep their future antibacterial efficacy. Moxifloxacin is a new broad-spectrum antibacterial agent against the most common bacteria involved in LRTI. Moxifloxacin is the commonly prescribed respiratory flouroquinolone drug in Yemen. Pneumonia is a major and an on-going public health problem globally. Thus, the aim of present study was to determine the trends of moxifloxacin and the distribution of resistant for different sample types among hospitalised patients in Sana'a, Yemen.

METHODS

This retrospective study was performed at a private hospital in Sana'a, Yemen. Moxifloxacin susceptibility samples were collected from January, 2017 to December, 2017 from the records of hospitalised patients. The moxifloxacin susceptibility was studied against several isolates. Full ethical clearance was obtained from the qualified authorities who approved the study design.

Statistical analysis

All data were analyzed using SPSS Statistics version 21.

RESULTS

According to the present study, the mean age of study sample (n=927) was 49 years (with SD ± 21.3 year) and ranged between 1 and 120 years. Out of 927 samples, 580 (62.6%) were moxifloxacin resistant isolates and only 30.1% were sensitive. Also (69.0%) of total patients were females and (31.0%) were males. Among 927 of patients, (28.2%) was aged between 41-60 years and 35.5% more than 60 years.

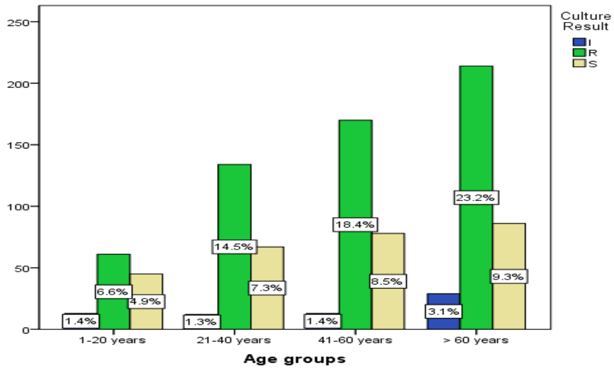

Figure 2: Distribution of age group and sex according to culture results.

The *E. coli* was observed in 24.4% of total sample isolates, followed by *Pseudomonas aeruginosa* (12.1%). From the study findings, 44.8% of total sample was isolated from sputum cultures (Table 1). Results in Table 3 indicated that the relationship between bacteria type and culture results was statistically significant ($P<0.001$). In the present study, 96.2% of *Acinetobacter species* were moxifloxacin resistant and all *Acinetobacter baumannii* isolates were moxifloxacin resistant. Also the study findings reported that 70.4% of *Escherichia coliisolate*s were resistant for moxifloaxin, followed by *Klebsiella pneumonia* (60.6%), methicillin resistant *staphylococcus aureus* (64.7%), *Pseudomonas aeruginosa* (46.4%). However, 86.1% of *staphylococcus aureus* isolates were moxifloxacin resistant. However, there was a statistically significant difference between culture results with age groups (*p*=0.02). Also 64.1% of male shadmoxifloxacin resistant and 36.9% of isolate resistant were aged >60 years (Table 3). The relationship between culture results and sample type was analyzed in the Table 4. Results in this table showed that there was high significantly relationship (*p*<0.001). Also 44.8% of sample isolates were from sputum cultures. Moreover, 74.2% of sputum cultures isolates were moxifloxacin resistant.

DISCUSSION

The primary objective in the development of moxifloxacin was to produce an appropriate spectrum antibiotic for the treatment of community-acquired RTIs with a good tolerability profile, and low propensity for the development of bacterial resistance, thus benefiting patients and helping clinicians to treat these diseases[10]. An effective new antimicrobial agent is necessary in light of the therapeutic problems posed by the increasing prevalence of antibiotic resistance of the common respiratory tract pathogens[11].

Table 1: Distribution of study variables.

Variable	Level of variable	Frequency	Percentage
Culture Result	I	68	7.3
	R	580	62.6
	S	279	30.1
	Total	927	100.0
Sex	M	287	31.0
	F	640	69.0
	Total	927	100.0
Age order	1-20 years	124	13.4
	21-40 years	213	23.0
	41-60 years	261	28.2
	60	329	35.5
	Total	927	100.0
Type of bacteria	*Acinetobacter baumannii*	24	2.6
	Acinetobacter species	185	20.0
	Alpha Hemolytic *Streptococcus*	2	0.2
	β-Hemolytic *Streptococcus*-Group-A	1	0.1
	β-*Hemolytic Streptococcus*-Group-D	1	0.1
	Citrobacter Spp	5	0.5
	Coagulase negative *Staphylococci*	57	6.1
	Enterobacter Spp	3	0.3
	Enterococcus Spp	19	2.0
	Escherichia coli	226	24.4
	Klebsiella pneumoniae	99	10.7
	Klebsiella Spp	50	5.4
	Moraxella Spp	4	.4
	Methicillin Resistant *Staphylococcus aureus(MRSA)*	17	1.8
	Neisseria Spp	1	0.1
	Nocardia Spp	1	0.1
	Proteus mirabilis	3	0.3
	Proteus Spp	10	1.1
	Proteus vulgaris	1	0.1
	Pseudomonas aeruginosa	112	12.1
	Serratia Spp	4	0.4
	Staphylococcus aureus	72	7.8
	Streptococcus pneumoniae	3	.3
	Streptococcus spp.	27	2.9
	Total	927	100.0
Type of sample	Aspirated fluid culture	1	0.1
	Blood culture	22	2.4
	Cerepro Spinal Fluid (CSF) C/S	144	15.5
	General swab for culture	17	1.8
	Pleural fluid for culture and Sensitivity	27	2.9
	Ascitic fluid c/s and sensitivity	6	0.6
	Pus for culture and sensitivity	91	9.8
	Sputum culture	415	44.8
	Throat swab culture	1	0.1
	Urine culture	120	12.9
	Wound swab for culture	83	9.0
	Total	927	100.0

Table 2: Distribution of bacteria type according to culture results.

Type of Bacteria	Culture Result			Total	*P*
	I	R	S		
Acinetobacterbaumannii	0	24	0	24	
Acinetobacter species	2	177	6	185	
Alpha Hemolytic *Streptococcus*	0	1	1	2	
B-Hemolytic *Streptococcus*-Group-A	0	1	0	1	
B-Hemolytic *Streptococcus*-Group-D	0	1	0	1	
Citrobacter Spp	2	1	2	5	
Coagulase negative *Staphylococci*	19	14	24	57	
Enterobacter Spp	2	0	1	3	
Enterococcus Spp	0	18	1	19	
Escherichia coli	7	159	60	226	
Klebsiella pneumoniae	10	60	29	99	
Klebsiella Spp	2	42	6	50	
Moraxella Spp	0	0	4	4	
Methicillin Resistant *Staphylococcus aureus* (*MRSA*)	6	11	0	17	0.001
Neisseria Spp	0	0	1	1	
Nocardia SPP	0	0	1	1	
Proteus mirabilis	0	3	0	3	
Proteus Spp	2	6	2	10	
Proteus vulgaris	0	0	1	1	
Pseudomonas aeruginosa	11	52	49	112	
Serratia Spp	0	0	4	4	
Staphylococcus aureus	3	7	62	72	
Streptococcus pneumoniae	0	0	3	3	
Streptococcus spp.	2	3	22	27	
Total	68	580	279	927	

Table 3: Distribution of age group and sex according to culture results.

Variable		Culture results			Total	*P*
		I	R	S		
Sex	F	26	170	91	287	
	M	42	410	188	640	0.25
	Total	68	580	279	927	
Age group	<20	14	62	48	124	
	21-40	12	134	67	213	
	41-60	13	170	78	261	0.02
	60	29	214	86	329	
	Total	68	580	279	927	

Table 4: Distribution of culture results according to sample type

Sample Type	Culture Result			Total	*P*
	I	R	S		
Ascitic fluid c/s and sensitivity	0	0	1	1	
Aspirated fluid culture	0	8	14	22	
Blood culture	18	62	64	144	
Cerepro Spinal Fluid (CSF) C/S	0	14	3	17	
General swab for culture	2	18	7	27	
Pleural fluid for culture and sensitivity	0	1	5	6	
Pus for culture and sensitivity	6	31	54	91	0.001
Sputum culture	28	308	79	415	
Throat swab culture	0	0	1	1	
Urine culture	7	83	30	120	
Wound swab for culture	7	55	21	83	
Total	68	580	279	927	

According to the study results, 62.6% of study sample were moxifloxacin resistant isolates and only 30.1% were sensitive. Moxifloxacin treatment failure is being increasingly reported, particularly in the Asia-Pacific region[12]. Fluoroquinolone resistance is rare in North America. Surveillance studies in the United States from 1987 to 2009 demonstrated low rates of resistance to moxifloxacin (0.1%)[13]. Although total per capita outpatient use of fluoroquinolones increased during this 10 yrs period, levofloxacin and moxi-floxacin resistance remained unchanged at <2% in the >26,000 isolates collected[14] . In contrast to study findings in Pakistan, the prevalence of Moxifloxacin resistant was 42.4%[15]. From the present study findings, 44.8% of total sample was isolated from sputum cultures. Moreover, 74.2% of sputum cultures isolates were moxifloxacin resistant. The increasing resistance to antibiotics by respiratory pathogens has complicated the use of empirical treatment with traditional agents and a definitive bacteriological diagnosis[16]. The study findings reported that 70.4% of *E. coli isolates* were resistant for moxifloaxin, followed MRSA (64.7%), *Klebsiella pneumonia* (60.6%), and *P. aeruginosa* (46.4%). Also results in this study showed that t there was a statistically significant difference between culture results with age groups and 36.9% of patients with moxifloxacin resistant isolates were aged>60 years**.** During the last several years, resistance to fluoroquinolones has remained very high among MRSA, *P. aeruginosa*. In addition, the recent reports of an overall increase in resistance to fluoroquinolones among bacteria causing community acquired infections. These surveillance data demonstrate that fluoroquinolone resistance has to be associated with both particular bacterial species and patient populations[13].

CONCLUSIONS AND RECOMMENDATIONS

LRTIs comprise a wide range of diseases from acute bronchitis to severe pneumonia leading to death. This study reveals that varieties of pathogens are responsible for LRTI and moxifloxacin resistance has become a great public health issue. The possibility of reducing resistance by controlling the use of antibioticsis a reasonable approach. Inappropriate and irrational drug usage should be avoided. This study may help the Government's regulatory authority to develop a policy about rational prescription of antibiotics to minimize resistance of new antibiotics and also to ensure the maximum safety to the health of patients.

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AUTHOR'S CONTRIBUTION

Alyahawi A: designed the study. **Alkaf A:** acquired the data. **Alnosary T:** analyzed the data and interpreted the results. All authors read and approved the final manuscript for publication.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

The authors declare that no conflict of interest is associated with this work.

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