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Impact of universal contact precautions and chlorhexidine bathing on the acquisition of carbapenem-resistant enterobacterales in the intensive care unit: a cohort study

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Abstract

Background For the prevention of carbapenem-resistant Enterobacterales (CRE) acquisition in the intensive care unit (ICU), the effectiveness of universal contact precautions (UCP) and chlorhexidine gluconate (CHG) bathing is controversial.

Methods With the aim of evaluating the effectiveness of UCP and CHG on CRE acquisition, this study was conducted in an ICU at a university-affiliated hospital in Seoul. Beginning in April 2017, all patients admitted to the ICU underwent weekly CRE screening and surveillance tests, and beginning in January 2018, UCP and CHG bathing were implemented for all patients. The pre-intervention period spanned from April to December 2017; the post-intervention period spanned from January 2018 to December 2019. The pre- and post-intervention CRE acquisition rates were subsequently compared using Kaplan–Meier analysis and log-rank tests, and independent risk factors for CRE acquisition were analysed using Cox proportional hazard modelling.

Results Of 1,747 patients, 35 acquired CRE during their ICU stay. The CRE acquisition rate was 1.94 and 1.45 per 1,000 patient-days before and after the intervention, respectively, with no significant difference ($p=0.357$). The incidence rate of multidrug-resistant organism (MDRO) colonisation decreased from 19.33 to 13.57 per 1,000 patient-days, with Poisson regression analysis showing a relative risk of 0.85 (95% confidence interval [CI] 0.738–0.945, $p=0.004$). Additionally, multivariable Cox regression revealed that CRE acquisition was significantly associated with carbapenem exposure (adjusted hazard ratio [aHR] 2.555, 95% CI 1.208–5.405, $p=0.013$) and the presence of more than four patients colonised with CRE during their ICU stay (aHR 2.639, 95% CI 1.157–5.243, $p=0.019$). However, UCP and CHG bathing were not significantly associated with CRE acquisition (aHR 0.657, 95% CI 0.301–1.433; $p=0.291$).

Conclusions UCP and CHG bathing did not affect the CRE acquisition rate in the ICU of a low-prevalence area. A multimodal strategy including antibiotic stewardship is necessary for controlling the nosocomial spread of MDROs.

Keywords Universal contact precautions, Chlorhexidine bathing, Carbapenem-resistant Enterobacterales

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Background

The global prevalence of carbapenem-resistant Enterobacterales (CRE) has risen significantly in recent years; in Korea specifically, there was a notable rise from 15,369 cases in 2019 to 30,548 cases in 2022 according to reports from the Korea Disease Control and Prevention Agency [1]. The therapeutic options for CRE infections are limited, and there is a growing concern about resistance to newly developed beta-lactam and beta-lactamase inhibitor combinations that constitute the primary treatment recommended in the guidelines of the Infectious Diseases Society of America [2, 3]. Recent data indicate that CRE infections are associated with higher mortality rates and prolonged hospital stays compared to those caused by carbapenem-susceptible Enterobacterales [4–6].

Universal contact precautions (UCPs) are not currently recommended as a standard infection control strategy. In a study by Harris et al., the universal gown and glove protocol (UCP) did not significantly reduce the acquisition of multidrug-resistant gram-positive bacteria, although it did lower the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) acquisition, a secondary outcome [7]. Subsequent studies have shown that UCP does not significantly reduce the acquisition of multidrug-resistant gram-negative bacteria, including carbapenemase-producing Enterobacterales, or *Clostridioides difficile* [8, 9]. However, those previous studies were conducted in intensive care units (ICUs) predominantly composed of single rooms, which limited the generalisability of their results to environments where multibed rooms are common and there is therefore a higher risk of multidrug-resistant organism (MDRO) transmission.

Chlorhexidine gluconate (CHG) bathing has been extensively investigated to reduce infection caused by gram-positive bacteria such as MRSA and vancomycin-resistant *Enterococci* (VRE). However, studies on gram-negative bacteria such as CRE are limited [10]. Previous studies have only demonstrated a reduction in CRE colonisation among ICU patients before and after intervention [11, 12]. Therefore, evidence on whether UCP and CHG bathing in ICUs with multibed rooms can effectively reduce CRE acquisition remains scarce.

Beginning in April 2017, all patients admitted to the ICU of a single university-affiliated hospital in Seoul underwent CRE screening and surveillance tests at 1-week intervals. UCP and CHG bathing were implemented for all patients beginning in January 2018, and we analysed the effect of these interventions on the acquisition of CRE infection in the ICU.

Methods

This study was conducted in an ICU that comprises a combined medical and surgical unit—with 4 isolated single rooms and 24 multibed bays—at a single university-affiliated hospital in Seoul (Additional file 1, Supplementary Figure). Beginning in April 2017, all patients admitted to the ICU underwent a CRE screening test on the day of admission, followed by subsequent surveillance tests conducted at 1-week intervals. Beginning in January 2018, UCP and CHG bathing were implemented for all ICU patients. Before the implementation of UCP, contact precautions were applied only to patients colonised with the following MDROs: MRSA, VRE, CRE, carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), and carbapenem-resistant *Acinetobacter baumannii* (CRAB).

To assess the effect of UCP and CHG bathing on CRE acquisition, we designated the time interval from April 2017 to December 2017 as the pre-intervention period. Owing to the reinforcement of infection control measures at the onset of the COVID-19 pandemic in January 2020, the post-intervention period was defined as the period from January 2018 to December 2019. During these study periods, other infection control measures such as environmental cleaning and disinfection procedures were not altered.

A rectal swab specimen was obtained from the patient on the day of ICU admission, and culture was performed using selective media for CRE (CHROMagar™ *Klebsiella pneumoniae* carbapenemase, Hangang Inc., Korea). CRE identification and antibiotic susceptibility testing were performed on clinical samples using the Microscan Walk Away 96 plus system (Beckman Coulter Inc.). Additionally, the presence/absence of carbapenem resistance was determined according to the guidelines of the Clinical and Laboratory Standards Institute. For all patients admitted to the ICU, CHG bathing was conducted once daily in the morning using a cloth impregnated with 2% CHG (Huons Meditech Inc.).

The medical records of patients admitted to the ICU between April 2017 and December 2019 were retrospectively reviewed. During this period, adults aged 18 years and above admitted to the ICU were enrolled while those who stayed in the ICU for less than 2 days were excluded. Patients in whom CRE was isolated by the screening test at the time of admission or from clinical samples obtained within 48 h of admission were also excluded. Patients whose hospital stay spanned the pre- and post-intervention periods were also excluded, as it was not possible to assess the effect of the intervention in such cases.

Baseline characteristics and variables known to be risk factors for CRE acquisition were collated [13], including age, sex, body mass index, comorbidities, Charlson comorbidity index, Sequential Organ Failure Assessment (SOFA) score at the time of ICU admission, history of antibiotic administration within 30 days, and receipt of invasive procedures. Exposure to a specific antibiotic was

defined as the administration of that antibiotic at least once within 30 days prior to CRE acquisition or ICU discharge. Invasive procedures included mechanical ventilation, tracheostomy, central venous catheter insertion, feeding tube insertion, urinary catheter insertion, and continuous renal replacement therapy. The duration of ICU stay and in-hospital mortality were also reviewed. The risk of acquiring CRE increases with the number of patients colonised with CRE during hospitalisation. Given that this can act as a confounder in CRE acquisition, we defined the colonisation pressure of CRE [14]; this was defined for each patient via a cumulative count of patients colonised with CRE who stayed in the ICU during the same period.

The primary outcome was CRE acquisition, defined as a case in which CRE was identified in the clinical samples or surveillance test performed 48 h after ICU admission but a negative test result was obtained on the initial screening test. CRE acquisition rates before and after the intervention were compared using Kaplan–Meier analysis and the log-rank test; for comparison between the pre- and post-intervention periods, continuous variables were analysed using the Mann–Whitney U test, and categorical variables were analysed using the chi-square and Fisher's exact tests. The independent risk factors for CRE acquisition were analysed using a multivariable Cox proportional hazard model. The multivariate analysis included the intervention (UCP and CHG bathing) and variables with $p<0.2$ from the univariate analysis, including a Charlson comorbidity index>3, exposure to carbapenem, and continuous renal replacement therapy.

The incidence rates of MDROs including MRSA, VRE, CRE, CRPA, and CRAB in the ICU during the study period were calculated. Additionally, compliance with hand hygiene and adherence to isolation precautions during the study period were evaluated. The temporal change in MDRO incidence, compliance with hand hygiene, and isolation precautions according to the year were also analysed using Poisson regression. Statistical analysis was performed using R software (version 4.3.3, R Foundation for Statistical Computing, Vienna, Austria).

The study protocol was approved by the Institutional Review Board of Soonchunhyang Seoul University Hospital (IRB No. 2023-09-017), which waived the need for informed consent owing to the retrospective study design.

Results

Of 1,747 patients who contributed 22,618 patient-days, 35 acquired CRE during their ICU stays. The CRE acquisition rate was 1.94 per 1,000 patient-days during the pre-intervention period and 1.45 per 1,000 patient-days during the post-intervention period. There was no significant difference in the acquisition rate of CRE according to the Kaplan–Meier analysis (log-rank $p=0.357$) (Fig. 1). The incidence rate of MDRO colonisation decreased from 19.33 per 1,000 patient-days in 2017 to 13.57 per 1,000 patient-days in 2019, and Poisson regression analysis revealed a relative risk of 0.85 (95% confidence interval [CI]: 0.738–0.945, $p=0.004$) (Table 1). The relative risk for gram-positive MDROs, including MRSA and VRE, was 0.92 (95% CI: 0.861–0.987) with a p-value of 0.02, indicating a statistically significant decrease. In contrast, the relative risk for gram-negative MDROs, including CRPA, CRAB, and CRE, was 0.90 (95% CI: 0.772–1.060) with a p-value of 0.214, showing no statistically significant decrease. During the study period, hand hygiene and isolation precaution compliance remained high, exceeding 90% and 80%, respectively, and Poisson regression did not reveal any statistically significant changes over time (Additional file 2, Supplementary Table).

Table 2 presents a comparison of baseline characteristics between the pre-intervention and post-intervention groups. In the post-intervention group, the median age and SOFA score were significantly higher at 70 years and 8 points, respectively, compared to the corresponding values of 69 years and 7 points in the pre-intervention group. First-generation cephalosporin exposure was significantly higher in the pre-intervention group at 17.7% compared to 13.5% in the post-intervention group, while carbapenem exposure was significantly higher in the post-intervention group at 27.9% compared to 20.8% in the pre-intervention group. In terms of therapeutic variables, the frequency of central venous catheter insertions was significantly higher in the post-intervention group at 65.5% compared to 56.8% in the pre-intervention group. Lastly, the length of ICU stay and in-hospital mortality rate did not differ significantly between the two periods.

The multivariable Cox regression model revealed that CRE acquisition was significantly associated with exposure to carbapenem [adjusted hazard ratio (aHR) 2.555, 95% CI 1.208–5.405, $p=0.014$] and the presence of more than four patients colonised with CRE during their ICU stay (aHR 2.639, 95% CI 1.226–5.684, $p=0.013$). No significant association was observed between UCP and CHG bathing and the acquisition of CRE (aHR 0.657, 95% CI 0.301–1.433, $p=0.291$) (Table 3).

Discussion

The findings of this study showed that the rates of CRE acquisition before and after the implementation of UCP and CHG bathing did not differ significantly. Additionally, the intervention was not identified as an independent risk factor for CRE acquisition. However, owing to the very low incidence of CRE acquisition in our study compared to other studies, these results lack generalisability [9, 15]. This study was also underpowered, which hindered the determination of the effect of UCP and

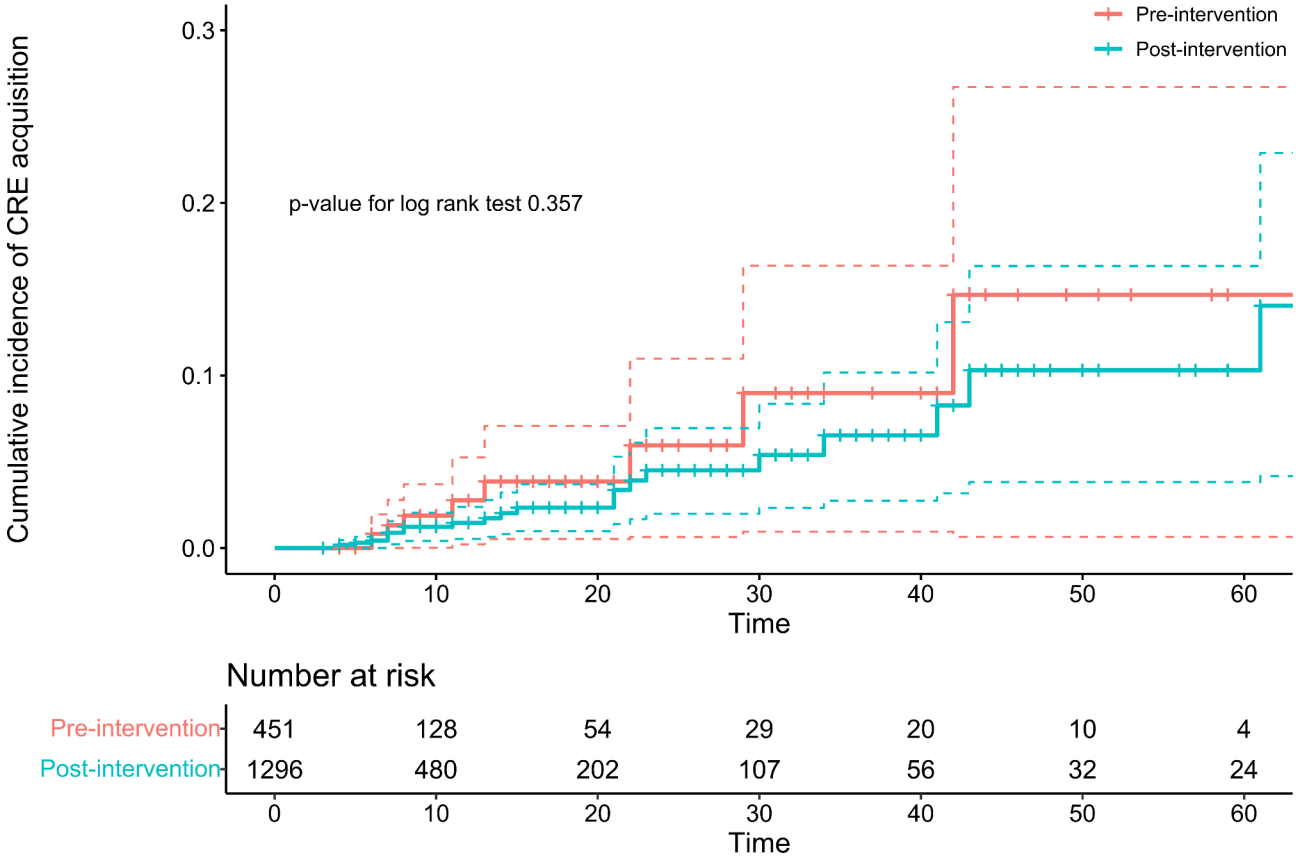

Fig. 1 Kaplan–Meier hazard plot of the acquisition of carbapenem-resistant Enterobacterales

Table 1 Annual incidence of multidrug-resistant organism colonisation (2017–2019)

	Incidence per year per 1,000 patient-days			Relative risk (95% CI)	*P*-value
	2017	2018	2019		
Total MDROs	19.330	18.189	13.567	0.85 (0.738–0.945)	0.004*
GP MDROs	9.320	6.098	5.087	0.92 (0.861–0.987)	0.020*
MRSA	7.59	5.05	3.18	0.65 (0.516–0.815)	0.000*
VRE	1.73	1.05	1.91	1.11 (0.733–1.692)	0.613
GN MDROs	10.010	12.091	8.479	0.90 (0.772–1.060)	0.214
CRPA	2.07	0.95	1.38	0.82 (0.534–1.266)	0.374
CRAB	7.08	10.41	6.78	0.94 (0.791–1.127)	0.524
CRE	0.86	0.74	0.32	0.63 (0.326–1.210)	0.165

*$P<0.05$; CI, confidence interval; MDROs, multidrug-resistant organisms; GP MDROs, gram-positive multidrug-resistant organisms; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococci*; GN MDROs, gram-negative multidrug-resistant organisms; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant Enterobacterales

CHG bathing on CRE infection. Nonetheless, the results suggest that in regions or hospitals with a low CRE incidence, UCP and CHG bathing have limited effects in addition to conventional infection control measures.

If we included other MDROs in addition to CRE or conducted the study in an area with a high CRE prevalence, the effect size and statistical power might have been higher, which may have led to different results [9, 15]. Since we only performed screening tests for CRE at admission, we could not compare the acquisition rates of other MDROs in our study. However, the significant decrease in the incidence rate of other MDROs, particularly gram-positive bacteria, in the ICU during the study period may be attributed to UCP and CHG bathing. Given the evidence supporting the effectiveness of these interventions on gram-positive bacteria—especially MRSA—as shown in previous studies [7, 10], and considering the effect of CHG bathing on the acquisition of gram-negative MDROs [10, 16], their introduction could be considered in situations where MDROs are prevalent.

Table 2 Comparison of baseline characteristics between pre-and post-intervention groups

Variable		Pre-intervention† (*n* = 451)	Post-intervention (*n* = 1296)	*P*-value
Age, years (IQR)		69 (54, 79)	70 (57, 79)	0.027*
Sex, M (%)		253 (56.1%)	727 (56.1%)	1.000
Body mass index (kg/m^2) (IQR)		22.4 (19.5, 25.2)	22.2 (19.5, 25.0)	0.661
Charlson comorbidity index (IQR)		2 (1, 4)	2 (1,4)	0.135
SOFA score (IQR)		7 (5, 10)	8 (5, 11)	0.023*
Single-room occupancy		10 (2.2%)	45 (3.5%)	0.213
Number of CRE colonisers present during ICU stay		3 (2, 3)	2 (1, 3)	0.184
Prior exposure to antibiotics				
	Beta-lactam and beta-lactamase inhibitor	240 (53.2%)	722 (55.7%)	0.379
	First-generation cephalosporin	80 (17.7%)	175 (13.5%)	0.030*
	Second-generation cephalosporin	10 (2.2%)	40 (3.1%)	0.414
	Third-generation cephalosporin	107 (23.7%)	254 (19.6%)	0.068
	Fourth-generation cephalosporin	44 (9.8%)	125 (9.6%)	1.000
	Aminoglycoside	7 (1.6%)	18 (1.4%)	0.819
	Fluoroquinolone	112 (24.8%)	321 (24.8%)	1.000
	Carbapenem	94 (20.8%)	362 (27.9%)	0.003*
	Vancomycin	119 (26.4%)	338 (26.1%)	0.901
Therapeutic variables				
	Mechanical ventilation	224 (49.7%)	678 (52.3%)	0.352
	Tracheostomy	55 (12.2%)	202 (15.6%)	0.089
	Central venous catheter	256 (56.8%)	849 (65.5%)	0.001*
	Feeding tube	262 (58.1%)	819 (63.2%)	0.056
	Urinary catheter	395 (87.6%)	1144 (88.3%)	0.736
	Continuous renal replacement therapy	85 (18.8%)	242 (18.7%)	0.944
Duration of hospital stay				
	Length of ICU stay (days) (IQR)	6 (4, 11)	7 (4, 14)	0.128
CRE acquisition		9 (2.0%)	26 (2.0%)	1.000
In-hospital mortality		142 (31.5%)	392 (30.2%)	0.635

†The intervention includes universal contact precautions and chlorhexidine gluconate bathing

*$P < 0.05$; IQR, interquartile range; M, male; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit; CRE, carbapenem-resistant Enterobacterales

Compliance of healthcare personnel with UCP and CHG bathing may have contributed to the findings of our study. Although adherence to isolation precautions in the ICU remained relatively high at over 80% throughout the study period, with no significant changes observed over time, evaluation solely by overt observers raises the possibility of overestimation due to the Hawthorne effect [17]. Additionally, CHG compliance is not monitored at our hospital, which may have impacted the study results. Inadequate CHG bathing may have also contributed. The concentration of CHG on patients' skin can be monitored using colourimetric assays to assess the appropriateness of CHG bathing. Feedback on the monitoring results can improve the appropriateness of CHG bathing by healthcare personnel [18]. If we had evaluated and provided feedback on the appropriateness of CHG bathing, it might have increased the effect size of the intervention and affected the significance of the results of this study.

Multivariable Cox regression identified recent exposure to carbapenem within the past 30 days as an independent risk factor for CRE acquisition, which underscores the importance of antibiotic stewardship in reducing the acquisition or transmission of MDROs. Studies on the effect of antimicrobial stewardship programs in reducing the incidence of multidrug-resistant gram-negative bacteria have accumulated substantial evidence [19]. Additionally, CRE colonisation pressure was also identified as an independent risk factor for CRE acquisition, suggesting the possibility that CRE acquisition during the study period occurred due to hospital transmission. This emphasises the importance of standard precautions such as environmental cleaning and hand hygiene.

As contact precautions have been recommended as part of infection control measures, studies have investigated their adverse effects [7, 20, 21]. Contact precautions can reduce the frequency of contact between healthcare workers and patients. It can also diminish patient satisfaction with medical care and lead to various psychological problems, such as depression and anxiety. Additionally, the use of disposable gowns and gloves can have a significantly negative impact on the environment [22]. Therefore, it is essential to consider the prevalence

Table 3 Risk factors for the acquisition of carbapenem-resistant Enterobacterales

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*-value	aHR	95% CI	*P*-value
Age						
≤65 years	1					
>65 years	1.113	0.544–2.278	0.769			
Sex						
Male	1					
Female	1.035	0.524–2.044	0.922			
Charlson comorbidity index						
≤3	1			1		
>3	1.756	0.886–3.482	0.107	1.478	0.729-3.000	0.279
SOFA score						
≤6	1					
>6	0.623	0.297–1.308	0.211			
Carbapenem						
Not exposed	1			1		
Exposed	2.753	1.332–5.691	0.006	2.555	1.208–5.403	0.014*
Beta-lactam and beta-lactamase inhibitor						
Not exposed	1					
Exposed	1.031	0.507-2.100	0.932			
Third- or fourth-generationcephalosporin						
Not exposed	1					
Exposed	0.866	0.419	1.789			
Vancomycin						
Not exposed	1					
Exposed	1.209	0.605–2.413	0.591			
Fluoroquinolone						
Not exposed	1					
Exposed	0.830	0.405–1.702	0.612			
Mechanical ventilation						
Not applied	1					
Applied	0.691	0.310–1.542	0.367			
Tracheostomy						
Not performed	1					
Performed	0.912	0.437–1.902	0.805			
Central venous catheter						
Not applied	1					
Applied	1.196	0.518–2.761	0.675			
Tube feeding						
Not applied	1					
Applied	0.875	0.293–2.620	0.812			
Urinary catheter						
Not applied	1					
Applied	0.845	0.297–2.407	0.753			
CRRT						
Not applied	1			1		
Applied	1.610	0.798–3.251	0.184	1.144	0.548–2.389	0.721
Number of CRE colonisers present during ICU stay						
≤4	1			1		
>4	2.715	1.256–5.869	0.011*	2.639	1.226–5.684	0.013*
Universal contact precautions and CHG bathing						
Before intervention	1			1		
After intervention	0.696	0.320–1.513	0.360	0.657	0.301–1.433	0.291

*$P<0.05$; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; SOFA, Sequential Organ Failure Assessment; CRRT, continuous renal replacement therapy; CRE, carbapenem-resistant Enterobacterales; ICU, intensive care unit; CHG, chlorhexidine gluconate

of MDROs in the region or hospital, the hospital setting (whether composed mainly of single rooms or multibed bays), and patient factors, and weigh the advantages and disadvantages before deciding to implement UCP.

Several studies have identified the effectiveness of CHG bathing in reducing the acquisition of gram-positive organisms, such as MRSA and VRE, as well as decreasing healthcare-associated infections [10, 23, 24]. However, evidence of its effectiveness against gram-negative bacteria remains limited [11, 12]. Our study was underpowered, which limits interpretation; however, we found that the effect size of UCP and CHG bathing on CRE acquisition in a low-prevalence area was not substantial. Therefore, it would not be appropriate to introduce CHG bathing solely as an intervention for multidrug-resistant gram-negative bacteria such as CRE in non-endemic areas.

A strength of this study was its large sample size and analysis of the effects of UCP and CHG bathing on CRE acquisition while considering various risk factors for CRE acquisition that could act as confounders. However, several limitations should also be considered. Surveillance cultures were not performed at discharge, potentially leading to an underestimation of CRE acquisition. Additionally, the study was statistically underpowered to detect significant differences. Temporal changes in variables, such as healthcare personnel compliance with infection control measures, which were not considered in the before-and-after design, may have acted as confounders. Furthermore, as both UCP and CHG bathing were implemented simultaneously, their independent effects could not be separated for analysis. Lastly, due to the inability to perform molecular typing, the epidemiologic relationships of the acquired CRE strains could not be assessed.

Conclusions

The implementation of UCP and CHG bathing did not affect the CRE acquisition rate in the ICU in a low-prevalence area in this study. However, the decrease in MDROs during the study period, particularly among gram-positive bacteria, may be related to the introduction of UCP and CHG bathing. These interventions should be implemented while considering factors such as the MDRO incidence in the local region, hospital facilities, and the risk to the patient population. A multimodal strategy including antibiotic stewardship should be implemented to control the nosocomial spread of MDROs.

Abbreviations

aHR	Adjusted hazard ratio
CHG	Chlorhexidine gluconate
CI	Confidence interval
CRE	Carbapenem-resistant Enterobacterales
ICU	Intensive care unit
MDROs	Multidrug-resistant organisms
MRSA	Methicillin-resistant Staphylococcus aureus
SOFA	Sequential Organ Failure Assessment
UCP	Universal contact precaution
VRE	Vancomycin-resistant Enterococci

Supplementary Information

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Supplementary Material 1: Supplementary Table. Compliance with hand hygiene and isolation precautions by healthcare workers according to year

Supplementary Material 2: Supplementary Figure. Floor plan of the intensive care unit

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Author contributions

Conceptualization, Methodology, Writing – original draft, Investigation, Data curation, Formal analysis: J.J, Y.J.B, E.L, T.H.K, Data collection and interpretation: H.P, S.O, J.C, S.A, Y.J, J.K, Writing – review & editing: J.J, Y.J.B, E.L, T.H.K. All authors have provided final approval for the final version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Soonchunhyang Seoul University Hospital (IRB No. 2023-09-017), which waived the need for informed consent owing to the retrospective study design.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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