

Trend of MRSA bacteremia in an
institution with a high rate of MRSA
after the reinforcement of antibiotic
stewardship and hand hygiene

Yong Chan Kim

Department of Medicine

The Graduate School, Yonsei University

Trend of MRSA bacteremia in an
institution with a high rate of MRSA
after the reinforcement of antibiotic
stewardship and hand hygiene

Yong Chan Kim

Department of Medicine

The Graduate School, Yonsei University

Trend of MRSA bacteremia in an
institution with a high rate of MRSA
after the reinforcement of antibiotic
stewardship and hand hygiene

Directed by Professor Jun Yong Choi

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Yong Chan Kim

December 2012

This certifies that the Master's Thesis
of Yong Chan Kim is approved.

Thesis Supervisor : Jun Yong Choi

Thesis Committee Member#1 : Dongeun Yong

Thesis Committee Member#2 : Young Goo Song

The Graduate School
Yonsei University

December 2012

ACKNOWLEDGEMENTS

Above all, I'd like to give thanks to Jun Yong Choi, my supervisor. He was motivating me and giving the purpose of this study. He also gave me a lot of advice and guidance in many ways. And I have to appreciate Dongeun Yong, M.D., Ph.D. and Young Goo Song, M.D, Ph.D. who gave lots of help to me in completing this paper, too.

I am grateful to Nam Su Ku, M.D. and Su Jin Jeong, M.D. fellowship of division of Infectious disease, department of internal medicine, Yonsei University health system for their constructive advice.

I wish to express my sincere thanks to my resident colleagues for many things and I am happy to work with them.

At last, I would like to thank my wife, sister, and parents who encouraging and helping me all the times. I dedicate this paper especially to my mother, with respect and love.

<TABLE OF CONTENTS>

ABSTRACT	1
I. INTRODUCTION	3
II. MATERIALS AND METHODS	5
1. Hand hygiene program	5
2. Antibiotic stewardship program	5
3. Amount of antibiotic consumption and rate of hand hygiene performance	6
4. Study population and data collection	7
5. Definitions	7
6. Statistical analysis	8
III. RESULTS	9
IV. DISCUSSION	20
V. CONCLUSION	22
REFERENCES	24
ABSTRACT(IN KOREAN)	27

LIST OF FIGURES

Figure 1. Incidence of methicillin-resistant <i>Staphylococcus aureus</i> bloodstream infection.	16
Figure 2. Amount of antibiotic consumption.	18
Figure 3. Rate of hand hygiene performance.	19

LIST OF TABLES

Table 1. Clinical characteristics of patients with methicillin-resistant <i>Staphylococcus aureus</i> bloodstream infection and primary focus of infection.	13
Table 2. Trend of methicillin-resistant <i>Staphylococcus aureus</i> bloodstream infection according to the epidemiologic type of infection, route of admission, and unit attributable for infection.	17

ABSTRACT

Trend of MRSA bacteremia in an institution with a high rate of MRSA after the reinforcement of antibiotic stewardship and hand hygiene

Yong Chan Kim

Department of Medicine

The Graduate School, Yonsei University

(Directed by Professor Jun Yong Choi)

Background : Some studies show that efforts to reduce health care-associated infections with methicillin-resistant *Staphylococcus aureus* (MRSA) are effective.

Method : Two infection control programs were reinforced in the hospital in South Korea where the MRSA rate is about 65%. “Antibiotic stewardship” was intensified starting in August 2008, when a computerized prescription restriction was implemented. “Hand hygiene”, consistent with World Health Organization (WHO) guidelines, started in December 2008. The incidence of MRSA BSI was evaluated using laboratory database.

Result : From January 2006 through November 2011, there were 568 episodes of MRSA BSI. Incidence of MRSA BSI was reduced in a year after these programs were implemented from 0.171 per 1,000 patient-days in 2009 to 0.116 per 1,000 patient-days in 2011 ($P = .009$). There was a decrease in antibiotic consumption from 690.54 ± 28.33 as the monthly mean defined daily dose (DDD) per 1,000 patients-days in 2008 to 652.47 ± 20.77 2011 ($P = .015$). The rates of performance in hand hygiene have been increased from 43% in 2008 to 83% in 2011 ($P = .043$).

Conclusion : Although we did not implement all components of the “MRSA bundle”, there was a decrease in MRSA BSI after the reinforcement of antibiotic stewardship and hand hygiene over a three year period in this institute which previously had a high rate of MRSA.

Key words : methicillin-resistant *Staphylococcus aureus*; bacteremia; infection control

Trend of MRSA bacteremia in an institution with a high rate of MRSA
after the reinforcement of antibiotic stewardship and hand hygiene

Yong Chan Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Jun Yong Choi)

I. INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most prevalent organisms that causes health care-associated infections. Incidence of MRSA infection has increased across the world, and is associated an increased mortality¹⁻³. Successful efforts to reduce MRSA infection have been investigated and the implementation of a “MRSA bundle”, comprising of universal active surveillance, contact precautions, hand hygiene, and a change in the institutional culture is linked to significant declines in health care-associated MRSA infections in large health care systems⁴⁻¹³.

The methicillin resistance rate of *S. aureus* in South Korean hospitals has rapidly increased since 1980 and remained at 65–70% during the past several years¹⁴⁻¹⁶. MRSA is a major pathogen isolated from patients with health care-associated infections in South Korea¹⁷, and is a national priority for disease control. However, because MRSA is now endemic in many Korean hospitals and the implementation of all components of the “MRSA bundle” requires excessive costs and facilities, the full control of MRSA may be beyond execution for many Korean institutes.

Since 2008, two infection control programs were reinforced to decrease multidrug resistant organisms in a tertiary-care teaching hospital in South Korea. They were an “antibiotic stewardship program” and a “hand hygiene program”. The “antibiotic stewardship program” was reinforced starting in May 2006 and associated bylaws were created in March 2007. The policy was intensified by use of a computerized prescription restriction of inappropriate prophylactic antibiotic use for surgery, inappropriate antibiotic combinations, and inappropriate antibiotic use from starting in August 2008. From December 2008, the “hand hygiene program” was reinforced due to the poor performance rates. The performance rates were investigated each quarter, and hospital-wide efforts were implemented to improve hand hygiene performances.

It is known that hand hygiene and antibiotic stewardship are associated with the prevention of transmission and infections of resistant organism, including MRSA¹⁸⁻²⁰. We hypothesized that our efforts to reinforce the hand hygiene and antibiotic stewardship programs would affect the incidence of MRSA blood stream infections (BSI), a surrogate for all MRSA infections. In this study, we

evaluated the epidemiologic characteristics of MRSA BSI and the trend of MRSA BSI incidence from January 2006 through November 2011 and analyzed the effect of the infection control programs.

II. MATERIALS AND METHODS

1. Hand hygiene program

Hand hygiene was reemphasized because of the poor rates of performance and a reinforced program was implemented to promote hand hygiene beginning in December 2008. Contents of program were consistent with the World Health Organization (WHO) guidelines²¹. We educated each department in the hospital on the contents and importance of hand hygiene. Hospital-wide monitoring of hand hygiene practice was conducted. The entire hospital was classified by special care units and their performance rates were investigated by professional groups every quarter. The results were recorded in the hospital newsletter which was mailed to all hospital workers. We did several internal campaigns and publicized the infection control program through posters, large sized electronic displays and screen savers.

2. Antibiotic stewardship program

There had been some efforts regarding antibiotic stewardship due to concern over the role of antibiotic overuse and overgrowth of multidrug resistant organisms in the hospital since May 2006. Associated bylaws were created in

March 2007, which aimed to limit inappropriate prophylactic antibiotic use for surgery, inappropriate antibiotic combinations, and inappropriate antibiotic use. The policy was reinforced by way of computerized prescription restriction of 3rd cephalosporin and aminoglycoside for surgery starting in August 2008. Inappropriate antibiotic combinations such as redundancy in antimicrobial coverage were also restricted using the computerized prescription system from August 2009. Exceptions and clinical indications were agreed upon by a group of infection specialists.

3. Amount of antibiotics consumption and rate of hand hygiene performance

The manager in the department of pharmacy aggregated the data for monthly prescribed antibiotics for monitoring consumption of drugs. To evaluate the amount of antibiotic use, J01 antibiotics of WHO anatomical therapeutic chemical (ATC) classification were extracted from prescribed antibiotics and the WHO defined daily dose (DDD) was used²². The amounts of antibiotic used were expressed as a monthly mean (\pm SD) DDD per 1,000 patient-days.

Hand hygiene performance was monitored by direct observation following the WHO guidelines²¹. Direct observations by trained and validated observers were used for monitoring hand hygiene compliance. Observed locations, times, and health-care workers (HCWs) were randomly identified to avoid selection bias. The rate of hand hygiene performance was calculated by dividing the number of observed hand hygiene actions performed when an opportunity occurs, by the total number of opportunities.

4. Study population and data collection

From January 2006 through November 2011, 515,703 patients were admitted to the hospital. All patients were eligible to be part of the hospital-wide infection control programs. We collected retrospective data, including age, sex, prior antibiotic use, predisposing factors, comorbid conditions, attributable unit for infection, route of admission, epidemiologic type of infection, and primary focus of infection, from patients identified as positive for MRSA BSI using the hospital database. Antimicrobial susceptibilities were determined using disk-diffusion methods or a VITEK-2 P600 card (bioMerieux, Hazelwood, MO., USA). The results were interpreted using the Clinical and Laboratory Standards Institute (CLSI) guidelines²³.

5. Definitions

A MRSA BSI episode was defined by a positive blood culture for the first time²⁴. MRSA BSI was classified as community acquired (CA), health care-associated (HCA), or hospital acquired (HA). HA BSI was defined by a positive blood culture from a patient who had stayed more than 48 hours in the hospital or was discharged from an acute care unit within the past 10 days. A positive blood culture within 48 hours after admission was defined as HCA BSI, if more than one of the following conditions was satisfied: a history of more than two days of hospitalization within the past 90 days; receipt of hemodialysis; receipt of intravenous therapy (IV) or specialized wound care within the past 30 days; residence in a long-term care facility or nursing home. CA BSI was defined by a positive blood culture within 48 hours after admission, if the

episode did not meet the HCA BSI criteria²⁵.

Prior antibiotic use was defined as use of any antimicrobial agent for more than three days in the previous 30 days. Predisposing factors to infection included neutropenia, steroid therapy, other immunosuppressive therapy, chemotherapy, and radiotherapy. Neutropenia was defined as an absolute neutrophil count less than $500/\text{mm}^3$ in the previous 30 days. Steroid therapy was defined as the daily receipt of the dose equivalent to 30 mg of prednisone for seven days or 20 mg for 14 days. If other immunosuppressive therapy, chemotherapy, or radiotherapy were used in the 30 days before MRSA BSI, each therapy was considered to be a predisposing factor to infection. All comorbid medical conditions were identified through a medical record review and defined according to the International Classification of Disease (ICD), tenth revision. We defined primary BSI including intravenous catheter associated infection according to the National Nosocomial Infections Surveillance (NNIS) System and classified any other primary focus of infection according to the Centers for Disease Control and Prevention (CDC)/ National Healthcare Safety Network (NHSN) surveillance criteria^{26, 27}. Units attributable for infection were determined to be places occupied for more than 48 hours prior to the BSI.

6. Statistical analysis

General linear model was used for trend of amount of antibiotic consumption. Incidence of MRSA BSI was expressed in annual episodes per 1,000 patient-days. Data for yearly percent change of incidence of MRSA BSI are reported with 95% confidence interval. The analysis of trends of both rates of

hand hygiene performance and incidence of MRSA BSI was performed by means of Poisson regression models. The chi-square test was used to compare the rates of MRSA BSI between groups according to the route of admission or units attributable for infection. All data were treated with SAS statistical program version 9.2 (SAS Institute Inc, Cary, North Carolina, USA). Statistically significance was considered for $P < 0.05$.

III. RESULTS

1. Clinical characteristics of patients, epidemiologic characteristics and primary focus of MRSA BSI

From January 2006 through November 2011, a total of 568 episodes of MRSA BSI were detected in the hospital. CA BSI accounted for 4% ($n = 25$) of all MRSA BSI, HCA BSI for 19% ($n = 109$), and HA BSI for 77% ($n = 434$).

Overall, 363 (64%) of the patients were male with a mean (\pm SD) age of 56.5 ± 22.7 years (Table 1). The mean age of patients with CA BSI, HCA BSI and HA BSI was 46.9 ± 31.1 , 55.9 ± 24.4 , and 57.1 ± 21.6 , respectively. The rate of prior antibiotic use was the highest in the group with HA BSI (83%), followed by HCA BSI (51%), and CA BSI (4%). The most frequent predisposing factor to infection was steroid therapy (16%), followed by chemotherapy (15%). HA BSI and HCA BSI groups had more predisposing factors than the CA BSI group (54%, 23%, and 8%, respectively). Cardiovascular disease was the most common comorbidity (48%, 66%, and 57% in the CA BSI, HCA BSI, and HA

BSI groups, respectively).

The most common primary focus of infection was primary BSI (47%, 38%, and 28% in the HA BSI, HCA BSI, and CA BSI groups, respectively), and followed by pneumonia in the HA BSI group (19%), and skin and soft tissue infection in HCA BSI and CA BSI groups (19% and 20%). Others, accounting for 32% in CA BSI group, consisted of bone and joint infections (12%), infective endocarditis (8%), and central nervous system (CNS) infections (12%).

2. Incidence of MRSA BSI

There was a difference in the rate of MRSA BSI according to the route of admission and unit attributable for infection. The rate of MRSA BSI during the study period was higher among patients admitted via the emergency department (ED) than patients admitted via the outpatient department (OPD) (0.181 per 1,000 patient days for ED vs 0.065 per 1,000 patient days for OPD, $P < .001$). According to unit attributable for infection, the rate of MRSA BSI during the study period was higher in the intensive care units (ICUs) than the non-ICUs (0.712 per 1,000 patient days for ICUs vs 0.069 per 1,000 patient days for non-ICUs, $P < .001$).

Incidence of MRSA BSI increased during the period before the reinforcement of antibiotic stewardship and hand hygiene programs from 0.122 per 1,000 patient days in 2006 to 0.171 per 1,000 patient days in 2009, a increase of 14% per year ($P = .003$). There was a decline in the incidence of MRSA BSI after 2009, a year after the renewed efforts, from 0.171 per 1,000 patient days in 2009 to 0.116 per 1,000 patient days in 2011, a decrease of 17% per year ($P = .009$).

(Figure 1). The same trends were observed in the incidence of MRSA BSI classified according to the route of admission and unit attributable for infection. From 2009 through 2011, incidence of MRSA BSI in ICUs decreased from 1.028 per 1,000 patient days in 2009 to 0.637 per 1,000 patient-days in 2011, a decrease of 22.8% per year ($P = .072$); in non-ICUs there was a 31.6% decrease per year (0.091 in 2009 to 0.04 in 2011, $P = .003$). Incidence of MRSA BSI in patients admitted via ED decreased from 0.232 per 1,000 patient-days in 2009 to 0.104 per 1,000 patient-days in 2011, a decrease of 30.8% per year ($P = .01$); OPD, 25% decrease per year (0.094 in 2009 to 0.054 in 2011, $P < .001$) (Table 2).

The decline of MRSA BSI incidence was significant only in HA BSI (0.142 per 1,000 patient days in 2009 to 0.072 per 1,000 patient days in 2011, $P < .001$), but not in HCA BSI or CA BSI (0.023 and 0.006 per 1,000 patient days in 2009, respectively, for HCA BSI and CA BSI a 0.032 and 0.013 per 1,000 patient days in 2011, respectively, for HCA BSI and CA BSI) (Table 2).

3. Amount of antibiotics consumption and Rates of Hand hygiene performance

Since the initial antibiotic stewardship program, the total amount of antibiotic use was reduced from 749.95 ± 23.22 monthly mean DDD per 1,000 patient days in 2006 to 652.47 ± 20.77 monthly mean DDD per 1,000 patient-days in 2011 ($P < .001$). During the same period, the consumption of 3rd cephalosporin was reduced from 295.14 ± 12.7 monthly mean DDD per 1,000 patient days in 2006 to 227.17 ± 15.93 monthly mean DDD per 1,000 patient-days in 2011 (P

< .001); glycopeptide, 55.3 ± 5.45 to 46.59 ± 4.74 ($P < .001$). But, the consumption of quinolone increased from 20.65 ± 1.87 monthly mean DDD per 1,000 patient days in 2006 to 38.93 ± 4.72 monthly mean DDD per 1,000 patient-days in 2011 (Figure 2).

The rate of hand hygiene performance increased from 43% in November 2008, which was about one month before the initial reinforcement of the hand hygiene program, to 83% in December 2009 ($P = .044$). The rate of hand hygiene performance was lower in the ED and ICUs as compared to the entire hospital (Figure 3).

Table 1. Clinical characteristics of patients with methicillin-resistant *Staphylococcus aureus* bloodstream infection and primary focus of infection

CA MRSA BSI HCA MRSA BSI HA MRSA BSI All MRSA BSI

Age, years	46.9 ± 31.1	55.9 ± 24.4	57.1 ± 21.6	56.4 ± 22.7
Male	16 (64)	63 (57.7)	284 (65.4)	363 (63.9)
Prior antibiotics use	1(4)	55(50.4)	361(83.1)	417 (73.4)
Predisposing factor				
Neutropenia	0 (0)	3 (2.8)	49 (11.3)	52 (9.1)
Steroid therapy	0 (0)	5 (4.6)	84 (19.4)	89 (15.6)
Immunosuppressive therapy	2 (8)	5 (4.6)	15 (3.5)	22 (3.8)
Chemotherapy	0 (0)	11 (10.1)	76 (17.5)	87 (15.3)
Radiotherapy	0 (0)	1 (0.9)	9 (2.1)	10 (1.7)
Comorbid medical condition				
Diabetes mellitus	7 (28)	42 (38.5)	116 (26.7)	165 (29)
Solid cancer	4 (16)	37 (33.9)	150 (34.6)	191 (33.6)
Hematologic malignancy	0 (0)	4 (3.7)	58 (13.4)	62 (10.9)
Solid organ transplantation	2 (8)	3 (2.8)	15 (3.5)	20 (3.5)
HSCT	0 (0)	1 (0.9)	7 (1.6)	8 (1.4)
Rheumatologic disease	0 (0)	4 (3.7)	10 (2.3)	14 (2.5)
Cardiovascular disease	12 (48)	72 (66.1)	246 (56.7)	330 (58.1)
COPD	0 (0)	8 (7.3)	13 (3)	21 (3.7)
Renal disease	8 (32)	54 (49.5)	173 (39.9)	235 (41.4)
Liver disease	9 (36)	25 (22.9)	180 (41.5)	214 (37.7)
HIV infection	1 (4)	0 (0)	1 (0.2)	2 (0.4)
Primary focus of BSI				
Primary BSI	5(20)	41(37.6)	205(47.2)	251 (44.2)
Venous catheter related	0(0)	18(16.5)	103(23.7)	121 (21.3)
Gastrointestinal tract infection	0(0)	9(8.3)	28(6.5)	37 (6.5)
Urinary tract infection	4(16)	9(8.3)	10(2.3)	23 (4)
Pneumonia	1(4)	9(8.3)	83(19.1)	93 (16.4)
Skin and Soft tissue	5(20)	20(19.3)	38(8.8)	63 (11.1)
Surgical site infection	0(0)	4(3.7)	38(8.8)	42 (7.4)
Others ^a	10(40)	17(15.6)	32(7.4)	59 (10.4)

NOTE. Data are the mean \pm SD or No (%).BSI, bloodstream infection; CA, community acquired; COPD, chronic obstructive pulmonary disease; HA, hospital acquired; HCA, health care-associated; MRSA, methicillin-resistant *Staphylococcus aureus*; HSCT, hematopoietic stem cell transplantation.

^aOthers includes bone and joint infections, endocarditis, central nervous system infections, and others.

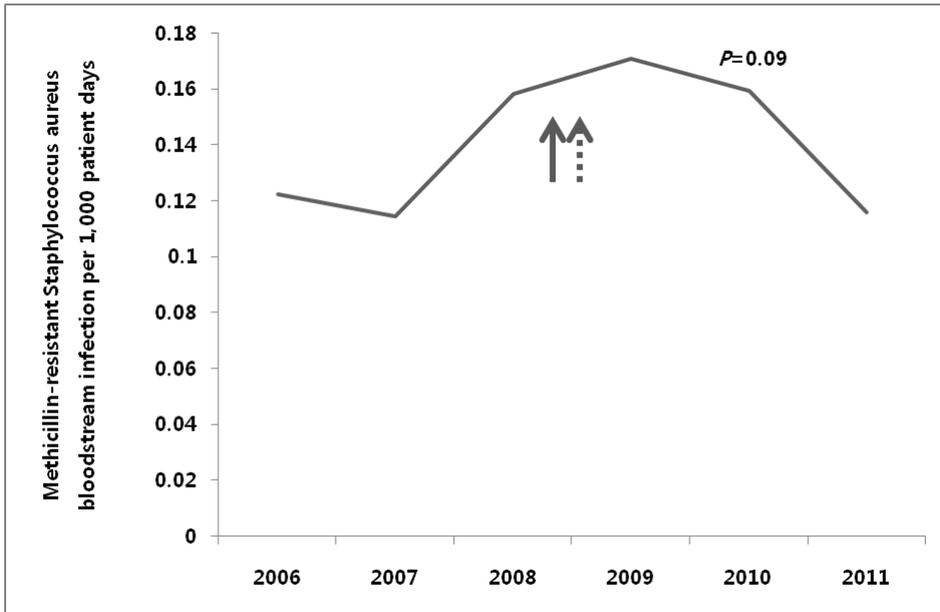


Figure 1. Incidence of methicillin-resistant *Staphylococcus aureus* bloodstream infection. The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI) from January 2006 to November 2011 is shown. The arrow indicates time, starting in August 2008, the antibiotic stewardship was intensified by use of a computerized prescription restriction and the dotted arrow indicates time, December 2008, at which point hand hygiene was reinforced. A year after the reinforcement of the two infection control programs, the incidence of MRSA BSI began to decline. Between January 2009 and November 2011, the incidence of MRSA BSI declined by 32% and Poisson regression was performed to analyze the trend.

Table 2. Trend of methicillin-resistant *Staphylococcus aureus* bloodstream infection according to the epidemiologic type of infection, route of admission, and unit attributable for infection

	2009		2010		2011		Yearly percent change ^a	P-value
	N	Incidence	N	Incidence	N	Incidence		
ICUs	34	1.028/1,000 patient days	23	0.626/1,000 patient days	19	0.637/1,000 patient days	-22.8 (-41.8 to 2.3)	.072
Non-ICUs	60	0.091/1,000 patient days	47	0.075/1,000 patient days	24	0.04/1,000 patient days	-31.6 (-46.8 to -12.2)	.003
ED	49	0.232/1,000 patient days	41	0.198/1,000 patient days	19	0.104/1,000 patient days	-30.8 (-47.7 to -8.4)	.01
OPD	45	0.094/1,000 patient days	29	0.063/1,000 patient days	24	0.054/1,000 patient days	-25 (-34.7 to -14)	<.001
HA	98	0.142/1,000 patient days	78	0.117/1,000 patient days	45	0.072/1,000 patient days	-27.6 (-38.7 to -14.4)	<.001
HCA	16	0.023/1,000 patient days	25	0.038/1,000 patient days	20	0.032/1,000 patient days	15.7 (-21.9 to 71.4)	.468
CA	4	0.006/1,000 patient days	3	0.005/1,000 patient days	8	0.013/1,000 patient days	57.1 (-13.8 to 186.6)	.14

NOTE. Poisson regression was performed as the trend test. BSI, bloodstream infection; CA, community acquired; ED, emergency department; HA, hospital acquired; HCA, health care-associated; ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; OPD, outpatient department.

^aYearly percent change is reported with a 95% confidence interval

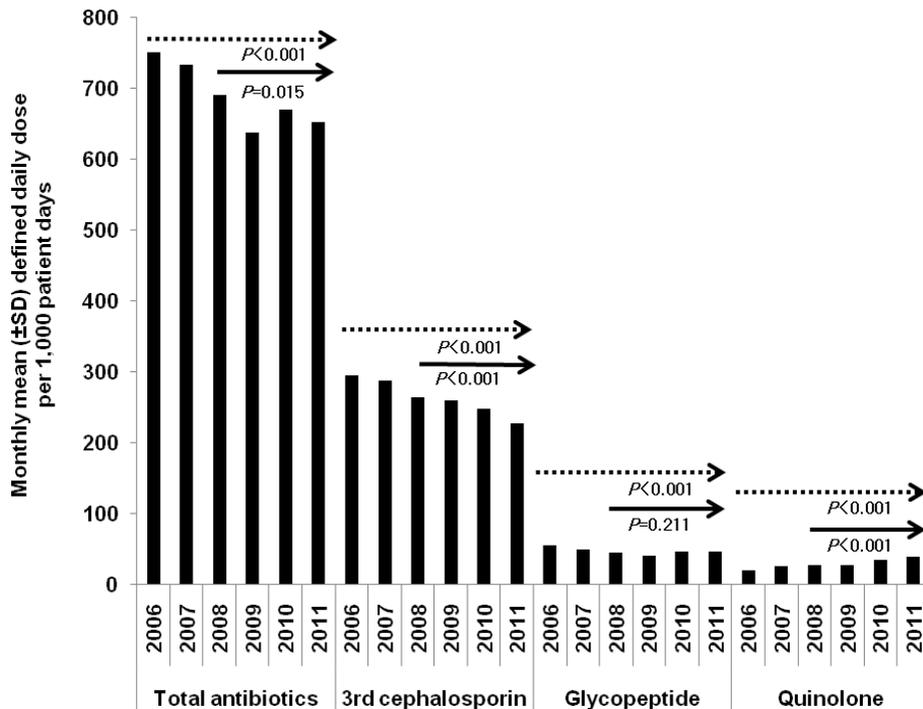


Figure 2. Amount of antibiotic consumption. A downward trend is shown in the amount of total antibiotics, 3rd cephalosporin, and glycopeptide consumption since 2006, when the antibiotic stewardship program was reinforced. There is no significant change in the amount of glycopeptide consumption after intensifying the antibiotic stewardship by computerized prescription restriction. An upward trend is shown in the amount of quinolone consumption. Trend test for amount of antibiotic consumption was performed with the use of a general linear model.

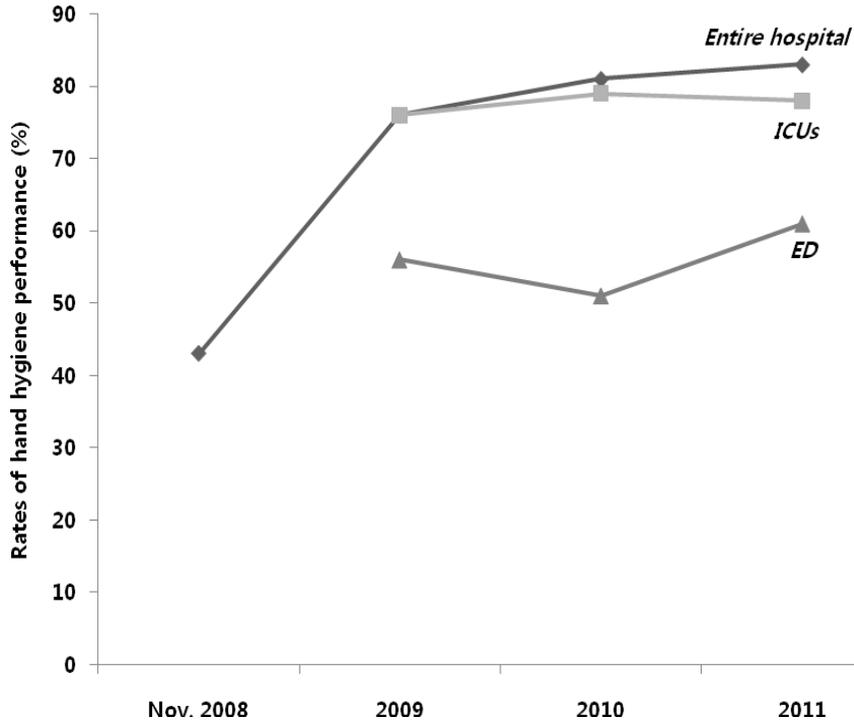


Figure 3. Rate of hand hygiene performance. The rate of hand hygiene performance was 48% in November 2008, before implementing the reinforced hand hygiene program. Between November 2008 and 2011, the rate of hand hygiene performance increased. There was a lower rate of hand hygiene performance in ICUs and the ED as compared to the entire hospital. ED, emergency department; ICU, intensive care unit.

IV. DISCUSSION

This study was designed to evaluate the epidemiologic characteristics of MRSA BSI and trend of MRSA BSI after the implementation of infection control efforts in a tertiary-care teaching hospital with high rate of MRSA. Since 2009, a year after the reinforcement of the antibiotic stewardship and hand hygiene programs, the incidence of MRSA BSI has decreased significantly. The incidence of MRSA BSI was 0.171 per 1,000 patient-days in 2009 and there was a 17% decrease per year, for a total 33.2% decrease over the 35-month long study period. Depending on the epidemiologic type of infection, this significant decrease was seen in HA MRSA BSI alone. Because our infection control programs were an in-hospital policy, the incidence did not decrease in HCA BSI and CA BSI after the reinforcement of the two infection control programs.

According to the route of admission, the rate of MRSA BSI was higher among patients admitted via the ED than OPD. This may be due to lower rates of hand hygiene performance in the ED compared to the performance throughout the hospital. It may also be affected by a higher rate of antibiotic prescription due to the disease severity of patients who visited the ED, although we did not investigate the amount of antibiotic use according to the route of admission. For the same reasons, the rate of MRSA BSI in ICUs may be higher than non-ICUs. Although the rate of MRSA BSI was high among patients who were hospitalized in ICUs and admitted via the ED, there was a remarkable reduction in MRSA BSI among these groups.

Patients infected with MRSA have role as a source of MRSA. As such, active surveillance or contact precaution may be useful. Several studies have already shown reductions in MRSA infections after implementation of infection control programs and most performed active surveillance for MRSA and contact precaution or isolation for carriers or patients⁴⁻¹³. However, it was difficult to implement these programs in our study because of the conditions of domestic hospital facilities, exempli.e, lack of beds, manpower shortage and financial problems. It was necessary to implement an infection control program that could meet the domestic situation. Therefore, we reinforced the pre-existing infection control programs, namely the antibiotic stewardship program and the hand hygiene program.

Inappropriate or excessive antibiotic use is a risk factor for MRSA infection and colonization²⁸. One meta-analysis demonstrated that MRSA isolation is clearly associated with previous antibiotic use, for example, quinolone, glycopeptides, cephalosporin and other beta-lactam²⁰. Of them, we investigated the amount of quinolone, 3rd cephalosporin, glycopeptide and total antibiotic consumption. The amount of quinolone consumption increased since 2006, although exposure to quinolone is a high risk factor for MRSA isolation^{20, 28-30}. Instead, there was a significant reduction in the amount of 3rd cephalosporin, glycopeptide and total antibiotic consumption during same period, but no further significant change in the amount of glycopeptide consumption after 2008, from which point the antibiotic stewardship program was intensified by use of

computerized prescription restrictions. Hand hygiene is one of the most important infection control programs in preventing the cross-infection of MDR pathogens in hospital. Several studies have shown that MRSA infection rates have been decreased through well-implemented hand hygiene programs^{18, 31, 32}. We also demonstrated a significant reduction in the incidence of MRSA BSI after a successful hand hygiene program during the study period. It is not possible to evaluate which component of the two infection control programs had a more powerful influence in reducing the incidence of MRSA BSI, as there were not control groups in this study.

Our study has two limitations. First, the results are data from three years after the reinforcement of our infection control program. Therefore, it is necessary to pursue an investigation of the prospective data of MRSA BSI. Second, we did not determine the cost-effectiveness of our infection control programs for controlling MRSA BSI. Estimated costs for the reinforcement of the “antibiotic stewardship program” and the “hand hygiene program” should be compared with the estimated costs of caring for patients infected by MDR pathogens, as well as MRSA. This is why the purpose of our infection control program was to reduce MDR pathogens, including MRSA.

V. CONCLUSION

MRSA is the most important hospital pathogen around the world. Many

infection control programs have been introduced. Among them, the implementation of a single method is likely to be insufficient to reduce MRSA infections. Several studies have shown decreases in the rate of MRSA infections after their infection control programs including active surveillance and contact precaution. Although we did not implement active surveillance and contact precaution or isolation due to the conditions of domestic hospital facilities, there was a significant decrease in MRSA BSI in this institution with a previously high rate of MRSA after efforts to reinforce antibiotic stewardship program and hand hygiene over a three year period.

REFERENCES

1. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32:470-85.
2. Johnson AP, Pearson A, Duckworth G. Surveillance and epidemiology of MRSA bacteraemia in the UK. *J Antimicrob Chemother* 2005;56:455-62.
3. Klein E, Smith DL, Laxminarayan R. Hospitalizations and deaths caused by methicillin-resistant *Staphylococcus aureus*, United States, 1999-2005. *Emerg Infect Dis* 2007;13:1840-6.
4. Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, et al. Veterans Affairs initiative to prevent methicillin-resistant *Staphylococcus aureus* infections. *N Engl J Med* 2011;364:1419-30.
5. Johnson AP, Davies J, Guy R, Abernethy J, Sheridan E, Pearson A, et al. Mandatory surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia in England: the first 10 years. *J Antimicrob Chemother* 2012;67:802-9.
6. Kallen AJ, Mu Y, Bulens S, Reingold A, Petit S, Gershman K, et al. Health care-associated invasive MRSA infections, 2005-2008. *JAMA* 2010;304:641-8.
7. Kotilainen P, Routamaa M, Peltonen R, Oksi J, Rintala E, Meurman O, et al. Elimination of epidemic methicillin-resistant *Staphylococcus aureus* from a university hospital and district institutions, Finland. *Emerg Infect Dis* 2003;9:169-75.
8. Vriens M, Blok H, Fluit A, Troelstra A, Van Der Werken C, Verhoef J. Costs associated with a strict policy to eradicate methicillin-resistant *Staphylococcus aureus* in a Dutch University Medical Center: a 10-year survey. *Eur J Clin Microbiol Infect Dis* 2002;21:782-6.
9. Huang SS, Yokoe DS, Hinrichsen VL, Spurchise LS, Datta R, Miroshnik I, et al. Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant *Staphylococcus aureus* bacteremia. *Clin Infect Dis* 2006;43:971-8.
10. Chowder MY, Paitan Y, Gottesman BS, Gerber B, Ben-Nissan Y, Shitrit P. Hospital-wide methicillin-resistant *Staphylococcus aureus* control program: A 5-year follow-up. *Infect Control Hosp Epidemiol* 2009;30:778-81.
11. Robicsek A, Beaumont JL, Paule SM, Hacek DM, Thomson RB, Jr., Kaul KL, et al. Universal surveillance for methicillin-resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Ann Intern Med* 2008;148:409-18.
12. Lawes T, Edwards B, Lopez-Lozano JM, Gould I. Trends in *Staphylococcus aureus* bacteraemia and impacts of infection control

- practices including universal MRSA admission screening in a hospital in Scotland, 2006-2010: retrospective cohort study and time-series intervention analysis. *BMJ Open* 2012;2:e000797.
13. Huang YC, Lien RI, Su LH, Chou YH, Lin TY. Successful control of methicillin-resistant *Staphylococcus aureus* in endemic neonatal intensive care units--a 7-year campaign. *PLoS ONE* 2011;6:e23001.
 14. Chong Y, Lee K, Park YJ, Jeon DS, Lee MH, Kim MY, et al. Korean nationwide surveillance of antimicrobial resistance of bacteria in 1997. *Yonsei Med J* 1998;39:569-77.
 15. Lee K, Chang CL, Lee NY, Kim HS, Hong KS, Cho HC. Korean nationwide surveillance of antimicrobial resistance of bacteria in 1998. *Yonsei Med J* 2000;41:497-506.
 16. Kim HB, Jang HC, Nam HJ, Lee YS, Kim BS, Park WB, et al. In vitro activities of 28 antimicrobial agents against *Staphylococcus aureus* isolates from tertiary-care hospitals in Korea: a nationwide survey. *Antimicrob Agents Chemother* 2004;48:1124-7.
 17. Cho YK. The nationwide surveillance system of nosocomial infection in Intensive care units. *Korean J Nosocomial Infect Control* 2011;16:S7-13.
 18. Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Infection Control Programme. Lancet* 2000;356:1307-12.
 19. Fukatsu K, Saito H, Matsuda T, Ikeda S, Furukawa S, Muto T. Influences of type and duration of antimicrobial prophylaxis on an outbreak of methicillin-resistant *Staphylococcus aureus* and on the incidence of wound infection. *Arch Surg* 1997;132:1320-5.
 20. Tacconelli E, De Angelis G, Cataldo MA, Pozzi E, Cauda R. Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis. *J Antimicrob Chemother* 2008;61:26-38.
 21. World Health Organization. WHO guidelines on hand hygiene in health care: first global patient safety challenge: clean care is safer care. Geneva, Switzerland: WHO; 2009.
 22. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2012.
 23. Cockerill FR, Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing : twenty-first informational supplement. M100-S22. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
 24. Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Intern Med* 2002;137:791-7.

25. Son JS, Song JH, Ko KS, Yeom JS, Ki HK, Kim SW, et al. Bloodstream infections and clinical significance of healthcare-associated bacteremia: a multicenter surveillance study in Korean hospitals. *J Korean Med Sci* 2010;25:992-8.
26. Horan TC, Emori TG. Definitions of key terms used in the NNIS System. *Am J Infect Control* 1997;25:112-6.
27. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309-32.
28. Shorr AF. Epidemiology of staphylococcal resistance. *Clin Infect Dis* 2007;45:S171-6.
29. Harbarth S, Liassine N, Dharan S, Herrault P, Auckenthaler R, Pittet D. Risk factors for persistent carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 2000;31:1380-5.
30. Weber SG, Gold HS, Hooper DC, Karchmer AW, Carmeli Y. Fluoroquinolones and the risk for methicillin-resistant *Staphylococcus aureus* in hospitalized patients. *Emerg Infect Dis* 2003;9:1415-22.
31. Stone SP, Fuller C, Savage J, Cookson B, Hayward A, Cooper B, et al. Evaluation of the national Cleanyourhands campaign to reduce *Staphylococcus aureus* bacteraemia and *Clostridium difficile* infection in hospitals in England and Wales by improved hand hygiene: four year, prospective, ecological, interrupted time series study. *BMJ* 2012;344:e3005.
32. Johnson PD, Martin R, Burrell LJ, Grabsch EA, Kirsa SW, O'Keeffe J, et al. Efficacy of an alcohol/chlorhexidine hand hygiene program in a hospital with high rates of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection. *Med J Aust* 2005;183:509-14.

ABSTRACT(IN KOREAN)

MRSA의 비율이 높은 한 기관에서 시행한 항생제 관리와
손위생의 강화 프로그램 후 MRSA 균혈증의 추세 변화

< 지도교수 최 준 용 >

연세대학교 대학원 의학과

김 용 찬

배경 : MRSA 감염은 1961년에 보고된 이후 전세계적으로 증가되어왔다. 외국의 몇 연구들에서 의료관련 MRSA 감염을 줄이기 위한 노력들이 효과적이었음을 보여주었다.

방법 : 2,000 병상을 가지는 국내 일개의 3차 대학병원에서 다재 내성균을 줄이기 위한 노력으로 2008년 8월부터 항생제 관리 프로그램, 2008년 12월부터 손위생 프로그램의 강화를 시작하였다. 2006년 1월부터 2011년 11월까지 병원에 입원한 환자 중 MRSA 균혈증이 확인된 환자를 대상으로 MRSA 균혈증의 발병률, 역학적 특징을 확인하고 두 감염관리 활동이 MRSA 균혈증의 추세에 미친 영향을 평가하였다.

결과 : 연구기간 동안 병원에 입원하였던 515,703 명의 환자 중 568건의 MRSA 균혈증이 발생하였다. 2006년부터 2009년까지 MRSA균혈증의 발병률이 증가하였으나, 항생제 관리와 손위생을 강화하는 감염관리 활동을 시행한 다음해인 2009년부터 감소하였다. 2009년에 1,000 입원일 당 0.171 건에서 2011년에 1,000 입원일 당 0.116 건으로 유의하게 감소하였다 ($p = 0.009$). 전체 항생제 사용량에서도 2008년에 월 평균 1,000 입원일 당 690.54 ± 28.33 일일사용량에서 2011년에 월 평균 1,000 입원일 당 652.47 ± 20.77 일일사용량으로 의미있는 감소를 보여주었다 ($p = 0.015$). 손위생 수행률의 경우 손위생 강화 프로그램 한달 전 수행률이 43%에 불과하였으나 2011년에는 83%까지 증가하였다 ($p = 0.043$).

결론 : MRSA감염 관리의 모든 항목을 시행하지는 않았지만, MRSA의 비율이 높은 일개의 국내 대학병원에서 항생제 관리와 손위생을 강화하는 감염관리 프로그램 후 3년 동안 의미있는 MRSA 균혈증 감소를 보여주었다.

핵심되는 말 : 메치실린-내성 포도상구균, 균혈증, 감염관리