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Reduction in *Clostridium difficile* infection (CDI) associated with the introduction of hydrogen peroxide vapor (HPV) automated room disinfection

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Conflicts: At time of writing, JAO was employed part-time by Bioquell, and he is now a consultant to Gama. JM, MP, ED and SM have no conflicts to declare.

Short title: Reduction in CDI due to HPV decontamination
Abstract

We evaluated the clinical impact of implementing hydrogen peroxide vapour (HPV) for disinfecting rooms vacated by Clostridium difficile infection (CDI) patients. Breakpoint time series analysis indicated a significant reduction (p<0.001) in the rate of CDI that occurred at the time when HPV was implemented, resulting in a reduction in the rate of CDI from 1.0 to 0.4 cases per 1000 patient days in the 2 years before vs. the first 2 years of HPV usage. HPV should be considered to augment the terminal disinfection of rooms vacated by patients with CDI.

Keywords: CDI, Clostridium difficile, HPV, hydrogen peroxide vapour, decontamination, disinfection
Introduction

*Clostridium difficile* is shed into the hospital environment, and contaminated surfaces are considered important in the transmission of *C. difficile* spores and *C. difficile* infection (CDI). In one study, admission to a room vacated by a patient with CDI increased the risk of acquisition for the incoming occupant; this association has been demonstrated for a number of other pathogens in other studies. Several studies have shown that improving the efficacy of disinfection, particularly at the time of patient discharge, reduces the rate of acquiring CDI. However, conventional disinfection relies on human operatives to assure adequate distribution and contact time for the disinfectant. Another approach is using automated room disinfection systems, most commonly hydrogen peroxide or UV based, which reduces reliance on the operator. Several studies have shown that hydrogen peroxide vapor (HPV) may reduce the transmission of CDI in hospitals. Therefore we implemented HPV for the terminal disinfection of CDI patients’ rooms.

Methods

All cases of CDI were attributed as healthcare-associated or non-healthcare-associated using CDC/NHSN criteria for national reporting purposes. Only healthcare-associated CDI (detected after 3 days of admission) were included in the analysis. From January 2012, rooms vacated by patients with CDI were disinfected using HPV using methods described by Passaretti *et al.* Briefly, HPV (Bioquell, Philadelphia, Pennsylvania, USA) was performed by placing an HPV generator and
aeration unit into each patient room, linked to a control panel situated outside the room; the system introduces vapour produced from 35% hydrogen peroxide unit microscopic condensation begins to form on surfaces. The presence of microscopic condensation on surfaces is inferred by an algorithm based on the rate of change in relative humidity measured in the room. The concentration of HPV inside the room was measured using a handheld sensor after the cycle to ensure that it is below 1 ppm before the process was considered complete. During the period before HPV disinfection was implemented patient rooms were cleaned daily and at the time of discharge using a sporicidal cleaner-disinfectant (Dispatch, Clorox, College Station, TX, USA) containing 6500 ppm sodium hypochlorite, which was applied with a 5 minute wetting time. After HPV was implemented, rooms were cleaned daily using Dispatch as described above; terminal cleaning before the HPV disinfection step was with a non-sporicidal cleaner-disinfectant (Virex II 256, Diversy). No other changes were implemented during the study period. A ‘breakpoint’ time series analysis model was performed to detect any significant changes in the monthly rate of CDI per 1000 patient days from 2010-2013 using methods described by Hughes et al. using the ‘Segmented’ package in R. The monthly number of patient days was not available for January 2010 – June 2011, so the monthly patient days data for this period was imputed using a mean of the annual number of patient days for 2010 and 2011. The breakpoint model identifies any significant change in rate, rather than specifying the breakpoint a priori. Once a breakpoint has been identified by the model, the timelines of when the intervention was introduced is overlaid. If the timeline of the intervention falls within the 95% confidence interval around the breakpoint, one can infer that the change in rate is linked to the intervention.
Results

The rate of CDI fell from 1.0 to 0.4 cases per 1000 patient days in the 24 months before HPV vs. the first 24 months of HPV usage (see Figure; 258 vs. 123 cases, 60% reduction). The breakpoint model identified two significant changes in rate: one in July 2011 (month 19) and one in January 2012 (month 25), when HPV was implemented.

3077 patient rooms and 727 other rooms were disinfected using HPV in 2012 and 2013. All rooms vacated by patients with CDI were disinfected using HPV. CDI was the reason for 670 (21.8%) of patient room disinfections and 98 (13.5%) of other room disinfections, of which 49 (50.0%) were in endoscopy / bronchoscopy procedure rooms, and 49 (50.0%) were in operating rooms. The median HPV cycle time was 1 hr 45 minutes.

Discussion

The breakpoint model identified two significant changes in the rate of CDI. The first occurred in July 2011, with 95% confidence intervals around this breakpoint spanning the spring and summer months from April to October 2011, suggesting that this first breakpoint is explained by seasonal variation. The second breakpoint occurred in January 2012, which was when HPV was first implemented. Whilst the 95% confidence intervals around the second breakpoint span from September 2011 (before HPV was implemented) to May 2012, we believe that this second breakpoint is likely to be explained by the introduction of HPV. Thus, our data suggest that
implementing HPV for the terminal decontamination of rooms vacated by patients with CDI reduced the exposure of patients to *C. difficile*-contaminated surfaces and resulted in a 60% reduction in the hospital-wide rate of CDI. Other studies have shown that improving disinfection results in a reduction of CDI. Two other before-after studies report a reduction in CDI associated with the implementation of HPV.\(^7\)\(^8\) Our 60% reduction was greater than the reductions reported by Boyce or Manian, who reported a 35% and 37% reduction, respectively.\(^7\)\(^8\) However, in these studies, HPV was only achieved on around 50% of the discharges that met the inclusion criteria.\(^7\)\(^8\) While not directly comparable, we were able to decontaminate all rooms following the discharge of patients with CDI, and this improved coverage of HPV may explain the larger reduction in the rate of CDI reported in our study.

We had already implemented sodium hypochlorite-based cleaning and disinfection of rooms before HPV use was implemented. Whilst other studies have shown that implementing sodium hypochlorite can reduce the rate of CDI,\(^5\) our findings suggest that HPV has an incremental clinical benefit over sodium hypochlorite disinfection; this is consistent with reports of surface contamination with *C. difficile* persisting after sodium hypochlorite disinfection.\(^2\)\(^7\) UV systems are appealing for automated room decontamination, because they are faster and easier to use than HPV.\(^6\) However, we chose HPV due to its improved ability to inactivate *C. difficile* spores.\(^10\) For example, one head-to-head comparison of the HPV system used in this study and a UVC system showed that the HPV system achieve a >6-log reduction on *C. difficile* spores, whereas the UVC system achieved approximately a 2-log reduction, and was significantly less effective out of direct line of sight.\(^10\)
Strengths of the study include the use of a breakpoint time series analysis model, which is less prone to bias than time series analyses where the breakpoint is specified a priori.\textsuperscript{9} Importantly, our study was performed in a low prevalence setting, with a baseline rate of 1.0 CDI cases per 1000 patients. Our study was performed over 4 years, with 2 years of pre-intervention data. We had already implemented sodium hypochlorite for terminal disinfection following cases of CDI and optimised the cleaning process. Weaknesses of the study include the before-after design, without a concurrent control unit or randomisation. Thus, we cannot rule out the possibility that other factors partly explain the difference in rate of CDI observed. However, no new infection control initiatives were implemented during this period. We did not perform any analysis of antimicrobial usage, changes in predominant strain types, compliance with hand or environmental hygiene procedures, or any changes in the patient population, which could have affected the rate of CDI. We did not perform a cost-effectiveness evaluation. However, the cost of the decontamination service per annum was less than the minimum estimate of HA-CDI cost, based on a recent review, associated with the 68 cases of CDI averted ($201,960);\textsuperscript{11} this suggests that the intervention may have been cost-saving to the hospital.

Our study suggests that improved disinfection at the time of patient discharge using HPV reduced transmission of CDI. HPV should be considered to augment the terminal disinfection of rooms vacated by patients with CDI.
**Figure:** The monthly rate of CDI in the 24 months prior to the implementation of HPV (2010 and 2011, study months 1-24) and the first 24 months of HPV usage (2012 and 2013, study months 25-48). The breakpoint model identified two significant changes in rate indicated by vertical lines at months 19 and 25; dotted vertical lines are 95% confidence intervals around the breakpoints.
References


