

Comparison of the effects of povidone-iodine and chlorhexidine solutions on skin bacterial flora among hospitalized infants

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ABSTRACT

Background: Infection control is an essential part of caring for hospitalized infants. With regard to the change of bacterial resistance over time and places, as well as the need for periodic studies on the effectiveness of antiseptics, this study aims to compare the effects of both solutions of povidone-iodine and chlorhexidine on skin bacterial flora among hospitalized infants. **Materials and Methods:** This clinical trial recruited 98 hospitalized infants and each of the above-mentioned solutions has been applied to a small area in the left or right side of the infants' bodies. Skin cultures were taken before, immediately after and 2 h after the randomly chosen infants' skin areas that were disinfected by each solution (588 skin cultures in total). Colony count and determination of microorganism types were done by only one person in a single laboratory. The study has been conducted in two teaching hospitals in Isfahan, Iran. **Results:** *Staphylococcus epidermidis* was the most common microorganism prior to skin disinfection by either solution. Two hours after disinfection, "*Staphylococcus epidermidis*" and "*Staphylococcus epidermidis* and *kelebsila*" had the highest frequencies of 3.1% and 3.1%, respectively. Before and 2 h after disinfection, distribution of different types of microorganisms had no significant difference between the two groups ($P = 0.84$ and 0.13 , respectively); however, the difference was significant immediately after disinfection, $P < 0.01$. **Conclusion:** The present study demonstrated that 10% povidone-iodine solution has more significant effect on reduction of skin pathogens promptly after application compared to 2% chlorhexidine. Therefore, prior to any catheterization procedures, it is imperative to use 10% povidone-iodine solutions for skin disinfection.

Key words: Chlorhexidine, Iran, neonates, povidone-iodine

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INTRODUCTION

Infections are among the major causes of infant morbidity and mortality worldwide. Nosocomial infections are responsible for death of 4-56% of hospital-born neonates in various countries.^[1] Thus, control of infectious agents is of much importance, particularly in the hospital environments.^[2] Control of infections is essential for survival and safety of the hospitalized infants.^[3]

Nosocomial infections lead a prolonged hospital stay, increased hospital costs, and anxiety of parents and families.^[4] Intravascular catheterization is a risk factor for nosocomial infections^[5] and insertion of catheters

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puts the patients at the risk of localized and systemic infections.^[5-8] However, using catheters are necessary for ill neonates to take medications, water, electrolytes, and nutrients. Therefore, appropriate skin antiseptics should be used before placing catheters to prevent infections.^[9] There are plenty of antiseptic agents available, such as 70% alcohol, chlorhexidine, and povidone-iodine. The most common antiseptics in the world are povidone-iodine and chlorhexidine, both of which are available in the forms of aqueous as well as alcoholic solutions.^[10] Many studies have suggested that the incidence of infections caused by inserted catheters was less in the patients whose catheter placement region was disinfected by chlorhexidine rather than povidone-iodine solution.^[5] In a meta-analysis study conducted by Chaiyakunapruk *et al.* (2002), 50% reduction rate in septicemia was found when 2% chlorhexidine solution or 0.5% alcoholic chlorhexidine were used in compare to 10% povidone-iodine.^[11] Yet, in a study conducted by Garland *et al.* in 2009 on infants, no significant difference was found for catheter's bacterial colonization when disinfection was done either with povidone-iodine or with chlorhexidine.^[12] With regard to the inconsistencies of the findings of different studies, it seems that povidone-iodine might not be the best choice.^[13] Nevertheless, according to the existing information aqueous povidone-iodine solution is the most common antiseptic used for skin disinfection in Iran.^[14] Given that bacterial resistance changes over time and places, and because no studies have yet compared the efficacy of disinfectant solutions on bacterial skin flora in Iranian infants, and as the efficacy of antiseptics should be evaluated periodically,^[15] this study aims to compare the effects of povidone-iodine solution and chlorhexidine solution on skin bacterial flora among Iranian hospitalized infants.

MATERIALS AND METHODS

This is a pre-post-test and single-blinded clinical trial with within-subjects design. The within-subjects design is a powerful design which provides the most control over subject variables because the same subjects are used in each group and undergo both interventions.^[16-18] The sample size computed based on confidence of 0.95, power of 0.8, and mean differences equal to 0.4 SD (standard deviation). Subjects were 98 bedridden infants who were hospitalized in a neonatal ward and neonatal intensive-care units of two teaching hospitals affiliated to Isfahan University of Medical Sciences, that are the main referral centers for ill newborns in Isfahan province, from 06.08.2011 until 06.11.2011. The neonates were hospitalized for a minimum duration of 24 h, their birth weights were > 1000 g, and their gestational age was more than 28 weeks. They were not suffering from any skin lesion or infectious diseases, and were selected by a continuous convenient sampling method. Subjects were excluded and replaced by another infant if one of the sampling sites of their skin was used for therapeutic procedures or disinfected by any solution, or if the infant died before taking all required culture samples. Before sampling, cleaning packages which contained

six pieces of cotton were placed in a graft paper, sealed by an operator and sterilized in an autoclave.^[19] For sampling, the regions at the back of hand, anterior medial elbow and ankle, were coded as 1, 2, 3 respectively, and via drawing lots one of the codes was selected. Through coin flipping (heads or tails), it was decided that which side of the body was supposed to get disinfected with 10% povidone-iodine solution and which side was to be disinfected by 2% chlorhexidine solution. Then, by using a drawing template, the researcher selected a 2 × 2 cm region on the skin of the randomly selected region of each hand.^[20] Before disinfecting, a skin culture sample was taken from the specified region. Then, the same region was disinfected from center to the periphery. Another two sets of culture samples were taken from the same region again, one immediately after the disinfection and the other one, 2 h after disinfection. The same procedure has been done for the other hand except for the applied disinfecting solution. Therefore, the sampling ended-up with 294 (98 × 3) skin cultures for each group of chlorhexidine or povidone-iodine. All the skin cultures were taken from a previously specified region by means of sterilized swabs moistened in sterile normal saline solution, rubbed five times horizontally and two times vertically on the skin area based on the method utilized by Darmstadt *et al.*^[20]

All samples were immediately immersed in an Amies transport medium (Amies transport medium with charcoal, for *Staphylococcus aureus* ATCC 25923, and for *Escherichia coli* ATCC 25922) and were immediately sent to the hospital laboratory within 2 h. In the laboratory, the swabs were cultured on agar eosin-methylene blue plates (ATCC 25922, PTCC 1609) and sheep blood agar (ATCC 25922, ATCC 33400, and ATCC 8668) by a microbiologist who was unaware of the utilized disinfection solutions and also the tie of sampling. To identify the kind and count of the bacteria, the culture media were kept in the temperature of 37°C for 48 h using an identical standard method^[19-23] by one laboratory technician. After 48 hours, efforts were made to identify the nine prevalent pathogens which are among the major causes of neonatal sepsis in developing countries including *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Acinetobacter* spp., *Enterobacter* spp., *Salmonella* spp., *Candida* spp., *Pseudomonas* spp., *Escherichia coli*, coagulase-negative staphylococcus in the culture media and count the colonies. Those skin-cultured samples that contained one or more of the aforementioned pathogens were considered positive.^[20]

The data were recorded in a data gathering sheet in two parts: demographic characteristics and the laboratory data about culture results.

The data were analyzed using SPSS version 14 software. χ^2 -test was used to compare the frequency distribution of microorganism types before and after disinfection with povidone-iodine or with chlorhexidine, and to compare the frequency distribution of the kinds of the microorganism types at different intervals between the two disinfection methods. At the end, it is worth mentioning that the researchers in this study did not receive

any monetary benefits from the companies which produced the solutions that were used in the current research, and the researchers were not biased toward any of the solutions.

Scientific and ethical content of this study have been approved by Isfahan University of Medical Sciences and all the parents agreed to enter their infants in this study by signing an informed written consent.

RESULTS

Out of the 98 infants who were enrolled in the study, 59 infants (60.2%) were males and 39 infants (39.8%) were females. Their gestational age was between 28 and 41 weeks and 95% confidence interval of their mean gestational age was 33 (3.5) weeks. Confidence interval of the subjects' average postnatal age was recorded at 9.94 (8.66) days ranging between 1 and 28 days. For average birth weight of the infants, it was 2005 (8.33) g ranging between 1010 and 4430 g. Five out of the total number of the infants were excluded (in two cases due to using the sampling site for insertion of peripheral intravenous line (PIV), in one case because the infant was referred to the neonatal surgery ward and in two other cases the losses were resulted from the contamination of the sampling site by the personnel). Therefore, another five newborns were replaced. A total of 588 skin cultures were taken as the samples for the study, of which 294 cultures were taken from the skin site which were disinfected by povidone-iodine, and 294 cultures were taken from the skin sites that chlorhexidine was used for disinfection.

The results of the skin cultures before, immediately after, and 2 hours after disinfection are given in Table 1, which shows a significant difference between povidone-iodine and chlorhexidine groups only immediately after disinfection in terms of frequency of positive skin cultures which is 3.1% in the povidone-iodine group compared to 17.3% in the chlorhexidine group ($P = 0.001$).

The frequency distribution of the microorganisms in positive skin cultures before, immediately, and 2 h after disinfection are shown in Table 2. In the povidone-iodine group, before disinfection, the most frequency pertained to *Staphylococcus epidermidis*, *Acinetobacter*, and *Enterobacter* with 37.1% ($n = 36$), 4.1% ($n = 4$), and 4.1% ($n = 4$), respectively. Two hours after disinfection, *Staphylococcus epidermidis* shrank to 3.1% ($n = 3$), *Enterobacter* decreased to 1% ($n = 1$), and *Acinetobacter* reduced to 0% ($n = 0$). Chi-squared tests indicated that the frequency distribution

of the types of the microorganisms in the povidone-iodine group has a significant difference at three aforementioned intervals ($P < 0.001$ and $\chi^2 = 132.99$) [Table 2].

In the chlorhexidine group before disinfection, the highest frequency was related to *Staphylococcus epidermidis*, *Klebsiella*, *Acinetobacter*, and *Enterobacter* with 36.1% ($n = 35$), 11.3% ($n = 11$), 7.2% ($n = 7$), and 3.1% ($n = 3$), respectively. In this group, *Staphylococcus epidermidis* and *Klebsiella* shrank to 3.1% ($n = 3$), *Acinetobacter* reduced to 1% ($n = 1$), and *Enterobacter* to 0% 2 h after disinfection. χ^2 -tests indicated that the frequency distribution of the types of the microorganisms in the Chlorhexidine group has a significant difference at three aforementioned different intervals ($P < 0.001$ and $\chi^2 = 79.82$) [Table 2].

Comparison between the frequency distribution of microorganism types in both groups showed that there were no significant differences between the frequency distribution of the kinds of microorganisms before disinfection ($P = 0.84$ and $\chi^2 = 4.16$) and also 2 h after disinfection ($P = 0.13$ and $\chi^2 = 7.01$). While the difference was significant immediately after disinfection ($P = 0.002$ and $\chi^2 = 19.18$) with higher frequency of negative skin cultures in the povidone-iodine group and higher frequencies of positive cultures with growth of *Staphylococcus epidermis*, *Klebsiella pneumoniae*, and *Acinetobacter* in the chlorhexidine group [Table 2].

The results also showed that there were no significant differences between the frequency distribution of the kinds of microorganisms immediately and 2 h after disinfection in the povidone-iodine group ($P = 0.48$ and $\chi^2 = 1.43$). This difference was not significant in the chlorhexidine group too ($P = 0.14$ and $\chi^2 = 6.58$).

DISCUSSION

This study indicated that the effectiveness of 2% chlorhexidine solution in the reduction of pathogens on the skin, immediately after disinfection, was significantly less than that of 10% povidone-iodine solution. Meanwhile, there was no significant difference in effectiveness of the solutions 2 h after disinfection.

Garland and colleagues (2009) showed that there was no significant difference between the bacterial colonization on catheter's tip in those infants whose catheter insertion site got disinfected by chlorhexidine solution (13%), and those infants whose insertion site got disinfected by povidone-iodine

Table 1: Frequencies of positive and negative cultures at three different times in two groups

Cultures	10% Povidone-iodine group n (%)			2% Chlorhexidine group n (%)		
	Before*	Immediately after**	After 2h***	Before*	Immediately after**	After 2h***
Positive cultures	59 (60.8)	3 (3.1)	4 (4.1)	58 (59.8)	17 (17.3)	7 (7.2)
Negative cultures	38 (39.2)	95 (96.9)	94 (95.9)	39 (40.2)	81 (82.7)	90 (92.8)
Total	97 (100)	98 (100)	98 (100)	97 (100)	98 (100)	97 (100)

* χ^2 test comparative frequencies of positive cultures before intervention between groups ($P=0.88$, $\chi^2=0.02$). ** χ^2 test comparative frequencies of positive cultures immediately after intervention between groups ($P=0.001$, $\chi^2=11.93$). *** χ^2 test comparative frequencies of positive cultures after 2 h intervention between groups ($P=0.34$, $\chi^2=0.87$)

Table 2: Comparative distribution frequency of microorganisms species, three different times within each group, and between groups

Microorganisms	10% Povidone-iodine group			P*	2% Chlorhexidine group			*P
	Before** n (%)	Immediately after*** n (%)	After 2h**** n (%)		Before** n (%)	Immediately after*** n (%)	After 2h**** n (%)	
None	38 (39.2)	95 (96.9)	94 (95.9)		39 (40.2)	81 (82.7)	90 (92.8)	
<i>Klebsiella Pneumonia</i>	10 (10.3)	0 (0)	0 (0)		11 (11.3)	4 (4.1)	3 (3.1)	
<i>Staphylococcus epidermidis</i>	36 (37.1)	1 (1)	3 (3.1)		35 (36.1)	11 (11.2)	3 (3.1)	
<i>Acinetobacter</i> spp	4 (4.1)	0 (0)	0 (0)		7 (7.2)	1 (1)	1 (1)	
<i>Enterobacter</i> spp	4 (4.1)	1 (1)	1 (1)	<0.001	3 (3.1)	1 (1)	0 (0)	<0.001
<i>Pseudomonas</i> spp	1 (1)	1 (1)	0 (0)		0 (0)	0 (0)	0 (0)	
<i>E. coli</i>	1 (1)	0 (0)	0 (0)		1 (1)	0 (0)	0 (0)	
<i>Klebsiella and Staph. epidermidis</i>	2 (2.1)	0 (0)	0 (0)		1 (1)	0 (0)	0 (0)	
<i>Acinetobacter and E. coli</i>	1 (1)	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	
Total	97 (100)	98 (100)	98 (100)		97 (100)	98 (100)	97 (100)	

* χ^2 test comparative distribution frequency of microorganism species, three different times in each group ($P < 0.01$). ** χ^2 test comparative distribution frequency of microorganism species, before intervention between groups ($P = 0.84$, $\chi^2 = 4.16$). *** χ^2 test comparative distribution frequency of microorganism species in immediately after intervention between groups ($P < 0.01$, $\chi^2 = 19.18$). **** χ^2 test comparative distribution frequency of microorganism species in after 2 h intervention between groups ($P = 0.13$, $\chi^2 = 7.01$)

solution (4%).^[12] The results of skin cultures 2 h after intervention of our study are in line with those of Garland's study; since, although seemingly the overall rate of positive skin cultures in the chlorhexidine group was higher than that of the povidone-iodine group, there was no significant statistical difference between those groups in the rate of bacterial colonization on the skin 2 h after disinfection. Another study, conducted in India by Jayakumar *et al.* (2011), showed that the effect of povidone-iodine solution on the reduction of the number of those pathogens which cause hospital infection was stronger than that of chlorhexidine solution.^[15] Valles and colleagues (2008), who compared the effect of three disinfecting solutions of 10% povidone-iodine, 2% chlorhexidine, and 0.5% alcoholic chlorhexidine on catheter's bacterial colonization, showed that the rate of catheter's bacterial colonization in the chlorhexidine group and the alcoholic chlorhexidine group was significantly higher than that of the povidone-iodine group ($P = 0.03$).^[5] The results of our study from those culture samples that got immediately after disinfection are similar to these results, since in this study, the percentage of positive skin cultures, immediately after disinfection, in the Chlorhexidine group was higher than the povidone-iodine group.

Suwanpimolkul and colleagues (2008) indicated that the infection rate in blood cultures was 3.2% after disinfecting with 2% chlorhexidine and alcoholic chlorhexidine while it was 6.9% after disinfecting with povidone-iodine and this difference was significant ($P < 0.001$).^[24] The results of Suwanpimolkul's study are not consistent with our study. This difference in the results can be because of using alcoholic chlorhexidine for disinfection in Suwanpimolkul's study rather than aqueous chlorhexidine in our study and also may be related to difference in sample sizes or in environmental factors such as bacterial resistance.

Chaiyakunapruk meta-analysis study (2002) indicated that only in those studies that alcoholic chlorhexidine solutions were used, there has been a significant decrease in the rate of catheter colonization compared to the studies which used

povidone-iodine solution.^[11] Other studies have shown that using alcoholic antiseptics has been more effective on the reduction of infection in blood cultures as well as catheter's infection compared with other antiseptics.^[25,26] In our study, because of lack of knowledge about the probable side effects of using chlorhexidine-ethanol on infants and the prohibition of its use in infants, alcoholic mixtures were not used.

Kasuda and colleagues (2002) indicated that in the two groups, *Staphylococcus epidermidis* was the most frequent bacterial species which was separated from the skin cultures at the catheter's insertion sites as well as the cultures of catheters' tip and there was no significant difference between the two groups in terms of bacteria types.^[22]

Suwanpimolkul and colleagues (2008) also showed that 80.6% of the blood cultures' infection after disinfecting the skin with povidone-iodine and chlorhexidine solutions pertained to coagulase-negative staphylococci, and the frequency distribution of the bacteria between the povidone-iodine group and the chlorhexidine group was the same.^[24] Our study supports the results of Kasuda and Suwanpimolkul, because in our study, the highest percent of bacteria species pertained to *Staphylococcus epidermidis* before and 2 h after disinfection too, and there was no significant difference between the two groups in terms of bacteria species. However, frequency of bacterial species was significantly higher in the chlorhexidine group immediately after disinfection than in the povidone-iodine group that shows greater impact of povidone-iodine on skin bacterial flora at the time frame in which insertion of IV devices usually takes place.

The results of the studies by Kasuda and Suwanpimolkulas also have a double emphasis on the fact that Bacterial skin flora enters internal body tissues through invasive methods including catheterization, venous puncture, and PIV insertion; causing nosocomial infections.

Darmstadt and colleagues (2007) showed that the rate of positive skin cultures 2 h after skin disinfection with chlorhexidine solution was decreased by 35-55%. This significant decrease was stable for 24 hours and even for 3 days.^[20] However, in our study, positive skin cultures in the chlorhexidine group, immediately and 2 h after disinfection, dropped by 70% and 88%, respectively. This difference could be due to the difference in the density of chlorhexidine solutions which were used in Darmstadt's study (0.25%) and the present study (2%). It can also be related to the difference in the sites which were used for sampling skin culture in the two studies. In Darmstadt's study, after a primary bathing and cleansing the skin, cultures were collected from the three sites of axillary, periumbilical regions, and inguinal regions. While in our study, the cultures were collected from the regions at the back of the hand, anterior medial elbow, and ankle. Therefore, it can be concluded that there is a higher probability of bacterial colonization in those regions where the skin is more wrinkled. Thus, the regions at the back of the hands, anterior medial elbow and ankle can be preferably used for the venous puncture, blood sampling and inserting central venous catheter or peripherally inserted central catheter (PICC) in newborns.

We did not evaluate clinical effects and possible side effects of the solutions. This could be a limitation as some researchers suggested potential absorption of chlorhexidine solution despite no observed irritation or systemic side effects.^[27-29]

CONCLUSION

The results of this study showed that 10% povidone-iodine solution is more effective than 2% chlorhexidine solution in reducing the skin bacterial flora immediately after disinfection. Thus, it is recommended to use 10% povidone-iodine solution to disinfect the skin before conducting procedures such as catheterization, venous puncture, and obtaining PIV and inserting PICC in neonatal sectors. The probable side effects of the used solutions including occurrence of allergic reactions, probable thyroid complications related to unwanted absorption of iodine, and neurologic responses to probable absorption of chlorhexidine were not examined and investigated in this study. However, mothers were asked to inform the researcher in case of any symptom of skin allergic reaction detected. However, no one referred to the researcher for this side effect.

Future studies should consider the measurement of the side effects of using these solutions for infants as antiseptic solutions.

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