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Major Article

Routine chlorhexidine gluconate use onboard navy surface vessels to reduce infection: A cluster randomized controlled trial

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Background: Hand disinfection with chlorhexidine gluconate (CHG) is commonly used for preventing the spread of infection in medical institutions and the community, but studies on its use in military settings have been inconclusive. We examined the effects of CHG on morbidity in Israeli Navy ships.

Methods: This was a controlled, cluster randomized study that took place at a major naval base in Israel. Ships were randomly selected into the study (347 sailors) and primary control (350 sailors) groups. Additional nonintervention control groups included other sailors serving on the base (n = 360) and logistics and support personnel (n = 859). CHG disinfection devices were installed on all ships in the study group, alongside soap and water. Morbidity was analyzed using a computerized patient record, subjective self-report questionnaires, and a sample of hand cultures. Compliance with hand hygiene was analyzed using a self-report hygiene attitudes questionnaire at the beginning of the trial and after 3 months. The study took place between May and September 2014.

Results: No significant differences were found between the groups in terms of sick days or light-duty days or in the number of acute gastrointestinal or respiratory cases. Sailors were found to have more skin infections than controls, but this was not significantly reduced by CHG. Hand cultures demonstrated that continuous use of CHG did not cause a reduction in colonization. There were no statistically significant differences in self-reported hygiene practices.

Conclusions: CHG did not demonstrate any medical benefit over the use of soap and water onboard Israeli Navy ships.

Handwashing is considered one of the most important means of controlling infection. The first description of handwashing as a preventive measure is famously attributed to Semmelweis' report in the middle of the 19th century, where hand hygiene was found to correlate with reduced postpartum mortality.[1] Another groundbreaking study in the field of hygiene was published by Mortimer et al in the 1960s describing a reduction in *Staphylococcus aureus* transmission in neonatal wards in which the nurses practiced handwashing.[2] The Centers for Disease Control and Prevention first published official guidelines on the subject in 1975, recommending handwashing with soap and water before and after procedures and on contact with patients.[3]

In addition to medical settings, hand hygiene has also been examined as a means of reducing infectious diseases in various community settings. The inquiry into sick days as a significant economic factor prompted a study in Germany that examined an intervention introducing hand sanitizers into an office setting. The study, using a moderate sample size, demonstrated a reduction in the number of sick leave days attributable to infectious diseases. Its most significant finding was a 10% reduction in sick days in the study group versus the control group because of diarrheal infections.[4] A meta-analysis published in 2008 reviewed a large number of community-based hand hygiene interventions. The various interventions were found to be more effective at preventing gastrointestinal morbidity than respiratory morbidity. Antibacterial soaps or hand sanitizers were not found to be superior to standard soap and water handwashing techniques.[5]

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Table 1
Hygiene interventions in the U.S. Armed Forces

	Study	Population	Protocol	N	Results
1	Van Camp and Ortega[6]	Aviation personnel	CHG hand sanitizing, cross over	117	1.5% reduction in illness
2	Mott et al[7]	Artillery basic training	Alcohol-based hand sanitizing	2,750	44% less lost training time
3	Whitman et al[8]	Officer candidate school	CHG-impregnated cloth for entire body	1,562	MRSA transmission decreased
4	Ellis et al[9]	Infantry trainees	CHG body wash, cluster randomized	30,209	SSTIs not prevented
5	Millar et al[10]	Infantry trainees	CHG body wash, cluster randomized	1,706	Reduced MRSA nasal colonization

CHG, chlorhexidine gluconate; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *SSTI*, skin and soft tissue infection.

Several studies have been performed in military settings examining the effect of hygiene intervention programs on infection prevention. Some of these are summarized in Table 1. Although some of these studies did demonstrate various benefits for hygiene interventions, overall their results can be said to be equivocal because no clear reduction in clinical infection in a large number of subjects was found.

The military setting is characterized by cramped quarters, use of shared gear, reduced hygiene infrastructure compared with other work places (eg, fewer handwashing stations), a military culture that does not encourage optimal hygiene, and an intensive, around the clock activity that requires soldiers to be in close contact with each other during most hours of the day.[11] It has been shown in the past that the military population is more susceptible to infectious diseases than its civilian counterpart.[12] In the naval setting, workstations are sometimes shared by shifts, and some operational considerations may call for berths shared by rotation. An additional factor that may be predisposing to the transmission of infection onboard ships is the abundance of doors and hatches that are frequently opened and closed by the hands of the entire crew. A study examining 6,522 pneumonia hospitalizations in the U.S. Navy and Marine Corps found that the most junior Navy and Marine Corps personnel were at highest risk.[13] Additional support for the possibility of navy-specific characteristics of infectious diseases may be found in a report from the U.S. Naval Ship Mercy during operation Desert Shield. The crew of the Mercy was found to have a lower risk of diarrheal disease than ground troops, with a higher predisposition for acquired respiratory illness.[14] Another study conducted among deployed troops showed a relatively larger burden of infectious disease in the naval branch of the U.S. Military.[15] Increased burden of infectious disease was also reported in the Israeli Navy; internal analysis from the 2013 emergency medical records showed that the incidence of acute respiratory infection in the Haifa Naval Base was 3.89 cases per 100 sailors per month. The incidence of acute gastrointestinal infection and skin and soft tissue infections was, respectively, 2.21 and 0.55 cases per 100 sailors per month.

We evaluated an intervention designed to improve hand hygiene in Israeli Navy fast missile boats and patrol boats using chlorhexidine gluconate (CHG) dispensers.

METHODS

Ethical approval for this study was obtained from the Israel Defense Forces Institutional Review Board (no. 1344-2014). Determination of the sample size allocated for this study took into account an estimated infection prevalence of 39.5%[15] per deployment; risk reduction with CHG was reported in previous studies to range between 10% and 40%.[5-10] An assumed risk reduction rate of 20% was made to calculate a power of 87.5% for a control and treatment group of 250 sailors each. We performed a cluster randomized prospective controlled study to evaluate the effect of introducing CHG dispensers to a population of sailors. Taking clustering into account yielded a suggested sample size of 350 sailors in each group. Ships from a single, central naval base were randomly assigned into either a study group (group A, n = 347) or a control group (group B, n = 350), stratified by vessel classes (corvette, fast missile boat, and patrol boat). Each group contained the same number of ships from each class. Both groups received hygiene instruction by a naval physician at the beginning of the study. Additional controls were randomly chosen from other sailors on the base (group C, n = 360) and littoral logistics companies (group D, n = 869).

Chlorhexidine dispensers were installed in key locations onboard ships in the study group (ie, adjacent to heads [toilets], mess decks [dining rooms], common areas). A virtually unlimited supply of CHG was provided to the study group. Refills were always replenished on demand and also actively sent to the ships regardless of replenishment demands. The study product was Septadine solution (Floris, Misgav, Israel), consisting of 70% alcohol and 0.5% CHG. Listed inactive materials included purified water, glycerin, propylene glycol, and methylene blue. Regular means of hygiene, such as soap and water for handwashing, were not removed from the study ships, but continued to be maintained alongside the CHG dispensers.

The groups were followed for 4 months from May 5-September 5, 2014. During this period, all subjects participated in security operations, routine exercises, and patrols. Data collected from all groups consisted of the entire database of clinic visits for all sailors and personnel both on and off the base from the Israeli Defense Forces computerized patient records system. We collected additional data from groups A and B, including the following: (1) a hygiene attitudes questionnaire adapted from Mody et al[16] (Supplementary Material A), administered at 0 and 3 months; (2) a self-reported symptoms questionnaire adapted from Riddle et al[15,17] (Supplementary Material B), administered at 1, 3, and 4 months; and (3) bacterial palm cultures from 30 sailors from each group, initially selected at random, using a modified bag broth technique with sterile brain-heart broth,[18] at 0 and 4 months (the same sailors were cultured). The laboratory procedure was conducted at the Rambam Medical Center Microbiology Laboratory. It included quantitative plating of the liquid samples at 3 serial 10-fold dilutions (:1, :10, and :100 dilutions). Samples were diluted in sterile saline, and 0.1 mL of each dilution was spread on a brain-heart infusion agar. Plates were incubated at 37°C under atmospheric conditions with 5% CO_2 for 5 days.

In addition, the total amount of CHG dispensed to the study group was tallied.

The outcomes evaluated were the incidence of infectious diseases reported by the computerized patient records system (Supplementary Material C lists all ICD-9 diagnoses tallied in this outcome). These were grouped into diarrheal, respiratory, and skin infections; the number of sick call visits; and the number of sick leave and light-duty days incurred by the sailors. Secondary outcomes included subclinical morbidity (ie, symptoms of self-reported infectious diseases), regardless of whether or not medical attention was sought, and hand colonization of the random sample.

Statistical analysis

Using SPSS 20 software (SAS Institute, Cary, NC), all statistical tests compared group A with all other groups. Categorical variables