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Original Article

Changing microbiology of the prosthetic joint infection and updating antibiotics strategy

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Abstract: Background: With the increasing number in total joint arthroplasty (TJA), prosthetic joint infection (PJI) is becoming difficult to treat. Although many efforts have been made to eradicate PJI, whether current treatments are sufficient is still unknown. Therefore by studying microbiology and their susceptibility to antibiotic agents, our purpose was to get better understanding of pathogenesis and provide advice to update strategies to prevent and treat PJI. Material and methods: A retrospective analysis of 126 patients diagnosed as PJI during 2003 and 2013 was performed. The microbiology and antibiotic susceptibility of PJI were studied. A theoretical model analysis was used to compare the susceptibilities of three most prophylactically used antibiotics and their dual combination. Results: Through the study period, coagulase-negative staphylococci (CoNS) was the most commonly isolated strain (35.4%). The rising numbers of CoNS and methicillin-resistant staphylococci were found through the study period. All gram-positive microorganisms were sensitive to vancomycin, teicoplanin and linezolid, while 16 of 51 (31.4%) aerobic gram-positive organisms were resistant to gentamicin, 33 of 58 (56.9%) gram-positive organisms were resistant to cefazolin. Gram-negative ones were all sensitive to amikacin, piperacillin-tazobactam, and carbapenem. Conclusion: The combination of vancomycin and gentamicin can be used prophylactically in bone cement for TKA and vancomycin and cefazolin can be used parenterally for cementless TJA to prevent PJI. The antibiotic can be used empirically depending on the classification of PJI before the final culture result is available, as well as vancomycin plus carbapenem in early and late infections, and vancomycin alone in delayed infection.

Keywords: Antibiotic prophylaxis, arthroplasty, vancomycin, cefazolin

Introduction

With the help of total joint arthroplasty (TJA), thousands of patients gain satisfactory outcomes every year. Despite of the high success rate, complications of TJA are still inevitable, especially prosthetic joint infection (PJI), which is one of the most devastating and fearing complications. Once it happens, PJI will be a catastrophe for both patients and surgeons. It is reported currently that the incidence of PJI is between 0.5% and 1.1% in primary total knee arthroplasty (TKA) [1-4] while 0.3% and 0.6% in total hip arthroplasty (THA) [3, 5]. Although the prevalence of PJI is relatively low, with the booming number in TJA, PJI will become a heavy burden for the society.

Great efforts have been made to prevent and eradicate PJI by using methods such as prophylactically used antibiotic [6] and antibiotic-impregnated cement [7]. Different medical therapies and surgical therapies are used depending on the type of PJI, duration of clinical symptoms, condition of implant and soft tissue, culture results of microbiology, and patients' comorbidities [8]. As the number of methicillin-resistant organisms increasing [6], whether current treatments are sufficient or not is left unknown. The microbiology and antibiotic susceptibility of PJI are the keys to selection of proper antibiotics for prevention and eradication of PJI.

The objectives of this study are to describe the microbiology of PJI, to identify the antibiotic susceptibility patterns of resistance and its changing trends over the last decades, and to offer a proper strategy for prophylactic and empirical use of antibiotics in treatment of PJI.

Table 1. Demographic of patients with PJI, 2003-2013

Factors	N	%
Gender (no. of patients)		
Male	52	41.2
Female	74	58.7
Primary diagnosis (no. of patients)		
Ankylosing spondylitis	5	4.0
Femoral neck fracture	29	23.0
Fracture of proximal part	2	1.6
Avascular necrosis of femoral head	16	12.7
Osteoarthritis	40	31.7
Rheumatoid arthritis	7	5.6
Traumatic arthritis	2	1.6
Developmental dysplasia of the hip	3	2.4
Unknown	22	17.5
Prosthetic (no. of patients)		
Hip	69	54.8
Knee	55	43.7
Shoulder	2	1.6
Treatment (no.)		
Debridement	20	23.0
Medical treatment	7	6.3
One-stage revision	13	18.3
Two-stage revision	50	50.0
Implant removal without replacement	3	2.4
Cultures (no.)		
Polymicrobial cultures	10	
Total	151	
	Range	Average
Age (year)	31-87	64.8
CRP (mg/L)	0.38-318	34.0
ESR (mm/h)	5-123	65.0
WBC (*10^9)	3-12.5	6.50
Time since joint replacement (year)	0.1-20	2.42

Table 2. Microbiology of prosthetic joint infection, 2003-2013

Microbiology	(%)
Coagulase negative Staphylococci	35.4
Staphylococcus aureus	21.2
Gram negative organisms	19.5
Others	15.0
Polymicrobial	8.8

Material and methods

This retrospective study was approved by the local institutional review and ethics board (2013-01-45). A retrospective analysis of 141 patients diagnosed as PJI from January 2003 to January 2013 at our hospital was performed. Our tertiary hospital performs about 1500 TJA operations per year. However, 15 of the 141 patients were excluded because they were treated at cooperative hospitals, and their medical records were not fully available. Finally, 126 patients were studied.

Diagnosis of PJI meets at least one of the following criteria [8, 9]: positive culture of the same microorganism in two or more cultures of synovial fluid or periprosthetic tissue (determined by the microbiologist), presence of purulence around the implant or of synovial fluid (determined by the surgeon), acute inflammation on histopathological examination of periprosthetic tissue (determined by the pathologist), or presence of a sinus tract communicating with the prosthesis.

During this study, identification of microbiology was gradually changed from tissue culture and synovial fluid culture to synovial fluid culture in the blood culture bottle and the fluid culture gained after sonication of prosthetic implants. Data about gender, age, primary diagnosis, surgical treatment, type of infection, and laboratory findings were collected from the medical records. The characteristics of 126 PJI patients are shown in **Table 1**. The infecting microbiology and its antimicrobial susceptibility were collected from microbiology laboratory culture reports. Finally, 151 culture results were available, 10 of which related to polymicrobial infection.

PJI was classified into early, delayed, or late infections, as suggested by Zimmerli [8]. The developing period is less than 3 months after surgery for an early infection, 3 to 24 months for a delayed infection, and more than 24 months for a late infection.

The antibiotic susceptibility of microbiology was reported as S (sensitive), I (intermediate) or R (resistant). The result was shown as the number of strains resistant to the given antibiotic divided by the total number of tested strains. Staphylococcal strains were tested for Oxacillin. For a result of R, the strains were considered as methicillin-resistant [10].

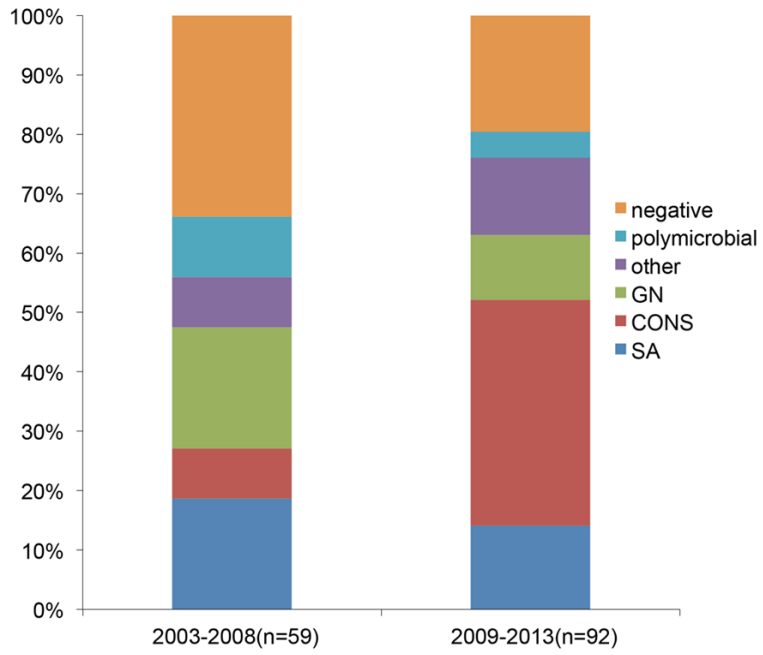

Figure 1. Changing patten of microbiological spectrum, 2003-2013.

The differences in patten of microbiological spectrum according to year categories were cross-compared by Chi Square test using SPSS 20.0. Univariate binary logistic regression analysis was performed to analyse the risk factors of antibiotics resistence. P<0.05 was considered as statistically significant.

Results

The theoretical model analysis is a theoretical calculation for dual antibiotic combinations, the combination was considered as sensitive if either or both of the antibiotics are sensitive.

The demographics of the 126 PJI patients are shown in **Table 1**. The three most common primary diagnoses before occurrence of PJI are osteoarthritis, femoral neck fracture, and avascular necrosis of femoral head.

Table 2 shows the prevalence of organisms related to culture positive PJI. Gram-positive organisms rank first among all. For PJI patients, Coagulase-negative Staphylococcus (CoNS) was the most commonly isolated strain, accounting for 35.4% of cases, followed by Staphylococcus aureus (SA, 21.2%), gram-negative organism (19.5%), other strains (15.0%), and Polymicrobial isolated ones. **Figure 1** shows the changing patten of microbiological spectrum throughout the study period. The difference between the spectrum during 2003-2008 and that during 2009-2013 was statistically significant (P<0.002). Specifically, the frequency of CoNS was higher during 2003-2008 than that during 2009-2013 (Chi-square test, P<0.001) and the decreasing of culture negative spectrum was found (Chi-square test, P=0.048), while changes of other spectra were not significant. Depending on the types of PJI (**Table 3**), methicillin-resistant CoNS (MRCoNS) was the most frequently isolated strain throughout the early, delayed and late infections (14.8%, 26.2%, and 36.4%, respectively), followed by Methicillin-sensitive Staphylococcus aureus (MSSA) (8.2%, 14.3%, and 15.2%, respectively). There is a relatively lower prevalence of gram-negative strains in delayed infections (3/42, 7.1%) than that in early infections (11/61, 18.0%, P=0.113) and late infections (5/33, 15.2%, P=0.29).

Vancomycin, teicoplanin and linezolid are the three most effective antibiotics for aerobic gram-positive PJI (**Table 4**). All the gram-positive organisms were sensitive to these three antibiotics. As the commonly used antibiotics for biofilm-related PJI, rifampicin and levofloxacin are also effective against aerobic gram-positive organisms, as 6 of 58 (10.3%) strains and 8 of 57 (14.0%) strains are resistant to them respectively. Moreover, 16 of 51 (31.4%) strains are resistant to gentamicin, the most commonly prophylactically used antibiotic in the bone cement; 33 of 58 (56.9%) gram-positive strains are resistant to cefazolin. Gram-negative ones are all sensitive to amikacin, piperacillin-tazobactam, and carbapenem (imipenem, meropenem), while 5 of 16 (31.3%) gram-negative strains are resistant to gentamicin. The susceptibilities of three most prophylactically used antibiotics and their dual combinations were compared by using theoretical model analysis (**Figure 2**). Gram-negative microbiology is considered resistant to vancomycin. When applied alone, vancomycin covers 76.4% of all the mi-

Table 3. Microbiology of prosthetic joint infection in different type of infection, 2003-2013

Microorganism		Type of infection					
		Early		Delayed		Late	
		N	% all	N	% all	N	% all
Gram-positive	MRSA	2	3.3	2	4.8	0	0.0
	MSSA	5	8.2	6	14.3	5	15.2
	MRCoNS	9	14.8	11	26.2	12	36.4
	MSCoNS	3	4.9	2	4.8	3	9.1
	Enterococcus faecalis	3	4.9	1	2.4	1	3.0
Gram-negative	Enterococcus faecium	0	0.0	1	2.4	0	0.0
	Pseudomonas aeruginosa	3	4.9	1	2.4	2	6.1
	Escherichia coli	3	4.9	0	0.0	3	9.1
	Acinetobacter	2	3.3	0	0.0	0	0.0
Others	Pseudomonas maltophilia	1	1.6	0	0.0	0	0.0
	Enterobacter cloacae	2	3.3	2	4.8	0	0.0
	Hemolytic streptococcus	0	0.0	0	0.0	0	0.0
	Streptococcus agalactiae	1	1.6	0	0.0	0	0.0
	Streptococcus dysgalactiae	0	0.0	1	2.4	0	0.0
	Pyogenic streptococcus	1	1.6	0	0.0	0	0.0
	Peptostreptococcus asaccharolyticus	1	1.6	0	0.0	0	0.0
	Candida parapsilosis	0	0.0	2	4.8	0	0.0
	Candida utilis	1	1.6	0	0.0	0	0.0
	Pichiapastoris	1	1.6	0	0.0	0	0.0
	Mycobacterium tuberculosis	2	3.3	0	0.0	0	0.0
	Polymicrobial	4	6.6	3	7.1	2	6.1
	Negative	17	27.9	10	23.8	5	15.2
		61	100.0	42	100.0	33	100.0

crobiology (68/89, 76.4%), while gentamicin and cefazolin cover only 67.2% (45/67) and 41.2% (40/68) respectively. Gentamicin plusvancomycin is the most efficient dual combination, with the highest sensitivity (78/89, 87.6%), which is much higher than that of cefazolin plusvancomycin (71/89, 79.8%), or cefazolin plusgentamicin (57/76, 75.0%).

All the strains and gram positive organisms isolated from PJI joint that fixed with bone cement had a lower cefazolin resistance rate than those fixed without bone cement (P=0.016, P=0.011) (**Tables 5** and **6**).

Discussion

With the booming number in TJA, the incidence of PJI is still relatively high [1-5]. Once it happens, it will be a catastrophe for both patients and surgeons. Although great efforts have been made to eradicate PJI, with the changing pattern of microbiology [11] and the increasing number of methicillin-resistant organisms [6], whether current treatments are sufficient or not is left unknown. Therefore, by analyzing the microbiology and antibiotic susceptibility of PJI, we tried to get better understanding of PJI pathogenesis and update the prevention and treatment strategy for PJI.

There are some limitations in our study. First, this retrospective study has its intrinsic shortcomings. Second, in vitro antibiotic test results should not replace in vivo ones, so further clinical outcome should be studied. Third, not all the PJI patients had their primary surgery at our institute; the different perioperative strategies taken to prevent PJI may cause confounding bias.

In our study, the most common isolates of PJI in our hospital are CoNS and SA, which account for 35.4% and 21.2% of total strains respectively. The results are consistent with other recent reports published by Stefansdottir [12],

Table 4. Microbiology susceptibility to antibiotic agents shown as the number of tested strains resistant to the given antibiotic divided by total number tested

Organism	Antibiotic																						
Aerobic gram-positive																							
	AUG	AMP	APS	PIP-TZB	PEN	CEP	IMI	ERY	CLI	SYN	RIF	LINEZ	FOS	CHL	NIT	TMP-SMX	TET	TEIC	VAN	AMI	GM	LEV	CIP
MRSA	0/0	0/0	0/1	0/0	4/4	3/4	0/0	3/4	3/4	0/0	1/4	0/1	2/4	0/0	0/0	1/4	0/0	0/3	0/4	1/3	1/1	1/1	2/3
MSSA	0/7	6/8	0/5	1/7	15/16	0/15	0/7	6/16	1/16	0/7	1/16	0/11	0/9	1/7	0/2	0/16	1/9	0/8	0/16	0/3	2/13	0/13	2/10
MRCoNS	28/28	28/28	0/2	0/1	31/31	30/31	28/28	19/31	8/31	1/28	2/31	0/29	0/5	3/28	0/0	14/31	6/28	0/5	0/31	0/1	11/29	6/30	8/29
MSCoNS	0/3	1/3	0/5	0/3	5/8	0/8	0/3	2/8	2/8	0/3	1/8	0/8	0/5	1/3	0/0	1/8	1/3	0/4	0/8	0/0	2/7	0/8	0/3
Enterococcus	0/0	1/6	0/0	0/0	1/3	0/0	0/0	4/4	0/0	1/3	1/3	0/5	0/0	1/3	0/4	0/0	2/3	0/4	0/6	0/0	0/1	1/5	1/4
Aerobic gram-negative																							
	AUG	AMP	APS	AZT	MERO	PIP	PIP-TZB	TICC	CEFE	CEFP	CFX	CEFO	CEFS	TAX	CAZ	CEP	TOB	IMI	TMP-SMX	AMI	GM	LEV	CIP
Pseudomonas aeruginosa	0/0	0/0	0/0	0/6	0/4	0/5	0/5	0/3	0/5	0/0	0/0	0/5	0/4	0/1	0/5	0/0	0/1	0/5	2/2	0/6	0/5	0/1	0/5
Escherichia coli	0/5	5/5	1/5	1/2	0/2	5/5	0/5	0/3	2/5	1/2	1/2	0/0	0/2	2/4	1/5	3/5	1/3	0/5	2/3	0/5	3/5	1/3	3/5
Acinetobacter	0/0	0/0	0/2	0/0	0/1	1/2	0/1	0/1	0/2	1/1	1/1	0/0	0/1	0/2	0/2	1/1	0/1	0/2	1/2	0/2	1/2	0/1	0/2
Enterobacter cloacae	3/3	3/4	3/4	2/3	0/1	3/4	0/4	2/3	3/4	0/1	0/1	0/0	0/1	3/4	0/4	3/4	2/3	0/4	2/4	0/4	2/4	1/3	1/4
Anaerobes																		Others					
	PEN	CEFT	TAX	ERY	CLI	NIT	LINEZ	TET	VAN	LEV	MOX						FLT	FLN	CLO	AMP	KET	ITR	
Streptococcus	0/3	0/1	0/1	1/3	1/3	0/1	0/3	1/1	0/3	0/3	0/1					Candida parapsilosis	0/2	1/2	0/2	0/2	0/2	0/2	
																Pichia pastoris	0/1	0/1	0/0	0/1	0/1	0/1	

Notes: AMI, Amikacin; AMP, Ampicillin; AMPB, Amphotericin B; APS, Ampicillin-Sulbactam; AUG, Augmentin; AZT, Aztreonam; CAZ, Ceftazidime; CEFE, Cefepime; CEFO, Cefoperazone; CEFP, Cefprozi; CEFS, Cefoperazone and sulbactam; CEFT, Ceftriaxone; CEP, Cefazolin; CFX, Cefuroxime; CHL, Chloramphenicol; CIP, Ciprofloxacin; CLI, Clindamycin; CLO, Clotrimazole; ERY, Erythromycin; FLN, Fluconazol; FLT, Flucytosine; FOS, Fosfomycin; FUS, Fusidic acid; GM, Gentamicin; IMI, Imipenem; ITR, Itraconazole; KET, Ketoconazole; LEV, Levofloxacin; LINEZ, Linezolid; MERO, Meropenem; MOX, Moxifloxacin; NET, Netilmicin; NIT, Nitrofurantoin; PEN, Penicillin; PIP, Piperacillin; RIF, Rifampicin; SYN, Synercid; TAX, Cefotaxime; TEIC, Teicoplanin; TET, Tetracycline; TICC, Ticarcillin/Clavulanate acid; TMP-SMX, Trimethoprim-sulfamethoxazole; TOB, Tobramycin; TZB, Tazobactam; VAN, Vancomycin.

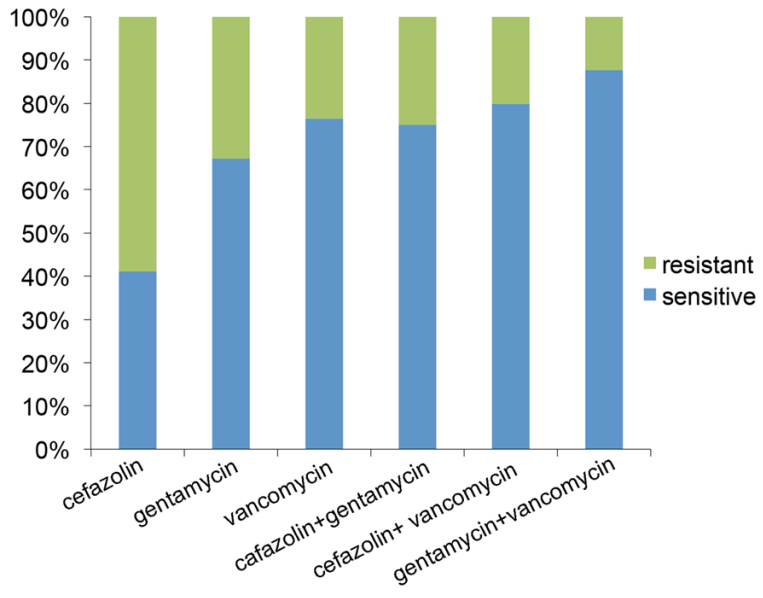

Figure 2. Mono and dual antibiotic susceptibility of PJI microbiology by theoretical model analysis.

Nickinson [11] and Rafiq [13], which show CoNS and SA account for 35.1-67% and 13-18.4% in infected knee and hip arthroplasty. Staphylococcus can typically form a biofilm on the surface of a prosthetic joint [14], which makes the infiltration of antibiotic and immunocyte difficult. Meanwhile, 59.4% (38/64) of these isolates are methicillin-resistant. The rising number of CoNS was found and the incidence of culturenegative strains decreasd. Two causes may lead to the changing pattens of microbiology. First, during the whole study period, culture methods were gradually changed from tissue and synovial fluid culture to BD BACTEC™Plus bottleculture of synovial fluid or to sonication of prosthetic joint. The sensitivity of BD BACTEC™Plus blood bottle culture of synovial fluid was higher than that of tissure and synovial fluidculture, which may cause the decrease of negative culture rate [15]. Secnod, the routine prophylactic use of vancomycin in bone cement in TKA may increase the incidence of CoNS. Sewick A et al [16] found the same result that the occurrence of CoNS in PJI patients rose when cefazolin plus vancomycin was used instead of cefazolin alone as the prophylaxis used antibiotic, but the definite mechanism is still unknown.

The most frequent isolate was MRCoNS throughout the early, delayed, and late infections, followed by MSSA. Stefansdottir et al [12] also found CoNS was the most common pathogen in all stages of infections (105/299, 35.1%), followed by SA (55/299, 18.4%). The majority of CoNS were methicillin-resistant with the predominant position in almost all stages of PJI. The high prevalence of MRCoNS makes it difficult to prevent PJI, because of their resistance to most prophylactically used β-lactam antibiotics including cefuroxime and cefazolin.

The number of methicillin-resistant staphylococci (MRS) also increases over time. The incidence of MRS has arisen from 18.2% (6/33) during 2003-2008 to 45.7% (32/70) during 2009-2013. As MRS is becoming the main cause of PJI, it is necessary to reconsider whether the prophylactically used antibiotics are proper. The current prophylactically used intravenous antibiotic (known as cefazolin or cefuroxime, recommended by AAOS [17]) alone may not be sufficient enough to prevent such a booming trend of MRS. Our theoretical model analysis shows that cefazolin alone only covers 41.2% of all the microbiology tested.

There is also a growing tendency to systematically use antibiotic and antibiotic-loaded bone cement together to prevent PJI [18]. Up to now, the most frequently used antibiotic in bone cement is gentamicin. However, our results showed that 32.8% (22/67) of all the PJI isolates were resistant to gentamicin. Rafiq et al [13] also found a declining effect of aminoglycoside antibiotic during the last three decades. However, vancomycin is thermostable [7] and can be eluted from polymethylmethacrylate (PMMA) in vivo [19], it is the optimal alternative choice. In order to improve the efficiency in preventing PJI, especially in TKA, adding additional antibiotics such as vancomycin in bone cement may be helpful. The combined use of vancomycin and gentamicin in bone cement was proved effective in vitro against methicillin-resistant Staphylococcus [20]. The theoretical model analysis in our study also shows that such combination covers 87.6% of all the microbiology

Table 5. Analysis of risk factors for all the microorganisms' resistance to gentamicin, cefazolin, and vancomycin

Risk factor	Gentamicin		Cefazolin		Vancomycin	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex-male	0.871 (0.313-2.423)	0.792	0.818 (0.311-2.154)	0.684	1.061 (0.375-2.998)	0.912
Age	1.013 (0.971-1.057)	0.559	0.999 (0.960-1.040)	0.962	1.048 (0.991-1.108)	0.103
Prosthetic joint fixation with bone cement	0.917 (0.295-2.850)	0.88	0.176 (0.043-0.722)	0.016	1.056 (0.330-3.380)	0.927
Type of infection		0.839		0.498		0.14
Early (less than 3 months)	Ref		Ref		Ref	
Delayed (3 to 24 months)	0.692 (0.191-2.512)	0.576	0.513 (0.159-1.659)	0.265	0.273 (0.067-1.102)	0.068
Late (more than 24 months)	0.900 (0.273-2.964)	0.862	0.575 (0.170-1.943)	0.373	0.436 (0.120-1.584)	0.207

Table 6. Analysis of risk factors for gram positive organisms resistance to cefazolin, gentamicin

	Cefazolin		Gentamicin	
	OR (95% CI)	P	OR (95% CI)	P
Sex-male	0.903 (0.319-2.558)	0.847	0.824 (0.251-2.706)	0.749
Age	0.996 (0.955-1.038)	0.833	1.013 (0.967-1.062)	0.577
Prosthetic joint fixation with bone cement	0.114 (0.022-0.604)	0.011	0.563 (0.149-2.123)	0.396
Type of infection		0.856		0.920
Early (less than 3 months)	Ref		Ref	
Delayed (3 to 24 months)	0.800 (0.229-2.793)	0.726	1.000 (0.234-4.278)	1.000
Late (more than 24 months)	1.143 (0.307-4.254)	0.842	0.769 (0.185-3.191)	0.718

Notes: OR = Odds ratio.

and provides the highest dual antibiotic sensitivity. According to the results of our studies, there is lower cefazolin resistance rates in organisms isolated for PJI joint that fixed with bone cement than those fixed without bone cement. It may also prove the safety of antibiotic-loaded bone cement. Therefore, it is proper to routinely mixgentamicin and vancomycin in bone cement to prevent PJI in TKA.

In THA where bone cement is used increasingly less, gentamicin and vancomycin cannot be topically used, and thus parenterally prophylactic antibiotics should be chosen. To avoid nephrotoxicity and ototoxicity, gentamicin would rather not be used routinely and systematically. The theoretical model analysis shows that vancomycin alone and vancomycin plus cefazolin cover 76.4% and 79.8% respectively of all the microbiology tested, while cefazolin alone only covers 41.2%. Instead of cefazolin alone, vancomycin or vancomycin plus cefazolin should be used as prophylactic antibiotics. Smith et al [21] found that changing cefazolin to vancomycin for routine perioperative antibiotic prophylaxis in TJA would significantly reduce the occurrence rate of PJI. Concerning PJI by gram-negative which cannot be covered by vancomycin, we do not use vancomycin alone. Sewick et al showed that compared with using cefazolin alone as antibiotic prophylaxis, vancomycin plus cefazolin would not reduce the occurrence rate PJI [16], but can still reduce the incidence of MRSA. As vancomycin and β-lactam acting at different stages of cell wall synthesis, Hagihara et al [22] found out that the combination of vancomycin and cefazolin could cause synergistic effect and improve the antibacterial effect against MRSA than vancomycin applied alone in vitro. Although AAOS [17] and some authors [16] were concerned that routine use of vancomycin may cause colonization and infection of vancomycin-resistant enterococcus (VRE), a recent study [21] showed no cases of VRE in any PJI patients when vancomycin was used as prophylactic antibiotic. Now we prefer to update prophylactically used antibiotic from cefazolin alone to vancomycin plus cefazolin in cementless TJA.

Empirical antibiotic treatment should be started when PJI is suspected and theated by surgical therapy while the intra-operative culture result is unavailable. According to our study, gram-positive strainswere dominant throughout all the stages of infection. With the rising

number of MRS, MRCoNS has become the most frequently isolated oganism in early, delayed and late stages. Considering the high prevalence of resistant microbilogy and the fact that all gram-positive organismsare sensitive to vancomycin in our study, it is proper to use it as an emprical antibiotic. Although all the isolated gram-negative organisms were sensitive to Amikacin, piperacillin-tazobactam, and carbapenem, we should select the antibiotic more carefully, as Sousa R et al [23] warned the emerging extended-spectrum beta-lactamase (ESBL) microbiology. These ESBLs will compromise vivo clinical outcome while vitro test turned out to be sensitive. Moreover, the potential nephrotoxicity and ototoxicity of amikacin drive us to choose carbapenem as a gram-negative empirical antibiotic. As there is a lower prevalence of gram-negative strains in the delayed infections, we do not use carbapenem in these patients. In summary, vancomycin plus carbapenem can be used empirically in early and late infections, and vancomycin alone in delayed infection. As soon as the final result is acquired, the antibiotics should be changed.

Conclusions

In conclusion, the most common microbiologies of PJIs in our hospital are CoNS and SA, and the most frequently isolated strains are MRCoNS throughout early, delayed, and late infection of PJI. A rising trend was found in both CoNS and MRS, while the incidence of culture negative strains was decreasing. The same concern was held by other authors [6, 11, 23]. They all thought the growing incidence of MRS would compromise the treating effectiveness of PJI patients. According to the theoretical model analysis, the combination of vancomycin and gentamicin covers 87.6% of all the microbiology and provides the highest dual antibiotic sensitivity, followed by the combination of vancomycin plus cefazolin which covers 79.8%. The combination of vancomycin and gentamicin can be used prophylactically in bone cement for TKA and vancomycin and cefazolin can be used parenterally for cementless TJA to prevent PJI. Further clinical studies will be designed to get more information. The antibiotic can be used empirically depending on the classification of PJI before the final culture result is available, as well as vancomycin plus carbapenem in early and late infections, and vancomycin alone in delayed infection.

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Disclosure of conflict of interest

None.

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