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The efficacy of very low-density sodium hypochloride washes in preventing healthcare-associated infections in pediatric intensive care units

Çocuk yoğun bakım ünitelerinde sağlık hizmeti ilişkili enfeksiyonları önlemede düşük konsantrasyonlu sodyum hipokloritli banyo uygulamalarının etkinliği

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Abstract

Aim: Healthcare-associated infections (HAIs) have increased in pediatric intensive care units (ICUs) within the last decade. Maintaining hand hygiene, performing invasive interventions in accordance with aseptic techniques, contact precautions and chlorhexidine gluconate showers are the usual prevention methods against HAIs. However, despite all prevention methods, HAI incidence has globally increased in pediatric ICUs. The purpose of this study is to investigate the preventive effects of 0.005% sodium hypochlorite (NaOCl) showers against HAIs in pediatric ICUs.

Methods: This case control study was conducted in a 17-bed pediatric intensive care unit. Patients were washed with water and soap during the first six months and water and 0.005% sodium hypochlorite during the following six months, after which the incidence of HAIs was compared. The diagnosis of HAIs was made according to Centers for Disease Control and Prevention National Healthcare Safety Network guidelines.

Results: Two hundred thirty patients (118 patients in control group, 112 patients in NaOCl group) who met the inclusion criteria were included in the study. 26 patients among the control group and 20 patients among the NaOCl group were diagnosed with HAIs. In the NaOCl group, we detected 100% and 66% reductions in *P. aeruginosa* and *S. aureus* infections, respectively. There was no statistically significant difference between the groups in terms of overall HAI incidences (P=0.510). Most frequently encountered HAIs in both groups were ventilator-associated pneumonia and bloodstream infections. The rates of multidrug resistant gram-negative bacterial isolation were 77.8% (14/18) in the control group and 66.7% (5/15) in the sodium hypochlorite group. The rates of extensive drug resistant gram-negative bacterial isolation were 38.9% (7/18) in the control group and 26.7% (4/15) in the NaOCl group. There was no statistically significant difference between the two groups (P=0.458). We did not encounter any local or systemic side effects in any of our patients.

Conclusion: We found that weekly 0.005% NaOCl showers reduced *P. aeruginosa* and *S. aureus* infections, although it did not change length of hospital stay, incidence of total HAIs and the sensitivity of gram-negative bacteria to antibiotics.

Keywords: Antibiotic resistance, Chlorhexidine gluconate, Gram negative bacteria, Healthcare-associated infections, Sodium hypochlorite

Öz

Amaç: Sağlık hizmeti ile ilişkili enfeksiyonlar (SHİE) son on yılda çocuk yoğun bakım ünitelerinde (YBÜ) artış göstermiştir. El hijyeni sağlamak, girişimsel uygulamalarda asepsi şartlarına uymak, temas önlemleri ve klorheksidin glukonat banyoları, SHİE'leri önlemenin en temel yollarıdır. Ancak, tüm önlemlere rağmen, SHİE insidansının global olarak pediatrik yoğun bakımlarda artış gösterdiği görülmektedir. Bu çalışmanın amacı çocuk YBÜ'de %0,005 sodyum hipokloritli (NaOCl) banyo uygulamalarının dirençli bakteriler ile ortaya çıkan SHİE önleyip önlemeyeceğini değerlendirmektir.

Yöntemler: Bu vaka kontrol çalışması, 17 yataklı çocuk BYÜ'de prospektif olarak yapıldı. Çalışmanın ilk altı ayında hastalar sadece su ve sabun ile yıkanırken ikinci altı aylık dönemde NaOCl ile yıkandılar. SHİE tanıları hastalık kontrol ve önleme merkezinin rehberine göre konuldu.

Bulgular: Çalışma kriterlerini karşılayan 230 hasta (118 kontrol grubu, 112 NaOCl grubu) çalışmaya dahil edildi. Kontrol grubundan 26 hasta ve NaOCl grubundan 20 hastada sağlık hizmeti ile ilişkili enfeksiyon saptandı. NaOCl grubunda kontrol grubuna göre *P. aeruginosa* ve *S. aureus* enfeksiyonlarında sırasıyla %100 ve %66 oranında azalma tespit edildi. SHİE sayısı açısından gruplar arasında istatiksel olarak anlamlı fark saptanmadı. Her iki grupta da en sık görülen SHİE ventilator ile ilişkili pnömoni ve kan dolaşım yolu enfeksiyonlarıydı. Çoklu ilaç dirençli gram negatif bakteri oranı kontrol grubunda %77,8 (17/18) iken, NaOCl grubunda %66,7 (5/15) olarak saptandı. Yaygın ilaç dirençli bakteri oranı kontrol grubunda %38,9 (7/18), NaOCl grubunda %26,7 (4/15) idi. Gruplar arasında anlamlı fark yoktu (P=0,458). NaOCl uygulanan hastalarda herhangi bir lokal veya sistemik yan etki gözlenmedi.

Sonuç: Haftalık %0,005'lik NaOCl banyo uygulamalarının *P. aeruginosa* ve *S. aureus* enfeksiyonlarında azalma sağladığı, ancak hastane kalma süresi, total SHİE sayısı ve gram negatif bakterilerin antibiyotik duyarlılıklarında ise bir değişikliğe sebep olmadığı gösterilmiştir.

Anahtar kelimeler: Antibiyotik direnci, Klorheksidin glukonat, Gram negatif bakteriler, Sağlık hizmeti ilişkili enfeksiyonlar, Sodyum hipoklorit

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Introduction

Healthcare-associated infections (HAIs) affect approximately 30% of patients in intensive care units (ICUs). It increases mortality and morbidity rates, length of hospital stay, and medical expenses [1]. Therefore, prevention and reduction of HAIs in ICUs is among the most imperative issues.

HAIs include surgical-site infections, bloodstream infections (BSI), central-line-associated bloodstream infections, urinary tract infections (UTI), and ventilator-associated pneumonias (VAP). Patients' skin may be colonized with methicillin-resistant *S. aureus* (MRSA) and carbapenem–resistant *Enterobacteriaceae* during hospitalization [2]. Nowadays, prevention of these infections has become the first step in the fight against HAIs. The usual prevention methods include hand hygiene, contact precautions, and aseptic techniques in performing invasive interventions. Chlorhexidine gluconate (CHG) shower has emerged as a new strategy to prevent skin colonization [3].

Sodium hypochlorite (NaOCl) application prevents *S. aureus* colonization and infections, including MRSA, in patients with atopic dermatitis (AD) [4,5]. At concentrations of 0.025-0.5%, NaOCl is used for treatment of wounds, burns, and decubitus ulcers [6]. Several studies have shown that NaOCl is safe at the concentration of 0.005% [6-10].

Intensive bacterial colonization is an important risk factor for HAIs [11]. Increasing antibiotic resistance and difficulties in treating infections have encouraged novel studies aimed at reducing colonization. In this study, we aimed to evaluate the efficacy of NaOCl wash at a bactericidal, non-toxic concentration in reducing the incidence of HAIs in pediatric ICU patients. We also evaluated patients for any metabolic or allergic side effects of NaOCl.

Materials and methods

Patients (between the ages of 1 month to 18 years old) without any dermal lesions, open wounds or any known allergic reactions to NaOCl, and who were hospitalized in pediatric ICUs for more than 72 hours were included in the study. A washing solution of 0.005% NaOCl was prepared by mixing 100 ml 5% NaOCl with 100 liters of water. Patients' whole bodies, except the eyes and mucosal membranes, were washed with the NaOCl solution using a washcloth for 30 minutes, after which they were washed with pure water. This washing procedure was performed once a week to all patients. During the research period, routine cleaning procedures and infection control measures, such as contact precautions for cases who were colonized or infected by multidrug-resistant organisms (MDRO), were continued. We did not actively survey MDRO colonization. Routine oral hygiene with 0.12% CHG was continued in both groups.

We evaluated the incidence of HAIs as a primary outcome and positive culture samples as a secondary outcome. HAI diagnoses were based on The Centers for Disease Control and Prevention guidelines [12]. We took samples from patients suspected of having infections to demonstrate the etiological agent.

The study was initiated in March 2015. During the first six months, patients were washed with soap and water. After a month-long gap, NaOCl-wash procedure was initiated in October 2015 and lasted until April 2016. Prospective active surveillance continued. The patients' demographic data, primary diseases, reasons for hospitalization in the pediatric ICU, hospitalization and discharge (or death) dates, presence of central or urinary catheters, duration of mechanical ventilation, isolated microorganisms, and their sensitivity to antimicrobials were recorded.

Statistical analysis

We used Statistical Package for Social Sciences Version 21.0 (SPSS, Chicago, IL, USA) for statistical analysis. *P*-value <0.05 was deemed statistically significant. Shapiro-Wilk test was used for normality analysis of numerical data. Mann-Whitney U test was used to compare numerical data that are not normally distributed, and Chi-square was used to compare categorical data.

Results

During the first and second six-month long periods, 420 and 405 patients, respectively, were hospitalized in the pediatric ICU. 118 patients in the first group and 112 patients in the NaOCl group met the inclusion criteria. The mean duration of hospitalization was 27.4 days in the control group and 32.8 days in the NaOCl group. 14 (11.9%) patients from the control group and 14 (12.5%) patients from the NaOCl group died during the study. The demographic data of the patients and statistical analysis results are presented in Table 1.

Among the control and NaOCl groups, 26 and 20 patients were diagnosed with HAIs, respectively. There was no difference between the two groups in terms of total HAI incidences (*P*=0.510) (Table 2). The most commonly isolated microorganisms were *A. baumannii, K. pneumoniae*, and *P. aeruginosa* (Table 3). Antibiotic resistance of Gram-negative bacteria (GNB) did not differ among groups (Table 4). The rates of multidrug resistant Gram-negative bacteria (MDRGNB) responsible for HAIs were 76.5% (13/17) in the control group and 66.7% (10/15) in the NaOCl group. There were no significant differences between the groups in terms of MDR rate (*P*=0.472). The rates of extensively drug-resistant bacteria isolates (XDRGNB) were 41.2% (10/17) in the control group and 26.7% (4/11) in the NaOCl group, which did not differ among the two groups (*P*=0.538) (Table 5).

Toxic, allergic, or metabolic reactions against NaOCl were not detected in any of our patients during the course of this study.

Table 1: Demographic data

		Control*	NaOCl*	Total*	*P*-value
Age (month)		43 (2-204)	41 (2-190)	43 (2-204)	0.440
Duration of hospitalization (days)		21 (4-217)	23 (4-179)	33 (4-217)	0.112
Duration of mechanical ventilation (days)		3 (0-217)	4 (0-156)	4 (0-217)	0.144
Duration of central catheters (days)		0 (0-34)	0 (0-19)	0 (0-34)	0.053
Duration of urinary catheters(days)		0 (0-20)	0 (0-34)	0 (0-34)	0.532
		Control n (%)	NaOCl n (%)	Total n (%)	*P-value*
Gender	Male	64 (54.2)	59 (52.7)	123 (53.5)	0.895
	Female	54 (45.8)	53 (47.3)	107 (46.5)	
Dead		14 (11.9)	14 (12.5)	28 (12.2)	1.000

* median (min-max)

Table 2: Total number of HAIs and their percentiles

	Control n (%)	NaOCl n (%)	Total n (%)	*P*-value
VAP	9 (7.6)	6 (5.4)	15 (6.5)	0.597
BSI	9 (7.6)	7 (6.3)	16 (7)	0.798
CABSI	1 (0.8)	2 (1.8)	3 (1.3)	0.614
Pneumonia	3 (2.5)	3 (2.7)	6 (2.6)	1.000
USI	2 (1.7)	1 (0.9)	3 (1.3)	1.000
CNSI	1 (0.8)	0 (0)	1 (0.4)	1.000
SSTI	1 (0.8)	1 (0.9)	2 (0.9)	1.000
Total	26 (22)	20 (17.9)	46 (20)	0.510

BSI: Bloodstream infection, CABSI: Central-line associated bloodstream infection, CNSI: Central nervous system infection, HAIs: Healthcare associated infections, SSTI: Skin and soft tissue infection, USI: Urinary system infection, VAP: Ventilator associated pneumonia

Table 3: Distribution of HAIs according to pathological agent (n,%)

HAIs	VAP		BSI		CABSI		Pneumonia		USI		CNSI		SSTI	
Pathological Agents	CG	SG	CG	SG	CG	SG	CG	SG	CG	SG	CG	SG	CG	SG
A.baumannii	1(0.8)	2(1.8)	0	1	1(0.8)	0	0	2(1.8)	0	0	1(0.8)	0	0	1(0.9)
C. albicans	0	0	1(0.8)	0	0	1(0.9)	0	0	0	0	0	0	0	0
C. parapsilosis	0	0	0	1(0.9)	0	0	0	0	0	0	0	0	0	0
C. freundii	1(0.8)	0	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter Spp.	1(0.8)	1(0.9)	0	2(1.8)	0	0	0	0	0	0	0	0	0	0
E. faecium	0	0	1(0.8)	0	0	0	0	0	0	0	0	0	0	0
E. coli	1(0.8)	0	0	0	0	0	0	0	1(0.8)	0	0	0	0	0
K. oxytoca	0	0	1(0.8)	0	0	1(0.9)	1(0.8)	1(0.9)	0	1(0.9)	0	0	0	0
K. pneumoniae	2(1.7)	2(1.8)	1(0.8)	1(0.9)	0	0	0	0	0	0	0	0	0	0
P. aeruginosa	2(1.7)	0	2(1.7)	0	0	0	1(0.8)	0	1(0.8)	0	0	0	0	0
S. marcescens	1(0.8)	0	1(0.8)	0	0	0	0	0	0	0	0	0	0	0
S. aureus	0	1(0.9)	1(0.8)	0	0	0	1(0.8)	0	0	0	0	0	1(0.8)	0
S. epidermidis	0	0	1(0.8)	1(0.9)	0	0	0	0	0	0	0	0	0	0
S. malthophilia	0	0	1(0.8)	1(0.9)	0	0	0	0	0	0	0	0	0	0
Total	9(7.6)	6(5.4)	9(7.6)	7(6.3)	1(0.8)	2(1.8)	3(2.5)	3(2.7)	2(1.7)	1(0.9)	1(0.8)	0	1(0.8)	1(0.9)

BSI: Bloodstream infection, CG: Control Group, CABSI: Central-line associated bloodstream infection, CNSI: Central nervous system infection, HAIs: Healthcare associated infection, SG: Study Group SSTI: Skin and soft tissue infection, USI: Urinary system infection, VAP: Ventilator associated pneumonia

Table 4: Antibiotic resistance rate of gram negative bacteria

Antibiotics	Control n (%)	NaOCl n (%)	*P*-value
Cefepime and ceftazidim	15/17 (88.2)	12/15 (80)	0.645
Piperacillin-tazobactam	15/17 (88.2)	11/15 (73.3)	0.383
Aminoglycoside	9/17 (52.9)	8/15 (53.3)	1.000
Carbapenem	11/17 (64.7)	7/15 (46.7)	0.503
Fluoroquinolone	12/17 (70.6)	9/15 (60)	0.978
Colistin	0/17 (0)	0/15 (0)	-

*Number of resistant bacteria/ number of total bacteria

Table 5: MDR and XDR rates of GNB

	MDR n (%)			XDR n (%)		
	CG	SG	*P*-value	C	SG	*P*-value
Escherichia coli	2 (100)	0	(-)	1/2 (20)	0	(-)
Klebsiella Spp.	2/5 (40)	3/6 (50)	0.740	1/5 (20)	1/6(16.7)	0.887
Acinetobacter Spp.	3/3 (100)	6/6 (100)	0.635	1/3 (33.3)	3/6 (50)	(-)
Pseudomonas Spp.	5/6 (83.3)	0	(-)	4/6 (66.7)	0	(-)
Enterobacter Spp.	1/1 (100)	3/3 (100)	0.248	1 (100)	1/3 (33.3)	(-)

CG: Control Group, GNBI: Gram negative bacteria, MDR: Multidrug resistant, SG: Study Group, XDR: Extensively drug resistant

Discussion

Around 30% of ICU patients are affected by HAIs. Along with mortality and morbidity rates, HAIs also increase duration of hospitalization and healthcare costs [1]. Prolonged hospital stay increases skin colonization, which in turn leads to an increase in HAIs, blood culture contamination, and hand contamination in healthcare personnel [13,14]. Skin colonization with resistant bacteria such as MRSA, vancomycin-resistant *enterococci* and *A. baumanii* cause severe HAIs [15-17].

Incompliance with hand hygiene and barrier precautions as well as disagreements about cost-effectiveness decreases the efficacy of infection control [18,19]. Infection control precautions are generally focused on patients, infected fomites, and contact with environmental surfaces. HAIs can develop despite contact precautions, compliance with hand hygiene as well as aseptic conditions during the performance of invasive interventions [18,19].

One of the most significant factors in decreasing the rate of HAIs is to decrease skin colonization, for which the scientists are always looking for new methods. One of the most frequently used methods to reduce HAIs is CHG shower, which is currently recommended by several guidelines [20]. It has been indicated that CHG application decreased *A. baumanii*, vancomycin-resistant *enterococci*, MRSA colonization and BSI rate [13,21,22]. Although the efficacy of this method has been proven, its application is not practical in daily routine because of the inadequacy of healthcare personnel. Besides, application of CHG is costly; and unnecessary application of CHG could cause an increase in bacterial resistance [23,24].

The objective of our study was to investigate whether 0.005% NaOCl solution could be an effective, low cost, and easily applicable agent in prevention of HAIs. We gave weekly 0.005% NAOCl washes. Several studies have reported that 0.005% NaOCl showers were effective and safe in reducing *S. aureus* (including MRSA) infections and colonization in patients with atopic diseases (AD) [6-10]. NaOCl has been safely used in environmental cleaning and disinfection. It is known to be bactericidal in concentrations that are used to prevent *S. aureus* infection and colonization in AD [25,26]. At concentrations of 0.025-0.5%, NaOCl is used for antiseptic purposes for the treatment of burns, wounds and deep ulcers [4,27-31].

When mixed with water, NaOCl is converted to hypochloric acid (HOCl), which has strong antibacterial and antifungal effects. HOCl produces superoxide radicals that cause oxidative damage and cell death. HOCl is quite effective against Gram-negative and positive bacteria, spores, fungi, and viruses [25,26].

Decolonization of patients is known to prevent HAIs [32,33]. Although we did not evaluate colonization of patients in this study, we evaluated HAIs, which is an indirect indicator of colonization. We found an insignificant reduction in HAIs in the NaOCl group compared to the control group. We also found a decrease in VAP and BSI which was not statistically significant. Despite the lack of significant difference between the groups, reduction in HAIs with NAOCl wash remains an important finding.

Although the rates change according to geographical regions, GNB are responsible for 70% of VAPs and UTIs and 30% of BSIs [34]. Moreover, the GNB are responsible for up to 97.8% of all HAIs in developing countries [35]. In this study we found that GNB were responsible for all VAP and UTI infections and 84.3% of HAIs. In addition, GNB were responsible of 83.1% of HAIs in the control group and 85.7% of HAIs in the NaOCl group. There were three HAIs caused by *S. aureus* and one caused by *E.faceum* in the control group, whereas there was only one HAI caused by *S.aureus* in the NaOCl group. Although sample size was small, this study shows that very low density NaOCl is effective in reducing Gram-positive infections (especially *S. aureus*) up to 66%.

MDRGNB and XDRGNB have become major problems in the ICUs. In some developing countries, MDR and XDR rates are as high as 96% and 43.3%, respectively [35]. Therefore, besides the usual precautions to prevent HAIs, daily wash with CHG or very low-density NaOCl (which was used in this study) gained importance. Although statistically insignificant, it is promising to find reductions in HAIs rates, GNB resistance rate, MDR rate, XDR rate, and 66% reduction in *S.aureus* infection rates with NaOCl.

The CHG and NaOCl washes cannot get ahead of contact precautions. These strategies are important in terms of preventing infections that develop despite all infection control precautions. They should be considered as complementary applications.

Limitations

We gave NaOCl washes just once a week owing to the limited number of healthcare staff. The NaOCl wash period was short (6 months). We were not able to use higher concentrations of NaOCl because of safety precautions (in the literature, higher concentrations were used locally only). We could not prevent lung colonizations with this method, which posed a risk for development of VAPs (responsible for most of HAIs).

Conclusions

We could not show that NaOCl wash was effective in reducing HAIs and epidemiologically important GNBS infections, except for *P.aeruginosa*. However, we demonstrated a significant decrease in Gram-positive bacterial infections, especially those caused by *S.aureus*. Although we could not detect a significant difference between two groups, the diminution in HAI rates is promising. We proved that NaOCl wash (at concentrations used in our study) does not have any toxic, metabolic, or allergic side effects on patients. Further multicenter studies with longer durations are required to determine the efficacy of 0.005% NaOCl in prevention of HAIs.

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