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Effectiveness and safety of chlorhexidine gluconate double-cleansing for surgical site infection prevention in neonatal intensive care unit surgical patients

Jin Ah Kwon[1], **Min Jeng Cho**[1,2]

[1]*Department of Surgery, Ulsan University Hospital, Ulsan, Korea*
[2]*Department of Surgery, University of Ulsan College of Medicine, Ulsan, Korea*

Purpose: This study assessed the efficacy and safety of preoperative chlorhexidine gluconate (CHG) double-cleansing in reducing the incidence of surgical site infections (SSI) in surgical patients in neonatal intensive care units.
Methods: A retrospective chart review involved 56 patients who underwent 73 surgical procedures in the neonatal intensive care unit (NICU) from 2013 to 2022. CHG double-cleansing involves the following 2 processes. Firstly, preoperative cleansing with 0.5% CHG for elective surgeries the night before or at least 1 hour before emergency surgery. The anterior trunk cleansing spanned from the neck to the pubis, including both axillary lines. Secondly, the surgical site underwent skin preparation using 2% CHG with 72% isopropyl alcohol before an incision. A control group (2013–2018) that used iodine and a CHG group (2019–2022) employing CHG double-cleansing were compared. The occurrence of SSIs within 30 days after the surgical procedure was assessed.
Results: The overall SSI rate was 16.4% (n = 12) in the total procedures. The SSI rate was significantly higher (22.6%) in the control group; no SSI occurred in the CHG group (P = 0.029). No significant differences were observed in the other parameters. No adverse effects were observed in the CHG group.
Conclusion: CHG double-cleansing, a modified approach for surgical patients in the NICU, effectively reduced the incidence of SSI compared to traditional iodine-based skin preparations. This study supports the safe use of CHG in neonates, including premature infants, without significant complications.
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Key Words: Chlorhexidine, Neonatal intensive care units, Safety, Surgical site infection

INTRODUCTION

Surgical site infections (SSIs) pose a significant clinical challenge, with reported rates ranging from 1.5% to 30% in adult and pediatric populations postoperatively [1,2]. In neonatal intensive care units (NICU), where vulnerability is increased, SSI rates vary from 4.3% to 19%, with a staggering 40% incidence in patients undergoing surgery for necrotizing enterocolitis (NEC) [3]. SSIs not only increase morbidity and mortality but also prolong hospital stays and impose a substantial economic burden. The urgency of addressing SSI in surgical patients in NICU is underscored by its higher incidence and more severe consequences than in older children [4]. Consequently, preventing SSI in this vulnerable population is paramount and efforts are being made to reduce SSI.

Chlorhexidine gluconate (CHG) is a topical antiseptic widely

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Corresponding Author: Min Jeng Cho
Department of Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, 877 Bangeojinsunhwando-ro, Dong-gu, Ulsan 44033, Korea
Tel: +82-52-250-8797, **Fax:** +82-52-250-8093
E-mail: 0733799@uuh.ulsan.kr
ORCID: https://orcid.org/0000-0001-5247-2606

used for its broad antimicrobial activity. Despite its efficacy, caution is warranted due to the potential for excessive skin irritation and increased drug absorption, current U.S. Food and Drug Administration (FDA) product labeling of 2% CHG with 70% isopropyl alcohol (IPA) preparation solution indicates "use with care in premature infants or infants under 2 months of age" [5,6]. Despite these guidelines, surveys have indicated widespread use of CHG in NICUs in the United States, escalating from 57% in 2009 to 86% in 2014 [7]. Although side effects have been reported, the efficacy of CHG in preventing and reducing central line-associated bloodstream infections (CLABSIs) in neonates has contributed to its increased usage [8,9]. However, research on the use of CHG in the NICU has focused mainly on CLABSIs, and there is no data on its use for preparation of neonates undergoing surgery.

Recommendations for SSI prevention practices include baths and/or wipes with an antiseptic agent before the operative day which are largely based on studies evaluating preventability in adults [10]. The U.S. Centers for Disease Control and Prevention (CDC) recommends that patients be cleansed with antimicrobial soap the night before surgical intervention and recommends the use of an alcohol-based solution to clean the surgical site before an incision [11]. Many studies in adult populations have shown that preoperative baths with CHG have broad antiseptic activity, reduce skin colonization, and are associated with significantly fewer SSIs [12]. However, there are limited data in children, and no data are available in neonates [13].

We endeavored to apply the CHG baths used in adult NICU surgical patients to neonates. Modification of CHG baths used in adults has become necessary owing to the practical challenges inherent in NICU environments, characterized by ventilators and intravenous lines that complicate bathing procedures. CHG cleansing was performed once the night before surgery or at least 1 hour before surgery and again before an incision; we called this new practice "CHG double-cleansing" and applied it to NICU surgical patients.

The primary objective of this study was to assess the efficacy of CHG double-cleansing skin preparation and the incidence of SSI compared with single application iodine skin preparations in the NICU patients undergoing abdominal or thoracic surgery. The secondary objective was to evaluate the safety of CHG in neonates, including premature neonates.

METHODS

This study was conducted in accordance with the principles embodied in the Declaration of Helsinki, and ethical approval was granted by our hospital's Human Research Ethics Committee (No. 2024-02-003). Written informed consent was waived from Ethics Committee due to its retrospective nature.

We retrospectively reviewed the charts of all neonates who underwent surgical repair at the NICU between October 2013 and March 2022. Demographic and clinical data extracted from medical records included gestational age at birth, birth weight, age and weight at the time of the procedure, gender, type of operation, type and duration of prophylactic antibiotics, presence of concomitant infection, urgency of the procedure, surgical site wound closure, wound cultures, SSI development, and type and duration of treatment for SSI.

This study included only patients who underwent an open laparotomy or thoracotomy. The exclusion criteria included patients who had undergone surgery by laparoscopy or thoracoscopy, as well as those who had undergone minor surgeries such as hernia repair. In addition, patients who died within 7 days after surgery were excluded because of difficulties in evaluating the SSI.

Prior to 2019, our institution used a 10% povidone-iodine (PI) solution for preoperative skin preparation, which was limited to the surgical area before an incision. In an effort to decrease the rate of postop SSI in our institution, preoperative CHG double-cleansing was adopted in 2019. The first CHG cleansing was conducted by NICU member for elective surgeries the night before, and for emergency surgeries, it was performed 1 hour prior to surgery. The 0.5% CHG was poured directly into a sterile bowl and a sterile cotton sponge was dipped in it. Anterior trunk cleansing was performed from the neck to the pubis and both axillary lines (Fig. 1). The second CHG cleansing involved treating the surgical site before an incision with a 2% CHG formulation containing 72% IPA by a pediatric surgeon. Our standard protocol emphasized using only a minimal volume of antiseptics, ensuring avoidance of pooling in dependent areas and not washing off. Careful attention was paid to skin integrity assessment as a safety measure, given

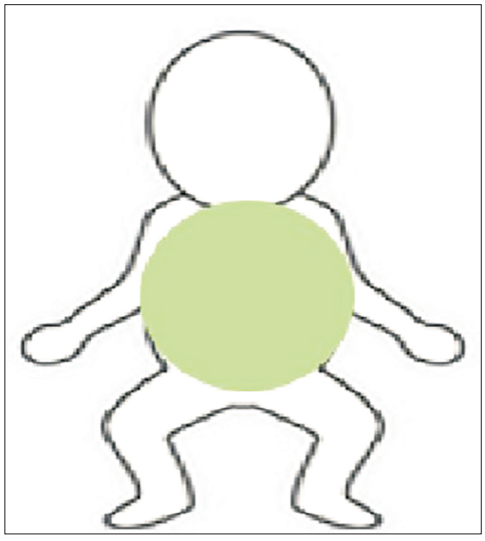

Fig. 1. The 0.5% chlorhexidine gluconate cleansing.

that skin irritation is the most reported adverse effect of CHG. A validated skin assessment of infants' skin condition included dryness, erythema, and breakdown prior to and after CHG application, with documentation in both the NICU flowsheet and operating room record.

Our institution is a level III NICU. During the study period, 2 pediatric surgeons and 2 neonatologists cared for the patients. Both specialties engaged in developing this new practice. Senior surgeons performed the surgical interventions from 2013 to 2016; and from 2017 onward, junior surgeons performed the surgeries. The infection control guidelines in our hospital's NICU state that for newborns born within the hospital, no specific screening is performed and routine blood cultures are required. However, for patients transferred from other hospitals, nasal, skin, and blood swab cultures were performed as part of the methicillin-resistant *Staphylococcus aureus* (MRSA) colonization screening. Preoperative antibiotic prophylaxis was administered within 1 hour before an incision, with antibiotics administered at a dosage based on the patient's weight. Patients who exhibited symptoms or signs of infection before surgery continued receiving antibiotic therapy. Although there is no standardized protocol for the duration of intravenous antibiotic treatment, cessation occurred once patient stability was ensured and there was no evidence of infection on blood tests.

SSIs were categorized according to the definitions set by the CDC, as outlined by the National Health and Safety Network. The patients were followed for SSI for 30 days after the surgical procedure and for all other infections until discharge. If a patient underwent more than 1 surgical procedure, the SSI was attributed to the most recent procedure unless the procedure was performed to treat an infection, such as wound debridement.

The authors compared 2 groups: controls (2013–2018) cleansed with 10% PI solution and the CHG group (2019–2022) who received CHG double-cleansing. Data are presented as the median (range). Proportions were compared using the Fisher exact test, and continuous variables were compared using the Mann-Whitney test. Statistical analysis was performed using IBM SPSS Statistics ver. 20.0 (IBM Corp.). Statistical significance was set at $P < 0.05$.

RESULTS

Fifty-two patients who underwent 73 surgical procedures were identified. Table 1 summarizes the demographic characteristics of the participants. There were 25 premature babies born before 37 weeks of age and 27 babies born after 37 weeks of age. The median age at the time of surgery was 40.1 days (range, 1–187 days). Although more patients underwent surgery immediately after birth, the median was calculated to be 40 days, as patients undergoing ostomy take-down were included. There were 27 patients who were born in our hospital and 25 were transferred from other hospitals. Among all patients, 3 premature babies died on postoperative days 31, 32, and 45 days after surgery from sepsis not related to SSI.

The patient diagnoses are presented in Table 2. There were 22 cases of NEC, 15 cases related to ostomy take-down or revision, 10 cases of midgut volvulus, 7 cases of small intestine atresia, 5 cases of meconium plug, and 5 cases of esophageal atresia. Of the 52 patients, 13 underwent 2 surgeries and 4 underwent 3 surgeries.

The overall SSI rate was 16.4% (n = 12) in all procedures. When comparing the control and CHG groups, SSI occurred in 22.6% of the patients in the control group, and in none of the cases in the CHG group ($P = 0.029$) (Table 3). There were no statistically significant differences in other parameters. No side effects were reported after CHG use.

When comparing the 12 cases with SSI and the 61 cases without SSI, there were no significant differences in gestational age, birth weight, or hospital stay (Table 4). The MRSA screening was performed in only 29 patients and the positivity rate did not differ between the 2 groups ($P = 0.785$). However, the infection rate was significantly higher in patients from other hospitals ($P = 0.018$) and in those with greater weight gain at the time of surgery ($P = 0.040$). There was no difference in the occurrence of SSI depending on the operator and there was no difference in the number of surgeries performed on the same patient. A statistically significant difference was observed when CHG double-cleansing was performed preoperatively ($P = 0.029$).

There were 12 cases of SSI (Table 5), which showed that SSI occurred not only in dirty wounds but also in clean-contaminated wounds, and 4 premature babies were included.

Table 1. Patient demographics

Characteristic	Data
No. of patients	52
Gestational age (wk)	32.9 (22–41)
≥37	27
<37	25
Birth weight (g)	2,131.9 (340–3,830)
Age at operation (day)[a]	40.1 (1–187)
Weight at operation (g)[a]	2,549.3 (440–5,510)
Birth hospital	
Ulsan University Hospital	27
Other hospitals	25
Mortality	3[b]

Values are presented as number only or median (range).
SSI, surgical site infection; UUH, Ulsan University Hospital.
[a]No. of procedures = 73. [b]Three premature babies. They died 31, 32, and 45 days after surgery because of sepsis unrelated to the SSI.

Table 2. Procedure of patients

Characteristic	Control group	CHG group	Total	P-value
Diagnosis[a]				0.440
NEC, gastric/colon perforation	18 (34.0)	4 (20.0)	22	
For stomy revision, take-down	11 (20.8)	4 (20.0)	15	
Midgut volvulus	6 (11.3)	4 (20.0)	10	
Atresia (duodenum, jejunum, ileum)	6 (11.3)	1 (5.0)	7	
Meconium plug	2 (3.8)	3 (15.0)	5	
Esophageal atresia	3 (5.7)	2 (10.0)	5	
Mechanical ileus	2 (3.8)	1 (5.0)	3	
Congenital diaphragmatic hernia	3 (5.7)	0 (0)	3	
Duplication cyst	0 (0)	1 (5.0)	1	
Intussusception	1 (1.9)	0 (0)	1	
Meckel's diverticulum	1 (1.9)	0 (0)	1	
Procedures per patient[b]				0.936
1	26 (68.4)	9 (64.3)	35	
2	9 (23.7)	4 (28.6)	13	
3	3 (7.9)	1 (7.1)	4	

Values are presented as number (%) or number only.
NEC, necrotizing enterocolitis.
[a]No. of procedures = 73. [b]No. of patients = 52.

Table 3. Control group *vs*. CHG group

Variable	Control group	CHG group[a]	P-value
No. of patients	53	20	
Sex, male:female[b]	26:9	9:8	0.378
Gestational age (wk)[b]	32.8 ± 6.4	32.9 ± 6.3	0.965
Birth weight (g)[b]	2,151.1 ± 1,188.0	2,080 ± 1,210.6	0.850
Transferred from other hospitals	21 (39.6)	8 (40.0)	0.067
MRSA[c]	8/18 (44.4)	3/11 (27.3)	0.466
Surgical site infection	12 (22.6)	0 (0)	0.029
Age at operation (day)	32.1 ± 39.2	61.2 ± 62.9	0.065
Weight at operation (g)	2,467.6 ± 1,277.9	2,766 ± 1,017.1	0.352
Operation time (min)	172.6 ± 73.6	207.0 ± 107.6	0.198
Hospital day (day)			
Preoperative	30.1 ± 39.6	56.7 ± 64.1	0.096
Postoperative	62.5 ± 46	63.2 ± 59.1	0.962

Values are presented as number only, mean ± standard deviation, or number (%)
CHG, chlorhexidine gluconate; MRSA, methicillin-resistant *Staphylococcus aureus*.
[a]No side effects were observed following CHG administration. [b]No. of patients = 52. [c]Positive cases/no. of patients examined.

Surgical site culture showed positive results in 8 patients, and MRSA or extended-spectrum β-lactamase was cultured in 4 cases. There was no mortality related to SSI, but 1 patient developed SSI immediately after surgery, which resulted in vacuum application and 5 wound revisions, followed by an enterocutaneous fistula. The fistula improved after conservative treatment.

DISCUSSION

Our study demonstrated the efficacy of a double-cleansing protocol using CHG in reducing SSI among surgical patients in the NICU and confirmed the safe use of CHG in newborns, including premature infants, without significant complications.

CHG, a chlorinated cationic polybiguanide, is the most widely used antiseptic agent [14]. Exhibiting bactericidal properties, CHG increases cell membrane permeability, resulting in rapid onset of action, and is effective against both Gram-positive and Gram-negative bacteria [15]. CHG is particularly noteworthy for its effectiveness against resistant organisms, including MRSA, vancomycin-resistant *Enterococcus*, and streptococci, which are significant causes of infection in NICU patients [12,16]. CHG

Table 4. No SSI *vs*. SSI cases

Variable	No SSI	SSI	P-value
No. of patients	61	12	
Gestational age (wk)[a]	32.2 ± 6.3	36.9 ± 4.9	0.054
Birth weight (g)[a]	2,019.8 ± 1,185.8	2,852.9 ± 934.9	0.083
Age at operation (wk)	41.9 ± 49.9	34.8 ± 39.3	0.684
Weight at operation (g)	2,420.7 ± 1,204.3	3,203.3 ± 1,074.5	0.040
MRSA[b]	8/21 (38.1)	3/8 (37.5)	0.785
CHG use	20 (32.8)	0 (0)	0.029
Transfer from other hospitals	18 (38.3)	7 (87.5)	0.018
Operator			0.112
Surgeon 1	20 (74.1)	7 (25.9)	
Surgeon 2	41 (89.1)	5 (10.9)	
Procedures per patient			0.306
1	45 (86.5)	7 (13.5)	
2	13 (76.5)	4 (23.5)	
3	3 (75.0)	1 (25.0)	
Operation time (min)	177.4 ± 85.6	205.4 ± 80.6	0.299
Hospital day (day)			
Preoperative	38.3 ± 50.5	32.9 ± 39.1	0.712
Postoperative	65.0 ± 52.0	47.4 ± 21.8	0.135

Values are presented as number only, mean ± standard deviation, or number (%)
SSI, surgical site infection; MRSA, methicillin-resistant *Staphylococcus aureus*; CHG, chlorhexidine gluconate.
[a]No. of patients=52, [b]positive cases/no. of patients examined.

also binds more strongly to proteins in the outermost layer of the skin, despite being removed by alcohol and promptly diminishing skin organisms after a single application [17].

Surgical sites face an increased risk of SSIs when tissue contains more than 10^5 microorganisms per gram of tissue. The use of CHG preoperatively reduces the microbial burden on the skin, thus minimizing intraoperative contamination at the surgical site [18]. A review of the literature indicated that CHG is more effective than iodine in reducing skin colonization, bacteremia, CLABSI, and culture contamination [19,20].

Despite the usefulness of CHG, safety issues associated with CHG preparations remain a concern for infants, including preterm infants. The national evidence-based guidelines in the United Kingdom recommend the use of 2% CHG with 70% IPA for skin antisepsis in "adults and older children" due to the lack of evidence and specific safety concerns in the infant population [21]. The CDC also offers research-based skin preparation recommendations for adults but lacks guidance for infants [11]. The immature skin of preterm infants, characterized by poor dermal-epidermal cohesion and a thin and poorly developed stratum corneum, makes them more susceptible to chemical burns, dehydration, infection, and systemic absorption of topical solutions such as CHG and iodine [22]. Owing to these characteristics, concerns about skin breakdown and percutaneous absorption are the most common reservations cited by clinicians for their hesitation to use CHG [17].

Skin irritation in the form of erythema and contact dermatitis is the most commonly reported adverse event following CHG use [14]. Although these episodes of dermatitis may have been secondary to CHG, local skin reactions after the use of CHG, particularly when associated with occlusive dressings, have been documented in multiple studies [19,23]. Interestingly, contact dermatitis has not been reported in infants undergoing full-body CHG skin cleaning when occlusive dressings are deemed unnecessary, even in very low birth weight and newborns as young as 28 weeks of gestational age [17,24]. Consistent with these findings, we did not observe any case of skin irritation, which is consistent with the perspective that skin irritation may be associated with the use of occlusive dressings. However, we emphasize the need for exercising caution during CHG use and advocate meticulous post-application skin observation. We acknowledge the importance of ongoing vigilance, as cases of skin burns have been reported after CHG use. Although rare, these instances have been observed primarily in neonates (<1,500 g) [19,25]. Caution is essential as chemical burns can cause hypothermia, excessive water loss, sepsis, and renal failure [26].

The clinical importance of detecting CHG in the blood is unknown because there are no established values that define its safe concentration. In this study, CHG concentrations in the blood of patients were not measured, preventing confirmation of systemic absorption of CHG. Mullany et al.'s review [27] revealed that after topical application of CHG, some

Table 5. SSI cases

No.	Diagnosis	Operation	Gestational age (wk)	Birth weight (g)	MRSA screening	Preoperative HD (day)	Postoperative SSI (day)	Wound culture	Antibiotics	Use of antibiotics	Complication
1	SB perforation	SB R&A	39	3,240	Negative	0	8		Ampicillin, gentamycin	6	
2	Meconium ileus	SB decompression	39	3,240		26	7		Meropenem	5	
3	Gastric perforation	Wedge resection, primary repair	41	3,800	Negative	0	20	*Escherichia coli*	Vancomycin, meropenem → meropenem	30	
4	Ileostomy due to NEC	Ileostomy T/D	22	600		103	5		Vancomycin, meropenem	14	
5	NEC	Ileal segmental resection, ileostomy	26	890	Negative	41	9	*Klebsiella pneumoniae*	Vancomycin, meropenem	8	
6	Colon perforation	Colostomy	38	3,420	MRSA(+)	0	1[b]	*Staphylococcus hemolyticus*	Vancomycin, meropenem	31	Enterocutaneous fistula
7	NEC	Colostomy T/D	28	780		78	5	*S. hemolyticus*	Vancomycin, meropenem	31	
8	Esophageal atresia	TEF ligation & EEstomy	38	2,790	Negative	3	7		Vancomycin, meropenem	12	
9	Ileal atresia	SB R&A	37	2,840	MRSA(+)	4	15	MRSA	Cefotaxime, metronidazole → vancomycin, meropenem	29	
10	Colonic atresia	Ileocolic anastomosis	30	1,310		93	1	MRSA, ESBL *E. coli*	Cefotaxime, metronidazole → vancomycin, meropenem	25	
11	Ileal atresia	Ileocecal R&A	39	2,990	MRSA(+)	2	3	MRSA	Cefotaxime, metronidazole → vancomycin, meropenem	23	
12	Jejunostomy due to midgut volvulus	Jejunostomy T/D	38	3,340	Negative	80	3	MRSA, ESBL *E. coli*	Cefotaxime, metronidazole → vancomycin, meropenem	15	

MRSA, methicillin-resistant *Staphylococcus aureus*; HD, hospital day; SSI, surgical site infection; SB, small bowel; R&A, resection and anastomosis; NEC, necrotizing enterocolitis; T/D, take-down; TEF, tracheoesophageal fistula; EEstomy, esophagoesophagostomy; ESBL, extended-spectrum β-lactamase.
[a]Gestational age, [b]open wound, vacuum application, [c]enterocutaneous fistula.

percutaneous absorption occurs, particularly in preterm infants, but only at trace levels. Although CHG was detected in the blood, none of the patients reported any side effects, including neurotoxicity or skin toxicity. However, the available safety data are incomplete. The clinical significance of elevated CHG concentrations should be determined in future clinical investigations.

Despite these issues, surveys have confirmed its use in patients with a wide range of ages and weights [16]. Surveys have shown that CHG use in the NICU increased from 57% in 2009 to 86% in 2014 in the United States [7,25]. In 2012, the FDA relaxed its labeling language for CHG from "do not use in infants of premature or low birth weight or children younger than 2 months of age" to "use with care in premature infants or infants younger than 2 months of age" [5].

However, CHG use in the NICU has primarily focused on CLABSI or cord care, with a noticeable lack of data on its application in NICU surgical patients. Despite the absence of comparative evidence of its effectiveness in SSI prevention and the documented risk of systemic toxicity through cutaneous iodine absorption and subclinical hypothyroidism, PI is commonly used as a skin preparation agent for neonatal surgery in most pediatric hospitals. A recent systematic review of 34 articles on preoperative preparation solutions for infants aged 24 weeks to 3 months revealed moderate quality evidence supporting the use of CHG over iodine for skin antisepsis before surgery [19]. The authors have also traditionally used PI; however, recent studies demonstrating the safe use of CHG in the NICU prompted a shift to CHG as a preoperative skin antiseptic for newborns, including premature infants, from 2019.

In the past, the practice of using antiseptic agents for full-body cleansing of newborns has declined in recent decades owing to the advocacy for dry skin care. Only a few studies have been conducted on whole-body CHG cleaning for neonatal infections [16]. In Norway and Nepal, the realm of complete CHG cleansing has been explored, demonstrating a reduction in superficial infections and mortality among newborns [16]. However, there is a notable absence of studies that have specifically investigated the use of CHG in surgical patients in the NICU. Berrondo et al. [13] reported the only study to evaluate the use of preoperative CHG baths in the pediatric population. The authors found that the use of preoperative antisepsis with CHG baths and wipes in pediatric patients undergoing outpatient hernia/hydrocele repair and/or orchiopexy did not affect the rate of postoperative SSI or adverse events. However, since SSI in pediatric inguinal hernia repair, hydrocele repair, and orchiopexy is low, ranging from 0.8% to 1.6%, and that studies have primarily focused on older children, Berrondo et al.'s study [13] differs from our study which targeted NICU patients and clean-contaminated/dirty wounds.

Many studies have demonstrated the efficacy of preoperative antiseptic agents using CHG baths and/or wipes in the adult population [11,21,28]. A 2017 study assessed the benefits of a pre-admission shower containing 4% CHG from a pharmacokinetic perspective by defining the appropriate dose, time, and duration [11]. Our CHG double-cleansing method, adapted from whole-body baths in adults, aims to minimize side effects and maximize the effect of the bath by covering the broadest surgical area possible, including the abdomen and chest.

Regarding the appropriate dose and presence of alcohol in CHG use, opinions in adults are still divided and there is less consensus on the appropriate guidelines for neonatal use. There have been several studies on the concentration of CHG in newborns, with contradictory results. Adams et al. [29] demonstrated that 2% CHG was more effective than 0.5% CHG at reducing colony-forming units. A systematic review indicated that 0.25% was more effective than 0.4% or 0.44% in reducing neonatal skin bacterial colonization [7]. In the study by Mullany et al. [27], the decline in skin bacterial colonization was highest in the 1.00% group, followed by the 0.50% and 0.25% groups. Therefore, the optimal concentration of CHG should be determined in future studies.

The CHG-alcohol product used for most preoperative preparations contains 70% IPA and 2% CHG. In addition to faster drying times, it is believed that the combination of alcohol and another antiseptic has synergistic effects to reduce microbial counts. In vitro studies have shown that alcohol-based CHG exhibits better bactericidal activity than aqueous CHG at the same concentration [29]. A NICU survey of the United Kingdom showed that more than half are currently using a CHG formulation containing 70% IPA [30].

The optimal number of applications of CHG to ensure the maximum concentration on the skin surface has not yet been determined. Most protocols recommend 2 to 3 separate applications of CHG prior to surgery because it is accepted that skin surface antimicrobial activity is improved after multiple applications [28]. However, there are no clinical or pharmacological data suggesting that 3, rather than 2.

In this study, a 0.5% CHG, and 2% CHG formulation containing 72% IPA was used. More detailed investigations on the concentration, presence of alcohol, and frequency and duration of CHG use are warranted. However, regardless of the concentration or application method, extreme caution is necessary regarding skin toxicity in neonates. Close observation of the skin before and after use is required, with efforts to minimize the amount of solution applied and careful attention to prevent the solution from spreading beyond the targeted area. Special care should be taken to avoid solution pooling in areas that are under or developing in infants. As demonstrated

in several studies, increased caution is crucial in extremely preterm infants.

Although this study confirmed that the use of CHG double-cleansing was effective and safe for the SSI rate in our patients based on the absence of toxicity, it has limitations, some of which are inherent in the study design. This study was retrospective in nature and compared patients with single control group, allowing the possibility of other confounding factors. Comparison solely with the PI-only group, specifically with the CHG double-cleansing protocol, limits our ability to discern whether the efficacy of preoperative skin preparation of CHG is superior to that of iodine or whether it is the result of additional cleansing associated with the modified bath concept. In addition, the inclusion of various types of procedures, different gestational ages, weights, duration of antibiotic use, specific patient situations such as septic conditions, and different times when applying CHG according to elective or emergency surgery introduces confounding factors that may affect SSI rates. More matched cohort studies are needed to identify the factors that influence SSI rates. In this study, SSIs were identified by reviewing medical records rather than in real-time evaluations, which could have led to incomplete or missing data. This study derived from a single institution experience, and the relatively small sample size emphasizes the need for larger multicenter trials to fully assess the efficacy and safety of CHG. In addition, these trials should explore variations in CHG formulations, concentrations, and combinations for use in NICU patients. Future research should focus on long-term safety considerations. Nevertheless, this study represents, to the best of our knowledge, this study represents the first attempt to apply a preoperative preparation involving CHG double-cleansing to reduce the incidence of SSI in NICU surgical patients, confirming its safety and efficacy. We anticipate that this study will serve as an initial step towards the establishment of safe standard skin preparation practices to reduce the incidence of SSI in NICU surgical patients.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID iD

Jin Ah Kwon: https://orcid.org/0000-0002-3547-7832
Min Jeng Cho: https://orcid.org/0000-0001-5247-2606

Author Contribution

All work was done by JAK, MJC.

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