Distribution and drug resistance profile of methicillin-resistant *Staphylococcus aureus* after orthopaedic surgery

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Abstract: This paper is aimed to comprehend clinical distribution and drug-resistance situation of methicillin-resistant *Staphylococcus aureus*. This study applied automatic microbe instrument Microscan W /A 96 for strain identification and drug susceptibility screening on the isolated strains. It was found that 312 MRSA strains were isolated in three years, which account for 58.1% of *Staphylococcus aureus*. MRSA were mainly focused in wound secretion, purulent sputum and prostatic fluid and a few of them were isolated from blood specimens; Endemic area distribution was mainly located in intensive care unit, neurosurgery, respiratory department, dermatology, orthopaedic burns and orthopaedics. MRSA strains showed high drug resistance of 82.37%~100% to most of the antibiotics including vancomycin, cotrimoxazole and rifampicin. Strain was 100% resistance towards ampicillin, amoxicillin/acid, cefalotin, cefazolin, tienam, benzylpenicillin, penicillin and tetracycline and 90% strains resisted clindamycin, cefotaxime, clarithromycin and gentamicin.

Keywords: Orthopaedic surgery, methicillin-resistant *Staphylococcus aureus*, drug resistance, clinical distribution.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* was the main pathogenic bacterium of hospital infection with high drug resistance. It was difficult to control if it spread in hospital and lead to infection prevalence or outbreak (Zhang and Wan, 2008). Some researchers held that infection causing to MRSA were on the top of the three infectious diseases worldwide, followed by AIDS and hepatitis B (Gao *et al*., 2009 and Shu, 2010). This research made a retrospective d on MRSA detection data (from 2007 to 2011), in order to discuss the effectiveness of intervention measure of MASA hospital infection in order to provide basis for prevention and control of MASA associated hospital infections.

Methicillin-resistant Staphylococcus aureus strains are wide spreading various hospitals at home and abroad. Methicillin was offered no-resistance along with various antibiotics that are widely provided in clinics (Xing *et al*., 2007). This paper discusses distribution of MRSA in clinical specimens and departments in People's Hospital of Zhengzhou and provides reliable therapeutic basis in clinics, timely and accurately.

MATERIALS AND METHOD

General information

A total of 312 strains of Staphylococcus aureus were isolated from the specimens of sputum, urine, blood, pus and the secretions of inpatients in People's Hospital of Zhengzhou dated back from January 2004 to December 2006.

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Instrument and susceptibility paper

Automatic microbial identification and drug susceptibility system were purchased from America Turin Corporation. Blood plate was purchased from Barrett Biotechnology Co. Ltd. MH plates were prepared in the laboratory, and reagents were purchased from Hangzhou Tianhe Microbial Reagents Co. Ltd. Susceptibility paper discs were 1 μg/ disc of oxacillin and 30μg/ disc of cefoxitin purchased from England Oxiod Corporation.

Quality control strains

Staphylococcus aureus ATCC25923 and ATCC29213.

Method

Collection and cultivation of bacterial strains for specimen: Collected specimens by regular method and inoculated them in corresponding medium for 18~24 hours of incubation at 37^{L}. Identification and drug resistance of bacteria: Adopted automatic microbe instrument Microscan W/A 96 and used manual method for the identification of bacterial isolate, 1. identification of *Staphylococcus aureus*: plasma coagulase and catalase tests were positive; Gram-cocci in grapes -like arrangement; reduction of nitrate; VP test was positive; anaerobic decompose glucose as acid production. 2. identification of methicillin resistant *Staphylococcus aureus*: drug resistance disc diffusion method. Prepared *Staphylococcus aureus* obtained by isolation into suspension of 0.5 McIntosh turbidity by sterile saline solution. Dipped bacterial solution by sterile swabs and smeared it on the surface of MH agar. Then placed drug impregnated discs paper, which contained 30μg/ disc of cefoxitin and 1μg/ slice of oxacillin on MH agar. Measured diameter of inhibition zone after 24 hours incubation at 37^{L}. The data included inhibition zones:

diameter by cefoxitin ≥19mm was drug resistance, ≥20 mm was sensitive; diameter of zones of inhabitation by oxacillin ≤10m was drug resistance, 11~12 mm was intermediate, and ≤13 mm was taken as sensitive (CLSL).

Data analysis: Made a statistical analysis of WHONET 5.6 software (Analyzed antibiotics result of the first strain from the same patient). Outpatient and hospitalization based strain; adopted x^2 to detect comparison of drug resistance rate of MRSA and MSSA and disposed it with SPSS16.0 software. P<0.05 was statistically significant.

RESULTS

Distribution analysis of MRSA

Among the 312 strains of Staphylococcus aureus, 58.1% was MRSA detection rate and 41.9% was MSSA detection rate Distribution status of MRSA and MSSA from 2004 to 2006 was in table 1. Distribution profile of MRSA in clinical specimens and departments were shown in table 2 and table 3. It can be seen from table 1 that detection rate of *Staphylococcus aureus* during three years was increasing year after year and constituent ratio of MRSA was also showing an increase. It could be seen from table 2 that 312 strains of MRSA specimen mainly were isolated from wound secretions, followed by phlegm and prostate fluid. Blood infection was at lower side. table 3 showed that 312 cases of MRSA patients were mainly distributed in intensive care unit, neurosurgery, respiratory medicine, dermatology, burns orthopaedics and orthopaedic department. Detection rate at intensive care unit was the highest and respiratory tract infection was most common; secondary was neurosurgery and respiratory medicine in which respiratory tract infection was most common; skin infection was most common in dermatology unit and burns orthopaedics; operative incision infection were orthopaedics and thoracic surgery. Department distribution: top three department for MRSA strains were brain surgery, pediatrics and general surgery, which accounted for 46.1% (table 1).

Table 1: Detection rate (%) of MRSA and MSSA from 2004 to 2006

Year	SA strain	MRSA	MSSA
2004	146	74(50. 68)	72(49. 32)
2005	174	102(58. 62)	72(41. 38)
2006	217	136(62. 67)	81(37. 33)

Specimen distribution: sputum and pharyngeal swabs were the main sources of MRSA strains, which comprised 209 strains and accounted for 49.6%, followed by incision, wound secretions and genitourinary tract specimens.

Drug resistance profile and transition of SAU on common antibiotics: resistance against penicillin was 94.0%~95.5% which is the highest in three years, followed by erythrocin resistance which was 57.6% ~68.7%; 5% against nitrofurantoin, 1.2% against rifampicin and 7.9% against moxifloxacin; Drug resistance rate against vancomycin and linezolid was 0.0%; compared with that in 2012 and 2010, drug resistance rate of clindamycin showed upward trend and drug resistance against oxacillin, gentamicin, levofloxacin and erythrocin showed a downward trend.

Table 2: Distribution of MRSA strains among 312 isolates

Specimen	Cases (%)
Wound secretion	156 (50.00)
Phlegm	91 (29.23)
Prostatic fluid	40 (12.71)
Blood	18 (5.67)
Others	7 (2.39)
Total isolates	312 (100)

Result of drug resistance profile

Drug resistance rate of 312 strains of MRSA was the least against vancomycin. So far, no showing of MR-SA could be isolated which was resistant to vancomycin, followed by 17.6% cotrimoxazole rate at MRSA stains and rifampicin rate at strains (40.96). Resistance to other drugs was more than 80.1% (table 3).

DISCUSSION

It could be seen from clinical specimen distribution that MRSA infection site of 312 cases of patients was most common in wound infection. Detection rate of wound exudate was 50.0%, which is due to large dose intake of antibiotic; followed by respiratory tract infection and detection rate of sputum specimen was 29.23%; detection rate of prostatic fluid was 12.71%; blood infection was rare with a detection rate of 5.67%. MASA were mainly isolated from in intensive care unit, neurosurgery, respiratory medicine, dermatology, burns orthopaedics and orthopaedics departments. Infection rate of intensive care unit was the highest and respiratory tract infections were primary. It was caused due to low immunity, difficult sputum excretion, reflux and aspiration of gastric content that were induced by protopathy. Invasive procedures such as using breathing machine, statistic or dynamic vein intubation. Indwelling catheter intubation and tracheotomy also increased the risk of MRSA spread. Further, repeated intake of antibiotics and hormones was also an important reason.

Spread of MRSA infection to other departments was very wide and respiratory tract infection was the most common (Gosbell, 2005 and Gupta *et al*., 2009), followed by wound secretion, prostatic fluid and so on. In view of age level, patients of <20 and >50 years accounted for 65.0%. Infants and old age had weak immunity and organism

Table 3: Distribution of department unit patients' cases

Department	Cases	Composition ratio (%)	Source of specimen	Age
Intensive care unit	67	21.47	Purulent sputum	43~89
Neurosurgery	55	17.63	Purulent sputum and wound exudate	19~76
Respiration medicine	42	13.46	Purulent sputum	11~82
Dermatology	31	9.94	Wound exudate	15~45
Burn and Plastic Surgery	26	8.33	Wound exudate	2~68

Table 4: MRSA department unit distribution and composition rate (%)

Department	2007	2008	2009	2010	2011	Total	
						Strains	Composition Rate (%)
Stomatology department	0	1	0	0	0	1	0.5
ENT department	0	0	0	0	1	1	0.5
Neurosurgery department	10	7	1	8	19	45	20.7
Cardiothoracic surgery department	3	2	0	0	0	5	2.3
Orthopaedics department	6	2	3	2	5	18	8.5
Urinary surgery department	1	2	1	0	1	5	2.3
Hepatobiliary surgery department	0	0	0	1	0	1	0.5
General surgery department	3	5	1	4	7	20	9.2
Oncological surgery department	1	1	0	1	4	7	3.2
Cardiology department	1	0	0	1	0	2	0.9
Nephrology department	0	2	1	1	4	8	3.7
Digestive system department	0	1	1	0	0	2	0.9
Neurology department	5	8	2	2	0	17	7.8
Respiration medicine department	4	3	0	0	1	8	3.7
Medical oncology department	2	2	1	3	5	13	5.9
Pediatrics department	0	3	1	1	4	9	4.1
ICU	20	16	0	2	17	55	25.3
Total	56	55	12	26	68	217	100.0

resistance. The aged often had underlying disease such as respiratory, cardiovascular and endocrine diseases. More serious the underlying disease was, the weaker was the resistance and easier to be infected of MRSA. Young and middle aged patients from 20 to 50 years accounted for 34.98% and majority had been infected via skin, wound and operative incision, due to large doses of antibiotic. Individuals of this age with underlying disease were uncommon.

External drug resistance experience of 17 kinds of antibacterial agents towards MASA showed that MASA strains were multi-drug resistant. Besides vancomycin, cotrimoxazole and rifampicin, drug resistance rate of MRSA for other antibiotics were all more than 80%, among which drug resistance rate for ampicillin, amoxicillin/ clavulanic acid, cefalotin, cefazolin, tienam, oxacillin, penicillin and tetracycline were 100% and that of clindamycin, cefotaxime, clarithromycin and gentamicin were more than 90%. MRSA strains were not only resistant to cephalosporins and other β-lactamase also to amino glycosides, macrolide, lincomycin and tetracycline. As for comparison with Gao Junfa's report:, resistance to cefotaxime, ciprofloxacin, erythrocin, gentamicin was low (resistance to these drugs was 100% in Gao Junfa's report) and was approaching equivalent resistance rate to other drugs. Compared with Zeng Jun's report, besides vancomycin, resistance to other drugs was high. Therefore, clinician should pay due attention to resistance monitoring of MRSA and avoid prescribing cephalosporins and other β-lactams in order to avoid inducing drug resistance that may lead to therapeutic failure (Shinabarger 1999 and Memmi *et al*., 2008). So far, it is reported that sensitivity to vancomycin of MRSA was downward because of increased MRSA infection. VISA had appeared in Japan, US, and China (all reported drug resistance strains). Three years drug resistance monitoring at our hospital had revealed that MRSA strains were 100% resistance to vancomycin, 17.6% to cotrimoxazole and 40.96% to rifampicin. Vancomycin showed a strong antimicrobial activity against MRSA strain. Once vancomycin was failed MRSA strains, then MRSA infection lead to a pathogenic disease that could not be cured but did induce outbreaks. Therefore, it is strict control warranted and used only when antibiotics were resistant to other drugs (to prevent MRSA from resistance against drugs). Cotrimoxazole is an oral drug, which slowed absorb and only could be applied in moderate infection. Rifampicin has a good antibacterial activity against MRSA and its toxic and side effects were less than vancomycin (Schmitz *et al*., 2001 and Skold, 2001). Therefore, rifampicin should be given as an alternate or

assist to vancomycin treatment which could reduce vancomycin intake.

According to NCCLS strain documents, MRSA showed sensetivity to cephalosporins or other β-lactams such as amoxicillin/clavulanic acid, ampicillin/sulbactam, ticarcillin/clavulanic acid, piperacillin/tazobactam and imipenem but had no clinically curative effect. Result of this research also indicated that MRSA strains were multi-drug resistant. Therefore, providing drug resistance result of MASA for clinic timely and accurately and monitoring drug resistance profile of MRSA could not only guide clinical rational drug use, but also control and slow down drug resistance of bacteria to antibiotics and extend service life of antibiotic.

CONCLUSION

MRSA accounted for a high ratio and invasive therapeutic measure should be reduced in clinics. It needs to apply antimicrobial agents rationally to prevent and reduce MRSA; strengthen monitoring of MRSA strains. Once found MRSA infection cases in carriers and infectors who were detected in early stage, it needs to be used with clear identity and implement along standard isolation measures. Hand washing and hygiene were specially emphasized to effectively hamper the spread and prevalance of MRSA inpatient areas and to prevent and control the occurrence and outbreak of hospital infection.

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