Two formulations of Copper-Nickel Alloy on High Touch Surfaces in Bone Marrow Transplant Patient Rooms show Consistent Reduction of Microbial Bioburden

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Abstract

Introduction: Copper surfaces have been promoted as a strategy to minimize environmental contamination but few studies have examined its antimicrobial efficacy over time.

Objective: This pilot project assessed the impact of re-engineered rooms on bacterial bioburden and protein load / organic matter as measured by colony counts and ATP bioluminescence.

Methods: Nine patients with acute myeloid?leukemia were randomized to a regular private room or re-engineered room with copper on high-touch surfaces, titanium dioxide coating on walls, water filters on bathroom faucets and shower heads and wall mounted ultraviolet C light in dedicated washrooms. Weekly RODAC cultures of air, water, and high-touch surfaces as well as ATP bioluminescence (ATPB) testing were performed during this 18 month long project.

Results: Average ATPB RLU in standard rooms was 500.8 ± 707.9 RLU compared to re-engineered rooms of 71.9 ± 302.6 RLU ($p<0.0001$). Copper alloy surfaces in re-engineered rooms contributed to an overall 85.7% reduction in RLU compared to standard room surfaces. Overall average RODAC™ plate count in standard rooms was 73.02 ± 301.3 CFU/plate compared to the overall average RODAC™ plate count for copper surfaces of 7.21 ± 17.7 CFU/plate ($p=0.008$). Copper alloy surfaces in re-engineered rooms contributed to an overall 90.1% reduction in CFU/plate compared to standard room surfaces. In a regression model that fit copper (Y/N), UVC exposure, surface type, and patient, copper surfaces were independently associated with a lower bioburden compared to non-copper surfaces

Conclusion: Copper on high-touch surfaces is a useful mitigation strategy to reduce microbial bioburden.

Introduction

Multiple studies have demonstrated that manual cleaning and disinfection of hospital surfaces is suboptimal with some articles reporting only 40-50% compliance with cleaning. [1-3] These findings, combined with studies demonstrating an increased risk of acquisition of an antibiotic resistant organism (ARO) in rooms previously occupied by a patient with an ARO have resulted in the development of adjunctive mitigation strategies such as self-disinfecting surfaces[4,5] A number of studies have demonstrated the potential for copper-containing surfaces to reduce healthcare acquired infections (HAI) in the clinical setting[6-8]. These studies assessed all solid copper surfacing or composite surfaces, and a few performed serial cultures over long periods of time. None of the previous studies used ATP bioluminescence (ATPB) in tandem with microbial colony counts, as a measure of both viable micro-organisms and organic matter..

This project examined the environment of nine patients undergoing myeloablative (allogeneic) transplantation who were randomized to stay either in a re-engineered room containing various formulations of copper on high touch surfaces or placed in a standard bone marrow transplant (BMT) room. The objective of the pilot was to assess the impact of re-engineered BMT rooms on microbial bioburden ?as measured directly by colony counts and indirectly by ATP bioluminescence[9] A secondary objective was to use the same methods to determine whether there were differences in microbial bioburden between the six high-touch copper alloy surfaces used in the pilot project.

Methods

Study Design and Setting: This 18 month pilot project was conducted in the 26-bed Bone Marrow Transplant Unit (BMTU) at Vancouver General Hospital, Vancouver, Canada from April 2015 to October 2016. Three single patient rooms with dedicated bathrooms were re-engineered with antimicrobial copper-alloy materials on the following high-touch surfaces: 1) overbed table tops; 2) bedside table top; 3) visitor chair arm rest; 4) bedrail; 5) toilet seat and 6) bathroom sink. Two out of the six high touch surfaces – the toilet seat and bathroom sink - were coated with a spray-on 80/20% copper-nickel product (Aereus Technologies™, Mississauga, Ontario) while the remaining four were covered with a solid 80/20% copper-nickel product (Trimco Hardware™, Los Angeles, California) custom fitted over the original surfaces (Figure1). Mobile items with copper surfacing in the three re-engineered rooms were clearly labelled with designated re-engineered room numbers to ensure they remained in that room for the duration of study. Re-engineered rooms also had ultraviolet C (UVC by Sanuvox Technologies) light wall mounted units installed in the patients' private bathroom, titanium dioxide paint on walls, and filters on bathroom faucets and shower heads. Low touch surfaces were replaced with Aereus and Trimco materials: patient room door hardware, patient bathroom door hardware, bedside table drawer pull handles, dresser cupboard pull handles, patient and bathroom wall electrical switch plates and the toilet flush handle. Also, all patient room and bathroom sink areas included no tough hand hygiene faucet plus no touch gel, soap and paper rowel dispensers

Patients: Only patients with acute myeloid leukemia admitted for myeloablative allogeneic transplantation were consented, enrolled into the pilot project, and randomized to receive a re-engineered or a standard room. One patient was enrolled at a time to ensure that the patient (and the mobile equipment) could remain in their assigned room for the length of their stay and to minimize disruption to the flow of the unit. All patients were routinely admitted seven days prior to transplant to begin conditioning chemotherapy treatment followed by bone marrow transplantation.

Sampling Collection Procedure: Following cleaning and disinfection, and just prior to patient admission, baseline environmental swabs of the six high-touch surfaces were taken. The surfaces of the patient room were then tested on Mondays between 0900 and 1000 as long as the patient was admitted. RODAC™ contact culture plates (Becton, Dickinson, New Jersey, USA) were applied to surfaces using consistent pressure for 30 seconds. Plates were then incubated at 35°C and colony growth counted and recorded at 24 and 48 hours. A template comparable to the surface area of the RODAC™ plate was used to ensure that ATPB swabs (SuperSnap™, Hygiena, Mississauga, Canada) were collected in a consistent manner; testing a uniform surface area. Samples were taken immediately adjacent to where RODAC™ plates were applied and the relative light units (RLU) measuredat the laboratory within one hour of swabbing. Surfaces were observed over the duration of the study for durability, evidence of wear, colour changes, staining, reaction to chemical cleaning and disinfecting agents and aesthetic appeal.

Statistical Analysis: The average CFU and RLU were calculated for each type of surface. Two tailed t-tests for paired samples were used to calculate differences between mean copper and non-copper results of the average CFU per plate and RLU for each type of surface. RODAC™ counts and ATPB data were visualized using density curves that were used to guide transformation of these outcome variables to achieve a distribution approximating normal. The effect of these transformations was confirmed using diagnostic plots such as quantile-quantile plots on the normal distribution.

Bivariate relationships were examined between the outcomes (a) transformed RODAC™ counts and (b) transformed bioburden data? and each of the following variables: surface material (copper vs non-copper); exposure to UVC; high-touch surface type; patient; and day and week of sample collection. Each outcome was regressed using multiple regression, with step-wise addition of variables. The final set of variables included in the analysis was based on minimizing residual errors and goodness of fit. Model fit was assessed using F-scores and residual error, as well as graphically, with diagnostic plots. A multilevel model using generalized estimating equations (GEE) was used as a sensitivity analysis, to explore the effect of possible collinearity and non-independence resulting from longitudinal data. All analysis was performed using R version 3.1.1 (https://www.R-project.org/).

Ethics: All patients were informed of the study and written consent obtained prior to admission. Study design, protocols, and patient consent procedures were pre-approved by the University of British Columbia and the Vancouver Coastal Research Institute's Clinical Research Ethics Board.

Training sessions were conducted with staff and physicians on the BMT unit for educational awareness plus environmental staff were instructed to ensure all surfaces in the control and non-control rooms were cleaned and disinfected with the same processes and chemicals.

Audits were done in each room on a weekly basis to ensure none of the mobile equipment had migrated to another room.

Aereus Technologies and Trimco Hardware donated their products to the pilot project. Installation of the products in the patient rooms were done through a donation of time and materials by CDC Construction Ltd. and also by the staff of the Vancouver General Hospital Facilities Department. Project management for the coordination of product supply and installation was done by Coalition Healthrcare Acquired Infection Reduction.

Results

Five of the nine patients enrolled between October 2015 and October 2016 were randomized to re-engineered rooms with an average admission of 29.6 days. Four patients stayed in standard rooms with an average admission of 30.3 days. Samples were taken for a maximum of seven weeks for each patient (min=28 days, mean=36.4 days). There were 336 opportunities for surface sampling; 329 (98%) data points were collected; 182 (55.3%) from copper surfaces, and 147 (44.7%) from non-copper surfaces. Each patient had between 28 and 42 samples tested with 26 samples taken of each copper surface and 21 from each standard room surface.

Average ATPB measurements for copper alloy surfaces in the re-engineered rooms were consistently lower on all six surfaces when compared to standard room surfaces (Table 1); with five out of six reaching statistical significance. The overall average ATPB RLU in standard rooms was 500.8 ± 707.9 RLU compared to re-engineered rooms of 71.9 ± 302.6 RLU ($p<0.0001$). Copper alloy surfaces in re-engineered rooms contributed to an overall 85.7% reduction in RLU compared to standard room surfaces.

Average RODAC™ culture plate counts for copper alloy surfaces in re-engineered rooms were consistently lower than those for standard room surfaces, with two out of six reaching statistical significance (Table 1). Overall average RODAC™ plate count in standard rooms was 73.02 ± 301.3 CFU/plate compared to the overall average RODAC™ plate count for copper surfaces of 7.21 ± 17.7 CFU/plate ($p=0.008$). Copper alloy surfaces in re-engineered rooms contributed to an overall 90.1% reduction in CFU/plate compared to standard room surfaces.

In a regression model (Table 2) that fit copper (Y/N), UVC exposure, surface type, and patient, copper surfaces were independently associated with a lower bioburden compared to non-copper surfaces (92.2% lower, p = 1.66E-11). UVC exposure had no independent effect on bioburden, after patients were controlled for (t=2.67, p = 0.82). This model had a residual variance of 0.5775, on 261 df, F-statistic = 20.41 (p < 2.2E-16) and adjusted R-squared = 0.57. Diagnostic plots indicated that the model was a good fit.

Sensitivity analysis: Plotting **RODAC™** counts and bioburden RLU's by patient demonstrated the potential for in-group effects, as patients may have distinct intercepts in an unadjusted model (Figure 2). In a GEE model for **RODAC™** counts, copper was associated with a 49% reduction in colony forming units (95% CI 46.2% - 51.5%, p=0.02) if samples with UVC exposure (n=52) were excluded. Copper and UVC exposure were collinear (i.e. all n=52 samples with UVC exposure were also from copper surfaces). GEE indicated an independent reduction in ATPB associated with copper of 92%, 95% CI = 82.5% - 96.8%. (Wald chi-sq = 35.80, p =2.2e-09). This effect remained even when exposure to UVC was excluded.

Discussion

The European Centre for Disease Prevention and Control estimated that, on any given day in 2011-2012, 80,000 patients had at least one hospital acquired infection.[9] A multistate survey of 183 American hospitals found that 4.0% of patients had one or more health care associated infections, with *Clostridium difficile* and *Staphylococcus aureus being* the most common pathogens - two organisms associated with transmission via the environment.[10] Traditional strategies (contact precautions, enhanced cleaning, hand hygiene) to control surface contamination are subject to human error and complementary strategies to decrease the risk of transmission are increasingly attractive. As a result, the use of copper alloys on high-touch surfaces and hospital equipment are of interest. Three clinical trials have suggested that copper alloy surfaces reduce the rate of HAIs or surface colonization with systematic reviews concluding that copper surfaces require further evaluation.[6-8,11,12, 14] A recent article demonstrated that copper surfaces accumulated a lower microbial bioburden over time compared to traditional surfaces.[13] Antimicrobial performance of copper over time, the effect of copper on total protein surface load and the impact of longer patient stays on the microbial burden of copper surfaces require further study.

Patients in this one and a halfyear pilot project were consented and randomized to either re-engineered rooms with self-disinfecting surfaces and UVC light in bathrooms or assigned to standard single rooms for the duration of their stay. Remarkably, no patients declined to participate, all room assignments were maintained, and all the resurfaced furniture and beds remained in their respective re-engineered rooms throughout the course of the pilot project. However, in order to accomplish this, it was necessary to enroll only one patient at a time and to assign a dedicated study nurse to visit the transplant unit daily; these factors accounted for the 98% compliance with environmental sample collection.

Multivariable regression on RODAC™ counts indicate that, after controlling for UVC exposure and surface type, copper surfaces were associated with a significant reduction in bacterial counts, of 43% (SE = 0.08, p= 0.0017). Although UVC exposure was also associated with a reduction in microbial bioburden independent of copper and surface type, sensitivity analysis indicated that UVC may be a confounder for copper in explaining the reduction in bacterial load. All surfaces exposed to UVC (n=52) were copper surfaces, making these two variables highly collinear, and the independent effect of UVC difficult to determine.

Copper also had a significant effect on ATPB results, of 90% reduction (SE=0.15, p=6.29E-11), independent of UVC exposure, surface type, and patient. UVC was not a significant covariate in this instance. Given that UVC exposure was significantly associated with ATPB RLUs in bivariate testing this suggested that UVC may be a confounder. The lack of significance for UVC exposure in sensitivity analysis by GEE, where within-patient variation is eliminated, supports this. Adjusted R-squared = 0.571 for the linear regression fitting copper, UVC exposure, surface type and patient indicated that 57% of variation in the ATPB data was explained by this model.

Two different formulations of copper alloy were tested; an integral solid surface and a spray-on application. Over the course of the one and a half year study, both solid and spray-on surfaces showed some staining, requiring the periodic use of a more abrasive cleaning agent (Emerel® Plus Alkaline Cream Cleanser, Diversey, Canada). Many of the stains for the solid surfaces were "rings" due to beverages while the undersides of toilet seats were discoloured from contact with urine or the toilet bowl chemicals for cleaning and disinfection. A few of the solid copper surfaces on table tops lifted at corners and had to be reattached with industrial adhesive. One of the toilet seats showed superficial crazing and some pitting of the material. Despite these aesthetic drawbacks, antimicrobial efficacy (as determined by RODAC™ colony counts) appeared to not be affected; however a full evaluation of the effect of cleaner/disinfectants on over-all durability was not performed.

Conclusion

Re-engineered patient rooms in the Leukemia/Bone Marrow Transplant ward were enhanced with antimicrobial copper on high-touch surfaces; these strategies were effective in decreasing microbial bioburden as measured by colony counts and ATP bioluminescence. The choice of surface used in health care must balance effectiveness in bioburden reduction, durability, aesthetic appeal and cost. Further studies are needed to determine effect of copper on microbial burden over time especially with respect to AROs and potential for transmission.

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Figure 1: Re-engineered patient rooms and bathrooms outfitted with antimicrobial copper and touchless disinfection technology

In the patient room, solid copper-nickel alloy was placed on A) visitor chair armrest B) patient bedrails C) patient over bed table and bedside table (not shown: overbed table); in the patient bathroom, D) in-built UVC wall units were installed as were spray-on copper products on the E) toilet seat and F) sink.

Table 1: Comparison of Average ATP Bioluminescence and Average Colony-Forming Units of Copper and Non-Copper High-Touch Surfaces

Surface	Average ATPB n=26 (copper n=26; non-copper n=21)			Average CFU n=25 (copper n=25;non-copper n=21)		
	Copper surface	Non-copper surface	p-value*	Copper surface	Non-copper surface	p-value*
Over-bed Table	245.9	830.9	0.066	8.84	9	0.97
Bedside Table	15.5	306.7	1.55E-07	6.16	9.76	1.60E-01
Visitor Chair Armrest	48.11	669.6	2.37E-06	5.69	35.71	2.30E-02
Bedside Rail	34.92	396.5	3.54E-05	15.88	28.86	2.70E-01
Toilet Seat	21.81	235	0.00021	3.48	272.38	0.062
Bathroom Sink	65.11	580.6	7.70E-05	3.24	82.38	8.40E-04

Table 2: Regression coefficients for bioburden – model 1

	Estimate (transformed)	Estimated effect (%)	t-value	p-value
(Intercept)	2.22	16354.32	14.69	2.00E-16
Copper surface	-1.11	-92.15	-7.04	1.66E-11
UVC exposure	0.39	46.04	2.67	0.82
Surface type				
B	-0.49	-67.55	-4.1	5.44E-05
C	0.05	12.05	0.42	0.6786
D	-0.09	-18.61	-0.75	0.4535
F	-0.6	-75.00	-4.18	4.04E-05
G	-0.2	-36.21	-1.35	0.1768
Patient				
2	0.38	141.73	2.57	0.0107
3	0.56	260.85	3.85	1.51E-04
4	0.32	109.17	2.01	0.0452
5	-0.41	-61.20	-2.69	0.0076
6	0.03	8.33	0.23	0.8159
7*	--	--	--	**--**
8	0.32	109.81	2.16	3.18E-02
9	0.16	45.16	1.12	2.65E-01

**Note:* *Patient 7 was excluded due to collinearity between variables. For n=35 samples from patient 7, all were from copper surfaces, with UVC exposure*.

SURFACES: A = Overbed table, B= Bedside table, C=Visitor Chair Armrest, D= Bedrail, , F=Toilet Seat, G=Bathroom Sink