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A comparative analysis of infection in patients with malignant cancer: A clinical pharmacist consultation study

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ABSTRACT

Background: Infection analysisamongst malignant cancer patients remains elusive. The objective of this study is to investigate the characteristics of both infection and anti-infection treatments in patients group with malignant cancer.

Methods: We retrospectively studied the clinical data of 148 patients with malignant cancer and 171 benign patients enrolled in the pharmacist consultation from April 2015 to April 2017. Statistical analysis was performed by chi-square test to compare the classification of primary disease, sites of infection, composition of pathogenic bacteria, and the effectiveness of drug treatment. P value <0.05 was considered statistically significant.

Results: A total of 102 pathogen strains were detected in the patients with malignant cancer and 129 pathogen strains were noted in the benign patient group, respectively. Statistics indicated that more abdominal infections were observed in malignant cancer patients rather than in non-cancer patients. Additionally, more *pseudomonas aeruginosa* infection was found in the malignant cancer patient group while more *Klebsiella pneumonia* infection was noted in the benign group. These findings were supported by statistical evidence. There were fewer extended-spectrum β-lactamases (ESBL) that produced *Escherichia coli*, which was commonly found in a gastrointestinal cancer patient group compared to patients under other types of cancer; it accounted for 51.3% of all malignant cases involved in the current study.

Conclusions: Patients with malignant cancer are more likely to suffer from an infection containing pathogenic bacteria in comparison to benign patients. There have been considerable differences in the composition of pathogenic bacteria and its resistance to drugs. Overall, evaluating pathogens plays an essential role in the anti-infection treatment of patients with malignant cancer.

Introduction

A strong link between cancer and microbial infections has been reported in many studies, which include bacterial, viral, and parasitic infections [1]. Infection is the leading cause of death in cancer patients overall and in the developing world, up to one in five cancer deaths is caused by infection [2]. At present, the main treatment methods for malignant tumors are chemotherapy, radiotherapy, and surgery treatments but they are likely to impair the normal organic functions. Cancer necrosis in conjunction with erosion also increases the risk of infection [3,4]. Therefore, infection constitutes the primary complication in malignant cancer patients and is also the major cause of death [5]. In addition, the infection sites are considerable different among a wide variety of cancer patients [3,6–7]. Although the National Comprehensive Cancer Network (NCCN) updates its cancer-related infection guidelines every year [8], infection specificity in malignant cancer patients is still unachieved [9].

In recent years, infections caused by resistant Gram-negative bacteria have drawn increased attention given its difficulty in treat-

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ment, as well as the high morbidity and mortality rates associated with it [10,11]. This type of bacteria has created a serious threat to public health around the world. According to the results of China's bacterial drug resistance surveillance network [12], the extended spectrum β-lactamases (ESBLs) producing *Enterobacteriaceae* bacteria has become more prominent. Meanwhile, the community acquired or associated ESBL producing (CA-ESBLs) *Enterobacteriaceae* bacteria have also been shown to be on the rise. The similar increase of infection resistant bacteria rates has also been observed throughout the United States since 2000. For example, cases of ESBL producing *Enterobacteriaceae*, carbapenem-resistant *Enterobacteriaceae* (CRE), and multidrug resistant (MDR) strains of *Pseudomonas aeruginosa* has been observed to increase particularly in hospitalized patients [11].

It is well known that the drug resistance in Gram-negative bacteria is highly complicated, which includes almost all of the currently known mechanisms. For instance, the major causes of resistance to third-generation cephalosporins in *Enterobacteriaceae* are Ambler class-A ESBL enzymes [11]. Some *in vitro* drug-sensitivity experiments have revealed that carbapenem-resistant *P. aeruginosa* is still sensitive to cephalosporins and additional attention must be focused on drug resistance through surveillance and mechanism.

In this study, we retrospectively analyzed the clinical data of cancer-related infections during consultations conducted by pharmacists to gain insights to differences present in infection sites, pathological bacteria characteristics, and anti-infection therapeutic methods. Furthermore, our work will aid in future experience-based treatments for malignant cancer patients who develop infections.

Materials and methods

Patient population

148 malignant cancer patients and 171 benign patients enrolled in the pharmacist consultation from April 2015 to April 2017 were analyzed in this study. Clinical data of these patients were collected and recorded. There were 73 males and 75 females within the malignant patient group with an average age of 60.20 ± 16.38 years (3–90 years), while there were 101 males and 70 females in the benign patient group with an average age of 60.31 ± 21.23 years (4 months to 93 years).

Clinical data of all patients was analyzed using statistical methods including age, gender, primary disease information, infection sites, availability of pathogenetic and sample sources, composition of pathological bacteria, drug treatment, physician compliance, infection situation, therapeutic effects and number of cases in each group. The infections were classified in accordance with the Clinical Applications of Anti-bacteria Drugs (2015 version) guidelines [13]. Regarding to the therapeutic effects, both the ability to cure and recover were regarded as direct results of effective treatments while the progression of infection and death were regarded as measures of ineffective therapy. A combination of symptom, microbiological, and image evaluation was used to judge the effectiveness of therapeutic effects.

Statistical analysis

Statistical analysis was conducted by SPSS 23.0 (SPSS Inc., Chicago, IL, USA). The comparison of infection sites, pathological bacteria composition, drug treatment, and therapeutic effects were analyzed using a chi-square test. $P < 0.05$ was considered statistically significant regarding the differences between malignant cancer groups and benign groups.

Table 1
Distribution of 148 primary malignant cases.

Primary lesion	Cases (%)	Primary lesion	Cases(%)
Colon cancer	15 (10.1)	Ampullary carcinoma	5 (3.3%)
Breast cancer	13 (8.8%)	Ovarian cancer	5 (3.3%)
Lung cancer	12 (8.1%)	Kidney cancer	5 (3.3%)
Cervical cancer	11 (7.4%)	Lymphoma	5 (3.3%)
Stomach cancer	11 (7.4%)	Multiple myeloma	3 (2.0%)
Rectal cancer	11 (7.4%)	Duodenal papilloma	3 (2.0%)
Pancreatic head cancer	9 (6.1%)	Pelvic cancer	2 (1.3%)
Cholangiocarcinoma	8 (5.4%)	Prostate cancer	2 (1.3%)
Esophageal cancer	7 (4.7%)	Others	15 (10.1%)
Liver cancer	6 (4.0%)	Total	148 (100%)

Table 2
Distribution of primary infection sites (%).

Group	Abdomen	Lung	Urinary tract	Others	Total
Malignant	50(33.8)	44(29.7)	13(8.8)	41(27.7)	148(100)
Non-cancer	27(15.8)	70(40.9)	21(12.3)	53(31.0)	171(100)
Total	77(24.1)	114(35.7)	34(10.6)	94(29.5)	319(100)
χ^2	14.03	4.338	1.019	0.414	–
P	<0.001	0.46	0.365	0.54	–

Results

Distribution of malignant patients

There were 76 cases of gastrointestinal cancer present out of 148 total cancer patient cases, which accounted for approximately 51.3% of all malignant cases. The distribution of different cancer types in our recruitment was denoted in Table 1.

Comparison of the top three primary infection sites among malignant patients vs. *benign patients*

The 3 top ranked primary infection sites, which were infections present in the abdomen, lung, and urinary tract, were compared between two cancer groups (see Table 2). Based on our findings, there were 50 cases of abdominal infection present in the malignant patient group and 27 cases in the benign patient group, which accounted for 33.8% and 15.8% of all cases, respectively. This difference was confirmed to have statistical significance ($\chi^2 = 14.03$, $P < 0.001$) (Table 2). In comparison, there were 44 lung infection cases (29.7%), 13 urinary tract infection cases (8.8%), 9 blood infection cases (6.1%), and 6 unexplained fever cases (4.0%) present in the malignant patient group. Similarly, there were 70 lung infection cases (40.9%), 21 urinary tract infection cases (12.3%), 16 blood infection cases (9.4%), 14 bone and joint infection cases (8.2%) in the benign patient group. There were no statistically significant differences found in lung infection sites ($\chi^2 = 4.338$, $P = 0.46$) and urinary tract infection sites ($\chi^2 = 1.019$, $P = 0.37$) between both groups (Table 2).

Furthermore, as shown in Table 2, there were 14 (9.4%) and 15 (8.8%) infection cases that incorporated two or more infection sites in the malignant and benign patient groups, respectively. No statistical significance was observed between the two groups ($\chi^2 = 0.848$, $P > 0.05$).

Composition of pathogenic bacteria

In the malignant cancer patient group, pathogenic bacteria were detected in 73 patients having an occurrence rate of 49.3%. At the same time, pathogenic bacteria were detected in 98 patients in the benign patient group, with an incidence rate of 57.3%. We then collected and compared the primary pathogenic bacteria between these two patient groups and results showed 102

Table 3
Distribution of pathogenic bacteria detected in two groups.

	Name of strain and number of isolates (strain)
Malignant cancer group (102 strains)	*E. coli* (13, which produces ESBL 10) *P. aeruginosa* (11) *E. faecium* (11, VRE 1) *S. aureus* (10, among them MRSA 5) *C. albicans* (9) *K. pneumonia* (6, which produces KPC 1) *A. baumannii* (5) *Enterococcus faecalis* (5) *Staphylococcus epidermidis* (3, which contains MRSE2) *S. maltophilia* (3) *Candida glabrata* bacteria (3) *Proteus mirabilis* (2) *Staphylococcus haemolyticus* (2) *Klebsiella oxytoca* (2) *Candida tropicalis* (2) *E. cloacae* (1) *Mycobacterium amyloliquefaciens* (1) Guinea pig airways (1) *C. albicans* (1) *Streptococcus angina* (1) *S. aureus* (1) *S. aureus* (1) *Ralstonia pneumoniae* (1) Difficile C. difficile (1) *Bacteroides fragilis* (1) B. puparus (1) *Streptococcus parahaemolyticus* (1) *Candida krusei* (1) Cooker's disease (1) *Enterobacter aeruginosa* (1)
Non-cancer group (129 strains)	*K. pneumoniae* (24, which produces ESBL 9, produces KPC 11) *E. faecium* (17) *E. coli* (15, which produces ESBL 7, produces KPC 1) *A. baumannii* (8) *E. cloacae* (5, which produces ESBL 1) *E. faecalis* (5) *C. albicans* (5) *C. glabrata* (5) *P. aeruginosa* (4) *S. aureus* (4) *S. epidermidis* (4, among them MRSCN 1) *S. maltophilia* (2) *S. haemolyticus* (2) *Streptococcus agalactiae* (2) *C. tropicalis* (2) Clostridium rolfsii (2) Enterobacter aerogenes (1, ESBL-producing Kochneria graminis (1) Aeromonas caviae (1) Serratia marcescens (1) Phytophthora latosus (1) Xylose-oxidizing leucobacter (1) Mendoza False Bacteria (1) Staphylococcus capricornicus (1) Streptococcus dysgalactiae (1) Trichoderma harzianum (1) Cryptococcus lunatus (1) Aspergillus (1) *K. oxytoca* (1)

Note: ESBL (extended-spectrum β-lactamase); VRE (vancomycin resistant *Enterococcus*); MRSA (methicillin-resistant *S. aureus*); KPC (carbapenemase-producing *K. pneumoniae*); MRSCN (methicillin-resistant coagulase-negative staphylococci).

pathogenic strains were detected in the malignant cancer group, which included 47 strains of Gram-negative bacteria (46.1%), 37 strains of gram-positive bacteria (36.3%), and 16 strains of fungi (15.7%). The 3 top ranked strains were *Escherichia coli*, *P. aeruginosa*, and *Enterococcus faecium*. As for the strains detected in the benign patient group, 129 strains in total were detected which included 65 strains of Gram-negative bacteria (50.4%), 47 strains of gram-positive bacteria (36.4%), and 17 strains of fungi (13.2%). The 3 top ranked strains were *Klebsiella pneumoniae*, *E. faecium* and *E. coli*. Results were displayed in Table 3.

We compared the primary pathogenic bacteria between the two previously indicated groups and the data was shown in Table 4. The 5 top ranked microorganisms detected in the malignant cancer group were *E. coli*, *P. aeruginosa*, *E. faecium*, *Staphylococcus aureus*, and *Candida albicans*. The 5 top ranked microorganisms detected in the benign patient group were *K. pneumoniae*, *E. faecium*, *E. coli*, *Acinetobacter baumannii*, and *Enterobacter cloacae*. The detection rate of *P. aeruginosa* in cancer patients was significantly higher than that in the benign patient group ($P < 0.05$), and the detection rate of *K. pneumoniae* in the non-cancer group was significantly higher than the rate found in the benign group ($P < 0.01$). Therefore, *Enterobacteriaceae* and non-fermentative bacteria were the most commonly observed pathogens found in nosocomial infections.

Due to the majority number of digestive tract cancer patients, we further divided malignant cancer subjects into the categories of digestive tract cancers and non-digestive tract cancers. As shown in Table 5, there were 51 strains of pathogenic bacteria in total isolated in the two groups. Interestingly, the infection of ESBL producing *E. coli* between two groups was found to be significantly different, which was believed to be responsible for its drug resistance. These results suggested that various infections were displayed among different cancer types.

Effects of drug treatment on patients with or without malignant cancer

Clinical pharmacist consultations primarily focused on providing the optimal drug treatment technique for patients with critical diseases. The anti-infection drugs including carbapenems, glycopeptides, and beta lactam/enzyme inhibitors shown in Table 6 received effective treatment effect. 113 and 135 patients in cancer and benign groups were cured or improved compared to 16 and 14 cases in cancer and benign groups who were sustained or dead (Table 6).

We compared the physician compliance and therapeutic effect between the malignant cancer patient group and benign patient group. Our results concluded that there were 112 and 128 effective cases of physician compliance in the cancer and benign patient groups, respectively, which accounted for 85.5% and 81.0% of all cases (See Table 7). The χ^2 and P values were 14.03 and 0.347 suggesting no statistically significant differences between these two groups. Regarding the incompliance of physicians, there were 9 effective cases in the cancer group and 3 effective cases in the benign group, which accounted for 52.9% and 23.1% of all cases (See Table 7). The χ^2 and P values were shown to be 2.738 and 0.141, which indicated no statistically significant differences present between these two groups.

Discussion

Previous study has reported that gastrointestinal cancer accounts for more than 20% of all cancers across the world [3]. Specifically, the most common types of gastrointestinal cancer are gastric cancer, colorectal cancer, and liver cancer. Among these types, colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide [14]. In our study, 72 of a total 148 patients experiencing malignant cancer were found to have gastrointestinal cancer, which accounted for the vast majority of all cancer cases. This statistic was consistent with the findings of the previous report.

Infection plays a prominent role in the death of cancer patients. Chang et al. reported a survey analyzed 112 patients who had advanced gastrointestinal cancer and found that toxic shock caused by infection ranked the first among all causes of death [15]. In this study, we compared the infection sites between cancer (148) and non-cancer patients (172) and found that the 3 top ranked infections were abdominal, lung, and urinary tract infections. Compared to the benign patient group, the incidence of abdominal infection was significantly higher in cancer patients ($P < 0.01$). Contrastingly, no significant difference was found in the occurrence of lung and urinary tract infections. Similarly, Li et al. also found that abdominal infections, which included gastrointestinal tract infections, were the most common types of infections and accounted for 34% of every 100 cases of cancer-associated infections [16]. Abdominal infections involved both primary and secondary infections and both of them were found among cancer patients, but they were especially prominent in digestive tract cancer patients.

Yao et al. studied the pathogens of nosocomial infections in malignant cancer patients and found that *Enterobacteriaceae* accounted for 65.3% the 118 pathogen strains detected, which included *Peria asiatica*, *E. coli*, and *Klebsiella pneumonia* [17]. In line with the findings of a previous report, our results showed that Enterobacteriaceae accounted for 46.1% in a benign patient group, which included *E. coli*, *P. aeruginosa*, and *K. pneumonia*. The significantly higher incidence indicated an important role of the *P. aeruginosa* infection in cancer patients.

It was also noted that the detection of *E. coli* was dramatically increased. Moreover, *P. aeruginosa* was a pathogen

Table 4
Cancer and non-cancer patients' pathogen distribution (strain) and composition ratio (%).

Group	*E. coli*	*K. pneumoniae*	*P. aeruginosa*	*E. faecium*	*Enterobacteriaceae* producing ESBL or KPC	Multidrug resistant G + bacteria
Cancer group	13(12.7)	6(5.9)	11(10.8)	11(10.8)	11(10.8)	8(7.8)
Non-cancer group	15(11.6)	24(18.6)	4(3.1)	17(13.2)	25(19.4)	5(3.9)
χ^2	0.067	8.159	5.538	0.306	3.199	1.688
P	0.841	0.005	0.029	0.686	0.099	0.253

Table 5
Distribution of pathogenic bacteria and strain ratio in patients with digestive and non-digestive cancers (%).

Group	Non-fermenting bacteria	Enterococci	Gram-positive cocci	ESBL-producing *E. coli*	Non-white rot fungus
Gastrointestinal cancer group	11	7	12	1	5
Non-digestive cancer group	9	9	9	9	2
χ^2	0.249	0.297	0.540	7.096	1.38
P	0.804	0.786	0.625	0.016	0.436

Table 6
Drug treatment and therapeutic effect in cancer and non-cancer groups which followed the recommendation from the pharmacist consultation.

	Cure or improved (cases)	Sustained or dead (cases)
Cancer group	Meropenem (34) Vancomycin (33) Imipenem Cilastatin (11) Piperacillin Tazobactam (14) Cefoperazone Sulbactam (10) Ceftazidime (6) Minocycline (5)	Vancomycin (9) Imipenem Cilastatin (5) Meropenem (2)
Non-cancer group	Meropenem (38) Vancomycin (45) Imipenem Cilastatin (12) Piperacillin Tazobactam (17) Cefoperazone Sulbactam (11) Ceftazidime (7) Minocycline (5)	Vancomycin (7) Imipenem Cilastatin (3) Meropenem (4)

Table 7
Consultation advice compliance and drug treatment results.

Group	Compliance (example, %)			Incompliance (example, %)		
	Effective	Ineffective	Total	Effective	Ineffective	Total
Cancer group	112(85.5)	19(14.5)	131(100)	9(52.9)	8(47.1)	17(100)
Non-cancer group	128(81.0)	30(19.0)	158(100)	3(23.1)	10(76.9)	13(100)
χ^2	14.03			2.738		
P value	0.347			0.141		

commonly acquired in hospitals. Studies have shown that patients with neutropenia and compromised immune functions caused by chemotherapy and radiotherapy for solid forms of cancer are more likely to suffer from *P. aeruginosa* infections in the lower respiratory tract. *E. coli*, as a gastrointestinal colonization bacterium, are easily detected due to the increased use of invasive operations and diverse treatments.

Potential risk factors for infections with drug-resistant bacteria include the exposure to antibiotics over the past 90 days, last admission to a hospital for more than 5 days, frequent detection of drug-resistant bacteria, and immune-deficient population [18]. Comparing the two patient groups, the detection rate of ESBL producing and KPC producing *Enterobacteriaceae* in the benign group was higher than that seen in the cancer group, and ESBL producing *E. coli* in the digestive cancer category was significantly lower than that found in the non-digestive cancer category, which suggested that cancer patients with digestive cancer needed to pay close attention to non-fermentative bacterial infections, such as *P. aeruginosa*.

The influence of infections containing drug-resistant bacteria on the prognosis of cancer patients has drawn an increasing attention. Previous studies have revealed that the mortality of patients with spontaneous bacterial peritonitis caused by multiple drug-resistant bacteria was four times higher than that caused by non-resistant bacteria [19]. Based on our comparison, the proportion of multidrug-resistant *Enterobacteriaceae* in cancer group was lower than that of the benign group (10.8% vs. 19.4%), while the proportion of *P. aeruginosa* in the cancer group was significantly higher than that of the benign group (10.8% vs. 3.1%). Therefore, individualized assessments should be strengthened to avoid overexposure to carbapenem drugs as well as to delay the process of acquired drug resistance.

Despite the increasing resistance of *Enterobacteriaceae bacteria* to carbapenems, which is related to the drug exposure, carbapenems remain the primary treatment option available for severe infections and complicated abdominal infections. From the statistical analysis, the combination of carbapenems and the beta lactam/enzyme inhibitor constitutes most of the drug treatment recommended by the pharmacist consultation, which assists with quinolones, aminoglycosides and tetracyclines. In conclusion, the initial empirical treatment of full-dose and full-time therapy are particularly important, because otherwise, it would be most likely to screen drug-resistant infections, such as *A. baumannii* and *Stenotrophomonas maltophilia* [20].

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Competing interests

All of authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have

approved the final version. Additionally, there are no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study received ethical approval by (protocol number: C2015-006). All methods were carried out in accordance with approved rules and regulations.

Informed consent was obtained from all subjects. No personal patient information was disclosed.

References

[1] Li J. Gastrointestinal tract tumors and microbial infections. Chin J Gastroenterol Hepatol 2013;22(2):109–15.
[2] Kuper H, Adami HO, Trichopoulos D. Infections as a major preventable cause of human cancer. J Intern Med 2000;248(3):171–83.
[3] de Martel C, Ferlay J, Franceschi S, Vignat J, Bray F, Forman D, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol 2012;13(6):607–15.
[4] Freire MP, de Oliveira Garcia D, Garcia CP, Campagnari Bueno MF, Camargo CH, Kono Magri ASG, et al. Bloodstream infection caused by extensively drug-resistant *Acinetobacter baumannii* in cancer patients: high mortality associated with delayed treatment rather than with the degree of neutropenia. Clin Microbiol Infect 2016;22(4):352–8.
[5] Peng WW. Xiandai Ganranxing Jibingyuchuangranbingxue [M]. Beijing Science Publication; 2000. p. 473–7.
[6] Mu XL, Yan SR, Wang ZR. Causes of infections in 168 tumor patients and prevention countermeasures. Chin J Nosocomiol 2013;23(15):3647–9.
[7] Kamboj M, Childers T, Sugalski J, Antonelli D, Bingener-Casey J, Cannon J, et al. Risk of surgical site infection (SSI) following colorectal resection is higher in patients with disseminated cancer: an NCCN member cohort study. Infect Control Hosp Epidemiol 2018;39(5):555–62.
[8] Baden LR, Swaminathan S, Angarone M, Blouin G, Camins BC, Casper C, et al. Prevention and treatment of cancer-related infections, version 2.2016, NCCN clinical practice guidelines in oncology. J Natl Compr Cancer Netw 2016;14(7):882–913.
[9] National Comprehensive Cancer Network. Prevention and treatment of cancer-related infections (version 2), 21; 2017. p. 1–159.
[10] Wilson AP, Livermore DM, Otter JA, Warren RE, Jenks P, Enoch DA, et al. Prevention and control of multi-drug-resistant gram-negative bacteria: recommendations from a Joint Working Party. J Hosp Infect 2016;92(Suppl 1):S1–44.
[11] Kaye KS, Pogue JM. Infections caused by resistant gram-negative bacteria: epidemiology and management. Pharmacotherapy 2015;35(10):949–62.
[12] Xiao YH, Wang J, Li Y, M.O.H.N.A.R.I. Net. Bacterial resistance surveillance in China: a report from Mohnarin 2004–2005. Eur J Clin Microbiol Infect Dis 2008;27(8):697–708.
[13] Yang F. Commentary on guideline principles for clinical use of antibiotics (version 2015). Chin J Clin Infect Dis 2016;5:390–3.
[14] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127(12):2893–917.
[15] Chang LL, Yang HJ, Wang L, Zhou XN, Zhang SM, Zhang ZH. Retrospective analysis on mortality of 112 patients with digestive tomor of late stage. Guide of China Medicine 2013;11(19):422–3.
[16] Li AM, Wang D. Clinical study of concurrent infection in the treatment of cancer patients with medical treatment. Clin Res Prac 2017;2(31):20–1.
[17] Yao DM, Cao W, Qing ZJ. Analysis of pathogen distribution and drug resistance of nosocomial infections accompanied in patients with malignant tumor. J Cancer Res 2008;20(2):155–8.
[18] Peleg AY, Hopper DC. Hospital-acquired infections due to gram-negative bacteria. N Engl J Med 2010;362(19):1806–13.
[19] Wiest R, Krag A, Gerbes A. Spontaneous bacterial peritonitis: recent guidelines and beyond. Gut 2012;61(2):297–310.
[20] Jia LH, Li ZD. Experience of clinical pharmacists participating in the treatment of one case of multidrug resistant *Acinetobacter baumannii* infection. Chin Pharm 2015;18(5):816–8.