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Original Article

Impact of broad-spectrum antimicrobial treatment on the ecology of intestinal flora

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Abstract *Background:* Suppression of intestinal flora by broad-spectrum antimicrobial agents facilitated risk of colonization or infection with resistant pathogen. We aimed to investigate the changes in bowel carriage of target resistant microorganisms (TRO) among patients treated with three different classes of *Pseudomonas*-sparing broad-spectrum antimicrobial agents (ertapenem, moxifloxacin and flomoxef) with anaerobic coverage. Risk factors for developing colonization of TRO were also analyzed.
Methods: We prospectively enrolled the adult hospitalized patients (>20 years old) who were indicated for at least 7-day course with either of ertapenem, moxifloxacin or flomoxef. Rectal swabs were performed for the patients who received at least 1-day course of study antibiotics during the treatment duration. The TROs included *Pseudomonas aeruginosa*, Enterobacteriaceae, and *Acinetobacter baumannii*. MacConkey agars with study antibiotics were used to isolate the TROs and evaluate the antimicrobial resistance.
Results: The mean age of our study population was 61.6 years, and 58.8% were males. The rates of rectal colonization for *Pseudomonas aeruginosa* was similar among the study medications (ertapenem 13.2%, flomoxef 20%, moxifloxacin 14.3%, $p = 0.809$). Compared with ertapenem, flomoxef (odds ratio [OR], 4.30; 95% confidence interval [95% CI], 1.28–14.48, $p = 0.019$) and moxifloxacin (OR, 6.95; 95% CI, 1.36–35.52, $p = 0.019$) had higher risk for colonization of ertapenem-resistant *Escherichia coli* colonization.
Conclusion: The patients who received treatment of ertapenem may have a lower risk of rectal colonization for ertapenem resistant *Escherichia coli* than those who received flomoxef or

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moxifloxacin. The rate of *Pseudomonas* colonization did not differ between the three study *Pseudomonas*-sparing agents.

Introduction

The normal flora of the gastrointestinal tract provides native barrier to colonization by antimicrobial resistant bacteria and fungi.[1] Suppression of intestinal anaerobic flora facilitates colonization and infection with pathogenic aerobic bacteria.[2] For example, the risk of colonization or infection with vancomycin-resistant enterococci (VRE) has been associated with the use of glycopeptides,[3,4] third generation cephalosporins,[5,6] and antibiotics with anti-anaerobic activity.[7] In contrast, the effects of the broad-spectrum antibacterial agents on colonization with resistant Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* had less been investigated.[8]

Gastrointestinal tract is the most common habitat of bacteria. It has been estimated to 10^{11-12} colony forming units habit in the colon, more than 99% are anaerobes.[9] Colonization of potential antimicrobial resistant pathogens could be selected under the pressure of using broad-spectrum antimicrobial agents. In vivo studies and an epidemiological study revealed colonization of carbapenem-resistant Enterobacteriaceae could developed after using broad-spectrum antibiotics, such as carbapenems.[10–12] Among the patients who received transrectal biopsy of the prostate, *Escherichia coli* was the most common pathogens.[13] Therefore, we focus on the ertapenem-resistant *E. coli* under the usage of broad spectrum antibiotics. In this study, the effect of three *P. aeruginosa*-sparing board spectrum antimicrobial agents (ertapenem, moxifloxacin and flomoxef) commonly used for intra-abdominal infections on the changes of bowel colonization with target resistant organisms (TROs) were accessed by serial cultures collected from rectal swabs. In addition, risk factors of bowel colonization of TRO were assessed.

Materials and methods

Study design

This is a prospective observational study of serial anal swabs for cultures among patients who were treated with three targeted broad-spectrum *Pseudomonas*-sparing antimicrobial agents (ertapenem, moxifloxacin and flomoxef) during the period of April 2008 to December 2009 at National Taiwan University Hospital. The inclusion criteria included all of the followings: (1) male or female patients over 20 years of age, (2) patients who were estimated for an at least 5 days of antimicrobial treatment with either of targeted antimicrobial therapy (ertapenem, moxifloxacin or flomoxef), (3) patients could receive anal swab culture within 72 h of initiating targeted antimicrobial therapy. The choices of these therapeutic regimens were decided by their attending physicians based on the clinical practice. Patients with the following condition were excluded: (1) patients received concomitant other antimicrobial agents in addition to these targeted antimicrobial medication or change to other antimicrobial agents, (2) patients who required more than 4-week duration of antimicrobial agent therapy, (3) patients had concomitant infections that might interfere with the evaluation of the response to studied medications, (4) patients underwent unscheduled surgery or requiring laparotomy for perforated or ruptured bowels or other acute conditions, (5) patients who were previously documented positive for TRO colonization and/or infection before or had received intravenous antimicrobial therapy within 1 year.

Data collection

Patients who met the inclusion criteria and had signed informed consents to participate the study were enrolled. A standardized case record form was used to collect information on demographic and clinical characteristics (age, sex, comorbidities), sites of infections, antimicrobial treatment course, baseline hemogram and blood biochemistry, clinical outcomes (septic shock, mortality), and adverse effects of antibiotics. Rectal swabs were performed within 72 h (early follow-up assessment) and the end of targeted antimicrobial therapy.

Laboratory investigations

Rectal Swabs were performed as following procedure: (1) insert the swab into the rectum as if taking a rectal temperature, (2) place one swab in a tube containing buffered-glycerol-saline (BGS), (3) cut or break the swab to fit in to the tube and screw the cap on tightly, (4) store the BGS tube at 4 °C and make sure the swab is moistened with the transport media. If the patient was withdrawn from the study prior to the early follow-up assessment, collected rectal swabs were discarded from the study.

Target resistant organisms (TROs)

The Target Resistant Organisms (TROs) of interest include ertapenem-resistant Enterobacteriaceae, extended-spectrum β-lactamases- (ESBL-) or APC β-lactamases-producing Enterobacteriaceae, *P. aeruginosa*, and *A. baumannii*. The methods of TRO isolation were performed according to the CLSI standards.[14] The swabs were cultures on the following selective media plates to isolate gram-negative bacilli, such as MacConkey agar with ertapenem

0.5 μg/ml; MacConkey agar with ceftriaxone 1 μg/ml, MacConkey agar with moxifloxacin 1 μg/ml and MacConkey agar with flomoxef 1 μg/ml. All swabs were only applied to selective agar to isolate the resistant microorganisms.

Ethics statement

This research conformed to the Helsinki Declaration and local legislation, and was approved by the Institutional Review Board National Taiwan University Hospital Research Ethics Committee (NTUH 200712004R). Written informed consent from the participants were performed of each patient in this study.

Statistical analysis

We used Fisher exact test or Chi square test for categorical variables among the three groups of patients (ertapenem, flomoxef, and moxifloxacin), and utilized unbalanced ANOVA analysis for the examination of continuous variables. We included the variables with a p-value <0.05 in the univariate analysis such as age, lung infection, urinary tract infection, underlying hepatobiliary diseases, and underlying endocrine diseases, and variables that were of biological significance such as sex and antibiotics treatment duration in the multivariate logistic regression models. The ertapenem group was used as the reference group in the logistic regression model. A p value of <0.05 was considered statistically significant. The confidence interval was set at 95%. The analysis was conducted using the statistical package SAS 9.3 (SAS Institute Inc., Cary, North Carolina, USA).

Results

During the study period, 97 patients who received study antibiotics were enrolled. There were 38, 45, and 14 patients in the ertapenem, flomoxef, and moxifloxacin groups, respectively. The mean age of the moxifloxacin group was significantly younger (51.1 ± 12.5 years) than those of ertapenem group and flomoxef group (64.0 ± 19.4 years and 62.7 ± 13.8 years, respectively, $p = 0.034$).

The overall clinical characteristics of the 97 study patients were shown in Table 1. Compared with ertapenem group and moxifloxacin group, the flomoxef group had higher proportion of patients who had hepatobiliary disease (66.7% versus 31.6% and 35.7%, $p = 0.004$) and suffered from hepatobiliary infection (44.4% versus 23.7% and 14.3%, $p = 0.039$). The ertapenem group had higher proportion of urinary tract infection (23.7% versus 4.4% and 0%, $p = 0.013$) and the moxifloxacin group had higher proportion of pulmonary infections (42.9% versus 15.8% and 11.1%, $p = 0.036$).

Table 1 Demographics characteristics, underlying diseases and sites of infections.

Case number	Total ($n = 97$)	Ertapenem ($n = 38$)	Flomoxef ($n = 45$)	Moxifloxacin ($n = 14$)	p Value
Age (mean ± SD)	61.6 ± 16.5	64.0 ± 19.4	62.7 ± 13.8	51.1 ± 12.5	0.034
Male sex, *n* (%)	57 (58.8%)	19 (50%)	30 (66.7%)	8 (57.1%)	0.304
Underlying diseases					
Connective tissue disease	10 (10.3%)	5 (13.2%)	4 (8.9%)	1 (7.1%)	0.899
Old stroke	5 (15.5%)	8 (21.1%)	5 (11.1%)	2 (14.3%)	0.402
HIV infection	2 (2.1%)	2 (5.3%)	0 (0%)	0 (0%)	0.42
Cardiovascular diseases	32 (32.9%)	16 (42.1%)	41 (31.1%)	2 (14.3%)	0.169
Respiratory diseases	21 (21.7%)	7 (18.4%)	8 (17.8%)	6 (42.9%)	0.148
Gastrointestinal diseases	36 (37.1%)	9 (23.7%)	22 (48.9%)	5 (35.7%)	0.059
Hepatobiliary diseases	47 (48.5%)	12 (31.6%)	30 (66.7%)	5 (35.7%)	0.004
Renal diseases	14 (14.4%)	4 (10.5%)	7 (15.6%)	3 (21.4%)	0.485
Metabolic diseases	20 (20.6%)	8 (21.1%)	12 (26.7%)	0 (0%)	0.08
Endocrine diseases	5 (5.2%)	5 (13.2%)	0 (0%)	0 (0%)	0.019
Solid cancer	14 (14.4%)	5 (13.2%)	7 (15.6%)	2 (14.3%)	>0.999
Leukemia	1 (1.03%)	0 (0%)	0 (0%)	1 (7.1%)	0.144
Operation within the previous 3 months	13 (13.4%)	6 (15.8%)	7 (15.6)	0 (0%)	0.33
Sites of infection					
Urinary tract	11 (11.3%)	9 (23.7%)	2 (4.4%)	0 (0%)	0.013
Bloodstream	5 (5.2%)	1 (2.6%)	3 (6.7%)	1 (7.1%)	0.564
Bone	5 (5.2%)	3 (7.9%)	2 (4.4%)	0 (0%)	0.694
Gastrointestinal tract	17 (17.5%)	5 (13.2%)	10 (22.2%)	2 (14.3%)	0.586
Liver/biliary tract	31 (31.9%)	9 (23.7%)	20 (44.4%)	2 (14.3%)	0.039
Lung	17 (17.5%)	6 (15.8%)	5 (11.1%)	6 (42.9%)	0.036
Head/neck	2 (2.1%)	0	0	2 (14.3%)	0.02
Skin	1 (1.0%)	0	1 (2.2%)	0 (%)	0.464
Others	8 (8.3%)	5 (13.2%)	2 (4.4%)	1 (7.1%)	0.356

HIV = human immunodeficiency virus.

The treatment duration and clinical responses were revealed by Table 2. The mean duration of therapy was 6.9 days for all the study patients, and there was no significant difference of treatment duration among the three study groups. The disease severity (septic shock, intensive care unit admission, acute renal failure, and 30-day mortality) and side effects profiles (skin rash, abdominal fullness, and decreased urine output) were also similar among the three study groups.

The microbiological profiles of anal colonization were shown in Table 3. The median duration from initiation of antimicrobial therapy to collection of rectal swab cultures was 3 days (min 1 day, max 14 days), and there was no significant difference among the three study groups. For *P. aeruginosa*, the overall colonization rate was 16.5%, and the proportion of colonization was similar among the three groups (13.2% versus 20% versus 14.3%, p = 0.809). The colonization rates of non-fermentative Gram negative bacilli (NFGNB) were similar among the three study groups. The overall colonization rate of Enterobacteriaceae was 59.8%. However, the colonization rate was borderline significant lower in the ertapenem group (44.7% versus 71.1% and 64.3%, p = 0.052). Compared with the other two groups, ertapenem group had lower rates of *E. coli* colonization (21.1% versus 53.3% and 57.1%, p = 0.004) but higher rates of *S. marcescens* colonization (10.5% versus 0% and 0%, p = 0.049).

The colonization rates of resistant Gram negative bacteria were shown in Table 4. The proportion of ertapenem-resistant *E. coli* colonization was significantly lower of the ertapenem group (13.2% versus 44.4% and 50%, p = 0.002). To do a sensitivity test, the ertapenem group had a significant lower colonization rate of ertapenem resistant E. coli than the flomoxef group (ertapenem versus flomoxef, 13.2% versus 44.4%, p = 0.002) and the moxifloxacin group (ertapenem versus moxifloxacin, 13.2% versus 50%, p = 0.01). The colonization rates of flomoxef- and moxifloxacin-resistant *E. coli* were also significantly lower in the ertapenem group. The proportions of resistant *Klebsiella pneumoniae* colonization were similar among the three study groups.

By multivariate logistic regression analysis to clarify the risk factors for colonization of ertapenem-resistant *E. coli*, we found that use of flomoxef or moxifloxacin would have a significantly higher odds ratio than use of ertapenem for colonization (Table 5). The adjusted odds ratios were 4.30 and 6.95 for flomoxef and moxifloxacin, respectively. The age, antibiotics treatment duration, and other possible confounding underlying medical diseases did not pose a significant effect on the anal colonization of ertapenem-resistant *E. coli*.

Discussion

In this study of anal colonization of Gram-negative bacteria after using pseudomonas-sparing broad spectrum antibiotics, it revealed 16.5% colonization rate of *P. aeruginosa* from the anal swab culture results among all the study patients. Previous reports revealed the colonization rate of *P. aeruginosa* were about 6% for healthy young adults and between 3% and 24% for hospitalized patients.[15,16] Our study is compatible with these results. The bowel source of *P. aeruginosa* may also plays some roles for nosocomial infections.[17] Therefore, the rectal colonization of *P. aeruginosa* was not significantly higher at our study subjects who receiving the broad spectrum pseudomonas-sparing antibiotics. From the experience of a 344-bed community teaching hospital, ertapenem was effective in their antimicrobial stewardship program after being added to the formulary and may improve the *P. aeruginosa* antimicrobial susceptibility to imipenem by decreasing the unnecessary usage and selective pressure of antipseudomonal agents.[18]

We found that the patients who underwent the use of ertapenem had a significant lower anal colonization proportion of ertapenem-resistant *E. coli* than the patients who received flomoxef and moxifloxacin. The rectal colonization rate of ertapenem-nonsusceptible *E. coli* was about 5% in hospitalized patients.[19] A previous bacteriological study revealed that the acquisition of the plasmid-mediated blaDHA-1 gene has led to flomoxef resistance in Lkp14 strain of *K. pneumoniae* after flomoxef exposure.

Table 2 Treatment durations, clinical outcomes, and side effects profiles.

Case number	Total (n = 97)	Ertapenem (n = 38)	Flomoxef (n = 45)	Moxifloxacin (n = 14)	p Value
Baseline leukocyte counts, mean ± SD	11,230 ± 5825	10,584 ± 6649	12,035 ± 5247	10,407 ± 5269	0.46
Duration of therapy, days, mean ± SD	6.9 ± 4.4	7.3 ± 4.6	6.9 ± 4.3	6.4 ± 4.4	0.759
Culture timing, after initiation of antibiotics, days, median (min, max)	3 (1, 14)	3 (1, 14)	2 (1, 13)	3.5 (1, 11)	0.625
Clinical outcomes					
Septic shock	4 (4.1%)	3 (7.9%)	0 (0%)	1 (7.1%)	0.109
Acute renal failure	4 (4.1%)	3 (7.9%)	1 (2.2%)	0 (0%)	0.364
ICU admission	4 (4.1%)	3 (7.9%)	1 (2.2%)	0 (0%)	0.364
30-day mortality	3 (3.1%)	2 (5.3%)	1 (2.2%)	0 (0%)	0.745
Side effects					
Abdominal fullness	1 (1.0%)	0	1 (2.2%)	0	>0.999
Decreased urine output	1 (1.0%)	0	1 (2.2%)	0	>0.999
Skin rash	1 (1.0%)	0 (0%)	1 (2.2%)	0 (0%)	>0.999

ICU = intensive care unit.

Table 3 Microbiological colonization of anal swabs.

Case number	Total (n = 97)	Ertapenem (n = 38)	Flomoxef (n = 45)	Moxifloxacin (n = 14)	p Value
Culture results					
Micro-organisms isolated	72 (74.2%)	24 (63.2%)	39 (86.7%)	9 (64.3%)	0.029
NFGNB	21 (21.7%)	7 (18.4%)	12 (26.7%)	2 (14.3%)	0.557
Pseudomonas aeruginosa	16 (16.5%)	5 (13.2%)	9 (20%)	2 (14.3%)	0.809
Stenotrophomonas maltophilia	1 (1.0%)	1 (2.6%)	0 (0%)	0 (0%)	0.536
Acinetobacter species	5 (5.2%)	1 (2.6%)	4 (8.9%)	0 (0%)	0.447
A. baumannii	2 (2.1%)	1 (2.6%)	1 (2.2%)	0 (0%)	0.367
A. johnsonii	2 (2.1%)	0 (0%)	2 (4.4%)	0 (0%)	0.633
A. lowffii	1 (1.0%)	0 (0%)	1 (2.2%)	0 (0%)	>0.999
Enterobacteriaceae	58 (59.8%)	17 (44.7%)	32 (71.1%)	9 (64.3%)	0.052
Enterobacter species	7 (7.2%)	3 (7.9%)	4 (8.9%)	0 (0%)	0.755
E. cloacae	5 (5.2%)	2 (5.3%)	3 (6.7%)	0 (0%)	>0.999
E. aerogenes	2 (2.1%)	1 (2.6%)	1 (2.2%)	0 (0%)	>0.999
Citrobacter species	5 (5.2%)	1 (2.6%)	3 (6.7%)	1 (7.1%)	0.564
C. koseri	2 (2.1%)	1 (2.6%)	1 (2.2%)	0 (0%)	>0.999
C. youngae	1 (1.0%)	0 (0%)	0 (0%)	1 (7.1%)	0.144
C. braaki	1 (1.0%)	0 (0%)	1 (2.2%)	0 (0%)	0.464
Escherichia coli	40 (41.2%)	8 (21.1%)	24 (53.3%)	8 (57.1%)	0.004
Klebsiella pneumoniae	16 (16.5%)	6 (15.8%)	9 (20%)	1 (7.1%)	0.567
Morganella morganii	2 (2.1%)	0 (0%)	2 (4.4%)	0 (0%)	0.633
Proteus mirabilis	4 (4.1%)	0 (0%)	2 (4.4%)	0 (0%)	0.075
Serratia species	5 (5.2%)	4 (10.5%)	1 (2.2%)	0 (0%)	0.224
S. marcescens	4 (10.1%)	4 (10.5%)	0 (0%)	0 (0%)	0.049
S. rubidaea	1 (1.0%)	0 (0%)	1 (2.2%)	0 (0%)	0.464
Candida species	1 (1.0%)	1 (2.6%)	0 (0%)	0 (0%)	0.536

NFGNB = non-fermentative Gram-negative bacilli.

Furthermore, the concomitant depletion of outer membrane protein (OmpK36) caused a collateral effect of ertapenem resistance and diminished susceptibilities to imipenem and meropenem.[20] The mechanism of collateral damage for flomoxef on carbapenem may explain the high proportion (44.4%) of ertapenem-resistant *E. coli* colonization in our study. The previous usage of quinolones had been noted as a risk factor for infection with ESBL-producing *Klebsiella* species and *E. coli* in nursing homes by a case—control study.[21,22] Moreover, in-hospital consumption of fluoroquinolones was significantly correlated with carbapenem resistance in *E. coli* by the analysis of the data from in the US military health system.[23] Comparing the pharmacokinetics of the three antibiotics, ertapenem and moxifloxacin had a more steady plasma concentration and longer half life than flomoxef.[24–26] A lower concentration below the minimum inhibitory concentration (MIC) can induce and select more resistant pathogens. Thus, it could affect the total colonization of resistant Gram negative bacteria, including *E. coli*. Due to a high fluoroquinolone resistance rate about 30% of *E. coli* in Taiwan,[27] it could make a lower rate of rectal colonization for *E. coli* in the ertapenem group.

Our study was under a prospective design. Therefore, we collected the anal swab specimens during the usage of study antibiotics under a standard protocol. We used MacConkey agar with a fixed concentration of tested antibiotics, and then the susceptibility of bacteria could be interpreted clearly by an all-or-none culture results. The susceptible minimum inhibitory concentration (MIC) breakpoint of Enterobacteriaceae for ertapenem was cut at 0.5 μg/ml, which was set according to the M100-S24 criteria published by Clinical and Laboratory Standards Institute (CLSI).[14] If the MIC equals 1.0 μg/ml, the cultured strain will be defined as intermediate for ertapenem. Therefore, some parts of the patients in our ertapenem-resistant *E. coli* group may belong to the intermediate susceptibility.

There were some limitations of our study. First, we included a relative small numbers of study patients and the unbalanced subject numbers between the three study antibiotics. The small case numbers of the moxifloxacin group may lead to some selection bias for the colonization status of the group. Second, we did not test the drug susceptibility of other anti-pseudomonal carbapenems, such as imipenem or meropenem, in this study. Therefore, we cannot reveal the whole picture of the carbapenem resistance in our isolates. The discordance of drug susceptibility for carbapenems had been notified before.[28] Third, the genotype assay for carbapenemase, including NDM-1 and KPC, was not checked here. Then we could not know the exact mechanisms for the ertapenem resistance. Fourth, the lower colonization rate of ertapenem-resistant *E. coli* may result from the uneven distribution of total *E. coli* colonization number among three groups. If we only focused on the proportion of the resistant *E. coli* and *K. pneumoniae* isolates number divided by the total number of isolated *E. coli* and *K. pneumoniae*, respectively, it would not reveal a statistical significance for the lower colonization of

Table 4 Isolated resistant pathogens.

N	Total (n = 97)	Ertapenem (n = 38)	Flomoxef (n = 45)	Moxifloxacin (n = 14)	p Value
Resistant bacteria					
Ertapenem resistant *E. coli*	32 (33.0%)	5 (13.2%)	20 (44.4%)	7 (50%)	0.002
Flomoxef resistant *E. coli*	24 (24.7%)	3 (7.9%)	14 (31.1%)	7 (50%)	0.002
Ceftriaxone resistant *E. coli*	21 (21.7%)	5 (12.1%)	12 (26.7%)	4 (28.6%)	0.228
Moxifloxacin resistant *E. coli*	26 (26.8%)	6 (15.8%)	13 (28.9%)	7 (50%)	0.048
Multidrug resistant *E. coli*[a]	14 (14.4%)	2 (5.3%)	9 (20%)	3 (21.4%)	0.096
Ertapenem resistant *K. pneumoniae*	10 (10.3%)	3 (7.9%)	7 (15.6%)	0 (0%)	0.248
Flomoxef resistant *K. pneumoniae*	10 (10.3%)	4 (10.5%)	5 (11.1%)	1 (7.1%)	>0.999
Ceftriaxone resistant *K. pneumoniae*	6 (6.2%)	4 (10.5%)	2 (4.4%)	0 (0%)	0.433
Moxifloxacin resistant *K. pneumoniae*	9 (9.3%)	4 (10.5%)	5 (11.1%)	0 (0%)	0.575

[a] Multidrug resistant *E. coli* were defined as at least two of the following antimicrobial agents (flomoxef, ceftriaxone, moxifloxacin, and ertapenem).

Table 5 Multivariate logistic regression for the risk factors of ertapenem-resistant *E. coli* colonization.

Factors[a]	Odds Ratio	95% Confidence interval	p Value
Ertapenem	1	As reference	
Flomoxef (versus ertapenem)	4.30	1.28—14.48	0.019*
Moxifloxacin (versus ertapenem)	6.95	1.36—35.52	0.019*
Age (per 1 year increase)	1.01	0.98—1.05	0.546
Male sex	2.11	0.75—5.90	0.156
Antibiotics treatment duration (per 1 day increase)	1.02	0.92—1.14	0.687

[a] The infection sites (urinary tract infection, lung infection) and underlying conditions (endocrine disease, hepatobiliary disease) with significant differences between the three groups were included in the multivariate model.

Table 6 Isolated resistant *E. coli* and *K. pneumoniae* versus total *E. coli* and *K. pneumoniae*.

	Total	Ertapenem	Flomoxef	Moxifloxacin	p Value
E. coli	(n = 40)	(n = 8)	(n = 24)	(n = 8)	
Ertapenem resistant *E. coli*	32 (80%[a])	5 (62.5%)	20 (83.3%)	7 (87.5%)	0.532
Flomoxef resistant *E. coli*	24 (60%)	3 (37.5%)	14 (58.3%)	7 (87.5%)	0.136
Ceftriaxone resistant *E. coli*	21 (52.5%)	5 (62.5%)	12 (50%)	4 (50%)	0.907
Moxifloxacin resistant *E. coli*	26 (65%)	6 (75%)	13 (54.2%)	7 (87.5%)	0.249
K. pneumoniae	(n = 16)	(n = 6)	(n = 9)	(n = 1)	
Ertapenem resistant *K. pneumoniae*	10 (62.5%)	3 (50%)	7 (77.8%)	0 (0%)	0.208
Flomoxef resistant *K. pneumoniae*	10 (62.5%)	4 (66.7%)	5 (55.6%)	1 (100%)	>0.999
Ceftriaxone resistant *K. pneumoniae*	6 (37.5%)	4 (66.6%)	2 (22.2%)	0 (0%)	0.118
Moxifloxacin resistant *K. pneumoniae*	9 (56.3%)	4 (66.7%)	5 (55.6%)	0 (0%)	0.779

[a] The % in each parentheses indicated the proportion which represented the number of isolated resistant *E. coli* and *K. pneumoniae* divided by the total number of isolated *E. coli* and *K. pneumoniae*, respectively.

ertapenem resistant *E. coli* in the ertapenem group (Table 6). Finally, we did not have the complete culture results before using and after ceasing the study antibiotics. Thus, we were unable to show the baseline colonization of the anal swabs before starting the antibiotics and clarify the flora changes after the course of using antibiotics.

In conclusion, the broad spectrum pseudomonas-sparing antibiotics may increase the anal colonization rate of ertapenem resistant *E. coli*. Use of flomoxef or moxifloxacin can have a significantly higher risk of ertapenem resistant *E. coli* colonization than administering ertapenem. Thus, the collateral damage for carbapenem resistance should be noticed while we use fluoroquinolones or oxacephams. The antibiotics had significant effects on the colonization flora of the patients.

Competing interests

All authors declare no competing interests.

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