American Journal of Infection Control 45 (2017) 401-3

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Reduction of health care–associated infection indicators by copper oxide–impregnated textiles: Crossover, double-blind controlled study in chronic ventilator-dependent patients

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Key Words:
Medical textiles
Clinical trial
Long-term care facility
Fever
Antimicrobial therapy
Mechanical ventilation

Background: Copper oxide has potent wide-spectrum biocidal properties. The purpose of this study is to determine if replacing hospital textiles with copper oxide–impregnated textiles reduces the following health care–associated infection (HAI) indicators: antibiotic treatment initiation events (ATIEs), fever days, and antibiotic usage in hospitalized chronic ventilator-dependent patients.
Methods: A 7-month, crossover, double-blind controlled trial including all patients in 2 ventilator-dependent wards in a long-term care hospital. For 3 months (period 1), one ward received copper oxide–impregnated textiles and the other received untreated textiles. After a 1-month washout period of using regular textiles, for 3 months (period 2) the ward that received the treated textiles received the control textiles and vice versa. The personnel were blinded to which were treated or control textiles. There were no differences in infection control measures during the study.
Results: There were reductions of 29.3% ($P = .002$), 55.5% ($P < .0001$), 23.0% ($P < .0001$), and 27.5% ($P < .0001$) in the ATIEs, fever days (>37.6°C), days of antibiotic treatment, and antibiotic defined daily dose per 1,000 hospitalization days, respectively, when using the copper oxide–impregnated textiles.
Conclusions: Use of copper oxide–impregnated biocidal textiles in a long-term care ward of ventilator-dependent patients was associated with a significant reduction of HAI indicators and antibiotic utilization. Using copper oxide–impregnated biocidal textiles may be an important measure aimed at reducing HAIs in long-term care medical settings.

Health care–associated infections (HAIs) contribute to morbidity, mortality, and hospitalization costs. Contaminated textiles are a potentially neglected source of nosocomial pathogens that contribute to HAIs because patients constantly shed bacteria and contaminate their linens[1-3]; bacteria readily proliferate on textiles;[2] changing linen discharges microorganisms into the air, contaminating the surroundings[4]; and personnel handling textiles can cross-contaminate other patients.[1,2] There is a correlation between microbial environmental contamination in clinical settings and infection risk.[5] Therefore, self-disinfecting surfaces are an appealing complementary strategy against HAIs.[1]

Copper kills bacteria, including antibiotic-resistant bacteria, fungi, and viruses.[6] Embedding nonsoluble copper oxide particles in textiles permanently endows them with potent broad-spectrum antimicrobial properties, which are not affected by harsh commercial laundry.[7] Its safety was demonstrated in clinical trials, without causing skin irritation, sensitization, or adverse reactions.[8]

This study examined if using copper-impregnated medical textiles would reduce HAI indicators, specifically antibiotic treatment initiation events (ATIEs), fever days, days of antibiotic treatment, and antibiotic defined daily dose (DDD) per 1,000 hospitalization days (HDs) in chronic ventilator-dependent patients in a long-term care facility.

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Funding/support: Supported by Cupron Inc.
Conflicts of interest: G.B. is an employee of Cupron Inc.

http://dx.doi.org/10.1016/j.ajic.2016.11.022

METHODS

We conducted a 7-month (February 15-September 15, 2015), double-blind, controlled, crossover study, divided into 2 intervention periods of 3 months, separated by a 1-month washout period. All patients in 2 similar ventilator-dependent wards in a long-term care hospital were included in the study. The study was approved by the institutional review board, and a waiver for informed consent was given. During period 1, one ward received copper oxide–impregnated linen and hospital patients' clothes and towels, and the other ward received control untreated textiles; in period 2, the ward that received the treated textiles received the control textiles and vice versa. During the washout period, both wards received usual hospital textiles. The treated textiles, listed as Food and Drug Administration class I medical devices, contained 1% wt/wt microscopic copper oxide particles.[7] The textiles were color-coded, and all personnel were blinded to which were the treated or control textiles. The textiles were used and laundered together in the same fashion. The infection control measures were the same in both wards. The decision to initiate antimicrobial therapy and its duration involved in all cases the same attending physician and infectious diseases consultant. The infection control nurse blindly recorded ATIEs, fever (axillary temperature >37.6°C) days, antibiotic treatment days, and antibiotic DDD calculated per 1,000 HDs. Only indicators that started at least 24 hours after the beginning of periods 1 and 2 until the last day of each period were recorded. The DDD was calculated according to the World Health Organization Collaborating Centre for Drug Statistics Methodology guidelines (http://www.whocc.no/atc_ddd_index/).

Patient's hospitalization duration, age, sex, presence of diabetes, colostomy, indwelling urinary catheters, feeding tubes, pressure sores (on admission), antimicrobial resistant bacteria, and being bed- or chair-bound were retrieved from patients' files.

Statistical analysis

The χ^2 and *t* tests were applied to compare patient's characteristics between the study groups. The χ^2 tests were applied for testing difference in rates of studied HAI indicators. All tests were 2-tailed, and $P \leq .05$ was considered statistically significant. The data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

When comparing the patients' characteristics according to the textiles used in both periods, there were no statistically significant differences between the groups (Table 1).

When ATIEs were stratified according to the textiles used and normalized to 1,000 HDs (Table 2), there was a 29.3% relative reduction in ATIEs when using treated textiles ($P = .002$). Furthermore, there was 55.5% decrease in the number of fever days in the patients in the wards that used the treated textiles ($P < .0001$). Consequently, there were 23.0% and 27.5% reductions in days of antibiotic treatment and DDD administrated in the treated versus control wards ($P < .0001$).

Similarly, when stratifying the data according to wards, there were statistically significant reductions in all indicators between both periods in each ward when using the treated textiles, except ATIEs in one of the wards. When stratifying the indicators according to periods 1 and 2, there were statistically significant reductions in all indicators, with the exception of DDD in period 1 (data not shown).

No skin irritation or adverse reactions occurred.

Table 1
Patients' characteristics according to the textiles used

Characteristic	Wards using control textiles	Wards using copper oxide–treated textiles	*P* value
No. of patients	54	58	NA
Hospitalization days	4,050	4,159	NA
Females/males			
No.	22/32	24/34	NA
Ratio	0.688	0.706	.61
Age (y)			
Mean ± SD	69.8 ± 15.0	71.3 ± 15.8	.42
Range	24-98	31-98	
Median	72	72	
Diabetes	10 (18.52)	10 (17.24)	.70
Colostomy	2 (3.70)	3 (5.17)	.72
Pressure ulcers	33 (61.11)	32 (55.17)	.45
Urinary catheter	41 (75.93)	36 (62.07)	.08
Bed- or chair-bound	52 (96.30)	56 (96.55)	.91
Feeding tube*	47 (87.04)	53 (91.37)	.43
Carriers of antimicrobial-resistant bacteria†	37 (68.52)	39 (67.24)	.74

NOTE. Values are n (%) or as otherwise indicated.
NA, not applicable.
*Either percutaneous endoscopic gastrostomy or nasogastric tube.
†Antimicrobial resistant bacteria: methicillin-resistant *Staphylococcus aureus*, carbapenem-resistant *Enterobacteriaceae*, vancomycin-resistant *Enterococcus*, and multidrug-resistant microorganisms.

DISCUSSION

The effect of copper oxide–containing textiles that are in contact with patients on bioburden or HAIs in clinical settings is being explored. Approximately 50% lower bioburden was found on sheets containing copper oxide than regular sheets when used by general ward patients.[7] Replacing linens and personnel's uniforms with copper oxide–impregnated products in a long-term-care ward for brain injuries resulted in 24%, 47%, and 32.8% reductions in HAI, fever days, and total number of days of antibiotic treatment per 1,000 HDs, respectively.[9] In a recent quasi-experimental study, the combined use of copper oxide–impregnated composite hard surfaces and linens in an acute care 204-bed, community hospital resulted in 78% ($P = .023$) lower HAIs caused by multidrug-resistant organisms or *Clostridium difficile*, relative to the baseline period.[10]

Our crossover-controlled study demonstrated that using copper oxide–impregnated textiles in chronically ventilator-dependent patients' wards results in reduction of HAI indicators. The reductions were statistically significant when analyzing the data according to the textiles used (combining both wards), and for most indicators when comparing both wards in each period and when comparing between both periods in each ward, therefore eliminating possible interferences (biases) produced by seasonal situations, outbreaks of infection, and differences among wards, nursing teams, and patients, which were not fully controlled in previous studies.

The decision to initiate antibiotic therapy is usually taken based, not only on the presence of fever, but also on a combination of other clinical and laboratory data. In this study, this decision involved the same attending physician and infectious diseases consultant in both wards, therefore strengthening the validity of the results. This was the decision process at the wards before the study initiation; therefore, the study results reflect the effect of the intervention of changing the medical textiles in the wards in real life.

We routinely measure patients' temperature 3 times a day via the axillary route, and we define fever as a temperature >37.6°C. Axillary measurement has its limitation, being inaccurate in comparison with rectal measurement, with a lower sensitivity in detecting fever.[11] Because the definition of fever was the same throughout the study, the effect of the intervention on the number of fever days is meaningful. Infections in older frail adults, and in younger patients with

Table 2
Health care–associated infection–related indicators: copper oxide–treated versus control textiles

Indicator	Control textiles	Copper oxide–treated textiles	P value	Relative reduction (%)
ATIEs	95	69	NA	NA
ATIEs per 1,000 HDs	23.46	16.59	.002	29.3
95% CI	19.09-28.69	13.02-21.08		
FDs (>37.6°C)	188	86	NA	NA
FDs per 1,000 HDs	46.42	20.68	<.0001	55.5
95% CI	40.24-53.47	16.67-25.60		
dAB	689	545	NA	NA
dAB per 1,000 HDs	170.12	131.04	<.0001	23.0
95% CI	158.71-182.09	121.01-141.76		
AB DDD	845	629	NA	NA
DDD per 1,000 HDs	208.6	151.2	<.0001	27.5
95% CI	196.2-221.5	140.5-162.5		

AB, antibiotic; *ATIE*, antibiotic treatment initiation event; *CI*, confidence interval; *dAB*, days of antibiotic treatment; *DDD*, defined daily dose; *FD*, fever day; *HD*, hospitalization day; *NA*, not applicable.

severe neurologic impairment, can present atypically without fever.[12] Reduction in fever days was the most pronounced result of the intervention (reduction of 55.5%).

The reduction in antibiotic treatment days is mainly caused by reduction in ATIEs. The DDD per 1,000 HDs, used in drug utilization research, reflects the amount of antibiotics used, which is influenced by the days of antibiotic therapy and daily dosage (influenced, for example, by renal impairment), and the number of antibiotics prescribed simultaneously.

We did not aim to define the source of infection that initiated antimicrobial therapy because in chronically mechanically ventilated patients, the clinical, radiographic, and laboratory data are nonspecific. It is difficult to define the source of infection, which can be from multiple potential sites, such as respiratory, urinary tract (high prevalence of indwelling urinary catheters), pressure ulcers, and so forth. Positive cultures from tracheal secretion or urine may represent colonization and do not necessarily indicate infection. Consequently, we could not ascertain the effect of the intervention on specific HAIs, which is a limitation of the study.

Reduction of antibiotic treatment not only reduces costs, but, also more importantly, is central in the combat against the development of antibiotic-resistant bacterial strains. Further studies are needed to assess the effect of copper oxide–impregnated textiles on infection rates, with a larger sample of patients in various acute settings and long-term care facilities.

In conclusion, our study adds an important layer to the in vitro studies and the previous open-label studies supporting the effect of copper oxide–impregnated medical textiles as a possible supplement to other measures aimed at reducing the rate of HAIs.

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