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Epidemiology and Drug Resistance Analysis of Mixed Infection in Orthopedic Surgical Sites

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Abstract

Background: Infection, including mixed infection, is not uncommon in orthopedic surgical incision. This study aimed to investigate the epidemiology and drug resistance of mixed infections after orthopedic surgical procedures.
Methods: We retrospectively analyzed 533 orthopedic surgical site infections (SSIs) in a university hospital from 2012 to 2017. Eighty-six patients (218 strains) with bacterial culture results showing more than one strain were screened to explore their epidemiology and drug resistance.
Results: Of 218 bacterial strains, 2–7 bacterial infections were noted in each wound. Most infections were caused by two kinds of bacteria (65.1%). The number of infections decreased with increased number of strains. The combinations of pathogenic micro-organisms were all gram-negative, 55.81%; gram-positive and gram-negative, 30.23%; all gram-positive, 12.79%; and gram-positive and fungi, 1.16%. Their resistance is consistent with the bacterial resistance of 447 cases of single bacterial SSI during the same period. Hospitalization duration was longer (9.8–20.6 d).
Conclusion: Our study shows no significant changes in epidemiology and drug resistance caused by mixed infections in the orthopedic surgical site because of coordination and competition among micro-organisms. These bacteria are difficult to control, leading to extended hospitalization. Antibiotic agents should be chosen strictly according to drug sensitivity, and ineffective antibiotic agents must be avoided.

Keywords: distribution of pathogenic bacteria; drug resistance; interaction between bacteria; mixed infection; orthopedic surgical procedures

Use of surgical procedures is one of the most important methods for the treatment of orthopedic patients [1]. Local soft tissue injury, internal fixation, surgical bleeding, long operation duration, and other factors lead to increased risk of incision infection [2]. Incision infection is still the most common early complication after operations. It directly increases the medical expenses of patients, prolongs hospitalization, delays fracture healing, necessitates reoperation or multiple operations, and makes patients lose the trust of surgeons [3]. If infection is difficult to control, amputation may be indicated, which can even be life-threatening [3].

The basic idea of bone infection control is to eliminate bacteria that cannot be killed by antibiotic agents, improve body immunity, create an environment conducive to enhance body immunity and function of antibiotic agents, and kill planktonic bacteria through antibiotic agents. Thus, in the management of post-operative infection, besides effective debridement and drainage, it is particularly important to analyze the epidemiologic status and drug resistance of pathogens.

Mixed infection refers to infection caused by two or more pathogens at the same time (e.g., a patient experiencing nasal gangrene and epidemic lymphangitis because of bovine tuberculosis and brucellosis). *Staphylococcus aureus* and *Pseudomonas aeruginosa* are often found in the wounds of patients with extensive burns and whose condition is complex and difficult. Such patients often need large doses of antibiotic agents, which may not always control the infection effectively. In addition, synergistic effects among various pathogenic

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micro-organisms in mixed infections, such as synergistic gangrene caused by hemolytic *S. aureus* and *Streptococcus microaerogenes*, promote the reproduction of anaerobic bacteria because of the consumption of oxygen by aerobic bacteria.

Initially, the wound appears as local cellulitis, with red periphery and purple center, then progresses to gangrene and ulcer, and gradually expands. The ulcer edge is purple-black and accompanied by severe pain. Therefore, one of the intractable aspects of surgical site mixed infection is the increase in the number of pathogenic bacteria, and adjustment of antibiotic doses is still not effective in controlling infection.

Many studies have investigated the interaction of pathogenic bacteria at the molecular level, but few studies have focused at the human ecologic environment level to determine whether epidemiologic and drug resistance of pathogenic bacteria varied because of the interaction between multiple pathogens on mixed infection. Infection and mixed infection are not uncommon in an orthopedic surgical incision because of its proximity to the body surface, long operation duration, excessive bleeding during operation, and the need for internal implants. Thus, to improve the control and management of mixed infection in orthopedic incisions, this study aimed to observe and understand the characteristics of pathogenic bacteria and drug resistance of mixed infection after orthopedic surgical procedures.

Methods

General information and patients

This study retrospectively analyzed 86 patients with mixed infection of a surgical incision among 533 patients with nosocomial infection after orthopedic operation in the First Affiliated Hospital of Nanchang University from March 2012 to July 2017. The inclusion criteria were as follows: (1) Complete clinical data; (2) sterile surgical treatment; (3) **diagnosis of surgical site infection** according to the criteria developed by the Joint International Commission Health Organization (2002) (i.e., a large amount of purulent material was drained from the wound; the wound split spontaneously with purulent drainage; wound drainage culture results were positive, or Gram stain results were positive; the surgeon noticed swelling or drainage from the incision, identified an infection, and opened the incision); (4) diagnosed as nosocomial infection according to the diagnostic criteria for nosocomial infection [4]; (5) positive bacterial culture in secretion or incision drainage fluid; and (6) more than one strain in a single culture.

The exclusion criteria were (1) repeated isolation of strains from the same surgical site in the same patient; (2) contaminated bacteria; (3) infectious diseases; (4) complicated with autoimmune diseases; (5) complicated with infectious diseases; (6) complicated with severe diseases; and (7) impaired organ function.

Examination method

The isolation media for the drug susceptibility tests were 90-mm Chinese blue agar medium (Shanghai Kemajia Biotechnology Co., Ltd.) and Colombian blood agar medium (Shanghai Kemajia Biotechnology Co., Ltd.). Pathogen identification and the drug susceptibility test were performed using the VITEK-2 Compact automatic bacterial tester (bioMerieux, Hazelwood, MO). Drug sensitivity was evaluated according to the 2017 Clinical and Laboratory Standards Institute standards.

The study was approved by the Ethics Committee of The First Affiliated Hospital of Nanchang University (approval #20170720), and all participants provided written informed consent.

Statistical methods

SPSS 19.0 Statistical Software was used to establish a database and perform statistical analyses. The data normality test was performed using a normal curve histogram, Q-Q graph, P-P graph K-S, and Shapiro-Wilk tests. These data were not normally distributed; therefore, non-parametric tests, such as Mann-Whitney and Wilcoxon non-rank sum tests, were used in comparing differences, which were deemed statistically significant if $p < 0.05$.

Results

Bacterial distribution

A total of 218 bacterial strains from 86 patients were included in this study. There were 152 gram-negative bacteria (69.72%), 65 gram-positive bacteria (29.82%), and one fungus (0.46%). *Enterobacter cloacae* (12.3%), *S. aureus* (9.6%), *P. aeruginosa* (7.7%), *Escherichia coli* (7.5%), and *Baumann/Acinetobacter haemolyticus* (6.8%) were the most common (Table 1). The foot (32.56%), leg (23.74%), forearm (16.96%), and knee (15.81%) were the most common sites of infection (Fig. 1).

There were 2-7 kinds of bacterial infections in each wound, of which two kinds of bacteria caused the most infections, accounting for 65.1% of the analyzed cases. With the increase in the number of strains, the number of infections decreased. There were four combinations of pathogenic bacteria: all gram-negative bacteria (55.81%), mixed gram-negative bacteria and gram-positive bacteria (30.23%), positive gram-positive bacteria (12.79%), and mixed gram-positive bacteria and fungi (1.16%). There are only two combinations of positive bacteria in the combinations of all gram-positive bacteria, but not in the combinations of all gram-positive bacteria. Mixed

Table 1. Distribution of Bacterial Species

Culture	*Number of bacteria*	*Constituent ratio (%)*
Enterobacter cloacae	27	12.3
Staphylococcus aureus	21	9.6
Pseudomonas aeruginosa	17	7.7
Escherichia coli	16	7.5
Acinetobacter haemolyticus	15	6.8
Aeromonas hydrophila	13	5.9
Staphylococcus epidermidis	10	4.5
Klebsiella pneumoniae	9	4.1
Enterobacter aerogenes	8	3.6
Xanthomonas maltophilia	7	3.2
Enterococcus faecalis	6	2.7
Morganella morii	4	1.6
Other	65	29.8
Total	218	100

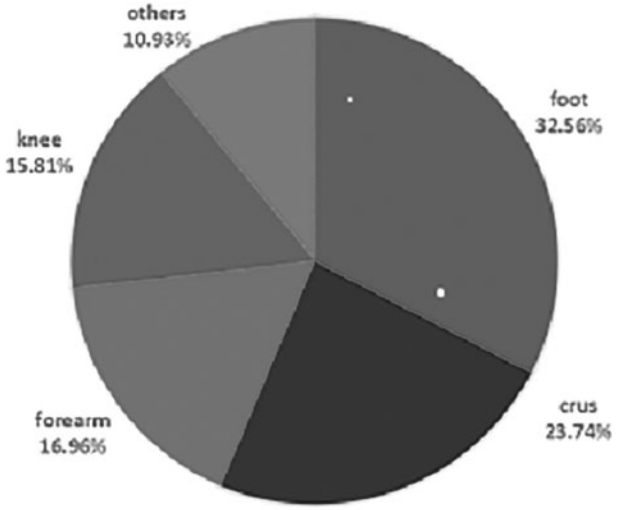

FIG. 1. Surgical site distribution of mixed infection.

infections caused by more than two gram-positive bacteria were found (Table 2).

Drug resistance of pathogenic bacteria

Gram-negative bacteria showed good susceptibility to cefoperazone/sulbactam sodium (11.1%) and meropenem (13.3%) and drug resistance to ampicillin (82%), aztreonam (70%), and amoxicillin/clavulanate potassium (75%) (Table 3). Gram-positive bacteria were highly susceptible to linezolid (0%). Furantoin (resistance rate 0%) showed good sensitivity, and ampicillin (resistance rate 100%) and amoxicillin/clavulanate potassium (75%) had high drug resistance (Table 4). This is consistent with the bacterial resistance of 447 cases of single bacterial surgical site infections during the same period (Table 5). Patients with mixed incision infection were defined as patients with simple postoperative infection. The 95% confidence interval for extended hospital stay was (9.8-20.6) days.

Discussion

Our results revealed the presence of two to seven kinds of bacterial infections in each wound, of which two kinds of bacteria, accounting for 65.1%, caused the most infections. The number of infections decreased as the number of strains increased. The four combinations of pathogenic bacteria present in our study included all gram-negative bacteria, mixed gram-negative and gram-positive bacteria, all gram-positive bacteria, and mixed gram-positive bacteria and fungi. In particular, only combinations of two gram-positive bacteria were found in mixed infections caused solely by the combination of pure gram-positive bacteria, and no mixed infections caused by more than two gram-positive bacteria were found.

In the ecosystem of orthopedic surgical sites, when the absolute amount of living space and nutrients is insufficient, two or more microbial groups compete for the same resources. Antagonistic micro-organisms can also capture water and nutrients, occupy space, consume oxygen, and other resources by rapid growth and reproduction to eliminate other groups of pathogens in the same habitat [5,6]. These resources include nutrients, oxygen, and space. Therefore, competition types are divided into nutritional competition and spatial competition. This competition results in fewer infections as the number of strains increase.

No relevant literature reports that the coexistence of more than two gram-positive bacteria will lead to strong interspecific competitions, which limits their strains. This may be related to the overall infection of bacteria—mainly gram-negative bacteria. From 2012 to 2017, 86 patients experienced mixed incisional infections after orthopedic operation. In all, the recorded 218 strains of bacteria, including 152 strains of gram-negative bacteria (69.72%), 65 strains of gram-positive bacteria (29.81%), and one strain of fungus (0.47%), confirm the report that the main infection after orthopedic surgical procedures is gram-negative bacterial infection.

E. cloacae, *S. aureus, P. aeruginosa*, *E. coli,* and *Baumann/A. haemolyticus* were the most common mixed infections in our hospital. This is generally consistent with the reported pathogenic bacteria in most orthopedic surgical site infections [7–9]. The foot, leg, forearm, and knee were the most common sites of infection. Gram-positive bacteria were susceptible to linezolid and furantoin, ampicillin, and amoxicillin/clavulanate potassium. Gram-negative bacteria are highly sensitive to cefoperazone/sulbactam sodium and meropenem and fairly sensitive to ampicillin, aztreonam, and amoxicillin/clavulanate potassium. This is consistent with the bacterial resistance of 447 cases of single bacterial surgical site infections during the same period.

TABLE 2. COMBINATION MODE OF BACTERIAL SPECIES

Combinations / *Strains* \ *Numbs*	*All G+*	*All G—*	*G+, G—mixing*	*G+, fungi mixing*	*Total*
2	28	11	17	1	56
3	10	0	5	0	15
4	8	0	4	0	12
5	1	0	0	0	1
6	1	0	0	0	1
Total	48	11	26	1	86

Numb = number of strains, G+ = gram-positive bacteria; G— = gram-negative bacteria.

Table 3. Resistance of Gram-Negative Bacteria to Antibiotic Agents

	Aerobacter cloacae		E. coli		Pseudomonas aeruginosa		Acinetobacter haemolyticus		Aeromonas hydrophila		*Amount*
	(n = 27)		*(n = 16)*		(n = 14)		(n = 13)		(n = 13)		*(n = 83)*
Antibacterials	*Numb*	*R (%)*	*Numb*	*R (%)*	*Numb*	*R (%)*	*Numb*	*R (%)*	*Numb*	*R (%)*	*Overall R (%)*
Ampicillin	26	100	15	53.3	1	100	1	100	6	66.7	82
piperacillin	27	40.7	15	53.3	13	7.7	13	61.5	0	0	41
Amoxicillin / clavulanic acid	24	83.3	15	33.3	9	100	9	88.9	12	83.3	75
Ampicillin / sulbactam	8	50	8	50	5	60	8	100	5	60	65
Cefoperazone / sulbactam sodium	9	11.1	4	0	3	33.3	5	20	3	0	12.5
Cefoperazone	11	45.5	8	37.5	9	33.3	7	71.4	6	16.7	41
Ceftazidime	27	22.2	16	37.5	13	30.8	13	69.2	13	30.8	35
Ceftriaxone	16	50	10	60	11	27.3	12	58.3	10	30	46
Cefotaxime	19	31.6	11	54.5	11	36.4	13	69.2	11	45.5	46
Cefepime	18	27.8	11	54.5	9	44.4	12	66.7	6	0	39
Cefoxitin	26	69.2	15	13.3	10	30	7	100	13	38.5	49
Aztreonam	20	80	11	81.8	3	33.3	1	100	11	45.5	70
Imipenem	27	63	15	46.7	11	81.8	7	100	8	62.5	66
Meropenem	15	13.3	7	28.6	3	33.3	5	80	7	28.6	30

The distribution, quantity, and drug resistance of bacteria in mixed surgical site infection after orthopedic operation are not significantly different from those caused by a single pathogen because of the interaction between pathogens. Mixed infections of orthopedic surgical sites form a small ecosystem. Its composition and stable population dynamics ultimately come from the interaction between organisms [10]. Various kinds and high concentration of micro-organisms exist in the biologic environment, but the existing and relatively small available space enables coevolution with unique physical and chemical interactions among species.

Table 4. Resistance of Gram-Positive Bacteria to Antibiotic Agents

	Staphylococcus aureus		*Staphylococcus epidermidis*		*Enterococcus faecalis*		Overall (%)
	(n = 21)		(n = 10)		*(n = 6)*		*(n = 37)*
Antibacterials	*Numb*	*R (%)*	*Numb*	*R (%)*	*Numb*	*R (%)*	*R (%)*
Penicillin	3	66.7	—	—	2	50	60
Ampicillin	9	100	5	100	3	0	100
Oxacillin	19	15.8	10	70	1	100	36.7
Gentamicin	20	10	10	60	3	33.3	29.3
Rifampicin	19	10.5	10	10	6	66.7	20
Levofloxacin	20	30	10	60	6	50	41.7
Clindamycin	1	100	—	—	2	0	33.3
Streptomycin	13	46.2	3	100	—	—	56.3
Erythromycin	19	31.6	10	60	6	66.7	45.7
Linezolid	15	0	10	0	4	—	0
Vancomycin	20	10	10	20	5	40	17.1
Achromycin	7	42.9	6	33.3	3	66.7	43.8
Nitrofurantoin	13	0	5	0	3	—	0
sulbactam sodium	13	15.4	4	25	2	50	21.1
Ceftazidime	14	14.3	4	100	3	66.7	38.1
Moxifloxacin	18	22.2	10	30	1	0	24.1
Amoxicillin/clavulanate potassium.	19	63.2	8	100	1	100	75
Cefotaxime	14	28.6	4	75	3	33.3	38.1
Gentamicin	20	10	10	60	3	33.3	27.3

Numb. = number of plants; R = drug resistance rate; "-" = not applicable.

Table 5. Drug Resistance of Single Bacterial Surgical Site Infections in Orthopedics

Baumann/Acinetobacter haemolyticus			Escherichia coli			Pseudomonas aeruginosa			Enterobacter cloacae			Staphylococcus aureus		
Antibiotics	*Num*	*R (%)*	*Antibiotics*	*Num*	*R (%)*	*Antibiotics*	*Num*	*R (%)*	*Antibiotics*	*Num*	*R (%)*	*Antibiotics*	*Num*	*R (%)*
Cefotetan	87	81	ceftetan	90	5.53	ceftetan	73	97.24	ceftetan	80	83.77	penicillin	95	97.89
Cefazolin	84	78	Amikacin	156	8.32	Amikacin	99	10.09	amikacin	140	52.15	Amoxicillin/ clavulanic acid	97	52.59
Ceftriaxone	103	77.01	Cefazolin	138	81.14	Cefazolin	74	100	Amoxicillin/ claulanic acid	111	71.18	Ceftriaxone	87	57.47
Cefepime	105	68.98	Ceftriaxone	136	77.18	Ceftriaxone	96	94.78	Cefazolin	125	98.39	Levofloxacin	125	20.81
Levofloxacin	106	57.99	Cefepime	139	41.72	Cefepime	101	16.82	Ceftriaxone	120	35.01	Tetracycline	119	30.24
Tobramycin	100	55	Levofloxacin	158	50.61	Levofloxacin	100	13.99	Cefepime	125	16.71	Moxifloxacin	111	8.1
Cefoperazone/ sulbactin	91	23.01	Tetracycline	68	67.66	Tobramycin	85	12.93	Levofloxacin	138	6.53	Ciprofloxacin	126	24.59
Ceftazidine	103	57	Tobramycin	143	27.28	Cefoperazone/ sulbactam	69	13.04	Piperacillin	108	26.86	Gentamicin	123	29.02
Ciprofloxacin	102	67	Cefoperazone/ sulbactam	117	5.96	Ceftazidine	97	22.69	Tetracycline	96	14.58	Compound neoprene	127	14.16
Gentamicin	106	62.04	Ceftazidine	154	47.41	Ciprofloxacin	101	17.83	Ciprofloxacin	125	18.41	Ticarcillin	29	0
Meropenem	95	59.99	Ciprofloxacin	158	49.87	Gentamicin	101	14.85	Cefoperazone/ sulbactam	108	7.4	Ampicillin/ sulbactam	84	59.51
Compound xinnomin	105	63	Gentamicin	148	50.66	Meropenem	71	18.32	Ceftadime	137	24.09	Ampicillin	97	100
Imipenem	92	58.99	Meropenem	137	8.02	Compound neoprene	87	86.2	Ciprofloxacin	135	11.1	Clocomycin	126	68.25
Ampicillin/ sulbactam	96	62.1	Trimoxazole	154	59.73	Impenem	101	15.84	Gentamicin	140	17.87	Erythromycin	124	70.16
Ampicillin	86	80	Ertapenem	133	9.01	Ampicillin/ sulbactam	65	96.93	Meropenem	126	8.73	Benzoxacillin	124	52.41
Ammonia quna	80	67	Imipenem	159	5.66	Ampicillin	79	97.47	Trimethoprim	137	21.15	Linezolid	122	0
Paracillin/tazobar	89	55	Ampicillin/ sulbactam	87	65.52	Paracillin/ tazobar	97	17.52	Ertapenem	118	12.71	Rifampicin	125	9.57
Nitrofurantoin	84	73.01	Ampicillin	157	93	Nitrofurantoin	71	97.17	Imipenem	140	12.87	Nitrofurantoin	34	0

Num = number of bacteria tested for drug sensitivity; R = drug resistance rate.

Some microorganisms have evolved mutually or even synergistically to promote cohabitation and efficient utilization of metabolic byproducts in the same ecosystem, while others have developed competitive antagonistic methods in the process of cocloning. One bacterium can affect the niche of the reproduction of another bacterium in the wound, making it easy to be colonized by pathogenic bacteria or caused by two or more non-pathogenic micro-organisms. For example, cystic fibrosis in the lung is often caused by *P. aeruginosa*, *S. aureus*, *Haemophilus influenzae, Burkholderia cepacia,* and other bacteria. These bacteria developed increased resistance through metabolic feeding or quorum sensing (QS)-related signaling mechanisms, bacterial tolerance, and biofilm development [11–14] in adults. *S. epidermidis* and *S. aureus* compete for nasal mucosal colonization and ESP-serine protease-producing *S. epidermidis* strains to eradicate *S. aureus* nasal colonization.

Mixed surgical site infection after orthopedic operation is not uncommon because the site is close to the body surface. Because *S. aureus* has always been a common bacterium in orthopedic surgical site infections, Regev-Yochay et al. [15] and Bogaert et al. [16] investigated another interaction: *S. aureus* carriers and the effect of pneumococcal conjugate vaccination on the increase of the carrying capacity of *S. aureus* and *S. aureus*-related diseases, and microbial interference with the protection ability of *S. pneumoniae* carriers, respectively.

Armbruster et al. [17] found that secretory staphylococcal protein ASpA inhibited biofilm formation of specific clinical isolates of *P. aeruginosa* and phagocytosis of neutrophils to all clinical isolates tested. Through reverse transcription polymerase chain reaction and other methods, Deng et al. [18] found that the cis-2-dodecanoic acid produced by *B. cepacia* mediated the communication with *P. aeruginosa* by interfering with the QS system and type III secretory system, which resulted in biofilm formation and virulence of *P. aeruginosa*. For down-regulation of force factor synthesis, Alex et al. [19] found that compared with single infection, the adhesion of *E. coli* and *Citrobacter freundii* to HeLa cells increased significantly. Moreover, *E. coli* carrying F-pili gene (traA) could form bacterial aggregates only in the presence of *C. freundii*.

Meanwhile, scanning electron microscopy analysis showed that both bacterial aggregates and enhanced biofilms formed by coinfection were mediated by flexible pili. In addition, the use of specific inhibitors of F-pili significantly reduced the formation of mixed infectious bacterial membranes. The results show, however, that the distribution, quantity, and drug resistance of mixed infections and post-operative infections caused by a single pathogen do not differ significantly because of the interaction between pathogens.

Our study shows that mixed surgical site infection significantly prolongs hospital stay. This may be related to the poor basic condition of patients with mixed infections, low immunity, and the difficulty of single antibiotic agents to cover the sensitive range of their bacteria. Other studies speculate that when mixed infections are found, doctors may extend the hospital stay to ensure infection control even after reaching discharge indications for fear that the infection will not be controlled completely.

Mixed infection after orthopedic operation is caused by many kinds of pathogenic bacteria and various combinations of pathogenic bacteria, which are difficult to control and prolonge hospitalization duration. It is difficult for conventional single or compound antibiotic agents to target surgical sites simultaneously caused by gram-negative bacteria and gram-positive bacteria. Moreover, published literature shows that more than two antibiotic agents are independent risk factors for infection after orthopedic surgical procedures, and various antibiotic agents aggravate the burden of patients, which necessitates strict matching of antibiotic agents sensitive to pathogenic bacteria according to drug sensitivity, so as to avoid unreasonable matching of antibiotic agents [20].

Age >60 years, body mass index >26.5 kg/m^2, hypertension, diabetes mellitus [21], coronary heart disease, chronic obstructive pulmonary disease, malnutrition, hypoproteinemia, and so on, are all risk factors of infection after orthopedic operation [19]. (Thus, it is necessary o improve immunity by active symptomatic treatment before operation.

Factors affecting the contact probability and time of pathogenic bacteria can be prevented by adjusting the treatment plan and making full use of protective factors, such as controlling the operation duration and laminar flow in operating rooms. In addition, the presence of infection before operation is an important reason for early infection after operation; thus, it is necessary to screen for occult infection to avoid infection.

Conclusion

The importance of multi-microbial diseases and interaction between human health and disease-related microbial communities have been recognized by the medical community. The multi-microbial causes of diseases and the effects of treatment, prevention, and prognosis have also been considered. Actively enhancing the immune capacity of patients and actively controlling factors affecting the probability of contact and time of pathogenic bacteria are strategies to prevent infections.

Our study indicated that the distribution, quantity, and drug resistance of bacteria in mixed surgical site infection after orthopedic surgical procedures are not significantly different from those caused by a single pathogen because of the interaction between pathogens. Various kinds of pathogenic bacteria are present in mixed infections after orthopedic operations. These bacteria are difficult to control, resulting in significantly prolonged hospitalization.

Use of conventional single or compound antibiotic agents may be ineffective in managing surgical sites, when both gram-negative and gram-positive bacterial infections are present. This necessitates that antibiotic agents sensitive to pathogenic bacteria should be matched strictly according to drug sensitivity to avoid ineffective antibiotic matching and minimize unnecessary administration of antibiotic agents to patients, which would create a greater burden to the body.

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Author Disclosure Statement

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References

1. Mu Y, Edwards JR, Horan TC, et al. Improving risk-adjusted measures of surgical site infection for the national health care safety network. Infect Control Hosp Epidemiol 2011;32:970–986.
2. Brophy RH, Wright RW, Huston LJ, et al. Factors associated with infection following anterior cruciate ligament reconstruction. J Bone Joint Surg Am 2015;97:450–454.
3. Uçkay I, Hoffmeyer P, Lew D, Pittet D. Prevention of surgical site infections in orthopaedic surgery and bone trauma: State-of-the-art update. J Hosp Infect 2013;84:5–12.
4. Ministry of Health of the People's Republic of China. Diagnostic criteria for nosocomial infection. Chin Med J 2001;81:460–465.
5. Cherif M, Loreau M. Stoichiometric constraints on resource use, competitive interactions, and elemental cycling in microbial decomposers. Am Nat 2007;169:709–724.
6. Chow SS, Wilke CO, Ofria C, et al. Adaptive radiation from resource competition in digital organisms. Science 2004;305:84–86.
7. Faxiang L, Ganghua C, Xiaokun S, Xinling H, Weishan W, Chenhui S. Characteristics of pathogens and risk factors of surgical site infection in orthopedic patients in five consecutive years. Chin J Infect Control 2016;15:466–470.
8. Yang L, Huang Y, Dong Y, et al. Distribution and drug resistance of pathogens isolated from surgical incisions in orthopedic patients. Chin J Nosocomiol 2015;25:552–3+61.
9. Huixiang Z, Shijuan Z, Dun-zhen L, Fu-ying L. The characteristics and drug resistance of pathogenic bacteria in operative incision infection of patients in orthopedic. Medical Innovation of China 2015;12:112–115.
10. Liujia Q, Jiahui W, Daijie C. Bacterial interspecific interactions and their influences on mixed infections. Chin J Antibiotics 2019;9:999–1007.
11. Baldan R, Cigana C, Testa F, et al. Adaptation of *Pseudomonas aeruginosa* in cystic fibrosis airways influences virulence of *Staphylococcus aureus* in vitro and murine models of co-infection. PLoS One 2014;9:e89614.
12. Brogden KA, Guthmiller JM, Taylor CE. Human polymicrobial infections. Lancet 2005;365:253–255.
13. O'Sullivan AK, Sullivan J, Higuchi K, Montgomery AB. Health care utilization & costs for cystic fibrosis patients with pulmonary infections. Manag Care 2011;20:37–44.
14. Filkins LM, O'Toole GA. Cystic fibrosis lung infections: Polymicrobial, complex, and hard to treat. PLoS Pathog 2015;11:e1005258.
15. Regev-Yochay G, Dagan R, Raz M, et al. Association between carriage of *Streptococcus pneumoniae* and *Staphylococcus aureus* in children. JAMA 2004;292:716–720.
16. Bogaert D, van Belkum A, Sluijter M, et al. Colonisation by *Streptococcus pneumoniae* and *Staphylococcus aureus* in healthy children. Lancet 2004;363:1871–1872.
17. Armbruster CR, Wolter DJ, Mishra M, et al. *Staphylococcus aureus* Protein A mediates interspecies interactions at the cell surface of *Pseudomonas aeruginosa.* MBio 2016:7.
18. Deng Y, Boon C, Chen S, et al. Cis-2-dodecenoic acid signal modulates virulence of *Pseudomonas aeruginosa* through interference with quorum sensing systems and T3SS. BMC Microbiol 2013;13:231.
19. Pereira AL, Silva TN, Gomes AC, et al. Diarrhea-associated biofilm formed by enteroaggregative *Escherichia coli* and aggregative *Citrobacter freundii:* A consortium mediated by putative F pili. BMC Microbiol 2010;10:57.
20. Jing-tang B, Yan-xia G, Ze-qing L, Mei-lin X. Incidence and causes of infection after orthopedic surgery. Modern Instruments & Medical Treatment 2019;1:1–4.
21. Chen YS, Liu YH, Kunin CM, et al.. Use of prophylactic antibiotics in surgery at a medical center in southern Taiwan. J Formos Med Assoc 2002;101:741–748.

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