Bridging the gap between knowledge and action for health: case studies

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Abstract Biomedical discoveries could improve people's health only if they are suited to the diverse political and social contexts, health systems and population groups. Knowledge generated through evidence-informed health policy and practice when applied to the local situation enhances the quality and efficiency of health care. This article describes four case studies on bridging the gap between knowledge and action for health in a tertiary care hospital in Bangkok, Thailand. Gaps between knowledge and action for health are classified into "know–do" and "do–know" gaps with knowledge implementation and knowledge generation being the key measures for bridging the gap.

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Voir page 606 le résumé en français. En la página 606 figura un resumen en español.

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Introduction

Health research findings impact policy, practice and patient outcomes if they are appropriately translated into healthcare practice. The 2004 *World report on knowledge for better health* stated that biomedical discoveries could improve people's health only if they are applied specifically to diverse political and social contexts, health systems and population groups. The report laid a strong emphasis on translating knowledge into action to improve health thereby bridging the gap between what is known and what is actually done.[1] Knowledge translation has been a cause for concern and strategies for bridging the gap between practice and evidence have been proposed.[2–5]

I describe four case studies chosen to illustrate how to bridge the gap between knowledge and action for health according to the framework in Siriraj Hospital, Bangkok where the "Knowledge Management to Promote Evidence-Informed Health Care Policy and Practice in Thailand" project has been conducted since 2001. The concept and the framework for knowledge management was based on my experiences at Siriraj Hospital over the first two years of the project (Fig. 1).[6]

Siriraj Hospital is a tertiary-care university hospital in Bangkok, Thailand with 2335 beds (2200 beds in 111 general wards and 135 beds in 10 intensive care units); approximately 10 000 personnel of which 1300 are physicians (700 faculty members and 600 residents) and 4200 are nurses; with around 1 000 000 outpatient visits and 100 000 inpatients per year.

I have classified the gaps between knowledge and action for health into "know–do" and "do–know" gaps with knowledge implementation and knowledge generation being the key measures for bridging the gap between knowledge and action for health.

Case Studies

Knowledge implementation for bridging the "do–know" gap

Heparinized saline flush and peripheral venous catheter patency

Many hospitalized patients require a peripheral intravenous catheter for the administration of drugs and fluids. The patency of indwelling peripheral intravenous catheters is maintained by a continuous drip of fluid via the catheter or by connecting the catheter to an intravenous catheter lock (IV lock). The IV lock is advantageous as the patient can move around without carrying the fluid bottle. However, an indwelling IV lock has to be periodically flushed with fluid to prevent clots.

The work instruction for the flush procedure in Siriraj Hospital (prepared in 2001 and revised in 2003) recommends using heparinized saline as flush fluid. A September 2004 survey, on the use of fluids for flushing peripheral intravenous catheters, found that the majority of the patients with IV lock received heparinized saline (89%) as flush fluid while the remaining (11%) received normal saline.[7] This occurred despite the known disadvantages of using heparin for flushing IV locks and the high cost of using heparin — an estimated 2.4 million baht (US$ 60 000) per year. Evidence from three meta-analyses found no significant difference in the incidence of catheter clot and phlebitis between peripheral intravenous catheters flushed with normal saline and those flushed with 10 units per ml or 50 units per ml of heparinized saline.[8–10] Results from two randomized controlled studies conducted by nurses at Siriraj Hospital and Ramathibodi Hospital in Bangkok reported findings similar to those from the meta-analyses.[11,12] Therefore, the practice of using heparinized saline as flush fluid for maintaining peripheral intravenous catheter patency of hospitalized patients in Siriraj Hospital was not evidence-based and had to be corrected. Many hospitals in Thailand use normal saline as flush fluid for IV lock and three patient-care areas in Siriraj Hospital have used normal saline flush for maintaining peripheral intravenous catheter patency for many years without any problems.

The knowledge management project at Siriraj introduced five knowledge

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implementation strategies/interventions for switching from heparinized saline flush to normal saline flush in 10 medical wards containing 240 beds.

1. Disseminating evidence-based clinical practice policy on using flush fluid for maintaining peripheral intravenous catheter patency to responsible personnel.
2. Reminding prescribers to use normal saline flush instead of heparinized saline flush.
3. Providing technical advice to nurses on using normal saline flush in the event of peripheral intravenous catheter clot.
4. Confirming the necessity of using heparinized saline flush with the prescriber.
5. Setting up a regulation that if the prescriber really wanted to use heparinized saline flush: an asterix should be placed next to the prescription otherwise the nurse would use normal saline flush. This regulation was added because many prescribers called the IV lock "heparin lock" and prescribed "heparin lock" even though they did not intend to use heparin.

The information on using flush fluids was collected from physicians' order sheets in the medical records at baseline in February 2005, and then every two to four weeks during the intervention period up to June 2005 and six months after implementing the interventions. All hospitalized patients in medical wards who had IV locks received heparinized saline flush at baseline. After knowledge interventions 1–4 were applied, from March to May 2005, in 75% of the patients with IV locks flush fluid was switched to normal saline. Normal saline flush completely replaced the practice of using heparinized saline flush after the inclusion of administrative intervention 5 from June to November 2005. The hospital administrator subsequently adopted these strategies as a policy for the entire hospital in January 2006. In addition to the publication of this observation[7] and its policy implications, this knowledge implementation resulted in enormous savings in terms of resources for the patients and the hospital.

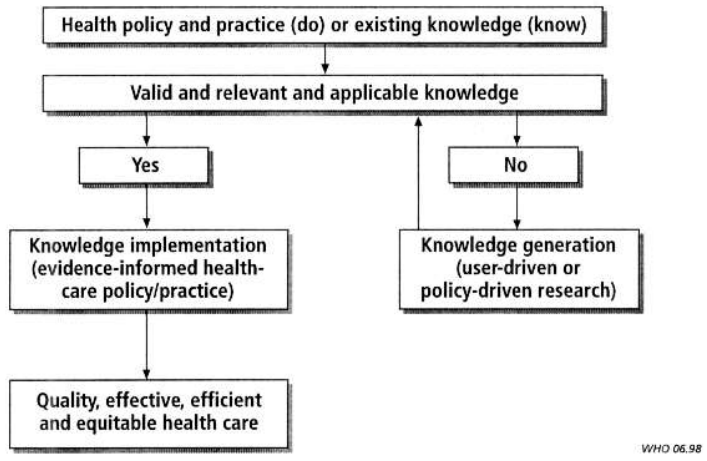
Knowledge generation for bridging the "do–know" gap: *Urinary drainage bag change regimen*

Urinary tract infection (UTI) is a common complication among patients with an indwelling urethral catheter. Each change of the urinary drainage bag predisposes the patient to developing UTI, and increases personnel time, expense and plastic waste. During the preparation meeting for Siriraj Hospital's accreditation in August 2001, there was a conflict between the nurse practitioners and the infection control committee regarding the frequency of urine bag changes for patients with short-term urinary catheter. The nurses' guideline recommended a urine bag change every three days but the infection control committee said it should not be changed on such a routine basis.

A review of the literature showed only one relevant study that compared urine bag changing regimens in 12 elderly long-term urinary catheterized patients.[13] The study found no significant clinical or microbiological differences between patients who had a daily urine bag change and those who had a weekly bag change. This study, however, was not applicable to Siriraj Hospital because it was conducted on long-term catheterized elderly patients. A guideline for preventing infections associated with the insertion and maintenance of short-term indwelling urethral catheters in acute care recommended that urinary drainage bags should be changed when clinically indicated, without any supporting evidence.[14] In this respect, neither the nurses' guideline nor the infection control committee's recommendation were based on valid evidence.

A randomized controlled trial on the incidence of UTI, among hospitalized patients with short-term indwelling urethral catheters, which compared a three-day urinary drainage bag change to a no-change found no significant difference in the incidence of UTI between the two groups.[15] This result was adopted as a policy endorsed by the Dean of Faculty of Medicine, Siriraj Hospital for the entire hospital from February 2002 and disseminated to infection control nurses during the national workshop on prevention and control of nosocomial infections in July 2002. In addition to a publication[15] and policy implications, it saved on costs, personnel time and plastic waste.

Fig. 1. **Framework for bridging the gap between knowledge and action for health**



Knowledge implementation for bridging the "know–do" gap *Semi-recumbent positioning to prevent ventilator/associated pneumonia*

Pneumonia is a common complication among patients on a respirator, causing high mortality and morbidity. While there is evidence that the supine position is a risk factor for ventilator-associated pneumonia (VAP),[16–18] a clinical study revealed that the semi-recumbent position prevented VAP with a relative risk reduction of 76% (95% confidence interval (CI): 27–93%) and number-needed-to-treat (NNT) of four.[19] An evidence-based clinical practice guideline recommends the semi-recumbent position as an intervention to prevent VAP.[20] These findings were valid, relevant and applicable to the

patients in Siriraj Hospital. A survey of the body position of patients on respirators in 14 medical wards of Siriraj Hospital during February–March 2003 showed that only 17% of the patients were in semi-recumbent position. A total of 27% of the residents and nurses in 14 medical wards recommended the semi-recumbent position for patients on respirators. However, the reasons for this response were not based on evidence for pneumonia prevention from the literature but mainly physiological, such as better lung expansion, better oxygenation and decreased intra-thoracic pressure.

The knowledge management project at Siriraj developed and executed strategies for knowledge implementation in the target populations — residents and nurses. These were:

1. informing the target population about the evidence during a quality improvement conference meeting in July 2003;
2. disseminating a one-page clinical practice policy in Thai containing information on the significance of the problem, the evidence, recommendation, grade of recommendation, contraindications for and warnings about the semi-recumbent position and the relevant references;
3. creating awareness among health-care personnel by placing a specific sign at the patient's bed. The front side of the sign would read, "This patient should be placed in a semi-recumbent position", while the back of the sign contained "indications, contraindications and warnings about the semi-recumbent position".

Because this was a no-cost simple intervention, a compliance rate greater than 90% was expected. However, a survey in July–August 2003, after the implementation of the aforementioned strategies, revealed that only 41% of patients on respirators in the 14 medical wards were placed in the semi-recumbent position, significantly higher than 17% at baseline (P <0.005), but the compliance was considered unsatisfactory. Therefore, additional strategies, such as feedback of observations to nurses, a reminder system and increasing awareness were implemented. Repeat surveys during November–December 2003 and March–April 2004 revealed that 56% and 76% of the patients on respirators in 14 medical wards, respectively, were placed in the semi-recumbent position. A survey of 739 adult patients on respirators in all intensive care units during October and December 2003 revealed that 68% of them were placed in a semi-recumbent position. The incidence of VAP per 1000 ventilation days decreased from 11.3 during January–December 2002 to 9.2 and 9.4 during October–December 2003 and January–June 2004, respectively. This decrease was not large because compliance with the semi-recumbent position was still modest. The lessons learned from these attempts showed that knowledge translation strategies are not easy even for implementing a simple and free intervention.

Knowledge generation for bridging the "know–do" gap

Antibiotic prophylaxis for preventing infection in cancer patients

The majority of patients who receive chemotherapy for the treatment of cancer develop neutropenia and thus are susceptible to bacterial infections. Bacterial flora in the oral cavity and gut of chemotherapy-induced neutropenic patients themselves cause these infections. Reports from two meta-analyses, which determined the efficacy of oral prophylactic antibiotics in afebrile neutropenic patients due to cancer chemotherapy, showed that oral prophylactic antibiotics, fluoroquinolones and cotrimoxazole, decreased bacteraemia and infection-related mortality due to bacterial causes during neutropenic episodes.[21,22] Although, evidence from these meta-analyses was valid and relevant to Thai patients, the issue of applicability was a concern. Most of the primary studies included in the meta-analyses were conducted in developed countries, where antibiotics are not available without prescription. In Thailand, however, antibiotics can be purchased without prescription, and fluoroquinolones and cotrimoxazole are commonly given to patients with acute diarrhoea and upper respiratory infections. Fluoroquinolones are also used as a growth stimulator in the shrimp industry in Thailand, and thus commonly available. Moreover, it is not known if bacterial flora in the oral cavity and gut of Thai patients who have cancer chemotherapy-induced neutropenia are susceptible to fluoroquinolones and cotrimoxazole, and whether they should receive such antibiotics.

This situation led the way for knowledge generation on the susceptibility of bacteria isolated from the oral cavity and gut of Thai patients with cancer chemotherapy-induced neutropenia. A study to determine the susceptibility of bacteria colonized in the oral cavity and/or gut of 140 Thai patients with cancer chemotherapy-induced neutropenia to oral antibiotics available in Thailand is currently being conducted. Preliminary results suggest that bacterial flora isolated from some patients are resistant to many oral antibiotics. By the end of 2006 it will be confirmed whether oral antibiotics would be beneficial for Thai patients before knowledge implementation of "to use" or "not to use" oral prophylactic antibiotics in Thai patients with cancer chemotherapy-induced neutropenia takes place.

Conclusions and recommendations

The gap between what we know and what we practice, i.e. the know–do gap, is mentioned in the literature, and translating research findings into practice by knowledge implementation has been attempted. The case studies described in this article found that another category of gap — the do–know gap, i.e. the gap between what we practice and what we know, is also common in health-care systems in developing countries. Knowledge generation is also an important measure to bridge the gap between knowledge and action for health and it is hoped that the above-mentioned case studies will encourage responsible institutions in developing countries to invest more resources in promoting professional communicators or intermediaries to narrow the gap as well as develop a culture where decisions taken by policy-makers, health professionals and the public are based on evidence. ■

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Résumé

Combler le fossé entre savoir et action en faveur de la santé : études de cas

Les découvertes dans le domaine biomédical ne peuvent déboucher sur des améliorations en matière de santé publique que si elles sont adaptées aux divers contextes politiques et sociaux, systèmes de santé et groupes de population. Les connaissances acquises à travers l'application à la situation locale de politiques et de pratiques sanitaires s'inspirant d'éléments factuels permettent d'améliorer la qualité et l'efficacité des soins de santé prodigués. L'article présente quatre études de cas examinant comment établir un pont entre les connaissances et les interventions en faveur de la santé dans un hôpital dispensant des soins tertiaire de Bangkok en Thaïlande. Les ponts à établir entre connaissances et interventions sanitaires sont répartis en deux catégories, «savoir-faire» et «faire-savoir», la mise en œuvre des connaissances et la génération de données étant des mesures clés pour créer de tels liens.

Resumen

Cerrar la brecha entre los conocimientos y la acción sanitaria: estudios de casos

Los descubrimientos biomédicos sólo redundan en mejoras de la salud de las personas cuando están adaptados a los diversos contextos políticos y sociales, sistemas de salud y grupos de población. Los conocimientos que generan las políticas y prácticas sanitarias basadas en la evidencia cuando se aplican a la situación local fomentan la calidad y eficiencia de la atención sanitaria. En este artículo se describen cuatro estudios de casos sobre la manera de corregir la brecha existente entre los conocimientos y la acción sanitaria en un hospital de atención terciaria de Bangkok, Tailandia. Las brechas teórico-prácticas en materia de salud son de dos tipos: «conocimientos-acción» y «acción-conocimientos», y las soluciones para corregirlas radican en la aplicación de conocimientos y la generación de conocimientos, respectivamente.

ملخص

رأب الفجوة بين المعارف والعمل من أجل الصحة: دراسة حالات

لا يمكن للمكتشفات الطبية والبيولوجية أن تحسِّن من حياة الناس ما لم تكن متناسبة مع السياق السياسي والاجتماعي ومع النظم الصحية ومع المجموعات السكانية. وتتولَّد المعارف من خلال السياسات والممارسات الصحية المسندة بالبيِّنات، وإثر تطبيقها على الوضع المحلي فإنها ستعزِّز الجودة والفعالية في الرعاية الصحية. ويصف هذا المقال أربع دراسات للحالات حول رأب الفجوة بين المعارف والعمل من أجل الصحة في إحدى مستشفيات الرعاية الثالثية في بانكوك في تايلاند. فالفجوات بين المعارف والعمل من أجل الصحة تصنَّف إلى فجوات المعرفة للعمل وفجوات العمل للمعرفة، ويبقى كل من تنفيذ المعارف وتوليدها الوسيلتين الأكثر أهمية في رأب هذه الفجوة.

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Original Article

In Vitro Activity of Tigecycline Against Methicillin-Resistant *Staphylococcus aureus* Isolated from the Patients at Siriraj Hospital

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ABSTRACT

An in vitro activity study of tigecycline against 51 clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) from different patients hospitalized at Siriraj Hospital, Bangkok, Thailand from 2002 to 2004 was performed by the disk diffusion method and E-test. All isolates had an inhibition zone of ≥ 20 mm, with the MIC_{50} and MIC_{90} of 0.125 and 0.25 mg/L, respectively. The study results indicated that all MRSA isolates tested were susceptible to tigecycline. (*J Infect Dis Antimicrob Agents 2006; 23:1-4.*)

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common causes of infections in hospitalized patients. The prevalence of MRSA among *S. aureus* isolates from hospitalized patients at Siriraj Hospital from January to May 2005 was 51.5 percent.[1] The common sites of MRSA infections were the skin and skin structures, the lower respiratory tracts, and the blood stream. Antibiotics currently used for therapy of MRSA infections include glycopeptides, fluoroquinolones, co-trimoxazole, fosfomicin, fusidic acid, and linezolid. However, these antibiotics had considerable drawbacks including the possibility of toxicity, emergence of resistance, and high monetary cost. Therefore, a search for any new agents effective against MRSA is ongoing.

Tigecycline is a glycylcycline antibiotic that shows a promising activity against a wide range of organisms.[2-4] Tigecycline is active against gram-positive cocci including methicillin-resistant staphylococci, penicillin-resistant *Streptococcus pneumoniae*, and vancomycin-resistant enterococci.

The objective of the study was to determine an in vitro activity of tigecycline against MRSA clinical isolates from Thai patients.

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Keywords: Tigecycline, Methicillin-Resistant *Staphylococcus aureus*

MATERIALS AND METHODS

MRSA Isolates

Fifty-one clinical isolates of MRSA from different infected patients hospitalized at Siriraj Hospital, Bangkok, Thailand from 2002 to 2004 were included. They were isolated from the lower respiratory tract (N=15), the pus (N=16), the blood (N=10), and the other specimens (N=10). All isolates had oxacillin minimum inhibitory concentration (MIC) of >4 mg/L and vancomycin MIC of <4 mg/L. Forty-six isolates were vancomycin-susceptible MRSA, and 5 isolates were vancomycin-hetero-resistant MRSA. Vancomycin-susceptible MRSA and vancomycin hetero-resistant MRSA were determined by a one-point population analysis and confirmed by a population analysis.[5,6]

Tigecycline Susceptibility Study

The methodology for susceptibility testing was done by direct colony suspension according to the guidelines recommended by the Clinical and Laboratory Standards Institute (CLSI).[7] The test isolate was grown overnight on blood agar at 35°C, and the colonies were picked and suspended in sterile normal saline equivalent to a 0.5 McFarland standard. The suspension was used to inoculate on Mueller-Hinton agar. The paper discs containing tigecycline 15 μg per disk (Becton Dickinson, USA) and E-test strips (AB BIODISK, Sweden) were placed according to manufacturer's recommendation. The agar plates were incubated at 35°C for 18 hours before the inhibition zone and MIC results were read. Quality control was performed by testing the susceptibility of *S. aureus* ATCC 29213 as recommended by Wyeth Research, USA.

RESULTS

The MIC of tigecycline against *S. aureus* ATCC 29213 was 0.064 mg/L which was within the reference range of 0.03-0.25 mg/L. A distribution of inhibition zone diameters of tigecycline against 51 MRSA isolates by the disk diffusion method is shown in Table 1. The inhibition zone of tigecycline against all isolates of MRSA was ≥20 mm. A distribution of MICs of tigecycline against 51 MRSA isolates by the E-test is shown in Table 2. The MIC_{50} and MIC_{90} values were

Table 1. Distribution of inhibition zone diameter of tigecycline against methicillin-resistant *Staphylococcus aureus* (MRSA).

Organism (No. of isolates)	Number of isolates with diameter of inhibition zone (mm)									
	20	21	22	23	24	25	26	27	28	30
All MRSA (N=51)	4	7	9	11	2	13	3		1	1
Vancomycin-susceptible MRSA (N=46)	2	7	9	8	2	13	3		1	1
Vancomycin-hetero-resistant MRSA (N=5)	2			3						

Table 2. Distribution of MICs of tigecycline against MRSA.

Organism (No. of isolates)	Number of isolates with MIC (mg/L)						
	0.032	0.064	0.094	0.125	0.19	0.25	0.5
All MRSA (N=51)	2	6	12	17	7	6	2
Vancomycin-susceptible MRSA (N=46)	2	6	12	15	5	5	1
Vancomycin-hetero-resistant MRSA (N=5)				2	2	1	

0.125 and 0.25 mg/L, respectively. Susceptibility profiles of tigecycline against vancomycin-susceptible MRSA and vancomycin-hetero-resistant MRSA were not significantly different.

DISCUSSION

According to the US Food and Drug Administration (FDA)-approved breakpoints of the inhibition zone of ≥19 mm and MIC of <0.5 mg/L indicating the susceptibility of *S. aureus* to tigecycline[8], all studied isolates of MRSA in one study were considered susceptible to tigecycline. These observations confirmed the worldwide data on in vitro susceptibility of tigecycline against MRSA.[9-14] Tigecycline was found to be effective and safe for treating patients with complicated intra-abdominal infections and complicated skin and skin-structure infections.[15-19] Tigecycline has been approved by the US FDA for treating patients with the aforementioned infections. However, the existing evidence proving the effectiveness of treating MRSA infections with tigecycline remains limited. Tigecycline may prove to be an important antibiotic for treatment of MRSA infections in Thailand in the near future once more clinical information on use of tigecycline in treating of MRSA infections becomes available.

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Original Article

In Vitro Activity of Colistin and Tigecycline Against Extended-Spectrum-Beta-Lactamase (ESBL)-Producing *Escherichia coli* and *Klebsiella pneumoniae* Isolated from Patients in Siriraj Hospital

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ABSTRACT

An in vitro activity study of colistin and tigecycline against extended-spectrum-beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from the patients hospitalized at Siriraj Hospital from 2004 to 2005 was conducted by the disk diffusion method and E-test. An in vitro activity of colistin revealed that 1) all 100 isolates had an inhibition zone of ≥11 mm, 2) the minimal inhibitory concentration MIC_{50} and MIC_{90} of colistin against 50 isolates of ESBL-producing *E. coli* were 0.5 mg/L and 1 mg/L, respectively, and 3) the MIC_{50} and MIC_{90} of colistin against 50 isolates of ESBL-producing *K. pneumoniae* were 0.5 mg/L and 0.5 mg/L, respectively. An in vitro activity of tigecycline revealed that 1) the MIC_{50} and MIC_{90} of tigecycline against 63 isolates of ESBL-producing *E.coli* were 0.5 mg/L and 1 mg/L, respectively, and 2) the MIC_{50} and MIC_{90} of tigecycline against 42 isolates of ESBL-producing *K. pneumoniae* were 1.5 mg/L and 2 mg/L, respectively. The study results indicated that ESBL-producing *E. coli* and *K. pneumoniae* isolated from the patients in Siriraj Hospital were susceptible to colistin and tigecycline. (*J Infect Dis Antimicrob Agents 2006;23:21-4.*)

INTRODUCTION

The prevalence of extended-spectrum-beta-lactamase (ESBL)-producing organisms and their antimicrobial resistance patterns may vary between geographic areas. The prevalence of ESBL-producing *E. coli* and *K. pneumoniae* causing infections,

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Keywords: colistin, tigecycline, ESBL, *Escherichia coli*, *Klebsiella pneumoniae*

especially hospital-acquired infections, in Thailand has been increasing. The prevalence of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from the patients of Siriraj Hospital in 2003 was 56.9 percent and 33.3 percent, respectively.[1] ESBL-producing *E. coli* and *K. pneumoniae* are usually more resistant to antibiotics than ESBL-non-producing strains. They are usually resistant to most beta-lactams including penicillins and cephalosporins. The choice of antibiotic therapy for ESBL-producing *E. coli* and *K. pneumoniae* is, therefore, limited. The most effective antibiotic for severe infections caused by such organisms is a carbapenem, and as a result, any new agents effective against ESBL-producing *E. coli* and *K. pneumoniae* are sought after.

Colistin has been shown to be active and effective against multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* including those isolated from Thai patients.[2,3] Tigecycline is a glycylcycline antibiotic that shows promising activity against a wide range of organisms.[4] Tigecycline is active against many Gram-negative bacilli including those resistant to multiple classes of antibiotics.

The objective of the study was to determine an in vitro activity of colistin and tigecycline against ESBL-producing *E. coli* and *K. pneumoniae* isolated from the patients hospitalized at Siriraj Hospital from 2004 to 2005.

MATERIALS AND METHODS

The studied organisms were 113 and 92 strains of ESBL-producing *E. coli* and *K. pneumoniae* isolated from different patients hospitalized at Siriraj Hospital from 2004 to 2005. The method for detection of ESBL-producers was the double-disk diffusion as recommended by the Clinical and Laboratory Standards Institute (CLSI).[5] The susceptibility of colistin was determined by the disk diffusion test, using a 10-μg colistin sulfate disk, and the minimal inhibitory concentration (MIC) was determined by the E-test method for 50 isolates of ESBL-producing *E. coli* and 50 isolates of ESBL-producing *K. pneumoniae*. A quality control was performed by testing the susceptibility of *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853. The MIC of tigecycline was determined by the E-test method for 62 and 42 isolates of ESBL-producing *E. coli* and *K. pneumoniae*, respectively. Quality control was performed by testing the susceptibility of *E. coli* ATCC 25922. The methodology for susceptibility testing was done by direct colony suspension as recommended by the CLSI.[5] The test isolate was grown overnight on blood agar at 35°C, and colonies were picked to suspend in sterile normal saline equivalent to a 0.5 McFarland standard. The suspension was used to inoculate on Mueller-Hinton agar, and the E-test strip was placed according to the manufacturer's recommendation. The agar plates were incubated at 35°C for 18 hours before the inhibition zone and the MIC results were read.

RESULTS

The inhibition zones of colistin against *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were both 12 mm, and their MICs were both 0.25 mg/L. The MIC of tigecycline against *E. coli* ATCC 25922 was 0.12 mg/L. All aforementioned values were within reference limits. An in vitro activity of colistin revealed that 1) all isolates had an inhibition zone of ≥ 11 mm, 2) the MIC_{50} and MIC_{90} of colistin against ESBL-producing *E. coli* were 0.5 mg/L and 1 mg/L, respectively, and 3) the MIC_{50} and MIC_{90} of colistin against ESBL-producing *K. pneumoniae* were 0.5 mg/L and 0.5 mg/L, respectively. An in vitro activity of tigecycline revealed that 1) the MIC_{50} and MIC_{90} of tigecycline against ESBL-producing *E.coli* were 0.5 mg/L and 1 mg/L,

respectively and 2) the MIC_{50} and MIC_{90} of tigecycline against ESBL-producing *K. pneumoniae* were 1.5 mg/L and 2 mg/L, respectively.

DISCUSSION

The susceptibility breakpoints of colistin against Gram-negative bacilli are the inhibition zone of ≥ 11 mm, and the MIC of ≤ 2 mg/L, whereas the susceptibility breakpoint of tigecycline against Enterobacteriaceae is the MIC of ≤ 2 mg/L. Therefore, nearly all strains of ESBL-producing *E. coli* and *K. pneumoniae* isolated from the patients hospitalized at Siriraj Hospital from 2004 to 2005 were susceptible to colistin and tigecycline. Our observations on susceptibility of ESBL-producing *E. coli* and *K. pneumoniae* to colistin and tigecycline were similar to several reports from other countries.[6-8] However, clinical studies on efficacy of colistin and tigecycline for infections caused by ESBL-producing *E. coli* or *K. pneumoniae* are needed before they can be recommended in clinical practice. In addition, there are two different bases between colistin used in an in vitro susceptibility (colistin sulfate) and in clinical indications (sodium colistimethate). Even though sodium colistimethate, after intravenous administration, will dissociate into colistin sulfate, conclusion from most studies between correlation of in vitro susceptibility and clinical outcome cannot be drawn. Colistin and tigecycline may prove to be important antibiotics for treatment of ESBL-producing *E. coli* and *K. pneumoniae* infections in Thailand in the near future once more clinical information on colistin and tigecycline therapy of such infections becomes available.

CONCLUSION

Colistin and tigecycline are found to be active against ESBL-producing *E. coli* and *K. pneumoniae* isolated from Thai patients. Both antibiotics have a potential for being alternative therapy for infections caused by ESBL-producing *K. pneumoniae* and *E. coli* in the near future.

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Effectiveness of the Royal Thai Traditional Massage for Relief of Muscle Pain

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ABSTRACT

Objective: To determine the effectiveness of Thai traditional massage for muscle pain relief.
Methods: Adults with muscle pain in the neck and/or shoulder and/or back without organic causes that needed specific treatment who attended the Ayuraved Clinic during April to May 2004 received royal Thai traditional massage performed by experienced personnel. An effectiveness of royal Thai traditional massage was determined by pain relief assessed by visual analog scale
Results: There were 115 participants; 88 (76.5%) were females. The mean age of the participants was 47.9 years; 45.2% of them had shoulder pain, 40.9% back pain and 26.1% neck pain. The median duration of the symptom was 4 months. The mean pain scores of the participants before and after the royal Thai traditional massage were 7.0 and 3.2, respectively ($p<0.001$). The participants who had a pain score < 3 before and after the royal Thai traditional massage were 3.5% and 79.1%, respectively ($p<0.001$). Adverse effects of the massage were not observed.
Conclusion: Royal Thai traditional massage is probably effective in relieving muscle pain of the neck, shoulder and back.

Keywords: Royal Thai traditional massage; Muscle pain; Myalgia

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Muscle pain is a common complaint of individuals presented to general medical practitioners. The causes of muscle pain are usually related to occupation or bad posture, without any specific organic diseases. These patients usually receive non-steroidal anti-inflammatory agents (NSAIDs) for symptomatic relief. This mode of therapy may lead to side effects such as gastritis, peptic ulcer and upper gastro-intestinal bleeding. In addition, a long-term use of NSAIDs, especially COX-2 inhibitors, is costly. Thai traditional massage has been used to relieve muscle pain in Thai people for centuries. The maneuver may be an appropriate alternative therapy in modern medicine for relieving muscle pain. A meta-analysis of randomized controlled trials of massage therapy in various conditions revealed that its single dose had insignificant effect on immediate pain whereas multiple-doses were found effective[1]. The aforementioned meta-analysis was not applicable to our setting in Thailand for two reasons. First, the massage used in the included studies was not Thai traditional massage. Second, the study patients had a wide variety of pain, including labor, post-operative and cancer pain. Therefore, the present study was carried out to determine whether a single session of the royal Thai traditional massage (RTTM) was effective in reliving muscle pain.

MATERIALS AND METHODS

This was an experimental self-controlled study at the Ayurved Clinic, Siriraj Hospital and Ayurved School, Phaholyotin Campus, Bangkok, from April to May, 2004. The study was approved by the Ethics Committee on Human Research, Faculty of Medicine Siriraj Hospital, Mahidol University.

Participants

The participants were adults, older than 18 years, who had muscle pain either in the neck, shoulder or back and agreed to participate in the study. A participant would be excluded if s/he had an organic cause of muscle pain that needed specific treatment, skin lesion at the massagesite or had been receiving massage. Sample size estimation was based on a pilot study of 14 subjects with muscle pain. The mean pain score before RTTM was 7 and the mean pain score after RTTM was ≤ 3.

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TABLE 1. Study participants' characteristics

Total	115
Males	27 (23.5%)
Females	88 (76.5%)
Age (Years)	
Mean ± SD	47.9 ± 13.8
Body weight (Kg.)	
Mean ± SD	61.2 ± 10.9
Site of pain	
Shoulder	52 (45.2%)
Back	47 (40.9%)
Neck	30 (26.1%)
Others	9 (7.8%)
Duration of pain	
Mean	1.8 years
Median	4 months
Range	1day to 20 years
Duration of pain	
Acute pain (≤6 months)	66 (57.4%)
Mean	1 month
Median	14 days
Range	1 day to 6 months
Chronic pain (> 6 months)	49 (42.6%)
Median	12 months
Range	8 months to 20 years
History of prior treatment	
Yes	93 (80.9%)
Modern medicine	56 (60.2%)
Current treatment	
Yes	45 (39.1%)
Modern medicine	26 (57.8%)

Approximately, 80% of the subjects had a mean pain score after RTTM ≤3. The aim of the study was to detect any response (mean pain score after massage ≤3) of 80% ± 10% with 5% type I error (2-sided). Therefore, the appropriate sample size was 108.

Intervention

The massage maneuver used in this study was the Royal Thai Traditional Massage. The practitioners were experienced personnel at the Ayurved Clinic, Siriraj Hospital, and the Ayurved School, Phaholyotin Campus, Bangkok. They used only palms and fingers to compress the area where the clients complained of having pain for 40 to 45 minutes. There was no bone and joint manipulation during the massage procedures.

Main Outcome Measurement

Each participant was asked to provide demographic and relevant clinical data to the study team before receiving the massage. The severity of pain was also assessed by each participant using a visual analog scale of 0 to 10 where 0 was "no pain" and 10 was "unbearable pain". The pain severity was reassessed by each participant immediately after finishing the massage, using the identical scale.

TABLE 2. Effectiveness of the royal Thai traditional massage in 115 participants

	Pain score Mean ± SD (Range)
Before massage	7.0 ± 1.9 (3 - 10)
After massage	3.2 ± 1.2 (0 - 7)
	Participants with pain score ≤3
Before massage	4 / 115 (3.5%)
After massage	91 / 115 (79.1%)

Data Analysis

The data were entered into SPSS for Windows. The data were analyzed by descriptive statistics, paired student t-test and chi-square statistics where appropriate.

RESULTS

In total, there were 115 participants. The characteristics of the studied participants are shown in Table 1. Most participants were middle-aged females. The common sites of pain were shoulder(s), back and neck. The median duration of the symptom was 4 months. Fifty-seven percent of the subjects had muscle pain for less than 6 months. Most subjects had used modern medicine for the treatment of their muscle pain. The effectiveness of RTTM is shown in Table 2. The mean pain scores of the participants before and after RTTM were 7.0 and 3.2, respectively ($p<0.001$). Subjects who had a pain score of ≤3 before and after RTTM were 3.5% and 79.1%, respectively ($p<0.001$). The response rates in participants with shoulder, back and neck pain were 82.7%, 74.5% and 76.7%, respectively ($p=0.6$). The response rates in participants with acute pain and chronic pain were 83.3% and 73.5%, respectively ($p=0.3$). Adverse effects of the massage were not observed.

DISCUSSION

We found that RTTM was safe and effective in relieving muscle pain of the shoulder(s), back and neck. The differences in the effectiveness of RTTM among various sites of pain or between acute and chronic pain were not observed. The explanations for pain relief achieved by the massage included the gate control theory of pain reduction,[2] promotion of parasympathetic activity,[2] influence on body chemistry, e.g., an increase in serotonin levels,[3] a release of endorphins,[4] mechanical effects to promote circulation of blood and the lymph[5]. The magnitude of the effects of treatment in our study was quite obvious. A mean decrease in the pain score was 4 and the response rate (pain score of ≤3) after the massage (79.1%) was much higher than that before the massage (3.5%). Since our study is a self-controlled study and there was no concurrent control group, a portion of the responses observed after massage could be due to placebo effect or Hawthorne effect.[6] The Hawthorne effect is often mentioned as a possible explanation for positive results in intervention studies. It is used to cover many phenomena, not only unwittingly confounding variables under study by the study itself, but also behavioral change due to an awareness of being observed, active compliance with the supposed wishes of researchers because of special attention received, or positive response to the stimulus being introduced. Therefore, the effectiveness and efficiency of RTTM should be confirmed in a randomized controlled study.

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บทคัดย่อ

ประสิทธิผลของการนวดแผนไทยแบบราชสำนักในผู้ที่มีอาการปวดกล้ามเนื้อ

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วัตถุประสงค์: เพื่อทราบประสิทธิผลของการรักษาผู้ที่มีอาการปวดกล้ามเนื้อบริเวณไหล่ หลัง และคอด้วยการนวดแผนไทยแบบราชสำนัก

วิธีการ: ผู้ที่มีอาการปวดกล้ามเนื้อบริเวณไหล่ หลัง และคอจำนวน 115 คนได้รับการนวดแผนไทยแบบราชสำนักที่คลินิกอายุรเวท โรงพยาบาลศิริราช และโรงเรียนอายุรเวท พหลโยธิน ระหว่างเดือนเมษายนถึงพฤษภาคม พ.ศ. 2547 ประเมินประสิทธิผลของการรักษาโดยสอบถามความรุนแรงของอาการปวดก่อนและหลังการรักษาด้วยการนวด ด้วยคะแนนความรุนแรงของอาการปวดตั้งแต่ 0 (ไม่ปวด) จนถึง 10 (ปวดมากที่สุดจนทนไม่ได้)

ผลการศึกษา: ผู้ป่วยจำนวน 115 คน เป็นหญิง 88 คน (ร้อยละ 76.5) อายุเฉลี่ย 47.9 ปี ผู้ป่วยร้อยละ 45.2, 40.9 และ 26.1 มีอาการปวดไหล่ หลัง และคอตามลำดับ ระยะเวลาที่มีอาการเฉลี่ย 4 เดือน คะแนนความรุนแรงของอาการปวดโดยเฉลี่ยก่อนการนวดมีค่า 7 และคะแนนความรุนแรงของอาการปวดโดยเฉลี่ยภายหลังการนวดมีค่า 3 ($p<0.001$), ผู้ที่มีอาการปวดกล้ามเนื้อก่อนได้รับการนวดมีคะแนนความรุนแรงของอาการปวดเท่ากับหรือน้อยกว่า 3 (ปวดเล็กน้อย) เพียงร้อยละ 3.5 ในขณะที่คะแนนความรุนแรงของอาการปวดเท่ากับหรือน้อยกว่า 3 ภายหลังได้รับการนวดมีเพิ่มขึ้นเป็นร้อยละ 79.1 ($p<0.001$), ไม่พบผลข้างเคียงและภาวะแทรกซ้อนจากการนวด

สรุป: การนวดแผนไทยแบบราชสำนักน่าจะมีประสิทธิผลในการรักษาผู้ที่มีอาการปวดกล้ามเนื้อบริเวณไหล่ หลัง และคอ

Cost-Effectiveness Analysis of Chlorhexidine Gluconate Compared with Povidone-Iodine Solution for Catheter-Site Care in Siriraj Hospital, Thailand

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Background: *Catheter-related bloodstream infections (CRBSI) are an important cause of patient morbidity, mortality, and increased health care costs. Use of an antiseptic solution for skin disinfection at the catheter insertion site helps prevent catheter-related infections. In Thailand, povidone-iodine solution is the most commonly used agent for this purpose. However, the results of several studies including a meta-analysis indicated that the use of chlorhexidine gluconate is more effective than the use of povidone-iodine as an antiseptic for preventing CRBSI. This study evaluated the cost-effectiveness of chlorhexidine gluconate versus povidone-iodine for catheter-site care using the Siriraj Hospital perspective.*

Material and Method: *We used a decision analytic modeling for estimating the cost-effectiveness of antiseptic solutions. The CRBSI rate was obtained from the Center for Nosocomial Infection Control at Siriraj Hospital, while the efficacy of cholorhexidine compared to povidone-idone was based on a meta-analysis. The cost of managing infections was derived from the Thai Drug Related Group (DRG). A series of sensitivity analyses were performed. Since the time horizon of the analysis was less than 1 year, there was no need for discounting.*

Results: *We found that the use of chlorhexidine, rather than povidone iodine, for central catheter site care resulted in a 1.61 % decrease in the incidence of CRBSI, a 0.32 % decrease in the incidence of death, and savings of 304 baht per catheter used. For peripheral catheter site care, the results were similar, although the differences were smaller.*

Conclusion: *Use of chlorhexidine gluconate in place of the current standard solution for vascular catheter site care is a cost-effective method of improving patient safety in Siriraj Hospital.*

Keywords: *Cost effectiveness, Chlorhexidine gluconate, Povidone-iodine, Catheter-related bloodstream infections*

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Intravascular catheters are commonly used in caring for hospitalized patients but can lead to catheter-related bloodstream infection CRBSI[1], particularly the central-line catheter[2]. Bloodstream infections related to the use of catheters are an important cause of morbidity, mortality, and increased duration of hospitalization and health care cost[2-6]. In Thailand, these infections result in an increased duration of hospitalization of 15 days and the additional cost of antibiotics for one episode of CRBSI was approximately 10,753 baht[7]. In addition, CRBSI has been associated with mortality of 12% - 25%[8-13]. Nowadays, there are several procedures, which help to prevent these infections, such as performing catheter insertion at the subclavian site, maximizing sterile barriers and avoiding the use of antibiotic ointment[14-15]. Moreover, disinfecting the skin at the catheter insertion site with antiseptic

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solution helps to prevent these infections as well, and povidone iodine is the agent most commonly used in several countries including Thailand for this purpose[16-18].

A recent meta-analysis and cost-effectiveness study[19-20] found that the use of chlorhexidine gluconate in place of the current standard solution for vascular catheter site care is a simple and cost-effective method of improving patient safety in the hospital setting. In addition, guidelines of the Infectious Diseases Society of America, and the Centers for Disease Control and Prevention (CDC) recommend the use 2% of chlorhexidine gluconate as an antiseptic for the prevention of catheter-related infections[21-22]. Because of these recommendations, Siriraj Hospital intends to switch from povidone iodine to chlorhexidine gluconate for skin disinfection at the catheter insertion site. However, the cost of chlorhexidine is more than povidone iodine and information on the cost-effectiveness of this switch is needed prior to implementing this intervention. Therefore, we evaluated the cost-effectiveness of the use of both antiseptics for vascular catheter site care for endorsing the policy on using chlorhexidine instead of povidone iodine for skin disinfection at the catheter insertion site of the patients in Siriraj Hospital.

Material and Method

Decision analysis model

A decision analytic model was developed to evaluate the outcomes associated with the use of chlorhexidine gluconate versus povidone iodine solutions for catheter site care as shown in Fig. 1[23]. Either solution could be used at the time that an intravascular catheter was inserted and then every 48–72 hr to clean the insertion site. Patients with a catheter could have one of the following outcomes: 1) CRBSI, defined as isolation of the identical pathogen from a peripherally obtained blood culture and from a colonized catheter; 2) local catheter-related infection, defined as the presence of purulence or signs of inflammation (e.g., erythema, tenderness, and induration) within two cm of the catheter exit site[24]; 3) catheter colonization without bloodstream infection or local catheter-related infection; and 4) no colonization or infectious complications. Colonization of the catheter was defined as growth of microorganisms from a catheter segment using quantitative (>1000 cfu/mL)[25] or semiquanti-

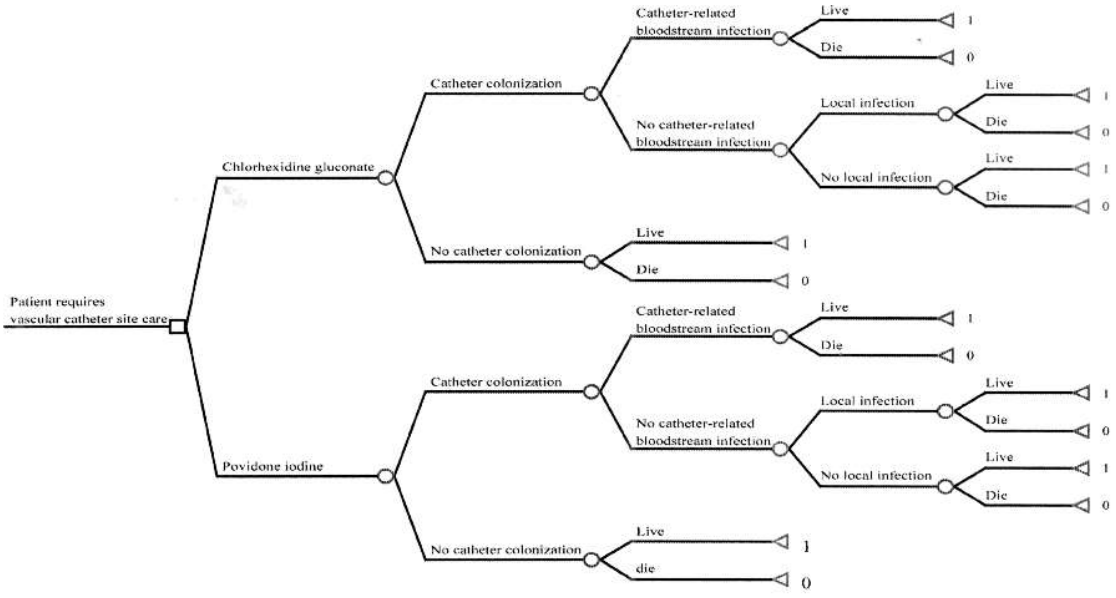

Fig. 1 Decision tree comparing the use of chlorhexidine gluconate with the use of povidone iodine for vascular catheter site care

tative (>15 cfu)[26] culture techniques. CRBSI was associated with a risk of dying. We assumed that local or systemic catheter-related infections did not occur without preceding catheter colonization. We performed the analysis using the hospital perspective; the time horizon was the period of hospitalization.

The hypothetical cohort in the decision analysis model included hospitalized patients requiring either a peripheral or central vascular catheter for short-term use (average duration, <10 days). Because the risk of CRBSI differs for central and peripheral venous catheters[24], we analyzed these cohorts separately. We considered "central vascular catheters" to include central venous, peripherally inserted central venous, pulmonary arterial, and hemodialysis catheters and introducer sheaths, whereas "peripheral vascular catheters" included peripheral venous and peripheral arterial catheters.

Likelihood of events

The probabilities of clinical events used in the decision analysis model are shown in Table 1. The probabilities of CRBSI with povidone iodine (the baseline risk) for central line were derived from Siriraj Hospital[7] and the study of Thongpiyapoom and colleagues[27]. The probabilities of catheter colonization were obtained from the literature[20]. The probability of CRBSI with chlorhexidine gluconate was determined by multiplying the probability of CRBSI when povidone iodine was used by the summary risk ratio of CRBSI when chlorhexidine gluconate was used, based on the results of the recently published meta-analysis[19].

The probability of catheter colonization when chlorhexidine gluconate was used was similarly derived (Table 1). All probabilities of clinical events for peripheral line were based on the study of Chaiyakunapruk and colleague[19]. These probabilities were similarly

Table 1. Probabilities of clinical events and comparison of the costs associated with chlorhexidine gluconate and povidone iodine solutions for vascular catheter site care

Probability of clinical event or cost	Base-case value (range)		Reference(s)
	Central line	Peripheral line	
Catheter-related bloodstream infection			
Probability when povidone iodine solution is used, %	3.16 (0.9–3.5)	0.92 (0.00-2.32)	[7,27]
Risk ratio for chlorhexidine gluconate solution*	0.49 (0.28-0.88)	0.49 (0.28-0.88)	[19]
Catheter colonization			
Probability when povidone iodine solution is used, %	18.09 (10.10–26.08)	7.91 (5.53-10.28)	[19]
Risk ratio for chlorhexidine gluconate solution*	0.49 (0.31-0.77)	0.49 (0.31-0.77)	[19]
Probability of death attributable to CRBSI, %	20.0 (4.40–25.0)	1.12 (0.47-2.11)	[8-13,27,29-33]
Probability of local infection if colonization occurs, %	20.0 (0.00–40.0)	20.0 (0.00-40.0)	[28]
Cost in Thailand in 2005, Baht			
Cost of 10% povidone iodine	22.39 (11.86-27.99)	3.73 (1.87-4.66)	[7]
Cost of 1% chlorhexidine gluconate	25.80 (13.67-30.96)	4.3 (2.15-5.16)	[7]
Cost associated with CRBSI per case	27,341.09 (18,907.60-53,127.34)	27,341.09 (18,907.60-53,127.34)	[34-35]
Cost of managing local infection per case	10,756.66 (8,770.56-18,694.45)	10,756.66 (8,770.56-18,694.45)	[34-35]

* To introduce a correlation between the probabilities of events in each treatment arm, the probability associated with the use of a chlorhexidine gluconate solution was calculated by multiplying the risk ratio by the probability associated with the use of povidone iodine solution. In the base case for the chlorhexidine arm, the probabilities that a catheter-related bloodstream infection would occur were 1.55% and 0.45% for central and peripheral lines, respectively, and the probabilities of catheter colonization were 8.86% and 3.88%

derived as central line (Table 1). We estimated that 20% of the colonized catheters were associated with local signs of infection[28]. All probabilities were calculated separately for central and peripheral catheter models. The probability of death attributable to CRBSI for a central venous catheter was calculated based on data from studies published elsewhere, which report excess mortality of 4%–25%. We used a 20 % attributable mortality for the base-case scenario and explored a range from 4% to 25% in sensitivity analyses because several studies in 2003-2004 found that the range of mortality rate was 22% to 25%[8-13,27,29-33] and a study in Thailand[27] reported a mortality rate of 20%. For patients with peripheral vascular catheters, we estimated an attributable mortality due to CRBSI of 1.12% (range, 0.47%-2.11%)[32].

Costs

We estimated the cost of antiseptic solution based on the total amount of solution used multiplied by the cost of the solution per ml. The total amount of solution used for the central line was estimated as 10 ml for clean skin at insertion on the first day, and 20 ml per day for 7.9 days while the amount of solution for the peripheral line was estimated as 5 ml per day for 5.6 day for clean skin at insertion (Table1).

Direct medical costs for patients with CRBSI were estimated based on data of the Thai Diagnosis Related Group (DRG) in year 2002-2003[34]. These medical costs were determined by multiplying the relative weight (RW) by cost per relative weight of these diseases. We used 16,000 Baht as cost per relative weight for university hospital in the year 2003 for calculation[34]. We estimated the relative weight for treatment of CRBSI as a septicemia adult, with moderate complication while the relative weight for treatment of a local infection was estimated as a minor skin disorder, with mild to moderate complication of Thai DRG[35]. These relative weights were 1.6547 and 0.6510, respectively[34]. For sensitivity analysis, we varied the cost of managing septicemia ranging from the treatment cost for septicemia without complication to those for patients with catastrophic complications. Likewise, we ranged the cost of managing local infection using the cost for minor skin disorder without complication and with catastrophic complication. All costs were adjusted to Thai baht in the year 2005.

Outcome assessment and sensitivity analyses

Outcomes calculated were the incidence of CRBSI, the incidence of death attributable to CRBSI, and the direct medical costs. The mean expected value for the differences in the incidence of death, the incidence of CRBSI, and the direct medical costs were determined. To assess uncertainty associated with the results, we conducted a series of one-way sensitivity analyses to evaluate the effect of varying individual parameters on the outcomes. To further test the robustness of the results, we set all parameters in the model to favor chlorhexidine gluconate in a best-case scenario and to favor povidone iodine in a worst-case scenario (Table 2).

Table 2. Results of decision analysis comparing chlorhexidine gluconate and povidone iodine solutions for vascular catheter site care in Thailand in 2005

Cathether type	Direct medical cost, Baht	Incidence of CRBSI, %	Incidence of death due to CRBSI, %
Central line			
Chlorhexidine gluconate solution	251.07	1.55	0.31
Povidone iodine solution	555.57	3.16	0.63
Difference	-304.49	-1.61	-0.32
Best-case scenario	-1740.48	-2.52	-0.63
Worst-case scenario	13.56	-0.11	-0.005
Peripheral line			
Chlorhexidine gluconate solution	92.09	0.45	0.005
Povidone iodine solution	192.23	0.92	0.01
Difference	-100.15	-0.47	-0.005
Best-case scenario	-632.35	-1.67	-0.47
Worst-case scenario	3.29	0.00	0.00

Main assumptions in the analysis

There were several main assumptions in our analysis: 1) the relative risk of death due to CRBSI was the same for central and peripheral vascular catheters; 2) the relative risks for CRBSI and catheter colonization for chlorhexidine gluconate, compared with povidone iodine, were the same in central and peripheral vascular catheters; 3) the cost of CRBSI was independent of survival outcome; 4) catheter colonization without local infection had no costs or adverse outcomes; 5) catheter-site erythrema without evidence of local infection did not affect survival outcome or cost; 6) the costs of medical care per case for all complications were the same in central and peripheral vascular catheters.

Results

Costs and outcomes

In the base-case analysis, use of chlorhexidine gluconate rather than povidone iodine for central line catheter site care led to an absolute decrease in the incidence of CRBSI of 16 cases/1000 catheters, and a decrease in the incidence of death attributable to CRBSI of 3 cases/ 1000 catheters (Table 2). In addition to these clinical benefits, use of chlorhexidine gluconate resulted in expected cost savings of 304.49 Baht for each catheter used, compared with the use of povidone iodine. Use of chlorhexidine gluconate rather than povidone iodine for peripheral line catheter site care led to an absolute decrease in the incidence of CRBSI of 5 cases/ 1000 catheters, and a decrease in the incidence of death attributable to CRBSI of 0.05 cases/1000 catheters. In addition to these clinical benefits, use of chlorhexidine gluconate resulted in expected cost savings of 13.56 Baht per catheter used, compared with the use of povidone iodine.

Sensitivity analyses

The use of chlorhexidine gluconate for central catheter site care resulted in cost-savings in most of the one-way sensitivity analyses as shown in Table 2. The cost of CRBSI was the most influential parameter in the model. Other influential parameters included the reduction in risk of CRBSI for chlorhexidine gluconate, the probability of death due to CRBSI, and the baseline risk of CRBSI. The use of chlorhexidine gluconate resulted in a dominant strategy in best-case but not in the worst-case scenario. In the worst case scenario, using chlorhexidine gluconate resulted in an increase of total medical costs of 18 Baht, while the incidence of CRBSI (decrease 0.11%) and death (decrease 0.005%) remained diminished. The threshold analysis indicated that the use of chlorhexidine gluconate would still provide cost-savings unless the cost of chlorhexidine gluconate exceeded 196.6 baht per 100 ml.

For peripheral vascular catheters, use of chlorhexidine gluconate for insertion site care was again found to be the best strategy in all one-way sensitivity analyses. The baseline risk of catheter-related bloodstream infection was the most influential parameter in the model. When the base-case scenario parameters were used in calculations, the use of chlorhexidine gluconate would save 100.15 Baht, and it still save cost as long as the cost of chlorhexidine gluconate was less than 373 Bath per 100 ml. In the worst-case scenario, use of chlor-hexidine gluconate resulted in an increase in direct medical costs of 3.29 Baht. However, it did not result in increases of the incidence of CRBSI and death due to CRBSI.

Discussion

To the best of our knowledge, this is the first study that has been performed to evaluate the cost-effectiveness of chorhexidine gluconate compared with povidone-iodine solution for catheter-site care in Thailand. Our analysis found that using of chlorhexidine gluconate for catheter site care reduces the incidence of CRBSI and decreases health care costs as shown by a prior study[20]. Our analysis was conducted from the perspective of the health care provider, rather than from that of society as a whole, as recommended by previous guidelines[39]. However, from a societal perspective, including indirect costs, such as time lost from work, the analysis would result in even greater cost savings for the chlorhexidine gluconate strategy.

Our analysis suggests that use of chlorhexidine gluconate for patients requiring short-term vascular catheterization, either with central or peripheral catheters, likely results in reductions of the incidence of CRBSI and health care costs. These results held true over a wide range of clinical and economic assumptions. This unusual combination of clinical benefits and decreased costs makes chlorhexidine gluconate attractive for routine use for both central and peripheral vascular catheter site skin care. Although, this study was conducted from the perspective of a university hospital, we believe that the use of chlorhexidine gluconate instead of povidone iodine could be generalized to general and other hospitals in Thailand, especially in university hospital where it may save more than our results because the actual cost of managing

septicemia and local infection might be higher than in other hospitals

The results from this study led to the production of 2% chlorhexidine gluconate in 70% alcohol by Siriraj Hospital Pharmacy Department and the implementation of using 2% chlorhexidine gluconate in 70% alcohol instead of 10% povidone iodine for catheter-site care of the patients hospitalized in three intensive care units (ICU) in Siriraj Hospital since January 2006. The preliminary results of this implementation from January to March in 70 patients revealed that the incidence of CRBSI was 3 per 1000 catheter days, which is less than the incidence of CRBSI observed in the same ICUs, 5 per 1000 catheter days, in the year 2005.

Conclusions

Our cost-effectiveness analysis shows that using chlorhexidine gluconate rather than povidone iodine for vascular catheter site disinfection in hospitalized patients requiring short-term vascular access is likely to result in decreased morbidity, mortality, and health care costs in the Thailand hospital setting. In addition, this simple method can be relatively easily implemented to improve patient safety, and, thus, should perhaps take priority in efforts to prevent vascular catheter–related infection.

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ต้นทุน-ประสิทธิผลของ คลอเฮ็กซิดีน กลูโคเนท เปรียบเทียบกับ โพวิโดน ไอโอดีน สำหรับทำลายเชื้อที่ผิวหนังบริเวณที่ใส่สายสวนหลอดเลือดที่โรงพยาบาลศิริราช

ราตรี แมนไธสง, ณธร ชัยญาคุณาพฤกษ์, วิษณุ ธรรมลิขิตกุล

ผู้ป่วยที่ได้รับการคาสายสวนในหลอดเลือดเสี่ยงต่อการติดเชื้อในกระแสเลือด น้ำยาทำลายเชื้อที่ผิวหนังบริเวณที่ใส่สายสวนหลอดเลือดของผู้ป่วยไทยที่ใช้กันทั่วไปคือโพวิโดน ไอโอดีน มีหลักฐานจากการวิจัยในต่างประเทศที่แสดงว่า คลอเฮ็กซิดีน กลูโคเนท ลดโอกาสติดเชื้อในกระแสเลือดได้มากกว่าโพวิโดน ไอโอดีนและคุ้มค่ากว่า การศึกษานี้จึงต้องการทราบต้นทุน-ประสิทธิผลของ คลอเฮ็กซิดีน กลูโคเนท เปรียบเทียบกับ โพวิโดน ไอโอดีน สำหรับทำลายเชื้อที่ผิวหนังบริเวณที่ใส่สายสวนหลอดเลือดที่โรงพยาบาลศิริราชโดยอาศัยข้อมูลจากโรงพยาบาลศิริราชและข้อมูลอื่นที่เกี่ยวข้องจากฐานข้อมูลต่าง ๆ ในประเทศไทยและต่างประเทศในกรณีที่ไม่มีข้อมูลในประเทศไทยซึ่งพบว่าคลอเฮ็กซิดีน กลูโคเนท มีต้นทุน-ประสิทธิผลดีกว่าโพวิโดน ไอโอดีนทั้งการคาสายสวนหลอดเลือดส่วนกลางและสายสวนหลอดเลือดส่วนปลาย ดังนั้นจึงควรใช้คลอเฮ็กซิดีน กลูโคเนทสำหรับทำลายเชื้อที่ผิวหนังบริเวณที่ใส่สายสวนหลอดเลือดแทนโพวิโดน ไอโอดีน

In Vitro Activity of Tigecycline against Clinical Isolates of Multidrug-Resistant *Acinetobacter baumannii* in Siriraj Hospital, Thailand

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In vitro activity of tigecycline against 148 strains of Acinetobacter baumannii isolated from different patients hospitalized at Siriraj Hospital, Bangkok, Thailand during 2002 to 2005 was conducted. These isolates were resistant to beta-lactams, aminoglycosides and fluoroquinolones. In vitro susceptibilities were determined by Kirby-Bauer disk diffusion, E-test and broth microdilution methods. The MIC_{50} and MIC_{90} values of tigecycline against A. baumannii determined by the broth microdilution method were 0.5 and 1 mg/L respectively. The MICs of tigecycline determined by E-test were 4-fold higher than those from the broth microdilution method. An inhibition zone of $\geq$13 mm was well correlated with a tigecycline MIC of $\leq$ 2 mg/L and had a sensitivity of 99% and a specificity of 100%. The study results indicated that 97.3% of MDR A. baumannii strains isolated from the patients hospitalized at Siriraj Hospital were susceptible to tigecycline. Tigecycline may prove to be an important antibiotic for treatment of multidrug-resistant A. baumannii infections in Thailand in the near future.

Keywords: *Tigecycline, Acinetobacter baumannii*

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Acinetobacter baumannii has emerged as a worldwide problem in causing infections in hospitalized patients[1-3]. *A. baumannii* is one of the most common causative pathogens in nosocomial pneumonia, bacteraemia, urinary tract infections, and skin and soft tissue infections, and the mortality associated with these infections is high. The incidence of infections caused by multidrug-resistant (MDR) pathogens, particularly *Acinetobacter baumannii* and *Pseudomonas aeruginosa,* in Thailand has dramatically increased[4]. A prospective study of 208 clinical isolates of *A. baumannii* recovered from patients in Siriraj Hospital from January to December 2002 revealed that 86 strains (41.3%) were isolated from infected patients and the remaining 58.7% were colonizers[5]. In this study, 57% of *A. baumannii* isolates were resistant to all antimicrobial agents available in Thailand including beta-lactams, aminoglycosides and fluoroquinolones, and the overall mortality rate of the patients infected with pandrug-resistant *A. baumannii* was 79%[5]. The study of 104 clinical isolates of *A. baumannii* from 100 hospitalized patients at Maharaj Nakorn Chiang Mai Hospital, Thailand also observed that 46% of the isolates were pandrug-resistant and the overall mortality was 52%[6]. The only available antibiotic effective for treating infections caused by *A. baumannii* resistant to all beta-lactams,aminoglycosides and fluoroquinolones is colistin[7], hence a search for new agents effective against MDR *A. baumannii* is needed.

Tigecycline is a glycylcycline antibiotic that shows promising activity against a wide range of organisms including multi-drug resistant gram positive cocci and gram negative bacilli[8]. The objective of the study was to determine in vitro activity of tigecycline against clinical isolates of MDR *A. baumannii* in

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Siriraj Hospital, Thailand.

Material and Method

One hundred and forty-eight strains of *A. baumannii* isolated from different infected patients hospitalized at Siriraj Hospital, Bangkok, Thailand during 2002 to 2005 were included. These isolates were resistant to all beta-lactams, aminoglycosides, and fluoroquinolones. In vitro susceptibilities of MDR *A. baumannii* to tigecycline were determined by Kirby-Bauer disk diffusion, E-test, and broth microdilution methods. Paper disc containing tigecycline 15 μg per disk (Becton Dickinson, USA), E-test strips (AB BIODISK, Sweden) and gram negative MicroScan MIC panels (Dade Behring Inc., USA) were provided by Wyeth Research. The methodology for susceptibility testing was done by direct colony suspension according to guidelines suggested by CLSI [9]. Quality control was performed by testing the susceptibility of *E. coli* ATCC 25922 as recommended by Wyeth Research.

Results

A distribution of inhibition zone diameters of tigecycline against *A. baumannii* is shown in Table 1. The MIC_{50} and MIC_{90} values of tigecycline against *A. baumannii* determined by E-test were 2 and 4 mg/L respectively. The MIC_{50} and MIC_{90} values of tigecycline against *A. baumannii* determined by the broth microdilution method were 0.5 and 1 mg/L respectively. There was a significant correlation between inhibition zone diameters and MICs determined by the broth microdilution method ($p<0.001$, $r = -0.8$), and between MICs of tigecycline determined by E-test and MICs determined by the broth microdilution method ($p<0.001$, $r=0.9$). The accuracy of the inhibition zone diameter of ≥13 mm in predicting susceptibility of *A.baumannii* to tigecycline is shown in Table 2. If the MIC of tigecycline at ≤2 mg/L was considered as a breakpoint for tigecycline susceptibility, the inhibition zone diameter of ≥13 mm had a sensitivity of 99% and a specificity of 100% in predicting the susceptibility of *A.baumannii* to tigecycline and 97.3% of MDR *A.baumannii* were susceptible to tigecycline.

Discussion

The previous studies on the in vitro activity of tigecycline against *A.baumannii* by the broth microdilution method revealed that the MIC_{50} and the MIC_{90} for tigecycline were 0.5-1 and 2 mg/L respectively, and more than 90% of these isolates had MICs ≤2 mg/L and were considered susceptible to tigecycline[10, 11]. Carbapenem-resistant *A. baumannii* isolates were still susceptible to tigecycline with comparable MICs to the aforementioned values[12, 13]. However, in vitro activity of tigecycline against *A. baumannii* by the agar dilution method observed that the MIC_{50} and the MIC_{90} for tigecycline against *A.baumannii* were 8 and 8 mg/L respectively[14]. These findings implied that the different methods of in vitro susceptibility testing of tigecycline against *A. baumannii* might yield different results. The breakpoints for the inhibition zone diameter and MIC of tigecycline against *A.baumannii* are not available. The US FDA-approved breakpoints of tigecycline against Enterobacteriaceae to be used by the local laboratory were inhibition zone diameter ≥19 mm and a MIC≤2 mg/L[9]. The previous studies on in vitro activity of tigecycline against *A. baumannii* used such a MIC breakpoint[10-14]. It is not known if the testing methods used in general microbiology laboratories, disk diffusion and E-tests, are accurate in predicting the MICs of tigecycline against *A. baumannii*.

The MIC_{50} and the MIC_{90} of tigecycline against *A. baumannii* determined by the broth microdilution method observed in our study were similar to those reported in the literature[10-13] and 97.3% of MDR *A. baumannii* isolated from the hospitalized patients at Siriraj Hospital were susceptible to tigecycline. However, our findings indicated that there was a discrepancy in the susceptibility results of tigecycline against *A. baumannii* for the different

Table 1. Distribution of the inhibition zone diameter of tigecycline against 148 isolates of MDR *A. baumannii*

Inhibition Zone Diameter (mm)	Number of Isolates (%)
11	1 (0.7)
12	4 (2.7)
13	4 (2.7)
15	8 (5.4)
16	11 (7.4)
17	20 (13.5)
18	34 (23.0)
19	21 (14.2)
20	17 (11.5)
21	16 (10.8)
22	8 (5.4)
23	3 (2.0)
26	1 (0.7)

Table 2. Accuracy of the inhibition zone diameter of ≥13 mm in predicting the susceptibility of *A.baumannii* to tigecycline

	MIC (MicroScan) ≤ 2 mg/L	MIC (MicroScan) > 2 mg/L
Inhibition Zone Diameter ≥13 mm	143	0
Inhibition Zone Diameter <13 mm	1	4

methods of testing. The MICs determined by E-test were usually 4-fold higher than those determined by the broth microdilution method and E-test might not be an accurate method for in vitro susceptibility testing of tigecycline against *A. baumannii*. Moreover, our study also observed that the US FDA-approved breakpoint of tigecycline against Enterobacteriaceae, to be used by the local laboratory, of an inhibition zone diameter ≥19 mm, was not applicable to tigecycline against *A. baumannii*. The breakpoint for an inhibition zone diameter ≥13 mm was more accurate in predicting susceptibility of *A.baumannii* to tigecycline with a sensitivity of 99% and a specificity of 100%. Our findings of good in vitro activity of tigecycline against MDR *A. baumannii* warrant a clinical study to prove its efficacy and to determine whether such proposed breakpoint and testing methods are valid.

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การทดสอบฤทธิ์ของ tigecycline ต่อ Acinetobacter baumannii ที่ดื้อยาต้านจุลชีพหลายขนานที่แยกได้จากผู้ป่วยในโรงพยาบาลศิริราช

สุรภี เทียนกริม, ชาญวิทย์ ตรีพุทธรัตน์, วิษณุ ธรรมลิขิตกุล

ผู้วิจัยได้ทดสอบฤทธิ์ของ tigecycline ต่อ Acinetobacter baumannii ที่ดื้อยาต้านจุลชีพหลายขนานที่แยกได้จากผู้ป่วยของโรงพยาบาลศิริราชระหว่าง พ.ศ. 2545 ถึง พ.ศ. 2548 จำนวน 148 สายพันธุ์ด้วยวิธี disk diffusion และวัด minimum inhibitory concentration (MIC) ด้วย E-test และ broth microdilution พบว่า 1) ค่า MIC_{50} และ MIC_{90} ของ tigecycline ต่อ A. baumannii ที่ดื้อยาต้านจุลชีพหลายขนานที่ทดสอบด้วยวิธี broth microdilution เท่ากับ 0.5 มก./ล. และ 1 มก./ล. ตามลำดับ 2) ค่า MIC_{50} และ MIC_{90} ของ tigecycline ต่อ A. baumannii ที่ดื้อยาต้านจุลชีพหลายขนานที่ทดสอบด้วยวิธี E-test มีค่ามากกว่าค่า MIC ที่ได้จากวิธี broth microdilution ประมาณ 4 เท่า 3) เส้นผ่านศูนย์กลางของ inhibition zone ของ tigecycline $\geq$13 มม.เป็นค่าที่เหมาะสม สำหรับพิจารณาความไวของ A. baumannii ต่อ tigecycline หากใช้เกณฑ์ MIC$\leq$2 มก./ล. ในการระบุว่า A. baumannii ไวต่อ tigecycline โดยมีความไวร้อยละ 99 และความจำเพาะร้อยละ 100, 4) Acinetobacter baumannii ที่ดื้อยาต้านจุลชีพหลายขนานร้อยละ 97.3 ไวต่อ tigecycline ดังนั้น tigecycline น่าจะมีประโยชน์ในการรักษาโรคติดเชื้อ Acinetobacter baumannii ที่ดื้อยาต้านจุลชีพหลายขนานในประเทศไทย

Epidemiology of *Staphylococcus aureus* Infections and the prevalence of Infection Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus* in Hospitalized Patients at Siriraj Hospital

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Background: *The CA-MRSA infections have emerged in many parts of the world over the past decade. To our knowledge, the prevalence of CA-MRSA infections in Thai patients is unknown.*
Objective: *To determine an epidemiology of Staphylococcus aureus (S. aureus) infections in hospitalized patients in Siriraj Hospital and the prevalence of infections caused by community-acquired methicillin-resistant S. aureus (CA-MRSA).*
Material and Method: *The study was carried out at Siriraj Hospital from January to May 2005. The eligible patients were hospitalized patients whom S. aureus were isolated from their clinical specimens submitted to Department of Microbiology. S. aureus isolate was classified into infection or colonization. S. aureus infections were further classified into methicillin-resistant S. aureus (MRSA) or methicillin-sensitive S. aureus (MSSA) infections, and hospital-acquired (HA) or community-acquired (CA) infections. CA-MRSA infection is defined as infection caused by MRSA isolated from the patient within 72-hour of hospitalization and has no features of HA MRSA infections.*
Results: *There were 669 S. aureus isolates from 448 patients. Two hundred and sixty two patients (58.5%) were MSSA whereas 186 (41.5%) were MRSA infections. CA-MRSA was found in three isolates (0.9% of total MRSA) from two patients.*
Conclusion: *The prevalence of CA-MRSA infections in hospitalized patients in Siriraj Hospital was uncommon and these patients could probably be HA MRSA infections.*

Keywords: *Prevalence, Staphylococcus aureus, Methicillin-resistant, Community-acquired, Cross sectional study, Cohort study,Thailand*

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The penicillinase-stable beta-lactams such as cephalosporins, methicillin and nafcillin became available in the late 1950s[1]. Ironically, the first methicillin-resistant *Staphylococcus aureus* (MRSA) was described at about the same time[2, 3]. The prevalence of MRSA progressively increased thereafter[4, 5]. A survey of the National Nosocomial infections Surveillance System reported that the hospital prevalence MRSA increased from 2.1% in 1975 to 35% in 1991[6]. It is currently as high as 70% in certain centers, but great geographic variations exists. The data from the SENTRY Antimicrobial Surveillance Program during 1997 and 1999 revealed that the MRSA prevalence varied as follows: Western Pacific region, 46%; United States, 34.2%; Latin America, 34.9%; Europe, 26.3%; Canada, 5.7%. Moreover, a variation of MRSA varied greatly among countries within a region. In European centers, the percentages of MRSA varied from less than 2% in the Netherlands to 54.4% in Portugal. In Western

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Pacific countries, MRSA ranged from 23.6% (Australia) to more than 70% in Japan and Hong Kong[7]. In Thailand, from a survey of 32 hospitals (1998-2001), the MRSA ranged from 24-36%. MRSA has traditionally been considered a healthcare-associated pathogen in patients with established risk factors[8-10]. MRSA has become a major cause of hospital-acquired (HA) infections over the past decade.[11]

MRSA is an emerging community pathogen. It was first reported in the early 1990s among closed communities of Aborigines in Western Australia[12]. Fatal community-acquired MRSA (CA-MRSA) infections were reported in USA in 1999[13]. Outbreaks of CA-MRSA infections in healthy children, adolescents, and adults were described worldwide[13-25]. CA-MRSA infections tend to occur in younger persons than do hospital-acquired MRSA (HA-MRSA) infections. They often cause sporadic cases of skin and soft tissue infections but cases of necrotizing pneumonia were also reported[26]. CA-MRSA was found to be associated with virulent strains producing Panton-Valentine leucocidin (PVL) and a variety of other exotoxins[27]. It showed resistance to methicillin, which is encoded by the *mecA* gene, mostly found on the type IV staphylococcal cassette chromosome (SCC)[16]. The spread of CA-MRSA strains was not limited to the community and might also be seen in the hospital setting[28]. A recent meta-analysis reported a pooled MRSA colonization prevalence rate of 1.3% in 10 studies testing a total of 8,350 persons in the community, whereas the respective prevalence rate was 0.2% in studies excluding persons exposed to healthcare services[29]. In this meta-analysis, it was also found that MRSA colonization was more frequent among persons in the community from whom cultures were obtained in the healthcare setting compared with those screened outside the healthcare setting[29]. Studies from some states in USA showed an increase in the number of CA-MRSA clinical isolates during the past decade[15, 21, 23], whilst this number remained stable in other states[14]. Factors that might facilitate the spread of CA-MRSA within hospitals included admission of unrecognized carriers from the community, prolonged asymptomatic colonization, inadequate laboratory identification and report, and inadequate adherence to hand hygiene and contact precaution measures.

The CA-MRSA infections have emerged in several parts of the world over the past decade. An emergence of CA-MRSA was reported from Taiwan with relatively high incidence (25-75%)[30, 31] whereas a true CA-MRSA infection was very rare in Singapore[32,33]. To our knowledge, a prevalence of CA-MRSA infections in Thailand is unknown. This study determines an epidemiology of *S. aureus* infections in hospitalized patients in Siriraj Hospital and the prevalence of infections caused by CA-MRSA.

Material and Method

Subjects and Study Procedures

The study was approved by the Ethics Committee on Human Research of Faculty of Medicine Siriraj Hospital. This cross sectional study was carried out from January 1 to May 31, 2005 at Siriraj Hospital, a 2,000-bed tertiary care university hospital in Bangkok, Thailand. The eligible patients were hospitalized patients whom *S. aureus* were isolated from their clinical specimens submitted to Department of Microbiology. *S. aureus* isolates were classified into infection or colonization. *S. aureus* infections were further classified into MRSA or MSSA; and nosocomial, HA or community-acquired (CA) infections. CA is defined as infection caused by MRSA isolated from the patient within 72-hour of hospitalization and has no features of HA MRSA infections, history of hospitalization, surgery, dialysis, or residence in a long-term care facilities within one year of the MRSA culture date or a permanent indwelling catheter or percutaneous medical device (e.g. tracheostomy tube, gastrostomy tube, or urethral catheter) present at the time of cultures, a known positive culture for MRSA prior to the study period or who had been discharged from an acute care hospital within 10 days. Nosocomial infection is the infection occur-

Table 1. Classification of cases with *S. aureus* isolated from their clinical specimens

Classification of cases		No. of cases (%)
MSSA*		262 (100)
	Community-acquired	68 (26.0)
	Nosocomial	117 (44.7)
	Healthcare-associated	77 (29.4)
MRSA**		186 (100)
	Community-acquired	2 (1.1)
	Nosocomial	154 (82.8)
	Healthcare-associated	30 (16.1)
Total		448 (100)

* Methicillin-Sensitive *Staphylococcus aureus*
** Methicillin-Resistant *Staphylococcus aureus*

ring in the patient who has been hospitalized for more than 72-hour or who had been discharged from an acute care hospital within 10 days. The isolates that are neither CA nor nosocomial-acquired therefore, belong to the "healthcare-associated" setting and are classified as HA infections. The medical records of the eligible subjects were reviewed. The relevant information regarding clinical data and microbiological data of each

Table 2. Demographics of 446 cases with *S. aureus* isolated from their clinical specimens

Demographic data		Type of *S. aureus*		p
		MSSA (N=262)	MRSA (N=184)	
Age	Mean (yr.)	44.9	55.3	<0.001
	Standard Deviation(yr.)	27.3	24.0	
	Minimum (d.)	1	7	
	Maximum (yr.)	93.0	95.0	
Gender	Male	129 (49.2%)	99 (53.8%)	0.39
Nationality	Thai	251 (95.8%)	179 (97.3%)	0.57
	Others	11 (4.2%)	5 (2.7%)	
Location of the residence	Central	218 (83.2%)	152 (82.6%)	0.72
	Northeast	17 (6.5%)	12 (6.5%)	
	South	11 (4.2%)	8 (4.3%)	
	North	7 (2.7%)	2 (1.1%)	
	Others	9 (3.5%)	10 (5.5%)	
Occupation	Nursing home	1 (0.4%)	0	NA*
	Government employee	15 (5.7%)	12 (6.5%)	
	Farmer	7 (2.7%)	6 (3.3%)	
	Student	28 (10.7%)	10 (5.4%)	
	Employee	46 (17.6%)	21 (11.4%)	
	Free	13 (5.0%)	16 (8.7%)	
	None	150 (57.2%)	117 (63.5%)	
	Others	2 (0.8%)	2 (1.1%)	
Living arrangement	Private	257 (98.1%)	181 (98.4%)	1.0
	Nursing home	5 (1.9%)	3 (1.6%)	

* Not available

Table 3. Clinical data of 446 patients

Clinical data		Type of *S. aureus*		p
		MSSA (N=262)	MRSA (N=184)	
Ward	Medicine	105 (40.1%)	118 (64.1%)	<0.001
	Surgery	87 (33.3%)	48 (26.1%)	
	OB&GYN	7 (2.7%)	1 (0.5%)	
	Pediatrics	38 (14.5%)	10 (5.4%)	
	EENT	16 (6.1%)	6 (3.2%)	
	Others	9 (3.5%)	1 (0.5%)	
History of healthcare-associated conditions		158 (60.3%)	145 (78.8%)	<0.001
Catheter or device		42 (16.0%)	40 (21.7%)	0.16
Prior presence of MRSA		2 (0.8%)	14 (7.6%)	<0.001
Hospitalization > 72 h*		108 (41.2%)	142 (77.2%)	<0.001
Prior hospitalization		150 (57.3%)	145 (79.2%)	<0.001

*Hospitalization more than 72 hours or who had been discharged from an acute care hospital within 10 days

Table 4. Underlying medical conditions of 446 patients

Underlying diseases / conditions		Type of *S. aureus* MSSA(N=262)	MRSA (N=184)	p
Pulmonary diseases	COPD	4 (1.5%)	14 (7.6%)	0.06
	Bronchial asthma	4 (1.5%)	1 (0.5%)	
	ILD	2 (0.8%)	0	
	Prior pneumonia	1 (0.4%)	0	
	Others	14 (5.3%)	16 (8.7%)	
Neoplastic diseases		57 (21.8%)	45 (24.5%)	0.58
Liver diseases	Cirrhosis	11 (4.2%)	17 (9.2%)	0.07
	Chronic active hepatitis	1 (0.4%)	1 (0.5%)	
	Others	4 (1.5%)	3 (1.6%)	
Heart diseases	CHF	5 (1.9%)	4 (2.2%)	0.13
	CAD	24 (9.2%)	25 (13.6%)	
	Valve replacement	1 (0.4%)	2 (1.1%)	
	Congenital heart diseases	7 (2.7%)	3 (1.6%)	
	Others	8 (3.1%)	9 (4.9%)	
Neurologic diseases	Stroke	22 (8.4%)	19 (10.3%)	0.01
	TIA	1 (0.4%)	0	
	Cerebral palsy	1 (0.4%)	0	
	Bed-ridden status	8 (3.1%)	14 (7.6%)	
	Others	14 (5.3%)	18 (9.8%)	
Renal diseases	Azotemia	7 (2.7%)	14 (7.6%)	0.13
	Chronic kidney disease	15 (5.7%)	10 (5.4%)	
	HD via catheter	15 (5.7%)	9 (4.9%)	
	HD via AVF	9 (3.4%)	7 (3.8%)	
	Peritoneal dialysis	2 (0.8%)	3 (1.6%)	
	Others	2 (0.8%)	4 (2.2%)	
Diabetes mellitus		55 (21.0%)	53 (28.8%)	0.07
High alcohol intake		16 (6.1%)	16 (8.7%)	0.20
Smoking		25 (9.5%)	19 (10.3%)	0.60
Neutropenia		5 (1.9%)	13 (7.1%)	0.01
Splenectomy		1 (0.4%)	1 (0.5%)	1.0
Metabolic disorder		2 (0.8%)	4 (2.2%)	0.24
Recent operation		15 (5.7%)	15 (8.2%)	0.52
Implanted devices	Pacemaker	0	1 (0.5%)	0.03
	Others	13 (5.0%)	19 (10.3%)	
Recent corticosteroid		8 (3.1%)	17 (9.2%)	0.02
Immuno-suppressives		21 (8.0%)	22 (12.0%)	0.28
Others		111 (42.4%)	83 (45.1%)	0.63

subject were retrieved and entered into the structured case record forms.

Data Analysis

Data were expressed as percentage and mean ± SD for nominal and continuous variables, respectively. Analyses were performed using SPSS 13.0 (SPSS Inc, Chicago, Illinois). Nominal variables were compared by Chi-square test or Fisher's Exact test and continuous variables were compared by two-tailed unpaired t-test or Mann-Whitney U test as appropriate. The statistically significant factors were confirmed by the multivariate analysis using a forward likelihood logistic regression model. A p- value < 0.05 was considered significant.

Results

From January 1 to May 31, 2005, 669 *S. aureus* isolates from 448 patients were enrolled. Two hundred and sixty two patients (58.5%) were MSSA whereas

186 (41.5%) were MRSA. CA-MRSA was found in three isolates (0.9% of total MRSA) from two patients as shown in Table 1.

Description of CA-MRSA patients

Case 1

A 46-year old Thai male presented with a three-month history of fever, malaise, weight loss, and hematemesis. He came to community hospital as an outpatient three times within three weeks. His underlying medical conditions included liver cirrhosis, hepatitis C infection, heavy alcoholic drinking, and smoking. He was admitted to general medical ward with dyspnea. He received endotracheal tube, nasogastric tube, and urethral catheter. Chest radiography revealed bilateral reticulonodular with patchy infiltration. MRSA was isolated from the sputum on the second day of hospitalization. Sputum examination was positive for acid fast bacilli. He was empirically treated with ceftriaxone, amikacin, and ciprofloxacin. He also received anti-tuberculosis drugs. He had clinical improvement and left the hospital six days after admission.

Case 2

A 52-year old female presented with chronic ulcer of her left leg. She had wound dressing at a community clinic everyday for two weeks and she took penicillin V 2 grams per day for two weeks. She was admitted to surgery ward for wound debridement and she was found to have diabetes mellitus. MRSA was isolated from pus and tissue on the first and second day of admission. She received ceftriaxone and clindamycin, wound debridement and diabetic control. She was improved and left the hospital seven days after admission.

MSSA and MRSA patients

The demographics of the patients who had

Table 5. Previous medical history of antibiotics use in 446 patients

Antibiotic	Type of *S. aureus*		
	MSSA (N=262)	MRSA (N=184)	p
Prior antibiotics use	74 (28.2%)	135 (73.4%)	<0.001
Cephalosporins	25 (9.5%)	82 (44.6%)	<0.001
Penicillins	31 (11.8%)	40 (21.7%)	0.07
Aminoglycosides	6 (2.3%)	23 (12.5%)	<0.001
Quinolones	6 (2.3%)	28 (15.2%)	<0.001
Macrolides	2 (0.8%)	3 (1.6%)	0.65
Tetracyclines	0	1 (0.5%)	0.42
Carbapenems	3 (1.1%)	27 (14.7%)	<0.001
Glycopeptides	3 (1.1%)	13 (7.1%)	0.002
Miscellaneous	13 (5.0%)	56 (30.4%)	<0.001

Table 6. Predisposing factors of 446 patients

Risk factors	Type of *S. aureus*		
	MSSA (N=262)	MRSA (N=184)	p
Arterial catheter	11 (4.2%)	6 (3.3%)	0.80
Central venous catheter	16 (6.1%)	30 (16.3%)	<0.001
Double lumen catheter	15 (5.7%)	15 (8.2%)	0.41
Endotracheal tube	62 (23.7%)	75 (40.8%)	<0.001
Tracheostomy	11 (4.2%)	25 (13.6%)	<0.001
Urethral catheter	88 (33.6%)	104 (56.5%)	<0.001
Nasogastric tube	70 (26.7%)	104 (56.5%)	<0.001
Surgical intervention	127 (48.5%)	98 (53.3%)	0.37
Others	33 (12.6%)	32 (17.5%)	0.20

Table 7. Category of infections of 446 patients

Type of infection		Type of *S. aureus* MSSA (N=262)	MRSA (N=184)	p
Infective endocarditis	Native valve	1 (0.4%)	0	1.0
Soft tissue infection	Abscess	50 (19.1%)	10 (5.4%)	<0.001
	Cellulitis	6 (2.3%)	0	
	Necrotizing fasciitis	3 (1.1%)	1 (0.5%)	
	Others	19 (7.3%)	9 (4.9%)	
Orthopedic infection	COM*	7 (2.7%)	2 (1.1%)	0.80
	AOM**	2 (0.8%)	0	
	Surgical site infect	3 (1.1%)	4 (2.2%)	
	Others	2 (0.8%)	2 (1.1%)	
Respiratory tract infection	CAP***	22 (8.4%)	10 (5.4%)	0.03
	HAP****	20 (7.6%)	39 (21.2%)	
	Lung abscess	0	1 (0.5%)	
	Empyema	2 (0.8%)	2 (1.1%)	
	Others	6 (2.3%)	0	
Urinary tract infection		5 (1.9%)	3 (1.6%)	1.0
Primary bacteremia		23 (8.8%)	9 (4.9%)	0.17
Other infections		23 (8.8%)	22 (12.0%)	0.35
Colonization		75 (28.6%)	74 (40.2%)	0.01

* Chronic osteomyelitis
** Acute osteomyelitis
*** Community-acquired pneumonia
**** Hospital-acquired pneumonia

Table 8. Source of clinical specimens containing *S. aureus*

Specimen	Type of *S. aureus* MSSA (N=262)	MRSA (N=184)
Blood	36 (13.7%)	17 (9.2%)
Joint fluid	5 (1.9%)	2 (1.1%)
Pleural fluid	2 (0.8%)	1 (0.5%)
Peritoneal fluid	0	1 (0.5%)
Pus	99 (37.8%)	39 (21.2%)
Sputum	82 (31.3%)	93 (50.5%)
Bronchial fluid	1 (0.4%)	2 (1.1%)
Urine	13 (5.0%)	7 (3.8%)
Others	24 (9.2%)	22 (12.0%)

MRSA infections were not significantly different from those who had MSSA except MRSA patients were older: 55.3 years vs 44.9 years as shown in Table 2. The variables that were significantly different between MRSA and MSSA patients are shown in Table 3 to 12. They were: 1) clinical data on type of wards (p<0.001), history of healthcare-associated factors (p<0.001), prior MRSA culture (p<0.001), hospitalization more than 72 hours or who had been discharged from an acute care hospital within 10 days (p<0.001), prior hospitalization (p<0.001); 2) underlying medical conditions on neurologic diseases (p=0.01), neutropenia (p=0.01), implanted devices (p=0.03), and recent corticosteroids (p=0.02); 3) previous history of prior antibiotic use (p<0.001), cephalosporin use (p<0.001), aminoglycoside use (p<0.001), quinolone use (p<0.001), carbapenem use (p<0.001), glycopeptide use (p=0.002), miscellaneous antibiotics (p<0.001); 4) predisposing factors on central venous catheter, endotracheal tube, tracheostomy, urethral catheter, and nasogastric tube (p<0.001); 5) category of infection on soft tissue infection (p<0.001), respiratory tract infection (p=0.03), and colonization (p=0.01); 6) clinical evaluation of infections on duration of fever (p<0.001), duration of admission (p<0.001), admission to ICU (p=0.04), and duration from hospitalization until death (p=0.03); 7) initial antibiotic regimen on number of initial antibiotics regimen (p<0.001), fourth generation cephalosporin use (p=0.003), penicillins use (p<0.001), quinolones use (p=0.001), carbapenems use (p<0.001), glycopeptides use (p<0.001), and miscellaneous use (p=0.006); 8) outcome on early outcome (p<0.001), complication (p=0.002), overall outcome (p<0.001), and cause of overall death (p<0.001). Six

Table 9. Clinical outcomes of infections

Duration (day)	Type of *S. aureus*		p
	MSSA (N=262)	MRSA (N=184)	
Duration of fever	113 (43.1%)	121 (65.8%)	<0.001
Mean	4.39	6.56	
Standard Deviation	9.26	7.24	
Range	1-90	1-35	
Duration of symptom	230 (87.8%)	161 (87.5%)	0.96
Mean	28.34	9.99	
Standard Deviation	242.72	15.10	
Range	1-3650	1-120	
Duration of hospitalization	262 (58.5%)	184 (41.1%)	<0.001
Mean	28.62	47.82	
Standard Deviation	36.01	52.53	
Range	1-213	1-348	
Admission to ICU	45 (17.2%)	65 (35.3%)	0.04
Mean	13	28	
Standard Deviation	20	45	
Range	1-101	1-348	
Duration from admission to death	50 (19.1%)	77 (41.8%)	0.03
Mean	18.21	18.60	
Standard Deviation	33.20	17.38	
Range	1-211	1-72	

variables associated with mortality were surgical wards, respiratory infections, use of endotracheal tube, category of *S. aureus*, indwelling urethral catheter, and having implanted devices as shown in Table 13.

Discussion

The recent report on *S. aureus* concluded that CA-MRSA in Thailand was extremely rare[34]. There was a report from a hospital in Thailand describing a child who had CA-MRSA infection[35]. He presented with submandibular lymphadenitis and MRSA was isolated from pus collected from incision and drainage of the lymph node on admission day. The molecular type of this isolate of MRSA was unknown. Our data suggests that the prevalence of CA-MRSA infections in hospitalized patients in Siriraj Hospital was uncommon, and both patients who met criteria of CA-MRSA infections could probably be HA MRSA infections since both of them had history of hospital visits just prior to their hospitalizations. Moreover, the antibiotic susceptibility profiles of MRSA isolated from both patients were multi-drug resistant. The universal definition of CA-MRSA has not been established and acceptable. In fact, the previous review revealed that at least eight different definitions have been used to classify MRSA infections as community acquired[29]: 1) isolation of MRSA within 24 h of admission, 2) isolation of MRSA within 24 h of admission, with other exclusions, 3) presence of MRSA at or within 48 h of admission, 4) isolation of MRSA within 48 h of admission, with other exclusions, 5) isolation of MRSA within 48–72 h of admission, 6) isolation of MRSA within 72 h of admission, 7) isolation of MRSA within 72 h of admission, with other exclusions, 8) isolation of MRSA from a patient from a community clinic or facility. An observation of a very low prevalence of CA-MRSA might not be valid since we did not include out-patients who could have minor *S. aureus* infections and these patients might have CA-MRSA infections. A recent outpatient visit within 12 months was found to be the risk factors for MRSA acquisition[29]. Other risk factors were recent hospitalization, recent nursing home admission, chronic illness, injection drug use, and close contact with a person with risk factor(s) for MRSA acquisition.

Table 10. Initial antibiotic regimens of 446 patients

Initial antibiotic regimen		Type of *S. aureus* MSSA (N=262)	MRSA (N=184)	p
Number of initial antibiotic regimens	Monotherapy	147 (56.1%)	76 (41.3%)	<0.001
	Duotherapy	72 (27.5%)	77 (41.8%)	
	Triple therapy	9 (3.4%)	11 (6.0%)	
	> 3 antibiotics	1 (0.4%)	4 (2.2%)	
	No treatment	33 (12.6%)	16 (8.7%)	
First generation cephalosporin		17 (6.5%)	4 (2.2%)	0.06
Second generation cephalosporins		2 (0.8%)	0	0.51
Third generation cephalosporins		90 (34.4%)	62 (33.7%)	0.97
Fourth generation cephalosporins		7 (2.7%)	18 (9.8%)	0.003
Penicillins		84 (32.1%)	27 (14.7%)	<0.001
Aminoglycosides		29 (11.1%)	17 (9.2%)	0.64
Quinolones		14 (5.3%)	27 (14.7%)	0.001
Macrolides		5 (1.9%)	2 (1.1%)	0.70
Tetracyclines		2 (0.8%)	1 (0.5%)	1.0
Carbapenems		7 (2.7%)	38 (20.7%)	<0.001
Glycopeptides		21 (8.0%)	37(20.1%)	<0.001
Miscellaneous		43 (16.4%)	51 (27.7%)	0.006
Susceptible to initial antibiotics	Susceptible to all antibiotics	66 (25.2%)	18 (9.8%)	NA*
	Susceptible to some antibiotics	19 (7.3%)	2 (1.1%)	
	Resistant to all antibiotics	3 (1.1%)	36 (19.6%)	
	Unknown	174 (66.4%)	128 (69.6%)	

* Not available

Table 11. Outcomes of 446 patients

Outcome		Type of *S. aureus* MSSA (N=262)	MRSA (N=184)	p
Early outcome *	Improve	202 (77.1%)	92 (50.0%)	<0.001
	Failure	51 (19.5%)	78 (42.4%)	
	Death	9 (3.4%0	14 (7.6%)	
Cause of early death**	Death	9 (3.4%)	14 (7.5%)	0.21
	Uncontrolled *S. aureus* infection	4 (1.5%)	10 (5.4%)	
	Other	5 (1.9%)	3 (1.6%)	
	Unknown	0	1 (0.5%)	
Complication	Uncontrolled *S. aureus* infection	9 (3.4%)	21 (11.4%)	0.002
	Unrelated to *S. aureus* infection	72 (27.6%)	77 (41.8%)	
Overall outcome	Improve	202 (77.1%)	101 (54.9%)	<0.001
	Failure	46 (17.6%)	75 (40.8%)	
	Undetermine	14 (5.3%)	8 (4.3%)	
Cause of death	Death	50 (19.1%)	77 (41.8%)	<0.001
	Uncontrolled *S. aureus* infection	8 (3.1%)	19 (10.3%)	
	Other	42 (16.0%)	57 (31.0%)	
	Unknown	0	1 (0.5%)	

* Outcome within 3-5 days of treatment
** Death within 72 hours

Table 12. Susceptibility of *S. aureus* to initial antibiotic regimen of 448 cases

Antibiotic	Type of *S. aureus*								
	MSSA (N=262)			MRSA (N=184)			CA-MRSA (N=2)		
	S*	R**	I***	S*	R**	I***	S*	R**	I***
Ampi/amoxy	18.2%	81.8%	0	0	100%	0	0	0	0
Cefazolin	100%	0	0	0	100%	0	0	0	0
Chloramphenicol	96.6%	3.4%	0	92.3%	6.7%	0	0	100%	0
Cotrimoxazole	99.4%	0.6%	0	13.1%	85.9%	1.0%	0	100%	0
Erythromycin	91.4%	7.4%	1.2%	1.1%	98.9%	0	0	100%	0
Gentamicin(10mcg)	98.2%	1.8%	0	8.1%	91.9%	0	0	100%	0
Methicillin	100%	0	0	0	100%	0	0	100%	0
Amoxy/clavulanate	100%	0	0	0	100%	0	0	0	0
Ampi/sulbactam	100%	0	0	0	100%	0	0	0	0
Cefoxitin	100%	0	0	0	100%	0	0	0	0
Ceftazidime	100%	0	0	0	100%	0	0	0	0
Ceftriaxone	100%	0	0	0	100%	0	0	0	0
Netilmycin	100%	0	0	0	100%	0	0	0	0
Ofloxacin	100%	0	0	0	100%	0	0	0	0
Tetracycline	59.7%	40.3%	0	12.9%	87.1%	0	0	100%	0
Ciprofloxacin	80.6%	5.0%	14.4%	1.0%	99.0%	0	0	100%	0
Clindamycin	94.8%	4.5%	0.7%	8.6%	91.4%	0	0	100%	0
Fosfomycin	100%	0	0	87.7%	9.2%	3.1%	100%	0	0
Fusidic acid	100%	0	0	91.8%	6.1%	2.1%	100%	0	0
Vancomycin	100%	0	0	100%	0	0	100%	0	0
Teicoplanin	100%	0	0	100%	0	0	100%	0	0
Linezolid	100%	0	0	100%	0	0	100%	0	0
Rifampicin	100%	0	0	46.2%	53.8%	0	50%	50%	0

* Sensitive, ** Resistant, *** Intermediate

Table 13. Variables associated with mortality by logistic regression

Variable	p	Adjusted OR	95% CI for OR
Ward			
Medicine	0.001	3.4	1.7-6.8
Others	0.40	0.7	0.3-1.7
Respiratory infection	<0.001	3.2	1.8-5.7
Retain endotracheal tube	0.001	2.8	1.5-5.2
Category of *S. aureus*	0.004	2.1	1.3-3.6
Urethral catheter	0.01	2.2	1.2-4.0
Implanted devices	0.21	4.6	1.3-16.9

MRSA colonization can persist for months to years[9,36], and one study reported an estimated half-life of MRSA colonization of 40 months among patients known to be colonized with MRSA who were admitted to a university hospital[36]. The majority of colonized patients remained completely asymptomatic. Therefore, acquisition of MRSA, whether it occurs in the hospital or in the community, frequently goes unrecognized unless clinical infection develops. Given the duration for which colonization with MRSA can persist, an infection may develop in a setting different from that in which the organism was initially acquired. Thus, in the absence of more epidemiological data, such as the results of surveillance cultures documenting time of acquisition, the true site of acquisition of MRSA is rarely known with certainty. The commonly used term "CA-MRSA" implies that it is known that the organism was acquired in the community. It appears, however, that this term is often used to refer to the detection of colonization or infection in the community, rather than to actual acquisition of MRSA in the community. The term "community-onset" MRSA (CO-MRSA), which simply describes the patient's location at the time of identification of MRSA, would be more technically correct than the currently used "CA-MRSA", which implies that the site of MRSA acquisition is known[29]. When a patient with nosocomially acquired MRSA spreads the

organism to multiple members of the patient's household or community, this should not be called "community acquisition".

In this study, we found that the patients who had MRSA isolated from their clinical specimens were significantly associated with health care-associated risk factors, prior antibiotic use, and predisposing factors when compared with those with MSSA. These observations were similar to the previous study[8-10]. MRSA patients were also associated with longer duration of fever, longer duration of hospitalization[9, 37], more frequent admission to ICU[9, 37] and higher mortality than MSSA patients. Most MRSA isolates were susceptible to several antimicrobial classes (including chloramphenicol, fosfomycin, and fusidic acid) and treatment of MRSA infections may not routinely require glycopeptides. CA-MRSA poses important challenges for public health officials. Surveillance data are needed to determine the geographic distribution of cases and to monitor the emergence of this important problem in the community. In addition, local information is needed to direct clinical decisions about treatment. However, public health resources for establishing new surveillance systems are limited. Creative approaches to surveillance, such as tracking infections from sentinel hospitals in areas that serve high-risk communities or performing periodic cross-sectional surveys, should be considered.

Conclusion

The prevalence of CA-MRSA infections in hospitalized patients in Siriraj Hospital was uncommon. These patients could probably be health care-associated MRSA infections. All CA-MRSA should be confirmed by molecular analysis.

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ระบาดวิทยาของการติดเชื้อ *Staphylococcus aureus* และความชุกของ *community-acquired methicillin-resistant Staphylococcus aureus* ในผู้ป่วยที่รับไว้รักษาในโรงพยาบาลศิริราช

ศรีเพชรรัตน์ เมฆวิวัฒน์วงศ์, สมพร ศรีเฟื่องฟุ้ง, กุลกัญญา โชคไพบูลย์กิจ, ดรินทร์ โล่ห์ศิริวัฒน์, วิษณุ ธรรมลิขิตกุล

ผู้วิจัยศึกษาผู้ป่วยที่รับไว้รักษาในโรงพยาบาลศิริราชที่แยกเชื้อ Staphylococcus aureus จากสิ่งส่งตรวจของผู้ป่วยระหว่างเดือนมกราคมถึงพฤษภาคม พ.ศ. 2548 เพื่อทราบระบาดวิทยาของการติดเชื้อ S. aureus และความชุกของการติดเชื้อ S. aureus ที่เกิดในชุมชน พบว่าจากจำนวนเชื้อ 669 สายพันธุ์ที่แยกได้จากผู้ป่วย 448 คน เชื้อจากผู้ป่วย 262 คน (ร้อยละ 58.5) เป็นเชื้อ MSSA ส่วนเชื้อจากผู้ป่วย 186 คน (ร้อยละ 41.5) เป็นเชื้อ MRSA ความชุกของการติดเชื้อ S. aureus ที่เกิดในชุมชนพบเพียง 3 สายพันธุ์จากผู้ป่วย 2 คนเท่านั้น ผู้ป่วยที่ติดเชื้อ MRSA มีลักษณะที่แตกต่างจากผู้ป่วย MRSA คือ 1) ผู้ติดเชื้อ MRSA มีอายุมากกว่า 2) ผู้ติดเชื้อ MRSA เป็นผู้ป่วย อายุรกรรม เคยรับการรักษาที่สถานพยาบาล เคยมีการติดเชื้อ MRSA เคยอยู่โรงพยาบาลมาก่อน และอยู่ในโรงพยาบาลนานกว่า 72 ชั่วโมง 3) ผู้ติดเชื้อ MRSA มีโรคปอดเรื้อรัง โรคระบบประสาท เม็ดเลือดขาวในเลือดต่ำ มีอุปกรณ์การแพทย์อยู่ในร่างกาย ได้รับคอร์ติโคสเตียรอยด์ และยาต้านจุลชีพ 4) ผู้ติดเชื้อ MRSA มีอุปกรณ์การแพทย์สอดใส่เข้าสู่ร่างกาย 5) ผู้ติดเชื้อ MRSA มีปอดอักเสบ การติดเชื้อที่ผิวหนังและเนื้อเยื่อใต้ผิวหนัง และ colonization 6) ผู้ติดเชื้อ MRSA มีเชื้อ S. aureus ในเสมหะ 7) ผู้ติดเชื้อ MRSA มีไข้นานกว่าอยู่โรงพยาบาลนานกว่า และอยู่ในหออภิบาลนานกว่า 8) ผู้ติดเชื้อ MRSA ได้รับการรักษาด้วยยาต้านจุลชีพหลายขนาน เชื้อ MRSA ทุกสายพันธุ์ไวต่อ vancomycin, teicoplanin และ linezolid ผู้ติดเชื้อ MRSA มีอัตราความล้มเหลวต่อการรักษา และอัตราการตายสูงกว่าผู้ติดเชื้อ MSSA ปัจจัยที่สัมพันธ์กับอัตราตายจากการติดเชื้อ S. aureus คือ ผู้ป่วยอายุรกรรม ปอดอักเสบ มีการติดเชื้อ MRSA และได้รับอุปกรณ์การแพทย์สอดใส่เข้าสู่ร่างกาย