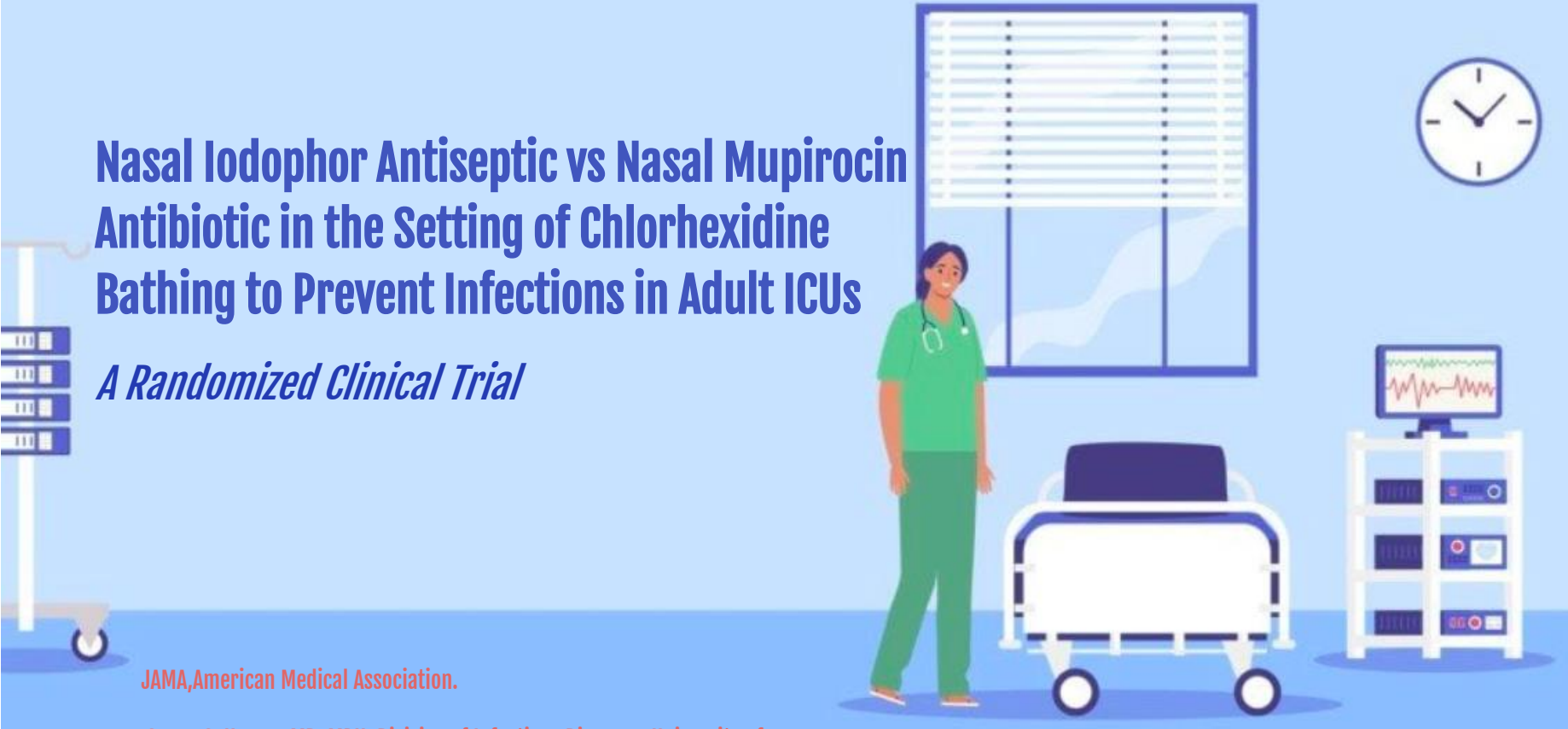
Nasal Iodophor Antiseptic vs Nasal Mupirocin Antibiotic in the Setting of Chlorhexidine Bathing to Prevent Infections in Adult ICUs

A Randomized Clinical Trial



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Susan S. Huang, MD, MPH, Division of Infectious Diseases, University of California Irvine School of Medicine, October 10, 2023,

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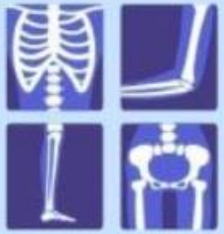


Introduction

staphylococcus aureus has remained a common pathogen in intensive care units (ICUs), with estimates in North American hospitals that S aureus has caused 23% of ICU infections.Both methicillin-susceptible S aureus and methicillin-resistant S aureus (MRSA) have produced a wide spectrum of ICU-associated infections, including ventilator- associated pneumonia, bloodstream infections, and surgical site infections

Universal nasal mupirocin plus chlorhexidine gluconate (CHG) bathing in intensive care units (ICUs) prevents methicillin-resistant Staphylococcus aureus (MRSA) infections and all-cause bloodstream infections.

While universal CHG antiseptic bathing has been broadly adopted in ICUs,adoption of mupirocin as a universal topical antibiotic has been slowed by concerns for engendering mupirocin resistance.

thus raising questions about whether an antiseptic could be advantageous for ICU decolonization.

XRFENG

Medical Iodophor Cotton Swab

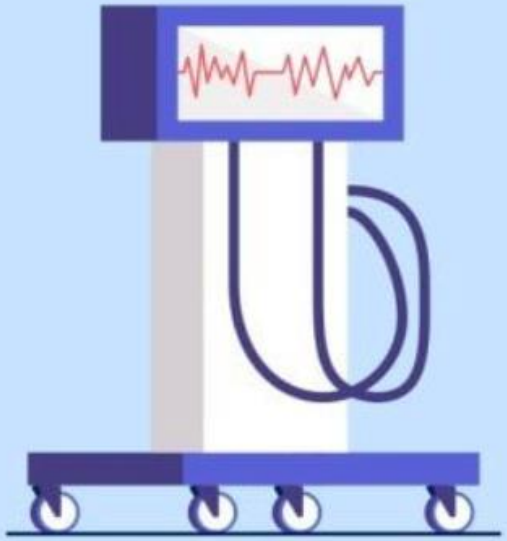
+ Easy carry
+ Individually packed
+ Cleaning and desinfaction

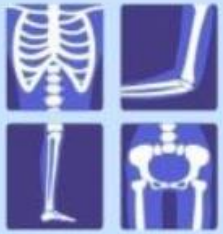
50 pcs

Iodophor removes germs that commonly live in the nose, including methicillin- resistant Staphylococcus aureus, or MRSA. MRSA is known to cause thousands of invasive infections in the United States annually. Many recent studies have shown the effectiveness of decolonization strategy in reducing risk of MRSA and other multidrug-resistant organism infections in hospitalized patients. Because having MRSA in the nose is a known risk factor for later infection

OBJECTIVE

To compare the effectiveness of iodophor vs mupirocin for universal ICU nasal decolonization in combination with CHG bathing.





METHODS

Two-group noninferiority, pragmatic, cluster-randomized trial conducted in US community hospitals, all of which used mupirocin-CHG for universal decolonization in ICUs at baseline.

Adult ICU patients in 137 randomized hospitals during baseline (May 1, 2015-April 30, 2017) and intervention (November 1, 2017-April 30, 2019) were included.

METHODS

Study Participants: 137 hospitals from 18 states participated.

ICU Details: These hospitals had 233 adult ICUs, with diverse specializations.

Intervention Period: During the 18-month intervention, there were over 353,000 admissions, contributing to 1.47 million ICU days.

Baseline Period: In the 24-month baseline, over 448,000 admissions contributed to 1.92 million ICU days.

Patient Characteristics: Patient characteristics were similar between the intervention and baseline periods.

Interventions: Two groups used different decolonization methods.

RESULTS

As-Randomized Analysis: Iodophor-CHG was less effective than mupirocin-CHG in preventing S aureus and MRSA clinical cultures. The hazard ratio for S aureus was 1.17 (18.4% higher risk with iodophor-CHG), and for MRSA, it was 1.13 (14.1% higher risk).

As-Treated Analysis: Similar results were observed when considering patients who received at least 2 doses of the intervention. The hazard ratio for S aureus was 1.27 (27.4% higher risk with iodophor-CHG), and for MRSA, it was 1.22 (21.5% higher risk).

Durability: Over 7 years, the mupirocin-CHG regimen consistently showed protective effects in reducing infections. Iodophor-CHG in the current trial outperformed the prior trial in reducing S aureus by 19.5%, MRSA by 36.6%, and all-cause bloodstream infection by 70.6%.

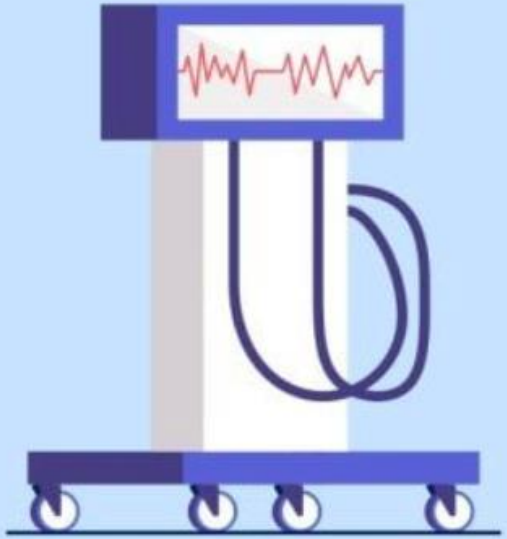


Table 1. Hospital ICU and Population Characteristics During the Baseline and Intervention Periods[a]

	24-mo Baseline period (5/1/2015-4/30/2017)		18-mo Intervention period (11/1/2017-4/30/2019)	
	Iodophor	Mupirocin	Iodophor	Mupirocin
Hospital-level ICU characteristics				
Hospitals, No.	69	68	69	68
Oncology/transplant hospital, No. (%)[b]	5 (7.2)	5 (7.4)	5 (7.2)	5 (7.4)
ICUs, No. (%)	122	111	122	111
Mixed medical/surgical	63 (51.6)	67 (60.4)	63 (51.6)	67 (60.4)
Cardiac	21 (17.2)	15 (13.5)	21 (17.2)	15 (13.5)
Surgical	15 (12.3)	10 (9.0)	15 (12.3)	10 (9.0)
Medical	12 (9.8)	10 (9.0)	12 (9.8)	10 (9.0)
Neurosurgical	11 (9.0)	9 (8.1)	11 (9.0)	9 (8.1)
Monthly ICU-attributable patient-days, mean (SD)[b]	607.3 (458.3)	560.7 (358.3)	630.7 (484.3)	568.1 (372.4)
ICU length of stay, median (IQR), d[b]	4.5 (4.1-5.3)	4.7 (4.4-4.9)	4.6 (4.2-5.0)	4.6 (4.2-4.8)
Elixhauser comorbidity count score, median (IQR)[b,c]	3.7 (3.4-4.0)	3.8 (3.6-4.2)	3.8 (3.6-4.1)	4.0 (3.8-4.3)
ICU nasal product (mupirocin or iodophor) adherence, median (IQR), %[b]	83.4 (74.1-91.2)	85.2 (73.8-91.0)	79.0 (70.6-84.2)	89.0 (84.5-94.0)
ICU chlorhexidine adherence, median (IQR), %[b]	80 (70-89)	79 (68-90)	86 (79-93)	88 (79-94)
ICU history of MRSA, median (IQR), %[b]	5.0 (3.7-7.6)	5.9 (4.2-7.6)	6.2 (4.6-8.5)	5.9 (4.7-8.6)
ICU surgery, median (IQR), %[b]	22.1 (15.3-28.3)	22.7 (13.4-27.8)	15.8 (10.1-21.1)	16.0 (9.9-22.0)
Mupirocin-resistant MRSA, mean (SD), %[b]	12.9 (10.6)	13.1 (10.9)	Not available	Not available

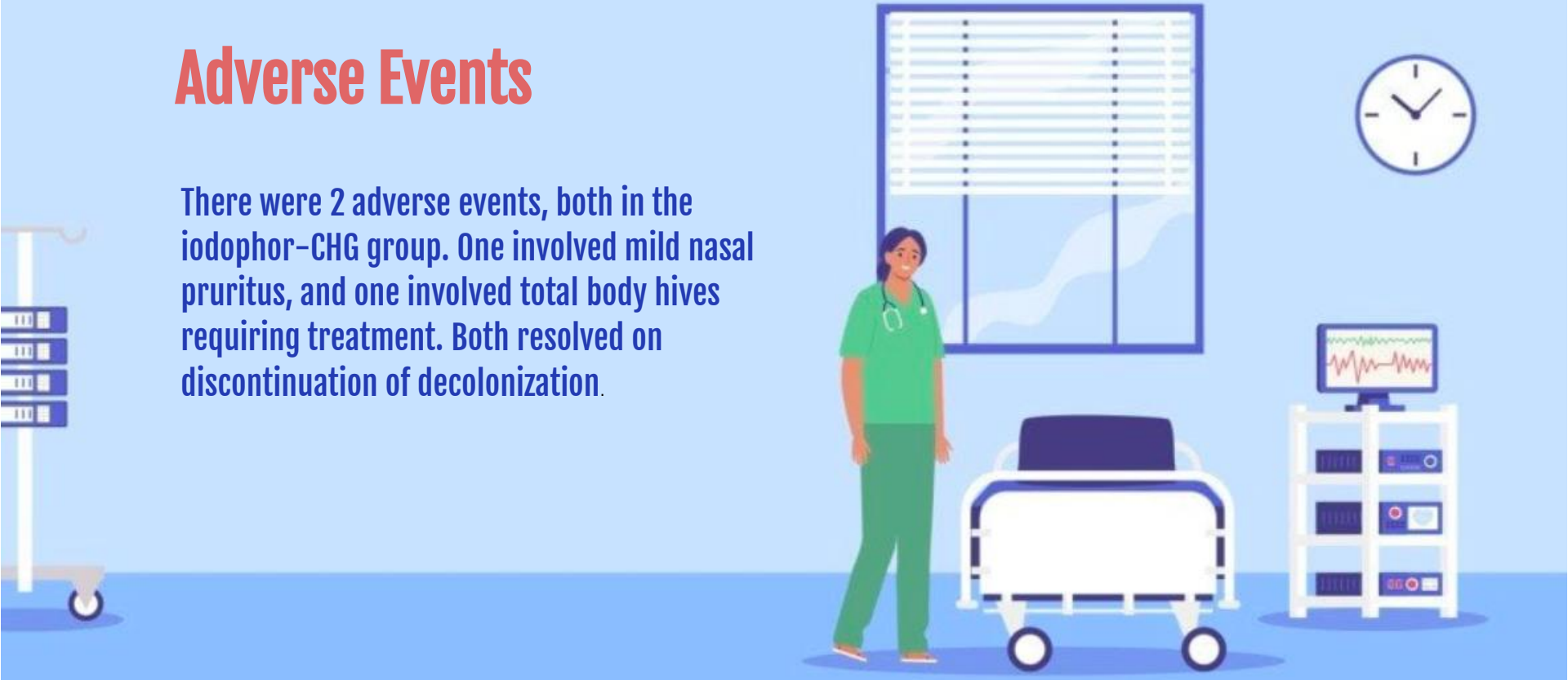
ICU population characteristics				
Admissions with ICU stay, No.	233 661	214 684	185 022	168 301
Attributable ICU patient-days, No.	1 005 648	915 141	783 346	685 169
ICU stay, median (IQR), d	3.0 (2.0-5.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)
Age, median (IQR), y	65.0 (53.0-76.0)	65.0 (53.0-76.0)	66.0 (54.0-76.0)	66.0 (54.0-76.0)
Sex, No. (%)	n = 233 578	n = 214 634	n = 184 950	n = 168 219
Male	125 796 (53.9)	115 097 (53.6)	99 756 (53.9)	90 145 (53.6)
Female	107 782 (46.1)	99 537 (46.4)	85 194 (46.1)	78 074 (46.4)
Race, No. (%)	n = 219 773	n = 200 857	n = 171 982	n = 155 666
Black/African American	34 296 (15.9)	27 932 (14.1)	27 776 (16.5)	21 901 (14.3)
White	172 946 (80.4)	162 723 (82.0)	135 060 (80.2)	126 749 (82.5)
Other[d]	12 531 (5.7)	10 202 (5.1)	9152 (5.3)	7018 (4.5)
Ethnicity, No. (%)	n = 224 084	n = 207 796	n = 176 794	n = 161 375
Non-Hispanic	196 618 (87.7)	174 731 (84.1)	154 370 (87.3)	134 092 (83.1)
Hispanic	27 466 (12.3)	33 065 (15.9)	22 424 (12.7)	27 285 (16.9)
Comorbidities, No. (%)				
Diabetes	81 134 (34.7)	76 754 (35.8)	65 689 (35.5)	61 517 (36.6)
With chronic complications	31 500 (13.5)	31 208 (14.5)	40 490 (21.9)	39 443 (23.4)
Without chronic complications	49 634 (21.2)	45 546 (21.2)	25 199 (13.6)	22 074 (13.1)
Chronic pulmonary disease	62 604 (26.8)	60 162 (28.0)	50 393 (27.2)	48 343 (28.7)
Kidney insufficiency	49 289 (21.1)	48 327 (22.5)	41 991 (22.7)	40 840 (24.3)
Obesity	38 423 (16.4)	37 461 (17.4)	37 082 (20.0)	36 143 (21.5)
Congestive heart failure	35 010 (15.0)	32 595 (15.2)	31 865 (17.2)	29 641 (17.6)
Cancer	16 010 (6.9)	14 294 (6.7)	13 495 (7.3)	12 133 (7.2)
Elixhauser comorbidity count score, median (IQR)[c]	3.0 (2.0-5.0)	4.0 (2.0-5.0)	4.0 (2.0-5.0)	4.0 (2.0-5.0)
History of MRSA, No. (%)[e]	15 940 (6.8)	13 437 (6.3)	11 704 (7.0)	13 809 (7.5)
Nasal product doses, median (IQR)	4.0 (2.0-8.0)	4.0 (2.0-8.0)	4.0 (2.0-7.0)	5.0 (3.0-8.0)
Died, No. (%)	16 903 (7.2)	14 398 (6.7)	10 305 (6.1)	12 331 (6.7)

Table 2. Group Comparisons for As-Randomized Outcomes of the Mupirocin-Iodophor Swap Out Trial[a]

	Iodophor-chlorhexidine, 69 hospitals			Mupirocin-chlorhexidine, 68 hospitals			Hazard ratio difference-in-differences	
	Raw events/1000 ICU-attributable days (No. of events/ No. of ICU-attributable days)			Raw events/1000 ICU-attributable days (No. of events/ No. of ICU-attributable days)				
	24-mo Baseline period	18-mo Intervention period	Clustered hazard ratio (95% CI)[b]	24-mo Baseline period	18-mo Intervention period	Clustered hazard ratio, (95% CI)[b]	Trial result main analysis[c]	*P* value
Primary outcome								
ICU-attributable *Staphylococcus aureus* clinical cultures	4.3 (4133/968 280)	5.0 (3563/710 051)	1.17 (1.12 to 1.23)	4.0 (3569/885 660)	4.1 (2708/663 439)	0.99 (0.94 to 1.04)	Mupirocin-CHG: 18.4% (95% CI, 10.7% to 26.6%) significant decrease over iodophor-CHG	<.001
Secondary outcomes								
ICU-attributable MRSA clinical cultures	2.1 (2036/987 177)	2.3 (1682/727 397)	1.13 (1.06 to 1.20)	2.0 (1829/899 953)	2.0 (1377/674 161)	0.99 (0.92 to 1.06)	Mupirocin-CHG: 14.1% (95% CI, 3.7% to 25.5%) significant decrease over iodophor-CHG	.007
ICU-attributable bloodstream infections	2.7 (2668/982 886)	2.7 (1956/727 346)	1.00 (0.94 to 1.06)	2.6 (2330/895 263)	2.6 (1766/672 092)	1.01 (0.95 to 1.07)	0.86% (95% CI, −8.95% to 7.96%) no difference between groups	.84

Adverse Events

There were 2 adverse events, both in the iodophor-CHG group. One involved mild nasal pruritus, and one involved total body hives requiring treatment. Both resolved on discontinuation of decolonization.

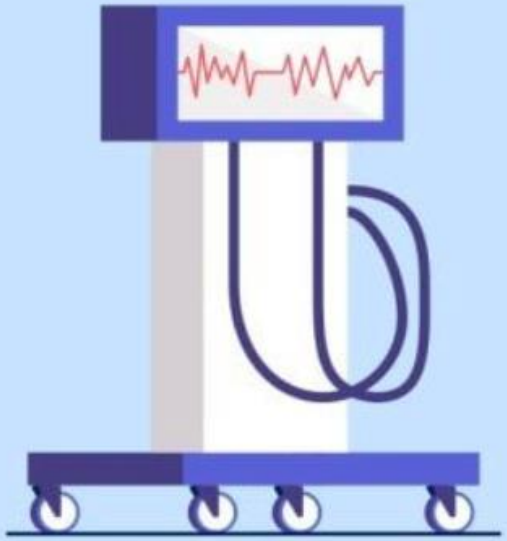


DISCUSSION

In a large-scale trial, universal mupirocin-CHG was found superior to iodophor-CHG in reducing S aureus and MRSA clinical cultures in ICU patients.

This unexpected superiority challenges previous expectations of mupirocin resistance. Despite iodophor's inferiority, it remains a viable alternative in specific situations.

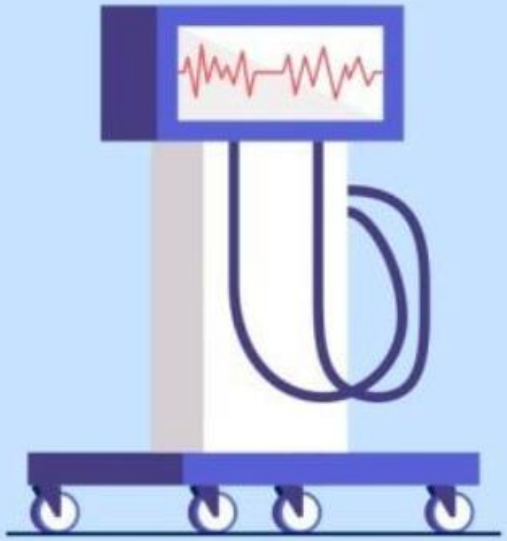
The durability of mupirocin-CHG benefits over seven years suggests no significant resistance development. Notably, the nasal product type did not impact bloodstream infection risk.



DISCUSSION

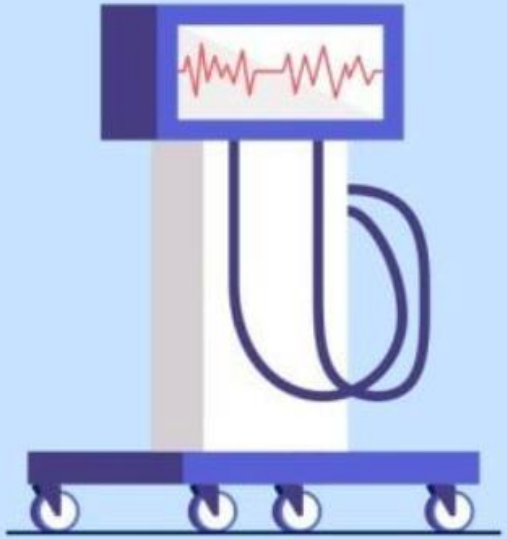
The trial, conducted in a health system familiar with universal ICU decolonization, supports mupirocin-CHG as a preferred strategy.

Limitations include potential variations in mupirocin resistance and the unexplored role of CHG alone. The findings emphasize the effectiveness of mupirocin-CHG in reducing ICU infections, particularly those caused by S aureus and MRSA.



CONCLUSION

Nasal iodophor antiseptic did not meet criteria to be considered noninferior to nasal mupirocin antibiotic for the outcome of S aureus clinical cultures in adult ICU patients in the context of daily CHG bathing. In addition, the results were consistent with nasal iodophor being inferior to nasal mupirocin.



THANK YOU FOR YOUR ATTENTION