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The Effect of Skin Bathing with Chlorhexidine Gluconate (2%) to Central Line-Associated Bloodstream Infections in Pediatric Intensive Care

Çocuk Yoğun Bakımda Klorheksidin Glukonat (%2) ile Cilt Banyosunun Santral Kateter İlişkili Kan Dolaşımı İnfeksiyonlarına Etkisi

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ABSTRACT

Introduction: *Central line-associated bloodstream infections (CLABSIs) are important causes of mortality and morbidity in pediatric intensive care units (PICUs). This study aimed to investigate the effect of a 2% chlorhexidine gluconate (CHG) bath on CLABSI.*

Materials and Methods: *Skin bathing was performed every other day with 2% CHG in patients as of 25.04.2019. The frequency of CLABSI pre and post-intervention was evaluated.*

Results: *A total of 226 patients were included in this study, 111 patients before CHG and 115 patients after CHG. CLABSI rates before and after using CGH were 10.11 and 5.52, respectively. The relative risk of CLABSI frequency during CHG bathing was compared to the control period and resulted in a significant reduction (13.0%, p< 0.0001, 95% CI= 2.5-4.2%).*

Conclusion: *Adding a 2% CHG bath every other day to CLABSI precaution bundles may be an effective strategy for reducing the frequency of CLABSI in PICUs.*

Key Words: *Bloodstream infection; Central venous catheter; Chlorhexidine bathing; Pediatric intensive care*

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ÖZ

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Giriş: *Santral kateter ilişkili kan dolaşımı enfeksiyonları (SKI-KDE), çocuk yoğun bakım ünitelerinde (ÇYB) önemli mortalite ve morbidite nedenleridir. Bu çalışma, %2 klorheksidin glukonat (CHG) banyosunun SKI-KDE üzerindeki etkisini araştırmayı amaçlamaktadır.*

Materyal ve Metod: *Hastalara 25.04.2019 tarihinden itibaren gün aşırı %2 CHG ile cilt banyosu yapıldı. SKI-KDE'nin müdahale öncesi ve sonrası sıklığı değerlendirildi.*

Bulgular: *Bu çalışmaya CHG öncesi 111, CHG sonrası 115 hasta olmak üzere toplam 226 hasta dahil edildi. CGH kullanımı öncesi ve sonrası SKI-KDE oranları sırasıyla 10.11 ve 5.52 idi. CHG banyosu sırasında SKI-KDE sıklığının relatif riski kontrol periyodu ile karşılaştırıldı ve önemli bir azalma olduğu görüldü (%13.0, p< 0.0001, %95 CI= %2.5-4.2).*

Sonuç: *SKI-KDE önlem paketlerine gün aşırı %2 CHG banyosu eklemek, ÇYB'lerde SKI-KDE sıklığını azaltmak için etkili bir strateji olabilir.*

Anahtar Kelimeler: *Kan dolaşımı infeksiyonu; Santral venöz kateter; Klorheksidin banyosu; Çocuk yoğun bakım*

INTRODUCTION

Central venous catheters (CVCs) are usually required for long-term treatments such as blood transfusion, inotropic agents, and parenteral nutrition in intensive care units (ICUs)[1]. Central venous line is not risk-free, and an estimated 30% of patients who have undergone CVC in ICUs have complications mostly including central line-associated bloodstream infections (CLABSIs)[2]. Central line-associated bloodstream infections are the most common healthcare-associated infection in pediatric intensive care units (PICUs) and are associated with high mortality, morbidity, and hospital costs[3,4].

Guidelines recommend "care bundles" for decreasing CLABSI's in different clinical settings. Central line bundles (CLBs) for prevention of infections generally includes all but not limited to the following steps including chlorhexidine gluconate skin preparations and complying with maximal sterile barriers during insertion, preferring the subclavian or internal jugular vein instead of the femoral vein, strict hand hygiene, and daily review of the necessity of central line infections. Central line bundles should be preventing CLABSI in PICUs[5-8]. Devrim et al. have reported a significant decrease in PICU in six months period, by applying a twelve-step CLB in PICU[9].

Risk factors such as inoperable cardiac disease, long catheter duration, and total parenteral nutrition had been identified for PICU patients for CLABSI[10]. However, it has been stated that it is complicated to develop strategies targeting risk factors since the determined risk factors are either minimally modifiable or non-modifiable[11-13]. Therefore, the preventive factors to be taken to prevent CLABSI formation stands out today.

Chlorhexidine is an effective antiseptic solution that limits colonization and microbial growth[13]. In the adult population, in intensive care, daily bathing with 2% CHG had decreased CLABSI rates between 40% and 50%[10,11,13-15]. To our knowledge, there is only one study focusing on usage in children[14]. Martinez et al. have evaluated the use of chlorhexidine 4% in the pediatric surgical intensive care unit. In their study, the investigators applied a 4% CHG bath daily

and evaluated its effect on CLABSI development in a retrospective, monocentric, cohort study. That study included a total of 775 patients before and after a year of CHG 4% application. However, they only included patient populations with the following risk factors they identified as; the presence of constitutive or acquired immunosuppression, presence of another invasive medical device (i.e. tracheotomy, cerebrospinal fluid drains, thoracic drains), and the carriage or previous infection with *Staphylococcus aureus* (regardless of methicillin sensitivity)[14].

The purpose of this randomized controlled study was to evaluate the clinical impact of the addition of 2% CHG skin bathing to the CLB for the prevention of CLABSI in PICU.

MATERIALS and METHODS

The study was conducted by the ethical standards stated in the 'Declaration of Helsinki'. The local ethics committee approved the study (Protocol number: 2019/343). Informed consent was obtained from all cases and/or their families included in the study.

Participants

This randomized controlled study was carried out at Pediatric Surgery Training and Research Hospital which is a 400-bed pediatric referral and tertiary care hospital with a 24-bed PICU in Izmir, Turkey. The study period was 16 months from August 2018-December 2019. In this study, the children who had central venous catheters for at least 48 hours were included. Patients who had a systemic infection when the catheter was inserted and patients who were transferred to PICU with a catheter were excluded from the study.

Before the CHG bath, our patients were bathing with only shampoo and water and 2% CHG bathing was initiated every other day in April 2019. For this reason, patients were allocated in the PICU for eight months (from August 2018 to April 2019) before and eight months (from April 2019 to December 2019) after the use of CHG. Data collection included days of hospitalization, total CVC days, and CLABSI numbers of patients in these periods.

Demographic characteristics (age, sex, weight), duration of mechanical ventilation, length of hospitalization, primary diagnosis, organ dysfunction, and mortality scores (PRISM-4: Pediatric risk of mortality score, pSOFA: Pediatric sequential organ failure assessment score), duration of CVC and CVC placement were recorded.

Central Venous Catheter Application And Dressing Properties

In the PICU population, the ICU specialists insert the non-tunneled central venous catheters. Central venous catheters were inserted by ultrasound-guided Seldinger method to the internal jugular, femoral and subclavian veins. In this institute a central line bundle protocol had used including the following elements: The selection of catheters with the minimal lumen and optimal insertion site, use of optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion (i.e., mask, cap, gown, sterile gloves, and sterile full-body drape), daily inspection of the catheter sites, prompt catheter removal, use of optimal hand hygiene, use of aseptic techniques, and use of transparent dressings, disinfection of the hub with isopropyl alcohol 70% solution, using needleless connectors (BD Q-Syte, BD, Franklin Lakes, NJ) and regular flushing of catheter lumens with sterile single-use prefilled syringes (BD Posiflush NaCl 0.9% 10-mL, BD, Franklin Lakes, NJ)[14]. After the first bundle period, skin bathing with 2% CHG was added to the bundle steps. Skin bathing with 2% CHG included all the body parts excluding the face and head starting from the neck, perineum, eye, and mucosal membranes. All side effects of CHG including skin rash, allergic reaction, or skin dryness were recorded twice per day by two nurses each day of the study period.

Definition of Central Venous Catheter-Associated Bloodstream Infection

The definition for CLABSI used for this research included, Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America is adopted[16]. Central line-associated bloodstream infection was defined as a patient with a catheter for

greater than 48 hours and a laboratory-confirmed blood circulation infection. Without a specific source for bloodstream infection other than a catheter, the detection of bacteremia or fungemia in one positive blood culture obtained from the peripheral vein in patients with clinical signs of infection such as fever and/or chills suggests CLABSI.

Statistical Analysis

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc; Chicago, IL, USA). Mean, standard deviation, minimum and maximum values were obtained by frequency analysis to evaluate the data. The rate of infections with the poisson 95% confidence interval in each bundle group and the relative risk reduction between groups were calculated and given as percentages. The relative risk ratio was also calculated to compare the risks for both groups with a 95% confidence interval for the incidence rate. Statistical analysis was performed using Medcalc v 11.6 (Ostend Belgium). The statistical significance level was taken as $p< 0.05$.

RESULTS

A total of 226 patients in whom 7-32 months range were included in this study, 111 patients before CHG, and 115 patients after CHG. Demographic characteristics (age, sex, weight), duration of mechanical ventilation, length of hospitalization, primary diagnosis, organ dysfunction and mortality scores (PRISM-4: Pediatric risk of mortality score, pSOFA: Pediatric sequential organ failure assessment score), duration of CVC, and CVC placement (jugular, subclavian, femoral) were similar between groups (Table 1).

The total hospital stay was 5557 days before CHG and 5380 days after CHG. The follow-up day with total CVC was 2078 days before CHG, and 1268 days after CHG. The number of CLABSI before the use of CHG was 21 and 7 after use. While the CLABSI rate was 10.11

Table 1. Demographic characteristics, catheter types, primary diagnosis, and critical illness severity of patients

	Before 2% CHG August 2018-April 2019	After 2% CHG April 2019-December 2019
Age (months) median (IR)	13 (7-26)	15 (9-32)
Gender (F-M) (%/%)	49-62 (44-56)	55-60 (48-52)
Weight (kg)-median (IR)	8 (7-15)	9 (7-18)
Duration of MV (days) median (IR)	45 (10-74)	38 (8-67)
Length of Hospitalization (days)	65 (16-138)	58 (21-142)
p-SOFA mean ± SD (min-max)	6 ± 4 (2-19)	5 ± 3 (2-21)
PRISM-4 median (IR)	4.91 (1.62-7.99)	4.32 (1.96-6.56)
Primary Diagnostic Groups N (%)		
Respiratory Diseases	28 (25)	26 (22)
Cardiovascular Diseases	15 (14)	19 (17)
Neuromuscular Diseases	22 (19)	27 (24)
Metabolic Diseases	24 (22)	21 (18)
Syndromic Diseases	15 (14)	17 (15)
Other	7 (6)	5 (4)
Duration of CVC (days) median (IR)	23 (11-34)	19 (9-29)
CVC Placement N (%)		
Jugular	85 (77)	81 (71)
Subclavian	13 (12)	18 (15)
Femoral	12 (11)	16 (14)

CHG: Chlorhexidine gluconate, F: Female IR: Interquartile range, Min: Minimum, M: Male, Max: Maximum, MV: Mechanical ventilation, N: Number, PRISM-4: Pediatric risk of mortality score, pSOFA: Pediatric sequential organ failure assessment score, SD: Standard deviation.

Table 2. Frequency of CLABSI before and after daily skin bathing with chlorhexidine gluconate

	Total number of patients hospitalized	Total day of hospitalization	Total CVC day	Number of CLABSI	CVC usage rate	Frequency of CLABSI*
Before 2% CHG August 2018-April 2019	111	5557	2078	21	0.4	10.11
After 2% CHG April 2019-December 2019	115	5380	1268	7	0.2	5.52

CVC: Central venous catheter, CLABSI: Central line-associated bloodstream infections, CHG: Chlorhexidine gluconate.
*Frequency of CLABSI: CLABSI per 1000 days.

before using CHG and 5.52 after use. In the period when chlorhexidine gluconate was used, the relative risk of seeing CLABSI compared to the control period was significantly reduced (13.0%, p< 0.0001, 95% CI= 2.5-4.2%) (Table 2).

One of the patients who underwent skin bathing with CHG had a mild rash on the skin, no other side effects were noted.

Microbial agents in catheter infections in total in both periods were determined as gram-negative (20; 71%), fungus (5; 18%), gram-positive (3; 11%). Microbial agents before skin bathing with CHG was determined as gram-negative (16; 76%), fungus (5; 14%), gram-positive (2; 10%) and after skin bathing with CHG was determined as gram-negative (5; 71%), fungus (1; 14%), gram-positive (1; 14%). Microbial agents were similar between the two periods and it was seen that gram-negative agents were the most.

When 28-day mortalities were compared; mortality of patients in the first period (8; 7.2%) and the mortality of the patients in the second period was determined as (8; 6.9%). The 28-day mortality of our patients was compared and no difference was found (1.0%, p= 0.76, 95% CI= -5.9-8%).

DISCUSSION

This study shows that skin bathing with 2% CHG every other day can be an excellent protection method to prevent CLABSI development and the CLABSI rate is decreased significantly with 2% CHG bathing. This study shows that the inclusion of skin bathing with 2% CHG every other day in PICU significantly decreased CLABSI and should be considered in the prevention strategies for CLABSI reduction and mortality, morbidity, and cost associated with CLABSI.

Central venous catheters provide safe and effective vascular access in PICUs. Central venous catheter use works with a high level of efficiency to provide nutrition or blood supply and to carry out blood tests[17]. However, CVCs also pose a risk to patients for bloodstream infections. The leading cause of nosocomial bacterial infections is CLABSI, and it is accounting for 69% of pediatric health-care-associated infections[18]. Central line-associated bloodstream infections prolong hospital stay and cause a significant increase in cost. Studies have shown that CLABSI doubles the risk of mortality in children[19,20].

When the literature was reviewed, it could be seen that most of the CLABSI studies include adult patients. When few studies were conducted in the pediatric age group, it was noticed that it is generally done in specific populations containing risk factors. These are studies conducted to determine risk factors and effects and to characterize incidence and infections (such as epidemiology and microorganism properties) [7,9,15]. While determining the risk factors was essential to prevent mortality and morbidity caused by CLABSI, studies over time have shown that risk factors for CLABSI are not preventable[9]. For this reason, developing various methods to prevent CLABSI is very popular recently.

Central line-associated bloodstream infections can consist of several sources. However, it is known that the most common reason is that organisms originating from the patient's skin migrate along the catheter surface and reach the blood

vessels from the catheter[21]. Central line insertion to prevent the colonization of these microorganisms migrating from the skin is "care bundles" for catheter care, antimicrobial catheters, and antimicrobial catheter solutions include catheters and equipment[21]. Also, catheter dressing with antiseptic agents such as CHG, novel silver-plated, and povidone-iodine are other recommended methods of protection[12,16,22]. The most effective of these is CHG disc dressing[13]. Therefore, CHG is preferred for bathing and toilet care today[13,14].

In intensive care, CHG baths are known to prevent the colonization of drug-resistant gram-positive cocci such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococ* spp. in patients[23]. Chlorhexidine gluconate baths provide a useful antiseptic feature on the skin, significantly reducing catheter colonization[24]. In most critical care studies, patients are administered the CHG bath daily[14,24]. However, we know that CHG has antimicrobial activity in human skin for at least 48 hours[25].

Martinez et al. have added a 4% CHG bath to the CVC care package every day for some of the patients with at least one of the few risk factors identified in PICU[14]. They have stated that not adding to all patients was related to increased care burden. As a result of their study, they have found that CHG bath significantly reduced CLABSI rates, so it would be good to do it in children with risk factors, even if the care load increased[14]. Unlike this study, we applied a 2% CHG without increasing our burden with the application every other day. Also, by applying this to all patients, not just a specific group of patients, the adverse effects of CLABSI may be eliminated.

Limitations of this study included 1) not compromised other disinfection materials 2) every other day application 3) lack of monitoring for resistance to bacteria.

CONCLUSION

In conclusion, the addition of 2% CHG bathing every other day appears to be a possible strategy for CLABSI prevention. By implementing 2% CHG bathing in the PICU central venous catheter routine care bundles CLABSI rates, morbidity, mortality, and the overall cost may be prevented.

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ETHICS COMMITTEE APPROVAL

This study approval was obtained from İzmir Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Clinical Researchs Ethics Committee (Decision No: 2019/343, Date: 19.12.2019).

CONFLICT of INTEREST

No conflicts of interest to be declared concerning the publication of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: ST, ID, HA

Data Collection or Processing: ST, ID, HA

Analysis/Interpretation: ST, ID, HA

Literature Search: ST, GA, MC, ES, EB, NY, NÖ

Writing: ST, GA, MC, ES, EB, NY, NÖ

Final Approval: ST, ID, UK, EB

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