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ARTICLE

Bacteria killing nanotechnology Bio-Kil effectively reduces bacterial burden in intensive care units

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Abstract A contaminated hospital environment has been identified as an important reservoir of pathogens causing healthcare-associated infections. This study is to evaluate the efficacy of bacteria killing nanotechnology Bio-Kil on reducing bacterial counts in an intensive care unit (ICU). Two single-bed rooms (S-19 and S-20) in the ICU were selected from 7 April to 27 May 2011. Ten sets of new textiles (pillow cases, bed sheets, duvet cover, and patient clothing) used by patients in the two single-bed rooms were provided by the sponsors. In the room S-20, the 10 sets of new textiles were washed with Bio-Kil; the room walls, ceiling, and air-conditioning filters were treated with Bio-Kil; and the surfaces of instruments (respirator, telephone, and computer) were covered with Bio-Kil-embedded silicon pads. Room S-19 served as the control. We compared the bacterial count on textiles and environment surfaces as well as air samples between the two rooms. A total of 1,364 samples from 22 different sites in each room were collected. The mean bacterial count on textiles and environmental surfaces in room S-20 was significantly lower than that in room S-19 (10.4 vs 49.6 colony-forming units [CFU]/100 cm^2; $P<0.001$). Room S-20 had lower bacterial counts in air samples than room S-19 (33.4–37.6 vs 21.6–25.7 CFU/hour/plate; $P<0.001$). The density of microbial isolations was significantly greater among patients admitted to room S-19 than those to room S-20 (9.15 vs 5.88 isolates per 100 patient-days, $P<0.05$). Bio-Kil can significantly reduce bacterial burden in the environment of the ICU.

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Introduction

Hospitals face higher costs as the number of patients with healthcare-associated infections (HAI) and the duration of hospital stay increase [1, 2]. Transmission of healthcare-associated pathogens takes place through air, droplets, and hand contact by medical staff [3–6]. Contamination of equipment has been identified as a major reservoir of pathogens associated with HAI [3–6]. Relevant studies have shown that surfaces in the rooms of hospitalized patients who have been infected with or colonized by methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE) are more likely to be contaminated with these bacteria than surfaces in rooms housing patients without MRSA or VRE infection [3, 4]. This indicates that pathogens like MRSA or VRE can be transmitted to the environment by patients. Although hand hygiene has already become a focal point at

various hospitals worldwide and is expected to have a major effect on reducing the rates of HAI, other measures are needed to reduce the colonization density in the hospital environment so that the chain of infection can be disrupted [7–18].

Bio-Kil (Cargico Group, Taiwan) is an antimicrobial agent comprising inorganic metal components and organic quaternary ammonium compounds (QACs) [19]. Bio-Kil molecules have a high-affinity structure and a strong electric field that effectively attracts pathogens [19]. Their strong electrical charge damages the membrane proteins of microorganisms, thereby killing the pathogens [19]. Bio-Kil forms a permanent, covalent bond with the surface of the textile fibers. Even after the textiles have been washed 50 times, the product still retains more than 90 % of its bacteria-killing power [19, 20]. Depending on the frequency with which the textiles are washed, treatment only needs to be repeated every 3 to 6 months in order to maintain a long-term bactericidal effect [19, 20]. In the same way, when the Bio-Kil® anti-bacterial catalyst is applied to the ICU environment and its instruments, such as nursing station desktops, workbenches, telephones, computer keyboards, and surfaces close to the patients, the catalyst will directly form a covalent bond with the surface of these objects, where it will have a long-term, bactericidal effect [19]. As it reduces the possibility of contamination of textiles, environments, and instruments, it lowers the environmental bacterial count in the hospital, thus reducing HAI due to bacterial colonization [20].

In the air filter system in the ICU, air circulates approximately 8–12 times per hour through an indoor air conditioning system, and each time the air passes through a system in which Bio-Kil has been applied, it comes into contact with the Bio-Kil platform where a catalyst reaction will take place, killing the bacteria [5, 19]. This way, as the air continues to circulate, it is continuously disinfected, thus reducing the amount of bacteria in the indoor air flow.

Although Bio-Kil has been shown to be a highly effective anti-microbial agent, no comprehensive studies have been performed on its effectiveness in clinical settings. In this study, we analyzed whether Bio-Kil when applied to different materials in the ICU, such as sheets, bedding, and clothing, desktops and the surfaces of instruments and equipment, reduces or eliminates bacteria in the environment, on the surfaces of surrounding items, and in the air.

Materials and methods

Setting

This study was conducted during the period 7 April to 27 May 2011 in two adjacent single-bed rooms (S-19 [control bed] and S-20 [experimental bed]) in a surgical intensive care unit of the Taipei City hospital, a 1,000-bed regional hospital in Taipei, Taiwan. During the study period, 3 patients were admitted to room S-19 and 5 patients were admitted to room S-20. Routine textile washing and replacement as well as infection control practices for nurses, physicians, visitors, and disinfection of environments and instruments in these two rooms were performed according to hospital regulations.

During the study period, ten sets of new textiles (pillow cases, bed sheets, duvet covers, and patient clothing) were provided by the sponsors for use by the patients who stayed in rooms S-19 and S-20. Clothing for physicians and nurses who worked in the two rooms and for people who visited the patients was provided by the hospital. The surfaces of the environment and the instruments were cleaned and disinfected (by 500 ppm sodium hypochlorite) every morning (8:00–9:00 am) as part of routine cleaning practice. Textiles were cleaned and replaced every day.

Embedding of textiles, environment, and instrument surfaces with Bio-Kil in room S-20

The ten sets of textiles to be placed in room S-20 were first washed for 5 min in 60 °C water with neutral detergents, rinsed with tap water, and then spin dried. The dry textiles were then soaked in Bio-Kil solution for 30 minutes and dried in a 50 °C oven (Fig. 1a). Bio-Kil solution was also treated evenly on the walls (cement and glass walls), ceiling, and in the air-conditioning filters of room S-20 (Fig. 1b, c). In addition, Bio-Kil antibacterial silicon pads (15 cm×10 cm) were placed over the instrument panel (respirator), computer keyboard, and telephone keypads in the nursing station associated with room S-20 (Fig. 1d).

Sampling of textiles and surfaces of the environment and instruments and bacterial counting

Samples were collected from surfaces of the environment and instruments with which medical staff and patients frequently come into physical contact. Moistened sterile cotton swabs were used to evenly wipe designated areas measuring 10 cm× 10 cm (100 cm^2; Fig. 2a–c). The samples were then inoculated into Trypticase Soy agar and placed in a 35 °C incubator for 48 h. The number of colonies was recorded as colony-forming units (CFUs)/100 cm^2.

Textiles and the surface of the environment and instruments in rooms S-19 and S-20 were sampled in the morning starting on the third day after the placement of new textiles and then every 2–3 days prior to routine cleaning practice by hospital cleaning staff.

Sampling of air and bacterial counting

Culture media (LB agar plates) were placed at four locations (right- and left-hand side of the entrance and head boards) in rooms S-19 and S-20 for 60 min to collect bacteria in the air (Table 1 and Fig. 2d). The plates were then placed in a 35 °C

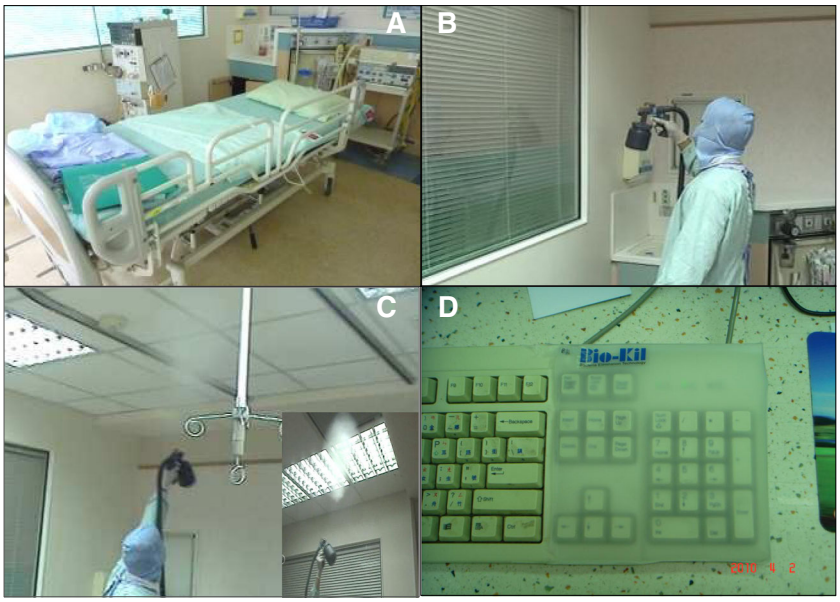

Fig. 1 Application of Bio-Kil bacteria killing nanotechnology in the intensive care unit. **a** Ten sets of new textiles (pillow cases, bed sheets, duvet covers, and patient clothing) were provided by the researchers for both S-19 and S-20. Clothing for family members, nurses, and doctors were routinely provided by the hospital. All the textiles placed in S-20 were treated by Bio-Kil solution. **b** All room walls in S-20 were treated evenly with Bio-Kil solution. **c** Bio-Kil solution was sprayed evenly on the air filter and the ceiling in S-20. **d** A Bio-Kil antibacterial silicon pad (15 cm×10 cm) was placed over the instrument panel and computer keyboard in the nursing station in the S-20 ward

incubator for 48 h. The bacterial colonies were counted and were recorded as CFU/hour/plate. Air samples in rooms S-19 and S-20 were taken in the morning along with sampling from textiles and environments.

Bacterial culture results for patients admitted to the rooms during the study period

Bacteria grown from textiles, the environment, and air samples were not identified to the species level and testing of susceptibility to antimicrobial agents was not performed. In order to evaluate the efficacy of Bio-Kil on microbial infections or colonization among patients admitted to the two rooms, all bacterial culture results and the resistant profiles of the isolates, particularly those resistant to extended-spectrum cephalosporins (ESC, ceftazidime or cefepime) or carbapenems (imipenem or meropenem), from all clinical specimens of all patients were evaluated during the study period. The density (per 100 patient-days) of microbial infections or colonization among patients admitted to rooms S-19 and S-20 was determined.

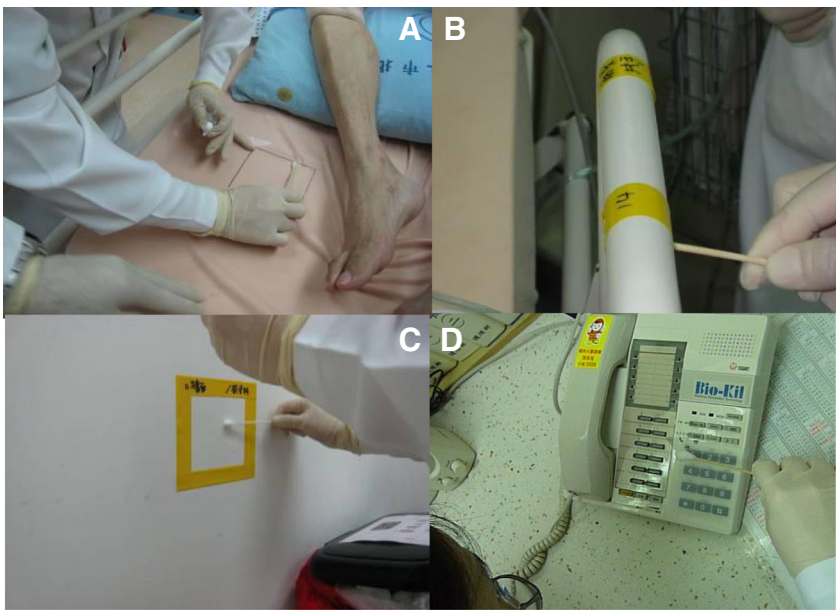

Fig. 2 Sampling of bacterial cultures by swabbing a 10 cm× 10 cm square of **a** bed sheet, **b** bedrail, **c** cement wall, and **d** a telephone keypad covered with a Bio-Kil silicon pad

Table 1 Bacterial count (colony-forming unit [CFU]/100 cm^2) in the control (S-19) and experimental (S-20) groups

Site	Control group (S-19)		Experimental group (S-20)	
	Number of samples	Mean (range) bacterial count	Number of samples	Mean (range) bacterial count
Environment surface		(CFU/100 cm^2)		(CFU/100 cm^2)
Patient clothing (chest/outer side)	31	50.6 (7–300)	25	10.7 (1–24)
Pillow case (left side)	31	46.0 (7–500)	25	11.5 (1–22)
Melamine table (right)	31	38.1 (2–300)	31	9.7 (2–33)
Melamine table (left)	31	37.8 (0–300)	31	10.7 (0–26)
Washbasin (left)	31	33.2 (1–500)	31	11.5 (0–35)
Bed sheet (right hand end)	31	32.5 (1–300)	25	8.2 (0–21)
Pillow case (right)	31	31.9 (9–102)	25	9.5 (1–19)
Bed sheet (left hand end)	31	28.8 (2–130)	25	10.3 (0–23)
Bed sheet (feet end)	31	25.9 (4–300)	25	5.5 (0–14)
Respirator panel	31	21.8 (0–400)	31	2.3 (0–13)
Duvet cover	24[a]	18.1 (3–127)	13	5.4 (0–12)
Bed rail	31	10.5 (0–50)	31	3.4 (0–11)
EKG panel	31	9.1 (0–90)	31	3.0 (0–16)
Nursing station desktop	31	7.8 (0–84)	31	3.7 (0–15)
Nursing station computer keyboard	31	6.0 (0–21)	31	3.9 (0–12)
Nursing station telephone keypad	31	5.3 (0–13)	31	3.0 (0–9)
Glass door (left inner side)	31	2.9 (0–33)	31	0.9 (0–6)
Wall	31	2.6 (0–24)	31	2.9 (0–28)
Air		(CFU/h/plate)		(CFU/h/plate)
Entrance (left)	30	37.6 (16–73)	29	25.7 (2–60)
Entrance (right)	30	32.5 (14–57)	29	24.4 (6–41)
Bed head side (left)	31	37.5 (15–200)	30	21.6 (5–48)
Bed head (right)	31	33.4 (13–57)	30	25.2 (8–55)

[a] Because bedding and clothing are used by all medical staff, it was not possible to take samples, resulting in insufficient samples

Statistical analysis

The independent-sample *t* test was used to compare the mean bacterial count of the two groups. Differences in mean bacterial count between the two groups were tested by the Student's *t* test and checked by one-way analysis of variance (ANOVA). A P value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed on a personal computer using the statistical package SPSS for Windows (Version 10, SPSS, Chicago, IL, USA).

Results

Bacterial counts from textiles and the environment of rooms S-19 and S-20

A total of 1,364 samples were taken from 22 sampling areas, including 18 environmental surfaces and four air samples in the control (S-19) and experimental (S-20) rooms. The ranges and means of bacterial counts from each sampling site are summarized in Table 1. With the exception of bacterial counts from the walls, the mean bacterial count from other sampling sites from room S-19 was higher than that from sampling sites from room S-20. The mean and 95 % confidence values of bacterial counts on the environment surfaces at five different time periods are illustrated in Fig. 3. The mean bacterial count from textiles and environment surfaces in room S-20 (10.4 CFU/100 cm^2) was significantly lower than that in room S-19 (49.6 CFU/100 cm^2; $P<0.001$).

Bacterial counts of air samples at rooms S-19 and S-20

The mean bacterial count from air samples was significantly higher in room S-19 than in room S-20 ($P<0.0001$), although there was no significant difference between the four sampling areas in the two rooms ($P=0.1108$).

Bacteria associated with infections and colonization

A total of 14 isolates were reported among the three patients hospitalized in room S-19. The isolates included methicillin-resistant coagulase-negative staphylococci ($n=1$), *Klebsiella pneumoniae* ($n=4$), including isolates resistant to ESC ($n=2$);

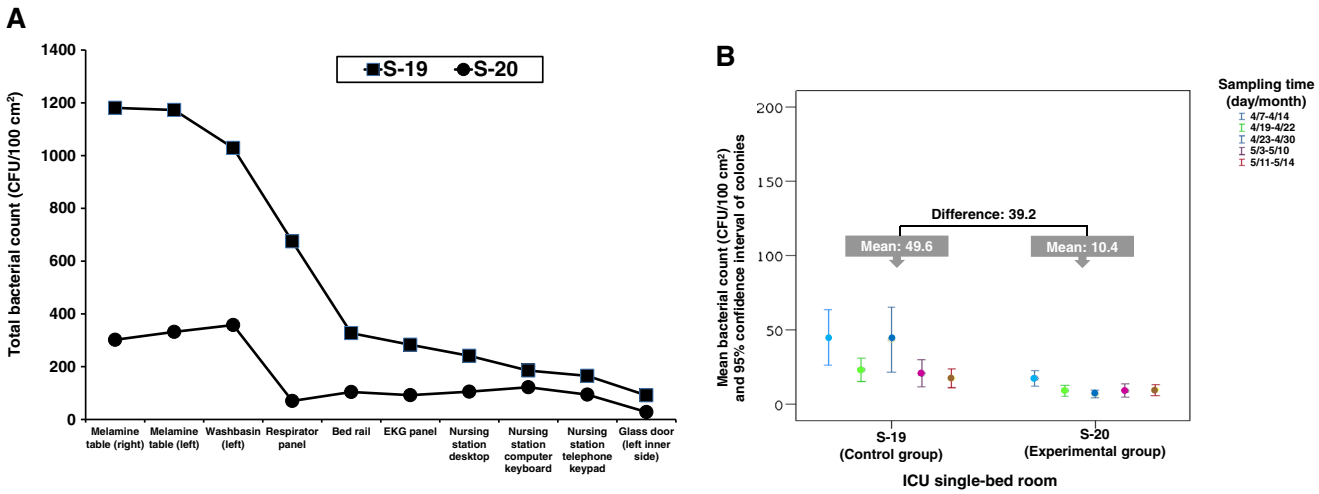

Fig. 3 **a** Total bacterial counts (colony-forming units [CFU]/100 cm^2) among 10 different sampling sites (environment and textiles) with the same sampling number ($n=31$) in S-19 (control) and S-20 (experimental) during the study period. **b** Mean bacterial count (colony-forming units [CFU]/100 cm^2) in rooms S-19 (control) and S-20 (experimental) during different time periods of sampling

ceftazidime-resistant *Enterobacter cloacae* ($n=2$); *Proteus mirabilis* ($n=1$), susceptible to ESC; *Pseudomonas aeruginosa* ($n=2$), both susceptible to carbapenems; *Acinetobacter baumannii* ($n=3$), all carbapenem-resistant; and *Stenotrophomonas maltiphilla* ($n=1$). As for the 5 patients admitted to room S-20, a total of 15 isolates were reported. They included methicillin-resistant coagulase-negative staphylococci ($n=3$), *Escherichia coli* ($n=1$), susceptible to ESC; *K. pneumoniae* ($n=1$), susceptible to ESC; *E. cloacae* ($n=2$), susceptible to ESC; *Citrobacter freundii* ($n=1$), susceptible to ESC; *P. aeruginosa* ($n=3$), 2 were susceptible to carbapenems and 1 was resistant to carbapenems; *A. baumannii* ($n=2$), both susceptible to carbapenems; *S. maltiphilia* ($n=1$); and *Candida albicans* ($n=1$). The density of microbial infections or colonization was significantly greater among patients admitted to room S-19 (9.15 isolates per 100 patient-days) than among patients admitted to room S-20 (5.88 isolates per 100 patient-days; $P<0.05$).

Discussion

In this study, we found that Bio-Kil significantly reduced the bacterial burden in the ICU. In health care settings, it is necessary to provide a safe environment and implement infection control measures to prevent HAI [21]. The majority of HAI are caused by colonization and subsequent infections due to endogenous flora and exogenous organisms from the environment have long been ignored as insignificant risk factors for HAI [17, 22]. Since cross transmission due to direct physician–patient contact plays a major role in HAI caused by exogenous pathogens [17], handwashing to break the chain of transmission has remained the most critical and preventing intervention in HAI control ever since the era of Semmelweis [7]. However, an average compliance rate of 30 % has always been a problem in real-world practice [7, 21].

Of the numerous infection control bundles and policies that were enacted in the era of zero tolerance after SARS [8, 23], the hand hygiene campaign has been shown to be the most cost-effective and widely accepted practice and has led to a trend toward reduction of MRSA nosocomial infections [24]. However, the incidence of MDR outbreaks such as carbapenem-resistant or pandrug-resistant *Acinetobacter baumannii*, or vancomycin-resistant enterococci has increased recently [3, 4, 13, 17, 18]. A series of studies have demonstrated that physician–environment–patient transmission of HAIs was the result of indirect contact with the hospital environment or the patient's surroundings [14, 23]. Ohl et al. suggested a potential link between transmission of pathogens to patients and healthcare workers (HCWs) who do not perform hand hygiene after touching the curtains [15]. As such, environmental disinfection has been emphasized in recent years to compensate for inadequate adherence to hand hygiene. In addition to cleaning on patient's discharge to reduce the chances of MDRO transmission from a previous occupant to a new occupant [16, 22], environmental disinfection of a patient's bed and surroundings should be performed to control MDR [17, 18]. However, for manual surface cleaning and disinfection there has always been a risk of quality instability due to poorly controlled processes or, arguably, the possibly undertrained and incompetent hands of housekeeping staff [17, 18].

A systematic renovation of automated environmental control may have to be considered to make up for the shortfalls of HCWs, whose behavior ultimately determines the exogenous factor responsible for HAI. Several environment disinfection

control models have been developed, including surface coating and photocatalyzing or ultraviolet germicidal irradiation (for surface and air sterilization), and copper and silver nanofilms [9–11, 22, 24, 25]. Yet, there are still barriers to overcome before they are adopted as standard clinical applications, some with long *D*-values and repopulation of bacteria in a short time. Instead, as we observed in present study, Bio-Kil reacts within seconds and maintains a constant effect for up to 6 months depending on the surfaces to which it is applied.

Airborne transmission of hospital pathogens and their contribution to the burden of HAI has been well described [5, 11, 26, 27]. A novel hydroxyl radical air disinfection system (Inov8 unit) has been reported to improve air quality and reduce environmental contamination in health care settings [11, 27]. A previous study in a regional hospital in Taiwan showed that the addition of Bio-Kil apparently reduced the bacteria count by up to 47 % (from 108.8 CFU/h/plate to 68.6 CFU/h/plate) [5]. Similar findings were also observed in the present study.

The main limitation of this study is the lack of assessment of the effect of Bio-Kil on other emerging health care-associated pathogens, including multidrug- or pandrug-resistant pathogens, *Clostridium difficile*, fungi (*Candida* and *Aspergillus*), and viruses in the hospital environment. These organisms were associated with an increasing incidence of life-threatening infections in hospitalized patients [17, 18, 28–30]. Furthermore, the low sample size (only two rooms) and the lack of detailed clinical characteristics of patients admitted to these two rooms (infections or contamination) and the following further infection prevention for the next patients admitted to these two rooms were also the limitations of this study. Further work is also required to validate whether reducing the burden of these organisms in the environment will minimize the risk of HAI.

In conclusion, we found that Bio-Kil nanotechnology can significantly reduce the bacterial burden in the environment (textiles, environmental surfaces, and air) and the bacterial density of microbial infections or colonization among patients in the ICU.

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Potential conflicts of interest The authors declare that they have no conflict of interest.

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Ethical approval This study was approved by the Taipei City Hospital Institutional Review Board (TCHIRB-1000901-E).

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