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-

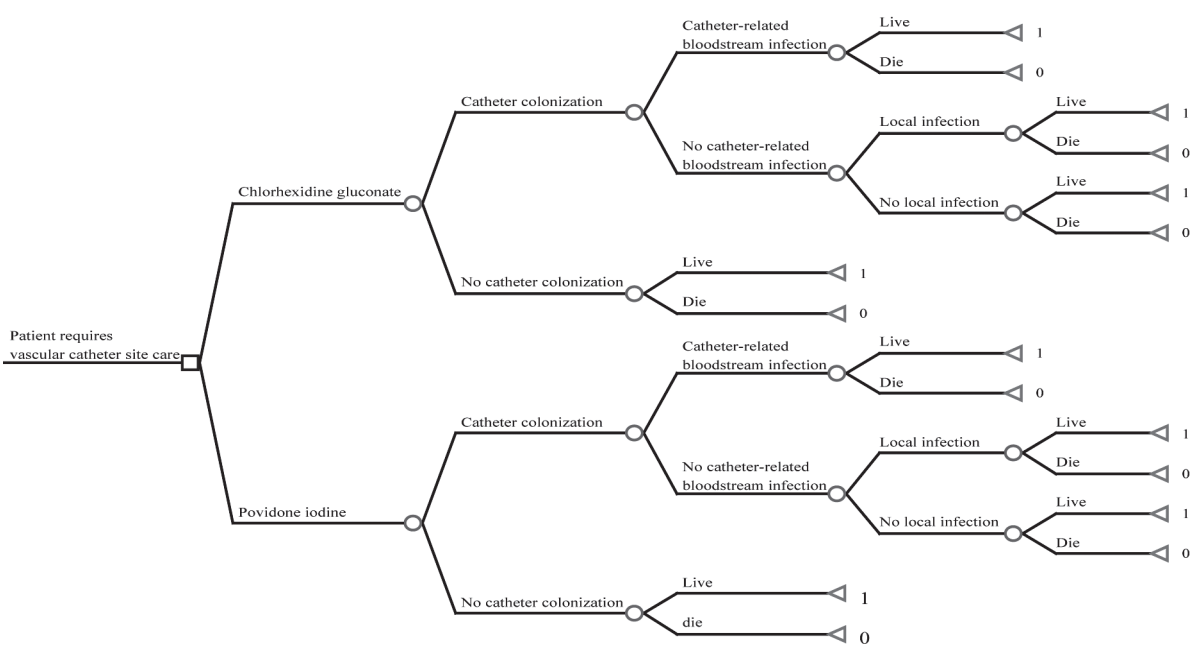

Fig. 1 Decision tree comparing the use of chlorhexidine gluconate with the use of povidone iodine for vascular catheter site care

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