**Effect of universal chlorhexidine decolonisation on the infection rate in intensive care patients**

Wiesława Duszyńska¹, Barbara Adamik¹, Karolina Lentka-Bera², Katarzyna Kulpa², Agata Nieckula-Schwarz², Agnieszka Litwin², Łukasz Stróżecki², Andrzej Kübler¹

¹Department of Anaesthesiology and Intensive Therapy, Wrocław Medical University, Wrocław, Poland
²Department of Anaesthesiology and Intensive Therapy, University Hospital, Wrocław, Poland

**Abstract**

**Background:** Healthcare-associated infections (HAIs), particularly intensive care unit- acquired infections (HAI-ICU), are an important cause of morbidity and mortality in hospitals. Most of these infections are caused by multidrug-resistant organisms. The results of recent studies have suggested that daily bathing with chlorhexidine (CHX)-universal decolonisation can prevent ICU infections. The purpose of the study was to determine the influence of CHX bathing on the rate and type of HAI-ICU in critically ill patients.

**Methods:** This observational study, conducted in a mixed, 16-bed tertiary ICU, compared the following three 3-month periods: I) pre-intervention (traditional soap-water bathing), II) intervention (bathing with 2% CHX clothes), and III) post-intervention (soap-water bathing). The type and rate of HAI-ICU were registered according to the European Centre for Disease Prevention and Control (ECDC) guidelines.

**Results:** A total of 272 patients were included in the study. During the intervention period, the total infection rate was significantly lower than in the pre-intervention period (12.7% vs 22.2%, respectively). Significant decreases in the rate and density of catheter-related infections (CRI) were observed during the intervention period. A decrease in the isolation rate of multidrug-resistant bacteria was also observed during the intervention and post-intervention periods.

**Conclusions:** Daily bathing of ICU patients with chlorhexidine-impregnated clothes significantly decreased the rate of HAI-ICU and the acquisition of CRI. This simple hygienic approach can be an important adjunctive intervention with the capability of reducing the burden of healthcare-associated infections in ICUs.

**Key words:** intensive care unit; healthcare-associated infections, catheter-related infections; multidrug-resistant pathogens; decolonization, universal; decolonization, skin, antiseptic, chlorhexidine

Healthcare-associated infections (HAIs) are a serious therapeutic problem in patients treated in intensive care units (ICUs). They considerably increase the morbidity and mortality of ICU patients. Moreover, they lengthen the ICU stay and substantially increase healthcare costs. ICU infections affect 30% to 50% of patients treated in ICUs [1]. They are divided into infections diagnosed on admission to the ICU, which can be non-hospital and hospital-acquired (from other hospital departments), and infections acquired during ICU treatment, i.e., HAI-ICU. The prevention of ICU infections exclusively comprises the infections that develop after 48 hours of ICU stay. HAI-ICU constitutes 10% to 50% of all infections diagnosed in ICUs, depending on the specificity of the ICU and the population of patients. Preventing HAI-ICU is one of the essential elements in the strategy of good clinical practice in ICUs. Despite the preventive measures implemented, infections still develop and their causes include impaired immunity of critically ill patients, numerous invasive interventions necessary for proper body function, intensive treatment and development of bacterial resistance to antibiotics. Multi-resistant pathogens are likely to cause up to 70% of infections that occur in ICUs [2]. Chlorhexidine is widely used for topical skin disinfection before invasive procedures are performed in ICU patients.
Because ICU infections are predominantly caused by microorganisms residing on the skin, the effective measure for preventing them is to disinfect larger skin areas and not only the catheter insertion sites. This type of management is called universal decolonisation. According to large randomised studies, universal decolonisation significantly reduces the incidence of ICU infections, particularly catheter-related bloodstream infections [3, 4].

The aim of the study was to evaluate the effects of a new prophylactic intervention, i.e., universal decolonisation using chlorhexidine, on the incidence and type of HAI-ICU. Another objective was to analyse the course of treatment during universal decolonisation and ICU as well as hospital mortality rates. Furthermore, the changes in bacterial flora causing HAI-ICU were analysed, and the safety as well as the efficacy of a new method of hygienic management were assessed.

**METHODS**

**PATIENTS**

The observational, prospective study was conducted in a 16-bed general intensive care unit between 01.09.2014 and 30.06.2015. The study design was approved by the Bioethics Committee (KB-595/2014); due to its observational nature, no informed consent from patients was required. The study included all patients treated in the ICU; however, the final analysis involved patients treated in the ICU for more than 48 hours. Three groups of patients were studied.

Group 1 — patients included in the pre-intervention period during which hygienic procedures were performed according to the traditional rules, e.g., soap-water bathing.

Group 2 — patients included in the intervention period with decolonisation conducted for all patients based on the interventional protocol of management presented below. Water and soap used during the first period were replaced with commercially available clothes impregnated with 2% chlorhexidine digluconate for skin disinfection and cleansing.

Group 3 — patients included in the post-intervention period during which the earlier management measures were applied (as in the pre-intervention period).

The exclusion criteria included an age < 18 years, skin injuries (burns and diseases) affecting more than 20% of the skin area, pregnancy and a history of hypersensitivity to chlorhexidine or skin reactions to chlorhexidine during decolonisation.

On ICU admission, all patients were assessed according to the Acute Physiology and Chronic Health Evaluation (APACHE II) score. Moreover, device utilisation (DU) was determined, i.e., the percentage of days with the use of artificial airways, central venous catheters and urinary catheters per total number of treatment days. The demographic data, microbiology results and adverse side effects associated with the use of 2% chlorhexidine digluconate were recorded in the individual patient’s medical records. The incidence and the density of HAI-ICU were compared among the three observational periods. Infections were diagnosed based on clinical symptoms as well as biochemical, imaging and microbiological findings according to the guidelines of the European Centre for Disease Prevention and Control (ECDC) [5]. The patients treated in the ICU for longer than 48 h were included for data analysis. The following infections were diagnosed: 1) intubation-associated pneumonia (IAP) (previously ventilator-associated pneumonia [VAP]); 2) catheter-related infections (CRIs) in three forms, local (CRI 1), general (CRI 2) and microbiologically confirmed (CRI 3); and 3) urinary tract infection (UTI). The incidence of infections was calculated based on the percentage of the total number of patients with hospital infections according to the total number of hospitalised patients enrolled in the study during the period analysed according to the ECDC criteria. The density of infection was calculated by dividing the total number of patients with HAI-ICU by the number of patient-days and then calculating the detailed indices, i.e., the number of IAP, CRI and UTI cases divided by a suitable number of days with the use of artificial airways, central catheters or urinary catheters, × 1,000. Infections were diagnosed by the hospital team who had long-term experience with ICU infection control. The microbiological diagnostic procedures were performed according to the accepted standards at the Microbiological Laboratory of the University Hospital in Wrocław.

**PROCEDURE OF UNIVERSAL SKIN DECOLONISATION USING CHLORHEXIDINE DIGLUCONATE**

The decolonisation procedure was performed by the nursing personnel daily at 7:15 a.m. for all ICU patients. The nursing personnel had been previously trained on how to perform proper decolonisation, and they were periodically monitored by the senior nurse. Chlorhexidine-impregnated clothes for skin disinfection and cleansing (2% Chlorhexidine Gluconate Cloth Patient Preoperative Skin Preparation, Sage Products, IL, USA) were used directly on the intact skin, avoiding the eye, mouth and ear areas. One package containing six cloths was used for one procedure. One cloth was used for a given body area and was disposed after a single use. The individual body areas were cleansed in the following order: 1) the neck, thorax and abdomen; 2) both upper extremities from the arms and armpits to the forearms and then hands; 3) hips, followed by the groin area; 4) both lower extremities, from the thighs to toes; 5) the back of the body, from the neck to the waist; 6) buttocks.
After completing the procedure, the skin was not rinsed; no liquids, moisturising lotion or other care cosmetics were applied. Skin contamination with blood, secretions or faeces occurring between the decolonisation procedures were removed using a 0.9% NaCl solution and chlorhexidine-impregnated tampons designed for this purpose. After the intervention period, the nursing staff completed the questionnaire assessing the usefulness and safety of the new hygienic intervention in the ICU.

**STATISTICAL ANALYSIS**

A statistical analysis was performed using STATISTICA 12.0 software (StatSoft, Inc., Tulsa, USA). The data were presented as the mean, standard deviation or percentage. The continuous variables were compared using the Kruskal-Wallis ANOVA test. The categorised data were compared applying the χ² test and contingency tables. \( P < 0.5 \) was considered to be statistically significant.

**RESULTS**

During the 9-month observational period, 289 patients were admitted to the ICU; 272 (94%) of them were enrolled for final analysis: 92 in group 1, 105 in group 2 and 75 in group 3. The characteristics of the patients are presented in Table 1. The clinical status of the patients assessed using APACHE II scores did not show statistically significant differences. The patients from the surgical departments constituted more than half (56%) of the hospitalised subjects. The mean duration of treatment of patients in the ICU was 13 days and 32 days in the hospital. The ICU mortality was 37% and the hospital mortality was 49%; there were no statistically significant intergroup differences observed. The analysis of groups regarding hospitalisation days (person/days), utilisation of devices such as artificial airways, central catheters, urinary catheters and indices of utilisation of individuals’ devices are presented in Table 2. The percentage of burden with invasive device utilisation was extremely high and was not considerably different in the individual study groups.

**INCIDENCE AND DENSITY OF HEALTHCARE-ASSOCIATED INFECTIONS IN THE ICU**

During the 9-month observation of 272 patients (3219 person/days of hospitalisation), hospital infections were diagnosed in 86 (31.6%) patients. The results of an analysis of the incidence of hospital-acquired infections are presented in Table 3. During the intervention period, the general incidence rates of infections (\( P = 0.04 \)) and of catheter-related infections (CRI 1–3, \( P = 0.005 \)) were found to be significantly lower. Moreover, the number of catheter-related infections confirmed microbiologically (CRI 3) decreased from 6.5% to 1.9% (66%); however, the difference was not statistically significant due to their small number.

The density of HAI-ICU is presented in Table 4. The general density of infections decreased by 48%; the difference, however, was not statistically significant. The density of catheter-related infections (CRI 1–3) was found to be substantially reduced (\( P = 0.017 \)). The density of catheter-related infections confirmed microbiologically was threefold lower (reduced from 6.3 to 2.0; \( P = 0.26 \)). The downward trend regarding the density of HAI-ICU was maintained during the post-intervention period (Fig. 1).

The most common pathogens causing HAI-ICU infections were Gram-negative bacteria (65–70%), Gram-positive bacteria (13–29%) and fungi (6–16%). The above proportions did not change considerably in the periods studied. Over half of the ICU infections were caused by alarming pathogens, i.e., *Acinetobacter baumannii* MDR (multidrug-resistant), *Klebsiella*
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Table 3. Incidence of health-associated infections in intensive care unit (HAI-ICU) in the individual groups

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>( p^a )</th>
<th>Group 3</th>
<th>( p^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 92</td>
<td>n = 105</td>
<td></td>
<td>n = 75</td>
<td></td>
</tr>
<tr>
<td>Incidence of HAI-ICU n (%)</td>
<td>38 (41.3)</td>
<td>22 (20.9)</td>
<td>0.04</td>
<td>26 (34.6)</td>
</tr>
<tr>
<td>Incidence of IAP n (%)</td>
<td>12 (13.0)</td>
<td>9 (8.6)</td>
<td>0.31</td>
<td>13 (17.3)</td>
</tr>
<tr>
<td>Incidence of CRI (1–3), n (%)</td>
<td>17 (18.5)</td>
<td>6 (5.7)</td>
<td>0.005</td>
<td>9 (12.0)</td>
</tr>
<tr>
<td>Incidence of CRI 3, n (%)</td>
<td>6 (6.5)</td>
<td>2 (1.9)</td>
<td>0.20</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Incidence of UTI, n (%)</td>
<td>9 (9.8)</td>
<td>7 (6.7)</td>
<td>0.42</td>
<td>4 (5.3)</td>
</tr>
</tbody>
</table>

*Comparison of groups 1 and 2; *comparison of groups 1 and 3; abbreviations in the text

Table 4. Density of health-associated infections in intensive care unit (HAI-ICU) in the individual groups

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<tr>
<th>Group 1</th>
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<td>n = 92</td>
<td>n = 105</td>
<td></td>
<td>n = 75</td>
<td></td>
</tr>
<tr>
<td>Density of HAI-ICU</td>
<td>36.2 ± 7.13</td>
<td>19.0 ± 2.79</td>
<td>0.09</td>
<td>25.7 ± 8.82</td>
</tr>
<tr>
<td>Density of IAP</td>
<td>16.7 ± 3.82</td>
<td>9.9 ± 0.6</td>
<td>0.22</td>
<td>16.4 ± 8.5</td>
</tr>
<tr>
<td>Density of CRI (1–3)</td>
<td>17.8 ± 15.7</td>
<td>6.1 ± 3.0</td>
<td>0.01</td>
<td>10.5 ± 3.84</td>
</tr>
<tr>
<td>Density of CRI (3)</td>
<td>6.3 ± 5.8</td>
<td>2.0 ± 1.76</td>
<td>0.26</td>
<td>2.3 ± 3.56</td>
</tr>
<tr>
<td>Density of UTI</td>
<td>9.3 ± 5.4</td>
<td>6.1 ± 1.1</td>
<td>0.40</td>
<td>4.0 ± 2.5</td>
</tr>
</tbody>
</table>

*Comparison of groups 1 and 2; *comparison of groups 1 and 3; abbreviations in the text

Figure 1. Mean density of health-associated infections in intensive care unit (HAI-ICU)

pneumoniae ESBL (extended-spectrum beta-lactamase), and Pseudomonas aeruginosa MDR. Only one methicillin-resistant Staphylococcus aureus (MRSA) infection was observed. The number of infections with alarming pathogens decreased by 32% in the intervention and post-intervention periods; however, the changes were not statistically significant.

ADVERSE EFFECTS

No redness, rash or other adverse side effects associated with the use of 2% chlorhexidine digluconate-impregnated clothes were observed. In the questionnaire, the nursing personnel assessed the procedures of universal decolonization positively or even enthusiastically.

DISCUSSION

Chlorhexidine is widely used as a topical broad-spectrum antiseptic with prolonged action against Gram(+), Gram(–) bacteria and some fungi. In the ICU, it is used for skin disinfection before the invasive placements of vascular catheters and other catheters, as an element of dressings placed over the site of catheter insertion and for impregnation of the walls of antibacterial vascular catheters [6]. Moreover, chlorhexidine is used for decontamination of the oral and nasopharyngeal cavity in critically ill patients [7]. Considering its antibacterial efficacy for topical use, chlorhexidine has been used for disinfection of larger skin areas, even the entire body, except the face (universal decolonisation).

A preliminary assessment of this method of decontamination was conducted with a retrospective control [8], and the results of the prospective study of alternating groups [9] demonstrated its effectiveness in reducing the incidence of catheter-related bloodstream infections in ICUs. Additional studies confirmed these findings [10, 11]. To objectively evaluate the effectiveness of the method, multicentre, prospective, randomised observational studies were performed. One of them involving 7727 patients demonstrated that daily skin decolonisation using chlorhexidine significantly reduced the incidence of catheter-related blood
infections, in particular the risk of infections with MRSA and vancomycin-resistant enterococcus (VRE) [3]. Another large study conducted in 74 ICUs and involving 74,256 patients revealed that daily universal decolonisation was more effective than targeted decolonisation in MRSA carriers and reduced the general incidence of healthcare-associated infections acquired in intensive care units [4]. Several critical reports were published, indicating this method’s limitations and lack of effectiveness [12–15]. Nevertheless, the recent meta-analysis demonstrated significantly reduced numbers of catheter-related bloodstream infections in ICUs and lower rates of MRSA and VRE infections [16].

Our findings demonstrated a significant 42% reduction in the total incidence of HAI-ICU during the intervention period. The density of infections decreased by 48% (not statistically significant). However, reductions in the incidence (by 65%) and density (by 66%) of catheter-related infections were found to be significant. According to the ECDE definitions, we evaluated both the incidence of catheter-related infections confirmed microbiologically (CRI 3), which is currently a standard in diagnosing catheter-related bloodstream infections, and the incidence of clinically confirmed infections without positive blood cultures (CRI 1, CRI 2). Therefore, the number of those infections was relatively high (CRI 1–3). Microbiologically confirmed bloodstream infections (CRI 3) were relatively rare; for this reason, their threefold decrease in the intervention period was not statistically significant. The reduced densities of IAP (by 41%) and UTI (by 33%) were not found to be statistically significant. The downward tendency found in the incidence and in the density of the total number of infections, in particular catheter-related infections, was observed, to a limited degree, in the post-intervention period. This finding may suggest, irrespective of chlorhexidine activity, that the improved outcomes observed in the post-intervention period could have been affected by repeated staff trainings and more attention focused on the proper bathing of patients.

The results of a large, randomised, prospective study performed by Noto et al. [15] with alternating groups involving 9340 patients from 5 ICUs of Vanderbilt University in Nashville did not demonstrate reduced HAI-ICU incidence rates in patients undergoing universal decolonisation using chlorhexidine; therefore, the authors considered this method to be ineffective. The findings of the above study have been often cited as an argument against the use of universal decolonisation in ICUs. However, our population was different from the population studied by Noto et al. In their study, the mean duration of treatment in the ICU was 2.5 days and 5 days in the hospital, whereas in our study, it was 13 days in the ICU and 32 days in the hospital. The hospital mortality in their study was 9% compared to 49% in our study. Thus, their population of patients was treated in the ICU for a short period of time and was characterised by a good prognosis as opposed to the patients treated in Polish ICUs. The incidence of HAI-ICU was also very low; and the authors stated that such a low percentage of HAI-ICU could have resulted in the lack of universal decolonisation-related benefits detected [15]. Martinez-Resendez et al. [17], who performed their study in Mexico in a population comparable to ours, confirmed the effectiveness of universal decolonisation for reduced incidences of respiratory tract and urinary tract infections. The effectiveness of universal decolonisation clearly depends on the severity of the conditions of ICU patients and their risk of HAI-ICU.

In our study, the dominating pathogens of HAI-ICU were Gram-negative bacteria, particularly from the Enterobacteriaceae family and non-fermenting bacilli. MRSA and VRE, often considered the objects of universal decolonisation, were not a clinical problem in our study. Recent reports have indicated the effectiveness of universal decolonisation with chlorhexidine in reducing the number of Gram-negative infections [18]. The recently published results of the study from South Korea demonstrated that chlorhexidine decolonisation was highly effective in reducing the incidence of carbapenem-resistant Acinetobacter baumannii [19], which is particularly important due to an increasing risk of such infections in ICUs. Our observations revealed a substantial decrease in the number of cultures with alarming pathogens in the intervention period. Although the result was not statistically significant, decreased numbers of positive cultures (by 32%) have suggested the usefulness of universal decolonisation for preventing infections with multidrug-resistant pathogens in the ICU.

A cost-effectiveness analysis was not within the scope of our study. Such an analysis will be warranted in additional multi-centre studies. However, it seems that significantly reduced incidence rates of infections should translate into economic benefits for the ICU budget.

Our study has many limitations. First, the study is based on a group of patients treated in a single centre, which may be the reason for the source of errors. Moreover, the effectiveness of the method would be better assessed in a larger population of patients and with decolonisation lasting longer than 3 months. Because the preliminary findings are encouraging, it seems well grounded to design a multi-centre research project to study the usefulness of universal chlorhexidine decolonisation in ICU patients. The findings should enable investigators to determine the role of universal decolonisation for the prevention of infections in Polish intensive care units.

**CONCLUSIONS**

1. Universal decolonisation of ICU patients using 2% chlorhexidine-impregnated clothes is an easy and effective
intervention, which is positively assessed by the nursing staff as a basic hygienic procedure in critically ill patients.
2. Universal decolonisation using chlorhexidine resulted in a reduced total incidence of HAI-ICU, especially catheter-related infections.
3. Universal decolonisation of ICU patients substantially decreased (by 32%) the number of infections with alarming pathogens.
4. Universal decolonisation using 2% chlorhexidine gluconate appears to be beneficial for reducing the incidence of HAI-ICU. Additional multi-centre studies are required to accurately determine the usefulness of this management procedure in ICU patients.

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2. Conflict of interest: none.
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Corresponding author:
Andrzej Kübler
Department of Anaesthesiology and Intensive Therapy, Wroclaw Medical University
Borowska 213, 50–556 Wrocław, Poland
e-mail: kai@umed.wroc.pl

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