The Efficacy of 2% Chlorhexidine Gluconate in 70% Alcohol Compared with 10% Povidone Iodine in Reducing Blood Culture Contamination in Pediatric Patients

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Background: *Blood culture is the gold standard for diagnosis of septicemia. However, false-positive blood cultures are associated with increased health care costs due to unnecessary treatment.*
Objective: *To evaluate the efficacy of 2% chlorhexidine gluconate in 70% alcohol compared with 10% povidone iodine in reducing blood culture contamination in pediatric patients.*
Material and Method: *This is a prospective study of pediatric patients who were admitted at a tertiary-care hospital. Pediatric patients who needed percutaneous blood cultures were recruited from two general pediatric wards and the pediatric intensive care unit. The authors used 10% povidone iodine as an antiseptic in odd months and 2% chlorhexidine gluconate in 70% alcohol as an antiseptic in even months in obtaining the blood culture samples.*
Results: *There were 1,269 blood culture specimens taken from 821 patients. 654 specimens used 10% povidone iodine as an antiseptic and 619 specimens used 2% chlorhexidine gluconate in 70% alcohol as an antiseptic. The 10% povidone iodine group and the 2% chlorhexidine gluconate in 70% alcohol group had the risk of blood culture contamination of 3.21% (95%CI: 2.00%-4.87%) and 2.28% (95% CI: 1.25%-3.79%) respectively. The risk difference of blood culture contamination was 0.93% (95% confidence interval: 0.86-2.72%) with p = 0.31. The most common contamination organism was Coagulase negative staphylococci (68.57%). No adverse skin reactions were observed in both antiseptic solutions groups.*
Conclusion: *Use of 2% chlorhexidine gluconate in 70% alcohol as an antiseptic seems to reduce the risk of blood culture contamination compared to use of 10% povidone iodine. In addition, neither of the antiseptic solutions resulted in adverse skin reactions.*

Keywords: *Blood culture, Contamination, Chlorhexidine gluconate, Povidone iodine*

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Blood culture is one of the most important laboratory tests for the diagnosis of septicemia. A false positive result from contamination leads to inappropriate antibiotic use, longer hospitalization and an increase in healthcare costs. Souvenir et al reported that almost half of the patients with a false-positive result were treated with antibiotics, often with vancomycin[1]. Lower contamination rates improve diagnoses, and help to avoid the inappropriate use of antibiotics, thus decreasing antibiotic-resistant organisms and minimizing risks for patients[2].

Blood culture contamination rates vary from 2% to more than 6%[3]. The American Society of Microbiologists target rate for contamination has been 2 to 3%[4,5]. The most common source of contamination is often from skin flora. Skin preparation plays an important role in reducing blood culture contamination. There are numerous antiseptic preparations that have been tested and shown to be effective in minimizing contamination. Among the most widely used are povidone iodine, isopropyl alcohol, tincture of iodine, and chlorhexidine.

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The blood culture contamination in pediatric patients at Thammasat University Hospital between 2002-2008 were reported. It was observed that 77% of positive blood culture samples were contaminated which generally used 10% povidone iodine as antiseptic[6]. The most common contamination organism was Coagulase negative staphylococci which is a common skin flora. Many studies have been performed to determine the best skin antiseptic to use for blood culture. Chlorhexidine gluconate is another antiseptic agent that may be used to reduce skin flora prior to the performing of procedures. However, few studies on the efficacy of antiseptic solutions have been conducted in pediatric patients. The purpose of this study was to assess the blood culture contamination rates when comparing 2% chlorhexidine gluconate in 70% alcohol and 10% povidone iodine in pediatric patients at a tertiary-care hospital.

Material and Method

Study population and design

This is a prospective study of pediatric patients between 0-15 years of age (excluding preterm newborn) who were admitted in three pediatric wards: general pediatric ward aged <5 years, general pediatric ward aged >5 years, and pediatric intensive care unit at a tertiary-care hospital. Patients who needed percutaneous blood cultures were eligible for enrollment and were classified into two groups according to antiseptic used: 10% povidone iodine in odd months and 2% chlorhexidine gluconate in 70% alcohol in even months. The sample size of 1,200 blood cultures (600 specimens per group) was needed to have 80% power to detect a contamination risk difference between groups of 3.7% with the significant level of 0.05[7]. Blood cultures were taken by ward nurses using standard techniques[8]. Adverse skin reactions were observed for 2 days.

The blood cultures were subsequently incubated at 37°C for 5 days and analyzed using the BACTEC (Versatrek, PCL Company). Isolated organisms and their antimicrobial susceptibilities were determined using standard microbiologic techniques.

Blood culture isolates were classified as a true pathogen or a contaminant by clinical observations combined with laboratory data. A blood culture was classified as contaminant if common skin flora was isolated from one of the blood culture samples without isolation of the same organism from another potential infection site (for example, intravenous catheter), or a common skin flora was isolated in a patient with incompatible clinical observations and improved without specific treatment for that organism. The common skin flora include coagulase-negative staphylococci, *Bacillus* species other than *Bacillus anthracis*, *Corynebacterium* species, *Propionibacterium acnes* and *Micrococcus* species.

The protocol was approved by the institutional review board of the Faculty of Medicine, Thammasat University.

Statistical analysis

The primary end point was the occurrence of blood culture contamination. All data were analyzed using the SPSS 11.5 software program. The categorical characteristics of both groups were described and compared using the Chi-square test. The continuous characteristics of both groups were described and compared by using an independent t-test, which showed a statistically significant level of 0.05. The risk of blood contamination of each group was presented with a 95% confidence interval.

Results

During June 2011-October 2012, 821 pediatric patients were enrolled. 1,269 blood culture specimens were obtained from these patients. 654 specimens used 10% povidone iodine as an antiseptic and 619 specimens used 2% chlorhexidine gluconate in 70% alcohol as an antiseptic. Referring to demographic features, there were no statistical differences in sex, age and admitted ward (Table 1).

Of these 1,269 cultures, 35 cultures (2.76%) grew an organism that was interpreted as being contaminated; 52 cultures (4.10%) were truly positive blood culture. The blood culture contamination rate was highest in children <1 month of age (4.21%) followed by 6-15 years (2.7%), 2 months-1 year (2.33%) and 2-5 years (2.02%) (Table 2).

The 10% povidone iodine group and the 2% chlorhexidine gluconate in 70% alcohol group had the risk of blood culture contamination of 3.21% (95%CI: 2.00-4.87%) and 2.28% (95%CI: 1.25-3.79%) respectively (Table 3). The risk difference of blood culture contamination was 0.93% (95% confidence interval: 0.86-2.72%) with $p = 0.31$.

The common contaminated bacteria in the blood culture were Coagulase negative staphylococci (68.57%), *Bacillus spp.* (17.14%), *Micrococcus spp.* (8.57%) and *Corynebacterium spp.* (5.71%). Comparing contaminated organisms between the 10% povidone iodine and 2% chlorhexidine gluconate in 70% alcohol

Table 1. Basic demographic features of patients comparing 10% povidone iodine group with 2% chlorhexidine gluconate in 70% alcohol group

Basic demographic features	Number (%)		*p*-value
	10% povidone iodine (n = 654)	2% chlorhexidine in 70% alcohol (n = 615)	
Sex			0.53
Boys	356 (54.43)	43 (55.77)	
Girls	298 (45.57)	272 (44.23)	
Age			0.96
≤1 month	158 (24.16)	151 (24.55)	
2 months-1 year	264 (40.37)	251 (40.81)	
2-5 years	154 (23.55)	143 (23.25)	
6-15 years	78 (11.93)	70 (11.38)	
Admitted ward			0.91
General pediatric ward aged ≤5 years	522 (79.82)	486 (79.02)	
General pediatric ward aged >5 years	24 (3.67)	25 (4.07)	
Pediatric intensive care unit (PICU)	108 (16.51)	104 (16.91)	

Table 2. The blood culture contamination rate based on age group

Age	Total of blood cultures	Contaminated blood cultures	
		Number	%
≤1 month	309	13	4.21
2 months-1 year	515	12	2.33
2-5 years	297	6	2.02
6-15 years	148	4	2.70

Table 3. Blood culture contamination rate in 10% povidone iodine and 2% chlorhexidine gluconate in 70% alcohol

Result of blood cultures	10% povidone iodine (n = 654)		2% chlorhexidine in 70% alcohol (n = 615)		*p*-value
	Number	Incidence risk (95% CI)	Number	Incidence risk (95% CI)	
Positive	41	6.27% (4.54-8.41%)	46	7.48% (5.53-9.85%)	0.23
Contaminated	21	3.21% (2.00-4.87%)	14	2.28% (1.25-3.79%)	0.20

groups, there were statistically significant differences in *Bacillus spp*. contamination rates ($p = 0.03$). The chlorhexidine gluconate in 70% alcohol group had a higher contamination rate of *Bacillus spp.* than the 10% povidone iodine group. The 10% povidone iodine group had a higher contamination rate of Coagulase negative staphylococci and *Corynebacterium spp.* than the 2% chlorhexidine gluconate in 70% alcohol group, but no statistically significant differences (Table 4).

In the case of the true pathogen in the blood culture, gram-negative organisms were more commonly identified (30/52, 57.69%) than gram-positive organisms (16/52, 30.77%). *Salmonella spp.* (10/52, 19.23%) were the most common isolates, followed by *Staphylococcus aureus* (6/52, 11.54%) and *Pseudomonas aeruginosa* (5/52, 9.62%) (Table 5). Two blood culture samples which positive for Coagulase negative staphylococci were classified as true pathogens according to isolate the same organism from the central intravenous catheter. No adverse skin reactions were noted with the two

Table 4. Distribution of contaminating organisms comparing 10% povidone iodine group and 2% chlorhexidine gluconate in 70% alcohol group

Microorganisms	Number (%)		*p*-value
	10% povidone iodine (n = 21)	2% chlorhexidine in 70% alcohol (n = 14)	
Coagulase negative staphylococci	17 (80.95)	7 (50)	0.05
Bacillus spp.	1 (4.76)	5 (35.71)	0.03
Micrococcus spp.	1 (4.76)	2 (14.29)	0.35
Corynebacterium spp.	2 (9.52)	0 (0)	0.35

Table 5. Distribution of true pathogens comparing 10% povidone iodine group and 2% chlorhexidine gluconate in 70% alcohol group

Microorganisms	Number (%)		
	10% povidone iodine (n = 20)	2% chlorhexidine in 70% alcohol (n = 32)	Total (n = 52)
All Gram-positive:	8 (40)	8 (25)	16 (30.77)
Staphylococcus aureus	1 (5)	5 (15.63)	6 (11.54)
Streptococcus group D not enterococci	2 (10)	1 (3.13)	3 (5.77)
Streptococcus pneumoniae	1 (5)	1 (3.13)	2 (3.85)
Streptococcus viridans	2 (10)	0	2 (3.85)
Coagulase negative staphylococci	1 (5)	1 (3.13)	2 (3.85)
Enterococcus species	1 (5)	0	1 (1.92)
All Gram-negative:	12 (60)	18 (56.25)	30 (57.69)
Salmonella spp.	4 (20)	6 (18.75)	10 (19.23)
Pseudomonas aeruginosa	1 (5)	4 (12.5)	5 (9.62)
Nonfermentative Gram negative bacilli	4 (20)	1 (3.13)	5 (9.62)
Burkholderia cepacia	0	3 (9.38)	3 (5.77)
Escherichia coli	2 (10)	0	2 (3.85)
Klebseilla pneumoniae	0	2 (6.25)	2 (3.85)
Haemophilus influenzae	1 (5)	0	1 (1.92)
Enterobacter cloacae	0	1 (3.13)	1 (1.92)
Pseudomonas stutzeri	0	1 (3.13)	1 (1.92)
All candida:	0	6 (18.75)	6 (11.54)
Candida albicans	0	3 (9.38)	3 (5.77)
Candida tropicalis	0	2 (6.25)	2 (3.85)
Candida krusei	0	1 (3.13)	1 (1.92)

types of antiseptic.

Discussion

To reduce contamination, antiseptics such as 2% chlorhexidine gluconate in 70% alcohol and 10% povidone iodine are generally used to clean the patients' skin before taking blood. Chlorhexidine gluconate is an alternative skin antiseptic, which has been reported as being superior to povidone iodine and comparable to iodine tincture for skin preparation prior to blood cultures[7,9,10].

Marlowe L et al reported blood culture, contamination rates after skin antisepsis with 3% chlorhexidine gluconate versus 10% povidone iodine in a pediatric, emergency department decreased after implementation of chlorhexidine[11]. Garland JS et al compared the efficacy of 10% povidone iodine with 0.5% chlorhexidine gluconate in 70% isopropyl alcohol

for the prevention of peripheral intravenous catheter colonization in neonates. They concluded that 0.5% chlorhexidine gluconate in 70% isopropyl alcohol appeared to be more efficacious than 10% povidone iodine for the prevention of peripheral intravenous catheter colonization in neonates. Catheter colonization occurred in 9.3% (38 of 408) povidone iodine group and 4.7% (20 of 418, $p = 0.01$) in chlorhexidine gluconate group[12].

The authors were comparing 2% chlorhexidine gluconate in 70% alcohol with 10% povidone iodine in reducing blood culture contamination in pediatric patients. The contamination rate when using 2% chlorhexidine gluconate in 70% alcohol was lower than using 10% povidone iodine, but these results were not statistically significant. In present study, the overall contamination rates were relatively low (2.76%) in comparison with previous studies (ranging from 2% to more than 6%)[3], probably due to different study designs and the definitions of contaminants and true pathogens. In addition, samples from emergency room and neonatal intensive care units (NICU) were excluded from the present study[13].

The present study has several limitations. First, a true, blinded comparison of these two skin-preparation techniques would not be possible because these antiseptics have distinctly different colors and application procedure. Second, contaminated blood culture is a particular challenge for infants and children. Mostly single blood cultures were collected as opposed to twice in adults. Two samples normally make discrimination between true bacteremia and contamination, particularly when Coagulase negative Staphylococci are grown in culture. Lastly, we did not collect the data of venipuncture nurses who take blood culture. Different experience and technical skills may have influenced the results.

The most common contaminated bacteria in the blood culture was Coagulase negative staphylococci, typically representing 70% to 80% of all contaminated blood cultures[1,2,14,15]. Comparing contaminated organisms between the 10% povidone iodine and 2% chlorhexidine gluconate in 70% alcohol, the chlorhexidine gluconate in 70% alcohol group had a higher contamination rate of *Bacillus spp.* than the 10% povidone iodine group in one ward only during the month of June. A variety of factors that can cause Bacillus spp. pseudobacteremia has been reported in the literature. These include an infected environment and contaminated biomedical equipment, such as gloves, alcohol swabs, ethyl alcohol, contaminated blood culture media, and contaminated automated blood culture analyzers[16-21]. However, in the present study, the isolates were identified in only one ward so that the possibility that the contamination originated in biomedical equipment is very likely.

Toxicity or adverse reactions due to chlorhexidine is infrequent[22-24]. In the present study, the authors did not find any adverse skin reactions with the chlorhexidine. However, the present study excluded preterm newborn that may frequently have irritation from skin antiseptic.

Conclusion

Use of 2% chlorhexidine gluconate in 70% alcohol as an antiseptic seems to reduce the risk of blood culture contamination compared to use of 10% povidone iodine. In addition, neither of the antiseptic solutions resulted in adverse skin reactions.

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Potential conflict of interest

None.

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ประสิทธิภาพของ 2% chlorhexidine gluconate in 70% alcohol กับ 10% povidone iodine ในการลดการปนเปื้อนของเชื้อที่ผิวหนังจากการเพาะเชื้อในกระแสเลือดในผู้ป่วยเด็ก

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ภูมิหลัง: การเพาะเชื้อในกระแสเลือดเป็นวิธีมาตรฐานที่ใช้ในการวินิจฉัยการติดเชื้อในกระแสเลือด แต่พบว่าผลการเพาะเชื้อในกระแสเลือดขึ้น เชื้อแบคทีเรียปนเปื้อนได้บ่อย

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิภาพของ 2% chlorhexidine gluconate in 70% alcohol กับ 10% povidone iodine ในการลดการปนเปื้อนของเชื้อจากการเพาะเชื้อในกระแสเลือดในผู้ป่วยเด็ก

วัสดุและวิธีการ: เป็นการศึกษาทางคลินิกชนิดไปข้างหน้าในผู้ป่วยเด็ก ตั้งแต่แรกเกิดถึงอายุ 15 ปี ที่เข้ารับการรักษาในหอผู้ป่วยกุมารเวชกรรม โรงพยาบาลระดับตติยภูมิที่สงสัยติดเชื้อในกระแสเลือดและแพทย์สั่งเพาะเชื้อในกระแสเลือด โดยแบ่งเป็น 2 กลุ่ม ตามเดือนได้แก่ กลุ่มที่ 1 อาสาสมัครที่ได้รับการเจาะเลือดเพื่อเพาะเชื้อในกระแสเลือดในเดือนคี่ ใช้น้ำยา 10% povidone iodine ทำความสะอาดผิวหนังก่อนเจาะเลือดเพื่อเพาะเชื้อในกระแสเลือด กลุ่มที่ 2 อาสาสมัครที่ได้รับการเจาะเลือดเพื่อเพาะเชื้อในกระแสเลือดในเดือนคู่ใช้น้ำยา 2% chlorhexidine gluconate in 70% alcohol ทำความสะอาดผิวหนังก่อนเจาะเลือดเพื่อเพาะเชื้อในกระแสเลือด

ผลการศึกษา: ผู้ป่วยทั้งหมด 821 ราย ได้รับการเจาะเลือดเพื่อเพาะเชื้อจำนวน 1,269 สิ่งส่งตรวจ แบ่งเป็นกลุ่มที่ใช้ 10% povidone iodine จำนวน 654 สิ่งส่งตรวจ และใช้ 2% chlorhexidine gluconate in 70% alcohol จำนวน 615 สิ่งส่งตรวจ กลุ่มที่ใช้ 10% povidone iodine ขึ้นเชื้อปนเปื้อนร้อยละ 3.21 (95%CI: 2.00-4.87%) ส่วน 2% chlorhexidine gluconate in 70% alcohol ขึ้นเชื้อปนเปื้อนร้อยละ 2.28 (95%CI: 1.25-3.79%) ค่า risk difference เท่ากับร้อยละ 0.93 (95% confidence interval: 0.86-2.72%) ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ เชื้อปนเปื้อนที่พบมากที่สุดคือ Coagulase negative staphylococci (ร้อยละ 68.57) จากการศึกษาไม่พบผลข้างเคียงต่อผิวหนังของน้ำยาทั้งสองชนิด

สรุป: การใช้น้ำยา 2% chlorhexidine gluconate in 70% alcohol ทำความสะอาดผิวหนังก่อนเจาะเลือดเพื่อเพาะเชื้อในกระแสเลือด มีอัตราการขึ้นเชื้อปนเปื้อนแนวโน้มน้อยกว่าการใช้ 10% povidone iodine และไม่พบอาการข้างเคียงจากการใช้น้ำยาทั้งสองชนิดในผู้ป่วยเด็ก