American Journal of Infection Control 000 (2021) 1–5

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Evaluation of an aerosolized hydrogen peroxide disinfection system for the reduction of *Clostridioides difficile* hospital infection rates over a 10 year period

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Key Words:
Aerosolized hydrogen peroxide
Clostridioides difficile
Environmental decontamination
Infection rate

A B S T R A C T

Background: *Clostridioides difficile* infections (CDI) cause significant morbidity and mortality in healthcare facilities worldwide. We examined the use of an aerosolized hydrogen peroxide (aHP) disinfection system for reduction of CDI rates.

Methods: We conducted a retrospective analysis of CDI rates at an acute care facility over a 10-year period. The first 5-year period investigated the before and after implementation of an aHP system followed by another 5-year period of continued use on CDI rates.

Results: The before and after period showed a reduction in CDI rates from 4.6 per 10,000 patient days down to 2.7 per 10,000 patient days after implementation ($P < .001$). The second study period for the continued aHP use exhibited a consistent decrease in CDI rates to 1.4 per 10,000 patient days at the end of the study.

Conclusions: The addition of a touchless aHP whole room disinfection system as part of terminal cleaning resulted in a significant reduction in CDI rates that have been sustained year after year.

BACKGROUND

Clostridioides difficile (formerly *Clostridium difficile*) infection (CDI) is the most common healthcare-associated infection (HAI), labeled an Urgent Threat by the Centers for Disease Control and Prevention.[1] Patients with CDI can be asymptomatic or have symptoms that range from mild to severe diarrhea to pseudomembranous colitis and toxic megacolon.[2] According to the CDC and The Joint Commission, *C. difficile* is responsible for 223,000 HAIs resulting in more than 12,000 deaths and $6.3 billion in costs in the United States.[1,3]

C. difficile is an anaerobic, gram-positive, spore forming bacillus bacterium that under certain stress factors will form an endospore. These stresses and resulting sporulation can occur in the human gastrointestinal tract or outside of the body.[4] Patients with CDI typically have frequent diarrhea which increases environmental contamination. The resiliency of this spore in the environment poses a significant acquisition risk to other susceptible populations.[5] The spore is resistant to temperature changes, hand sanitizers, and most disinfectants.[6] The recovery of *C. difficile* from the environment of rooms housing patients with *C. difficile* ranges from 29% for asymptomatic carriers to 49%-100% for patients with CDI.[7] In addition, patients occupying rooms in which a prior occupant had CDI can be at significantly higher risk of CDI acquisition.[8]

There are many environmental interventions available to reduce fomite acquisition. Unlike clinical treatment, there is no specific environmental intervention used in the industry as best practice. In this study, we retrospectively examined the implementation of a hydrogen peroxide based no touch decontamination system for reduction of CDI rates over a 10-year period.

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Conflicts of interest: All authors report no conflicts of interest relevant to this article.

https://doi.org/10.1016/j.ajic.2021.11.021

METHODS

Study design

This study compared the implementation of an aerosolized hydrogen peroxide (aHP) system and the rates of healthcare associated CDI before and after hydrogen peroxide utilization. The Halo Disinfection System (Halosil International, New Castle, Delaware) consisted of an EPA registered (#84526-6) whole room fogging unit that generated an aerosolized dry-mist fog resulting in coverage of all exposed surfaces without wetting. The disinfection formulation delivered 5.0% w/w hydrogen peroxide and 0.01% ionic silver to all surfaces.

The study period before usage of aHP was 27 months (July 2009-September 2011), and the implementation period was 33 months (April 2012-December 2014). The months of October 2011 through March 2012 were excluded because aHP disinfection was not used consistently throughout this 6-month period. We also examined the effects of continued aHP usage from January 2105 through December 2019. The study was conducted at Pennsylvania Hospital, a Penn Medicine facility, in Philadelphia, PA. It is a 475-bed acute care, urban teaching hospital. During this study, all infection data was collected and calculated using the National Healthcare Safety Network (NHSN) criteria.

Room protocols

Upon discharge or transfer of a CDI patient, the following room protocol was utilized. A contact isolation sign was used to identify treatment rooms for environmental services (EVS). This alert advised EVS for contact isolation procedures with use of only soap and water for hand hygiene. EVS were required to remove isolation signs as a method to ensure rooms were properly treated. As a backup, the EVS and Patient Care Coordinators were also notified of the CDI room to ensure rooms were not skipped. Infection Prevention (IP) maintained a running list of current CDI room locations and sent the list directly to the EVS supervisors at least twice weekly to ensure room treatments. A log of treated rooms was maintained by EVS and available to IP on a shared drive. The IP tracked CDI patient transfer and discharge rooms while monitoring EVS logs to ensure proper room treatment. When a room was missed, feedback was given, and a high alert was created to ensure the room was treated when available. An overall compliance report was generated quarterly for EVS administration and shared with EVS staff.

All rooms were cleaned with 10% bleach (sodium hypochlorite) solution daily and upon discharge prior to aHP treatment. The bleach solution was mixed daily and added to a task bucket for microfiber charging and applied to high touch surfaces. Cleaning effectiveness was monitored through a fluorescent gel program from 2009 to 2016 and switched to an ATP monitoring process in 2017. Real time feedback was given to EVS when possible while data on both monitoring programs and aHP compliance were formally presented weekly at staff meetings.

The aHP treatment procedures were standardized as follows. In each room, the unit was placed in the furthest corner facing inward. The bathroom door was opened, and privacy curtains pulled partially opened to allow contact with the aerosol. The vents were sealed with a plastic cover and a towel was placed at the bottom of the main door to prevent any leakage of the hydrogen peroxide. An indicator strip was placed in each room to ensure sufficient concentration of hydrogen peroxide aerosol. The room was closed for a total of 2 hours to allow the chemical to disinfect and passively break down.

Definitions

CDI cases were defined with a stool diagnostic test positive for CDI on unformed stools specimens that conformed to the shape of the container. Prior to October 2018, glutamate dehydrogenase assay plus enzyme-linked immunosorbent assay for toxin was the laboratory test used to determine CDI. If there was a discrepancy in the results, nucleic acid amplification test was utilized. Starting in October 2018, a 2-step algorithm was utilized with nucleic acid amplification test testing administered first followed by toxin testing if the *C. difficile* antigen was detected. NHSN definition was utilized through a multi-step algorithm for CDI on the same unformed stool specimen. The finding of the last test performed on the specimen was documented in the patient medical record and determined if a CDI positive laboratory assay definition was met. CDI cases were considered healthcare associated if there was no history of recent *C. difficile* in the prior 8 weeks and the onset of symptoms that led to recovery of the organism was present after 3 days of hospitalization. Incidence rates of CDI were defined as new healthcare-associated CDI (HA-CDI) cases per 10,000 patient-days. Beginning January 2015, we began classifying infections as hospital-onset CDI (HO-CDI). We no longer used the gap day concept to determine criterions were met and did not include the use of laxatives as a cause for diarrhea that quickly resolved. Rate data were extracted from Infection Prevention and Control databases without any links to individual patient information.

Statistical analysis

Two-tailed tests were used for analyses and differences were considered statistically significant when $P < .05$ (StataCorp, College Station, TX).

RESULTS

During this study, there were a total of 192 HA-CDI. Before implementation of aHP, 120 cases were observed over a 27-month interval with a CDI rate of 4.6 per 10,000 patient days (total patient days of 262,656). After implementation of the aHP system, 72 cases were observed over a 33-month interval with a CDI rate of 2.7 per 10,000 patient days (total patient days of 262,106). The rate of CDI fell from 4.6 to 2.7 cases per 10,000 patient days with a *P* value < .001 (Table 1).

The aHP system utilization on HO-CDI rates were followed an additional 60 months. The HO-CDI rate in 2015 was 5.4 per 10,0000 patient days and consistently decreased to 5.2 in 2016 to 3.7 in 2017 to 3.5 in 2018 and down to 1.4 in 2019. The standardized infection ratio (SIR) has also decreased from 0.77 in 2015 down to 0.5 in 2019.

Table 1
Healthcare-associated *Clostridioides difficile* infection rates before and after aerosolized hydrogen peroxide/silver disinfection fogger implementation.

Date	Length	Total patient days	Healthcare associated CDI	CDI per 10,000 patient days
Before implementation (Jul-09 through Sep-11)	27 mo	262656	120	4.6
After implementation (Apr-12 through Dec-14)	33 mo	262106	72	2.7*

CDI, *Clostridioides difficile* infection
*$P < .001$

Table 2
Hospital-onset *Clostridioides difficile* infection rates from the consistent use of the aerosolized hydrogen peroxide/silver disinfection fogger.

Year	Total Patient Days	HO-CDI	Expected Infections	SIR	P-value	CDI per 10000 patient days
2015	74160	40	52	0.77	0.1001	5.4
2016	76373	40	52	0.77	0.0777	5.2
2017	72161	27	50	0.54	0.0005	3.7
2018	71448	25	44	0.57	0.0024	3.5
2019	70120	10	33	0.30	<0.0001	1.4
Total	364262	142	231	0.62	<0.0001	3.9

HO-CDI, hospital-onset *Clostridioides difficile* infection; CDI, *Clostridioides difficile* infection; SIR, standardized infection ratio

The overall CDI data from 2015 through 2019 was 142 HO-CDI for 364,262 patient days resulting in a 3.9 infections per 10,000 patient days. The SIR data over the same period was 0.62 with a *P* value < .0001 (Table 2).

DISCUSSION

We report a 41% reduction in HA-CDI rates associated with aHP implementation. To our knowledge, this is the first study showing the effectiveness of aHP in reducing CDI rates in a clinical setting. Other studies have demonstrated the effectiveness of whole room decontamination in reducing CDI rates; however, they used a hydrogen peroxide vapor (HPV) system. For example, a before-after study by Boyce et al[9] reported a non-statistically significant hospital-wide CDI reduction of 38% after HPV implementation. Similarly, Manian et al[10] reported a significant CDI reduction of 38% with HPV plus an enhanced bleach disinfection program. Horn and Otter[11] also reported a statistically significant 47% reduction in CDI rates with HPV and hand hygiene improvements.

HPV contains a higher concentration of hydrogen peroxide (30%-35% w/w) and can be used as a vapor with a particle size of less than 1 micron.[12] Following exposure, the HPV units utilize a secondary system to actively break down the hydrogen peroxide into water vapor and molecular oxygen. The HPV systems are sporicidal and registered as a sterilant with the Environmental Protection Agency (EPA).[13] Conversely, the aHP system we implemented produced a fine mist by aerosolizing a solution containing 5% w/w hydrogen peroxide and 0.01% ionic silver. The aerosolized product was introduced via a unidirectional nozzle which consisted of a charged particle approximately 10 microns in diameter. After disinfection, the hydrogen peroxide passively decomposes. This fogging application system is registered as an EPA sporicidal.[14]

We also report a 74% reduction in HO-CDI from 2015 to 2019 with continued use of a whole room aHP disinfection system. This system has been utilized at our facility with great success over the last 8 years along with an environmental cleaning program which included the use of daily bleach cleaning and an environmental monitoring system. The quarterly analysis illustrated in Figure 1 shows that the sustained use of the aHP system and environmental disinfection program continued the reduction in CDI rates as shown with a linear regression trend line over the 5-year period. This study period initiated when we changed the method of reporting HA-CDI to HO-CDI that corresponded with the 2015 rebaseline from NHSN.[15] This resulted in more cases of CDI being recorded versus the original study period from 2009 to 2014.

A few studies have examined aHP systems based on laboratory studies or evaluation of experimentally contaminated carriers assessed in hospital rooms. An aHP system was able to kill >4 $\log_{10}$ methicillin-resistant *Staphylococcus aureus* (MRSA) and *Acinetobacter baumannii* using a carrier test in a hospital room.[16] Another study reported a >5 $\log_{10}$ reduction of two spore suspensions of *C. difficile* dried onto ceramic tiles and exposed to 7.5% hydrogen peroxide

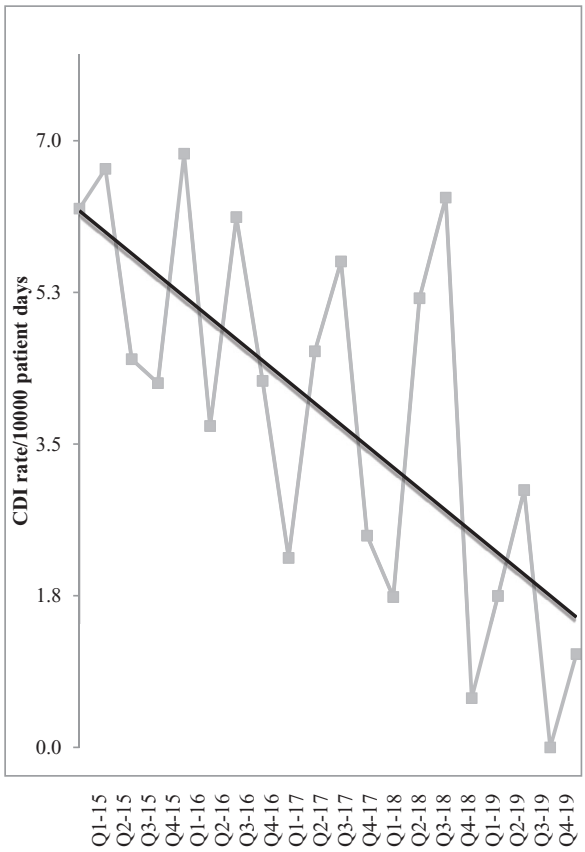

Fig. 1. Quarterly data of *Clostridioides difficile* infection rates per 10,000 patient days with consistent use of aerosolized hydrogen peroxide system from 2015 through 2019. Linear regression trend line for same period is shown.

aerosol for two hours.[17] A clinical study by Michell et al[18] using a 6% aHP system showed a significant 41% reduction in MRSA with hand hygiene compliance plus other infection control initiatives. We also observed during our study period that MRSA and vancomycin-resistant enterococci rates did not significantly change.

Our study has several important strengths. It was performed over a period of 10 years, with a 60-month study period, which is considerably longer than other before-after studies evaluating the impact of no touch technologies such as HPV, ultraviolet C and pulsed xenon ultraviolet (PX-UV).[8-10,19-24] Also, the adequacy of terminal manual cleaning was assessed through fluorescent gel or ATP sampling which was standardized to decrease variability in the evaluation process by different supervisors. There were no new infection control initiatives during the study period such as hand hygiene compliance or antibiotic stewardship programs.

Limitations of our study include a retrospective analysis of data that would not consider possible changes in practices over time, lack

of specific antimicrobial use data, and other confounders, such as, hand hygiene compliance and colonization pressure which could affect CDI rates. Furthermore, the before and after implementation of aHP design with the lack of a crossover study arm does introduce an inherent weakness. Throughout the study, we did not evaluate antibiotic utilization; however, a vigorous and successful antimicrobial stewardship program has been in place for decades with the only significant new intervention being a reduction in fluoroquinolones hospital wide.

Device cost is significantly less than other no touch disinfection systems such as HPV, ultraviolet C, PX-UV.[25] Some costs were incurred to train EVS staff to properly use and maintain the devices; however, the ease of use and device automation minimized these expenditures. The primary economic burden of elevated CDI rates can influence hospital reimbursement through pay-for-performance programs and could have a secondary impact through reduced patient satisfaction, extended length of stay, and increased recurrence or readmission.[26] We performed one cost analysis with privacy curtains over a 4-month period where a $45 per curtain replacement cost resulted in an annualized saving of over $10K not including labor. In comparison, the healthcare costs attributable to primary CDI is approximately $25K[27] and assuming there were 6 fewer infections in one fiscal quarter, this would result in a cost avoidance up to $150K. Return of investment could easily be returned in this time frame.

Before aHP implementation, a typical CDI room would require approximately 30 minutes to clean and another 45 minutes for changing privacy curtains with a total room turnover time of 1 hour and 15 minutes. With the addition of aHP, clean time was still 30 minutes and system run time with unit and vent cover removal was 2 hours for a full room turnover time of 2 and 30 minutes. Turnover time increased two-fold; however, we did not experience any significant backlogs or availability issues. Over time, staff included the increased duration in day-to-day activities without any major disruptions in room assignments. Even though a few aHP in vitro studies have achieved greater than 10^3 log reduction of *C. difficile* spores,[25] we were still able to prove significant reductions in CDI with reasonable room turnover although there was added work in implementation.

Asymptomatic shedding of *C. difficile* endospores is a major concern with environmental spread.[28] It is difficult to explain why rates did not significantly drop from 2015 to 2016 while observing a 60% decrease from 2018 to 2019; however, infection control measures, demographics, hand hygiene and other possible confounders were mostly consistent throughout the study periods. We hypothesize the likely reason for decrease was the continued elimination of environmental spores over time, along with improved implementation of aHP units in additional areas including rooms with other multidrug resistant organisms.

CONCLUSIONS

It is difficult to prove a direct cause and effect of *C. difficile* rates solely from aHP treatment because of the study design and potential confounders such as hand hygiene compliance, antibiotic usage, patient demographics, and cleaning practices. We did not directly monitor all these potential variables over the 10-year study; however, we did consistently monitor and record aHP utilization. With over 90% fogging compliance year after year, we are very confident our results suggest that aHP contributed to a reduction in CDI rates over the 5 years before and after period along with another 5 years of continued success as an addition to standard cleaning practices. Future studies are needed and should include a large cluster randomized trial of aHP, and in a high-risk environment such as an oncology unit like Anderson et al,[29] to compare the significance of terminally cleaned rooms with bleach and aHP versus rooms cleaned with only bleach for *C. difficile* transmission.

Acknowledgments

The researchers would like to thank all the EVS staff who did the work throughout this study.

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