

**RESEARCHARTICLE/KLİNİK ÇALIŞMA** 

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# Does Skin Bathing With Chlorhexidine Gluconate (2%) Affect the Carbapenem-resistant *Enterobacteriaceae* and Vancomycin-resistant *Enterococcus* Colonization in Pediatric Intensive Care?

## Klorheksidin Glukonat (%2) ile Cilt Yıkama Pediatrik Yoğun Bakımda Karbapenem-dirençli Enterobakter ve Vankomisin-Dirençli Enterokok Kolonizasyonunu Etkiler mi?

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#### ABSTRACT

Introduction: Carbapenem-resistant Enterobacteriaceae (CRE) and vancomycin-resistant Enterococcus (VRE) colonization and infections are important in the pediatric intensive care unit (PICU). This study aimed to investigate the effect of a 2% chlorhexidine gluconate (CHG) bath on VRE and CRE colonization.

*Materials and Methods:* Skin bathing was performed every other day with 2% CHG as of April 2019. The frequency of CRE and VRE colonization pre and post-intervention was evaluated. Rectal swab samples were taken within 7 days before and after skin bathing with CHG. Besides, VRE and CRE spontaneously negation rates within 14 day periods were examined.

**Results:** The number of CRE positive patients within the CHG group were detected as 10 (47.6%) before using CHG and as 8 (38%) after using (OR: 1.5, p = 0.131, 95% CI: 0.87-1.98). The number of VRE positive patients were detected within the CHG group as 15 (71.4%) before using CHG and as 10 (47.6%) after using (OR: 2.7, p = 0.044, 95% CI: 1.09-2.42). Also, when we compared the control group with the CHG group; there was no significant difference in CRE when comparing the negation rates (p = 0.804). There was a significant difference between the two groups in VRE (p = 0.048).

**Conclusion**: It shows that performing skin bathing with 2% CHG every other day in the PICU significantly reduces VRE colonization but cannot decrease the risk of CRE colonization. We think that skin bathing with 2% CHG every other day in the PICU can be used as one of the resistant microorganism colonization and infection prevention methods.

Key Words: Carbapenem-resistant Enterobacteriaceae; Chlorhexidine gluconate; Pediatric intensive care; Skin bathing with chlorhexidine; Vancomycin-resistant Enterococcus

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#### ÖΖ

#### Klorheksidin Glukonat (%2) ile Cilt Yıkama Pediatrik Yoğun Bakımda Karbapenem-dirençli Enterobakter ve Vankomisin-Dirençli Enterokok Kolonizasyonunu Etkiler mi?

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Giriş: Karbapenem-dirençli Enterobakter (CRE) ve vankomisin-dirençli Enterokok (VRE) kolonizasyonu ve infeksiyonları çocuk yoğun bakım ünitesinde (ÇYBÜ) önemlidir. Bu çalışma, %2 klorheksidin glukonat (CHG) banyosunun VRE ve CRE kolonizasyonu üzerindeki etkisini araştırmayı amaçlamaktadır.

Materyal ve Metod: Klorheksidin ile cilt banyosu, Nisan 2019 itibariyle gün aşırı %2 CHG ile gerçekleştirildi. Müdahale öncesi ve sonrası CRE ve VRE kolonizasyon sıklığı değerlendirildi. Rektal sürüntü örnekleri %2 CHG ile cilt banyosu başlanmadan önce 7 gün ve başlandıktan sonra 7 gün içinde alındı. Ayrıca, VRE ve CRE'nin 14 günlük periyotlar içerisinde kendiliğinden negatifleşme oranları incelendi.

**Bulgular:** CHG grubundaki CRE pozitif hastaların sayısı, CHG kullanılmadan önce 10 (% 47.6) ve kullanıldıktan sonra 8 (%38) tespit edildi (OR: 1.5, p= 0.131,% 95 CI: 0.87-1.98). VRE pozitif hastalar, CHG kullanılmadan önce 15 (% 71.4) ve kullanıldıktan sonra 10 (%47.6) saptandı (OR: 2.7, p= 0.044, %95 CI: 1.09-2.42). Ayrıca kontrol grubunu CHG grubu ile karşılaştırdığımızda, CRE'de negatifleşme oranlarında anlamlı bir fark bulunmadı (p= 0.804). VRE'de iki grup arasında anlamlı fark saptandı (p= 0.048).

**Sonuç:** Çocuk yoğun bakım ünitesinde gün aşırı %2 CHG ile cilt banyosu yapmanın VRE kolonizasyonunu önemli ölçüde azalttığını, ancak CRE kolonizasyonu riskini azaltmadığını göstermektedir. Çocuk yoğun bakım ünitesinde gün aşırı %2 CHG ile cilt banyosunun dirençli mikroorganizma kolonizasyonu ve infeksiyon önleme yöntemlerinden biri olarak kullanılabileceğini düşünmekteyiz.

Anahtar Kelimeler: Karbapenem-dirençli enterobakter; Klorheksidin glukonat; Pediatrik yoğun bakım; Klorheksidin ile cilt banyosu; Vankomisin-dirençli enterokok

#### **INTRODUCTION**

The incidence of drug-resistant microorganisms is increasing day by day in hospitals, especially in intensive care units (ICUs). Increasing the use of antibiotics to treat infections has made it the primary source of the spread of drug-resistant microorganisms in ICUs. Risk factors for infection and colonization with resistant microorganisms are severe illness, immunosuppression, prolonged hospitalization, young age, presence of an intravenous catheter, presence of mechanical ventilation, surgical and other interventions, broad-spectrum antibiotic use, chronic kidney failure, chemotherapy, and other immunosuppressive treatments. These microorganisms are associated with increased morbidity and mortality[1-3]. Therefore, proper management of drug-resistant microorganisms is essential. However, especially the treatment process has various difficulties due to antibiotic resistance<sup>[1]</sup>. For this reason, taking preventive measures (such as hand hygiene, gloves, antiseptic baths) in the ICUs to prevent colonization and especially to reduce the bacterial load on the skin is at the forefront<sup>[4,5]</sup>.

Bathing with chlorhexidine gluconate (CHG) or skin bathing is one of the standard infection control measures<sup>[6]</sup>. Previous studies have shown that CHG reduces infection and colonization rates<sup>[6,7]</sup>. While there are a limited number of studies on drug-resistant microorganisms, they were generally evaluated for the effect of CHG on the microorganism load on the skin or the bloodstream infection, ventilator-associated pneumonia and surgical site infections observed in patients hospitalized in the ICU. These studies have been performed in adult ICUs and evaluate adult patients<sup>[5-7]</sup>. As far as we know, there is no study performed using the material method like in our study on this subject in pediatric patients.

Our study aimed to evaluate the effect of skin bathing with 2% CHG every other day in the pediatric intensive care unit (PICU) on carbapenem-resistant *Enterobacteriaceae* (CRE) and vancomycin-resistant *Enterococcus* (VRE) colonization by following a positive rectal swab sample.

### 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: 2019/04-05).

#### Participants and Skin Bathing Application With Chlorhexidine Gluconate

The study was performed at the 24-bed PICU at our Pediatric Surgery Training and Research Hospital, which is a 400-bed pediatric referral and tertiary care hospital in Izmir, Turkey. The study included rectal swab samples from the patients in 14-day periods before the CHG application for the control group and rectal swab samples 7 days before and after the CHG application for the CHG group. After the first bundle period, skin bathing with 2% CHG was added to the bundle steps as of April 2019. We included patients who met the inclusion criteria in our study from 1 November 2018 to 7 April 2019. Patients were evaluated as the control group divided into 14-day periods between 1 November 2018 and 24 March 2019. Patients were evaluated as the CHG group into a 14-day period between 25 March 2019 and 7 April 2019. Skin bathing with 2% CHG included all age groups except patients under 2 months and all the body parts excluding face and head starting from the neck, perineum, eye, and mucosal membranes. The side effects of CHG including skin rash, an allergic reaction, and skin dryness was recorded by the same two nurses during everyday visits twice a day. Patients who were hospitalized at least seven days before and seven days after this date were included in our CHG group. Gastrointestinal decolonization was not performed to the patients. Patients with insufficient hospitalization time, those with gastrointestinal symptoms, and

those who took probiotics were excluded from the study.

#### **Rectal Swab Sampling**

A rectal swab sample is routinely taken within the scope of infection control measures at our hospital's PICU two days a week. If the sample is positive, the patient is considered positive until the next routine swab scan. If the sample is negative, it is repeated at 48-hour intervals until the number of samples is 3, and when three samples are found consecutively negative, the patient is considered negative. Rectal swab samples are taken by experienced nurses working at the PICU. Materials that are 'visible soiling' in the swab sample are not sent for review.

In our clinic, apart from standard measures for the colonization control of patients, only soap and water baths are used for skin bathing, and as of April 2019, every other day skin bathing was started with 2% CHG. Therefore, CRE and VRE results obtained from the rectal swab samples of patients before and after this date were evaluated. Besides, VRE and CRE spontaneously negativity rates within 14 day periods were examined before the CHG application was initiated and compared with the CHG group. Because CRE and VRE may become negative spontaneously with other bundle applications without CHG.

It was evaluated whether CHG would be used as an infection control method by looking at the positive or negative status of swab samples of CRE and VRE before and after skin bathing with CHG.

#### **Statistical Analysis**

Statistical analysis was performed 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 for CRE and VRE ratio between the groups were calculated. Also, binary logistic regression analysis was used to evaluate CRE and VRE ratios before and after the 2% CHG skin bathing. Statistical significance level was taken as p< 0.05.

#### RESULTS

In our study, a total of 21 patients, 13 (62%) males and 8 (38%) females with a median age of 23 (IR-interquartile range: 9-48) months were included for the CHG group. Moreover, a total of 63 patients was included for the control group; 36 (57%) males and 27 (43%) females with a median age of 18 (IR: 7-32) months (Table 1). Only one of the patients who underwent skin bathing with CHG had a mild rash on the skin, there were no side effects except for this during 8 months of skin bathing every other day with CHG.

In rectal swab samples before 2% CHG, CRE was positive in 10 patients and VRE was positive in 15 patients; after 2% CHG, CRE was positive in 8 patients, and VRE was positive in 10 patients in rectal swab samples. The number of CRE positive patients was 10 (47.6%) before using 2% CHG and was 8 (38%) after using (OR: 1.5, p= 0.131, 95% CI: 0.87-1.98). Although 2% CHG decreased CRE positivity, no statistical difference was observed. However, skin bathing with CHG every other day was shown to reduce the risk of CRE colonization 1.5 times. The number of VRE positive patients was 15 (71.4%) before using CHG and was 10 (47.6%) after using (OR: 2.7, p= 0.044, 95% CI: 1.09-2.42). VRE positivity significantly decreased by 2% CHG. Every other day skin bathing with CHG reduced the risk of VRE colonization 2.7 times (Table 2).

CRE and VRE may become negative with other bundle applications in the period when CHG is not applied. In the period before the CHG 2% bathing, we looked at self-negative rates of the patients within 14 days. In this period, before bathing with CHG was initiated, 63 patients with similar age and demographic characteristics to the CHG group were included in the study as the control group. Negative rates of the patients were compared during and before CHG. Among the 63 patients in the control group, 27 patients were CRE positive, 5 (19%) were negative in 14 days and 22 (81%) patients remained CRE positive. With CHG 2% became negative in 14 days and 8 (80%) patients remained CRE positive. There was no statistically significant difference became negative in 14 days and 34 (87%) patients remained VRE positive. With CGH 2% bathing, among the 21 patients; 15 patients were VRE positive, 5 (33%) became negative within 14 days, and 10 (67%) remained VRE positive. There was a statistically significant difference between them (p=0.048) (Table 3).

#### DISCUSSION

Our study shows that every other day skin bathing with 2% CHG significantly reduces the risk of VRE colonization in PICU. It shows that it reduces the risk of CRE colonization although it is not statistically significant. We think that skin bathing with 2% CHG every other day may be one of the infection control methods for VRE and CRE in PICU.

Table 1. Demographic and clinical characteristics of the patients					
	CHG Group	Control Group			
Gender					
Male, n (%)	13 (62.0)	36 (57.0)			
Female, n (%)	8 (38.0)	27 (43.0)			
Age (months)-median (IR)	23 (9-48)	18 (7-32)			
CHG: Chlorhexidine gluconate, IR: Interquartile range, n: Number.					

Table 2. Positivity of the VRE and CRE before and after CHG for the case group					
	Before 2% CHG n (%)	After 2% CHG n (%)	р		
VRE positive	15 (71.4)	10 (47.6)	0.044		
CRE positive	10 (47.6)	8 (38.0)	0.131		
CHG: Chlorhexidine gluconate, CRE: Carbapenem-resistant Enterobacteriaceae, VRE: Vancomycin-resistant Enterococcus.					

Table 3. Control group and CHG 2% group VRE and CRE negation rates						
	Negation in 14 days					
	Positivity	n (%)	р			
CRE-before CHG	27	5 (19.0)	0.804			
CRE-after CHG	10	2 (20.0)				
VRE-before CHG	39	5 (13.0)	0.048			
VRE-after CHG	15	5 (33.0)				

CHG: Chlorhexidine gluconate, CRE: Carbapenem-resistant *Enterobacteriaceae*, N: Number, VRE: Vancomycin-resistant *Enterococcus*.

CRE and VRE have become a significant health problem, especially in the  $ICUs^{[8,9]}$ . Transmission of microorganisms from patient to patient occurs by the caregiver's hand or other contaminated appliance in the environment. If this colonization causes colonization and infection in patients, it creates a severe burden by increasing morbidity and even mortality rates in the  $ICUs^{[8-10]}$ .

Although preventing the growth of drug-resistant microorganisms is the primary intention, long-term use of antibiotics is inevitable in chronic diseases<sup>[11]</sup>. Especially in the ICUs, it is tough to prevent these microorganisms due to the use of multiple and long term antibiotics. Therefore, the use of infection control measures has become essential to prevent the spread of microorganisms recently<sup>[12]</sup>. Standard measures such as caregiver's use of hand hygiene, gloves, apron, and transmission-based measures to prevent transmission by contact, droplet, and respiration are recommended<sup>[4]</sup>. The primary purpose is to prevent potential transmission routes instead of isolating the patient<sup>[11]</sup>.

Skin bathing with 2% CHG reduces skin colonization of multidrug-resistant microorganisms such as methicillin-resistant *Staphylococcus aureus* (MRSA), CRE, and VRE. In some studies, while high CHG concentration does not correlate with low bacterial load; in some studies, it is stated that the CHG concentration increases while the bacterial load decreases<sup>[5,13]</sup>. Generally, the daily application of skin bathing with various concentrations (2% or 4%) of CHG is preferred in the ICUs. However, we know that CHG has antimicrobial activity in human skin for at least 48 hours<sup>[14,15]</sup>. Skin bathing with CHG, which is

applied every day, creates a severe burden for the caregiver in the ICUs with a high number of beds like ours. We think that skin bathing with CHG is more appropriate to continue patient care, other infection measures, and treatment processes without interruption.

CHG bathing has been shown to reduce healthcare-acquired bloodstream infections and central-line associated bloodstream infections (CLABSI) rates with various multicenter and randomized controlled trials<sup>[16,17]</sup>. In addition, Urbancic et al. have evaluated the effect of 2% CHG bathing and 1% triclosan application on CLABSI rates comparatively. They have demonstrated that 2% CHG application is superior to 1% triclosan, and significantly reduces methicillin-resistant Staphylococcus aureus skin colonization and thus CLABSI rates<sup>[18]</sup>. In our study, there was no other skin sterilization method that we compared with CHG bathing. With future studies, a comparative evaluation can be made with different skin sterilization methods.

In our study, while skin bathing with 2% CHG had a significant effect on VRE, there was no statistically significant decrease for CRE, although it decreased the rate of positivity. This may be related to the fact that CHG provides more effective antibacterial properties, especially in gram-positive bacteria such as MRSA and VRE. Most epidemiological studies have shown that CHG decreases bloodstream infections of MRSA and VRE<sup>[19,20]</sup>. However, Nadimpalli et al. have shown that CHG reduces the risk of colonization for both microorganisms in their studies where CHG evaluated the swab samples taken from the antecubital fossa and chest skin for both VRE and CRE<sup>[5]</sup>. In our study, althou-

gh the statistical effect of CHG seems only to decrease the colonization of VRE. Perhaps if we had evaluated the bacterial load in our study, we could have obtained different results.

We see that there is a need for large-scale studies on the importance of CHG and skin bathing in preventing resistant microorganisms colonization and infections. As far as we know, there is no study on this subject in our country. The evaluation of the CHG bath on resistant microorganisms and pediatric patients with different studies can provide important information to clinicians.

The main limitation of our study may be its retrospective design. We applied every other day instead of the standard daily used, it may reduce the risk of colonization for CRE even more everyday application. We did not scan for resistance to bacteria for CHG. In addition to looking at the positivity or negativity of the swab samples; in future studies, evaluation of the bacterial load can also provide relevant information to the literature.

#### CONCLUSION

In conclusion, our study showed that every other day skin bathing with 2% CHG significantly reduces the risk of VRE colonization when evaluated with a rectal swab sample. Besides, it showed that it reduced the risk of CRE colonization but no statistically significant results could be obtained. Skin bathing with 2% CHG seems to be an excellent method to prevent drug-resistant microorganism colonization.

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#### ETHICS COMMITTEE APPROVAL

The approval for this study was obtained from SBU İzmir Dr. Behçet Uz Children's Education and Research Hospital Ethical Committee (Decision no: 32 Date: 13.02.2020).

#### **CONFLICT of INTEREST**

The authors declare that they have no conflict of interest.

#### AUTHORSHIP CONTRIBUTIONS

Conception/Design: ST, EB, HA, MC, ÖS, İD, GC

Data Acquisition: ST, GA, MÇ, HA, ES

Analysis/ Interpretation: ST, UK, İD, EB, HA, MÇ

Revision and Correction: ST, NY, İD, EB, FY, ES, GA

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