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Respiratory Symptoms in Hospital Cleaning Staff Exposed to a Product Containing Hydrogen Peroxide, Peracetic Acid, and Acetic Acid

Brie Hawley*, **Megan Casey**, **Mohammed Abbas Virji**, **Kristin J. Cummings**, **Alyson Johnson**, **Jean Cox-Ganser**

Respiratory Health Division, National Institute for Occupational Safety and Health, CDC, 1095 Willowdale Road, Morgantown, WV 26505, USA.

Abstract

Cleaning and disinfecting products consisting of a mixture of hydrogen peroxide (HP), peracetic acid (PAA), and acetic acid (AA) are widely used as sporicidal agents in health care, childcare, agricultural, food service, and food production industries. HP and PAA are strong oxidants and their mixture is a recognized asthmagen. However, few exposure assessment studies to date have measured HP, PAA, and AA in a health care setting. In 2015, we performed a health and exposure assessment at a hospital where a new sporicidal product, consisting of HP, PAA, and AA was introduced 16 months prior. We collected 49 full-shift time-weighted average (TWA) air samples and analyzed samples for HP, AA, and PAA content. Study participants were observed while they performed cleaning duties, and duration and frequency of cleaning product use was recorded. Acute upper airway, eye, and lower airway symptoms were recorded in a post-shift survey (n = 50). A subset of 35 cleaning staff also completed an extended questionnaire that assessed symptoms reported by workers as regularly occurring or as having occurred in the previous 12 months. Air samples for HP (range: <11 to 511.4 ppb) and AA (range: <8.8 to 319.4 ppb) were all below established US occupational exposure limits (OEL). To date, no full-shift TWA OEL for PAA has been established in the United States, however an OEL of 0.2 ppm has been suggested by several research groups. Air samples for PAA ranged from <2.2 to 48.0 ppb and were well below the suggested OEL of 0.2 ppm. Hospital cleaning staff using a sporicidal product containing HP, PAA, and AA reported work-shift eye (44%), upper airway (58%), and lower airway (34%) symptoms. Acute nasal and eye irritation were significantly positively associated with increased exposure to the mixture of the two oxidants: HP and PAA, as well as the total mixture (TM) of HP, PAA, and AA. Shortness of breath when hurrying on level ground or walking up a slight hill was significantly associated with increased exposure to the oxidant mixture (P = 0.017), as well as the TM (P = 0.022). Our results suggest that exposure to a product containing HP, PAA, and AA contributed to eye and respiratory symptoms reported by hospital cleaning staff at low levels of measured exposure.

*Author to whom correspondence should be addressed. BHawley@cdc.gov.

Supplementary Data

Supplementary data are available at *Annals of Work Exposures and Health* online.

Keywords

acetic acid; cleaning; health care; hydrogen peroxide; lower airway; occupational asthma; peracetic acid; respiratory; sporicidal; upper airway

Introduction

Cleaning and disinfectant products are widely used in health care settings to minimize health care-acquired infections (HAIs). HAIs are estimated to cost the US health care industry $8.5–11.3 billion annually (Zimlichman *et al.,* 2013). The high costs associated with HAIs have increased demand for effective cleaning and disinfection products that can reduce infectious bacteria like methicillin-resistant *Staphylococcus aureus,* vancomycin-resistant *Enterococcus*, and *Clostridium difficile* (C. diff) in health care environments (Weber *et al.,* 2010). C. *diff* alone is estimated to cause ~15 000 deaths and cost the health care industry ~ $1–5 billion annually (Dubberke and Olsen, 2012; CDC, 2016). Because *C. diff* spores are highly resistant to many chemical and physical agents and can persist on hospital surfaces for months, health care cleaning and disinfecting practices often rely on chemicals with sporicidal activity to attain disinfection (Weber *et al.,* 2010). Glutaraldehyde, formaldehyde, chlorine compounds, hydrogen peroxide (HP), and peroxy acids are known to have sporicidal activity; however, inhalational exposure to each of these chemical agents may contribute to adverse health outcomes such as upper airway irritation and irritant or sensitizer induced asthma (Russell, 1990; Rideout *et al.,* 2005; AOEC, 2015). Of the chemicals with sporicidal activity, glutaraldehyde, formaldehyde, and peroxy acids are typically used for sterilization of medical equipment. Sporicidal mixtures composed of chlorine compounds, and mixtures of HP and peroxy acids, are often used in areas throughout a health care facility as surface cleaners and disinfectants (Russell, 1990; Weber *et al.,* 2010; Abreu *et al.,* 2013). Cleaning and disinfecting products containing a mixture of HP, peracetic acid (PAA), and acetic acid (AA) are currently widely used as surface cleaners and sterilants in hospitals and are promoted as a safer alternative to chemical sterilants like glutaraldehyde and formaldehyde; however, there are few studies to support these claims (Rideout *et al.,* 2005).

Previous studies observed an increased risk for dermatitis, chronic bronchitis, and work-related rhinitis and asthma in workers exposed to cleaning and disinfectant chemicals in many different occupational settings (Rosenman *et al.,* 2003; Medina-Ramón *et al.,* 2005; Maçãira *et al.,* 2007; Arif *et al.,* 2009; Charles *et al.,* 2009; Vizcaya *et al.,* 2011; Arif and Delclos, 2012; Dumas *et al.,* 2012; Folletti *et al.,* 2014). Exposure to cleaning products has been associated with work-related asthma in agriculture, construction, manufacturing, transportation, whole sale, retail trade, services, and government industries (Rosenman *et al.,* 2003). Although respiratory effects have been well documented in workers exposed to cleaning and disinfecting products, few previous studies have simultaneously evaluated (i) cleaning workers' full-shift personal exposures to cleaning and disinfectant chemicals and (ii) upper and lower airway symptoms reported as having occurred during the workers' shift. Additionally, despite widespread use of products containing a mixture of HP, PAA, and AA,

few assessments of hospital cleaning workers' exposure to HP, PAA, and AA have been performed to date.

In 2015, the National Institute for Occupational Safety and Health (NIOSH) conducted a health hazard evaluation at a hospital where a new sporicidal product (Product A), consisting of HP, PAA, and AA, was introduced in the previous year to aid in the control of health care-associated infections. The product was used as a one-step disinfectant and sporicidal agent on all surfaces throughout the hospital, except floors. Hospital cleaning staff cited concerns about exposure to Product A, and occurrence of symptoms related to product use that included eye and nasal problems, asthma-like symptoms, shortness of breath, wheeze, chest tightness, and cough. We collected personal, time-weighted average (TWA) air samples for HP, PAA, and AA on participants while they performed their regular cleaning duties, and administered a post-shift survey to evaluate acute upper and lower airway symptoms that occurred across their work shifts. Some participants also completed an extended questionnaire that assessed symptoms reported as regularly occurring or as having occurred in the previous 12 months. To our knowledge, no previous studies have assessed acute (cross-shift) and chronic upper and lower airway symptoms in hospital cleaning staff exposed to a mixture of HP, PAA, and AA.

Methods

Study population

Hospital cleaning staff on all three shifts, and in all hospital departments, were invited to participate in the air sampling, post-shift survey, and extended questionnaire. Participation was voluntary. Workers gave informed consent before participating in the air sampling, post-shift survey, and extended questionnaire. Demographic information was collected in the extended questionnaire.

Exposure assessment

We collected 50 TWA, full-shift samples while participants performed their regular cleaning duties throughout the hospital. Full-shift samples of 41 participants were collected from workers' breathing zones while eight samples were mobile-area samples. For the mobilearea samples, we followed participants while they performed their cleaning duties and placed the samplers near the participants in the rooms while they cleaned. TWA samples were collected from participants assigned to the following hospital areas: main operating rooms, birth center, birth center triage, birth center operating room, ante- and post-partum, medical-surgical, orthopedic surgery, intensive care unit, oncology, neonatal intensive care unit, outpatient clinic, and public bathrooms. Four samples were collected from 'float' cleaning employees who were assigned to cover regular cleaning duties in multiple areas of the hospital. One sample was collected on an employee assigned to clean floors in multiple areas of the hospital and who did not use Product A during their cleaning duties.

All air samples were analyzed for HP, PAA, and AA content. HP and PAA were simultaneously collected on a cassette in-line with a glass tube sampler at a flow rate of 1 liter per minute (lpm), and were analyzed according to the method specified by Hecht *et al.*

(2004). HP was collected on two quartz filters coated with titanium oxysulfate hydrate preloaded in a 25 millimeter (mm) two-piece polystyrene cassette with no support pad (SKC 2016). PAA was collected on a glass tube containing 800 mg silica gel coated with methyl p-tolylsulfoxide with two glass wool separators, downstream of the HP quartz filters (SKC 2016). AA was collected using glass sampling tubes containing coconut shell charcoal at a flow rate of 0.2 lpm and analyzed according to Occupational Safety and Health Administration (OSHA) Method PV2119 [OSHA 2003]. The limits of detection were 4 μg of HP, 2 μg of PAA, and 3 μg of AA per sample, respectively.

We also observed participants while they performed their regular cleaning duties and recorded task duration, cleaning products used, duration of cleaning product use, and use of any personal protective equipment. In addition to Product A, participants also used other products that contained asthmagens including ethanolamine, bleach, and quaternary ammonium compounds. Use of other asthmagen-containing products was summed to create an asthmagen score to account for use of all other asthmagen-containing products. Other asthmagen-containing products were defined as products that contained chemicals listed as an asthmagen by the AOEC (AOEC 2015). A summed asthmagen score of 0 to 3 was assigned to evaluate use of all other asthmagen products by workers during their regular cleaning duties. A minimum score of zero indicated that a participant did not use any products containing ethanolamines, bleach, or quaternary ammonium compounds during their shift whereas a maximum score of three indicated a participant used products containing ethanolamines, bleach, and quaternary ammonium compounds during their shift.

Post-shift survey of acute symptoms

We administered a voluntary post-shift survey to workers ($n = 50$) who participated in the air sampling survey. The post-shift survey asked if participants had experienced eye, upper airway, or lower airway symptoms during their shift. When workers reported symptoms that occurred during their work shift, we asked (i) if their symptom had worsened during their shift; (ii) what they were doing when the symptom first began; and (iii) if they had that symptom upon arrival at work that day. We focused our analyses on work-related symptoms, which were defined as symptoms that occurred during the participants' shift that were not present upon arrival at work that day. Participants were asked about the following symptoms: burning, itchy, runny nose; sneeze; burning, itchy, watery eyes; burning, dry, sore throat; cough; wheeze; chest tightness; shortness of breath; difficulty breathing; and dizziness. Upper airway symptoms were defined as nasal, eye, and throat symptoms. Lower airway symptoms were defined as cough, wheeze, chest tightness, shortness of breath, and difficulty breathing.

Extended questionnaire

As part of the health hazard evaluation, we administered a questionnaire to 79 cleaning workers 1 week prior to the air sampling survey, which included 35 air sampling and post-shift survey participants from the present study group. Questions addressed respiratory and dermatological symptoms, asthma and other diagnoses, smoking history, work history and practices, and demographic information. Respiratory symptom and asthma questions were taken from the Third National Health and Nutrition Examination Survey (NHANES III)

(Department of Health and Human Services, 1996) and the European Community Respiratory Health Survey (Grassi *et al.,* 2003).

Asthma-like symptoms were defined as having responded 'yes' to any of the following questions: (i) 'Are you currently taking any medicine (including inhalers, aerosols or tablets) for asthma?' (ii) 'Have you had wheezing or whistling in your chest at any time in the last 12 months?' (iii) 'Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?' (iv) 'Have you been woken by an attack of asthma at any time in the last 12 months?'

Statistical analyses

We used the American Conference of Governmental Industrial Hygienists (ACGIH) Additive Mixture Formula to create mixture exposure groups for the total mixture (TM) of HP, PAA, and AA as well as the oxidant exposure mixture (OM) of HP and PAA (ACGIH 2016). Measurements below the LODs were replaced by imputations, which were randomly simulated from 0 to the corresponding LODs (Ganser and Hewett 2010). Measured parts per million (ppm) concentrations of HP and AA were divided by their established OSHA permissible exposure limit (PEL) and NIOSH recommended exposure limit (REL) of 1 ppm and 10 ppm, respectively [equations (1) and (2)]. Measured ppm concentrations of PAA were divided by the occupational exposure limit (OEL) proposed by multiple researchers, of 0.2 ppm (Gagnaire *et al.,* 2002; Pacenti *et al.,* 2010; Pechacek *et al.,* 2015). TM and OM exposure was determined using equations (1) and (2),

$$TM = \frac{[HP]}{1ppm} + \frac{[PAA]}{0.2ppm} + \frac{[AA]}{10ppm} \quad (1)$$

$$OM = \frac{[HP]}{1ppm} + \frac{[PAA]}{0.2ppm} \quad (2)$$

where [HP], [PAA], and [AA] represent the measured full-shift TWA concentrations for HP, PAA, and AA. ACGIH states that when two or more chemicals have been observed to have similar toxicity on the same target organ or system, the mixture formula can be used to assess if an exposure exceeds the threshold limit of the mixture, which is defined as one (ACGIH, 2016). The summed values from the additive formula were divided into tertiles to create TM and OM exposure variables with low, medium, and high exposure categories. TM exposure was analyzed as continuous or categorical, with categories defined as (1) low = <0.088, (2) medium = 0.088 to 0.228, or (3) high = >0.228. OM exposure was analyzed as continuous or categorical with categories defined as (1) low = <0.08, (2) medium = 0.080 to 0.218, and (3) high = >0.218. TM and OM exposure variables were used for exposure and health outcome analyses.

Statistical analyses were conducted using SAS software version 9.3 (SAS Institute, Inc., Cary, NC). An alpha of 0.05 was used to establish significance for all hypothesis testing. SAS PROC GENMOD's log-binomial regression was used to calculate prevalence ratios and

95% confidence intervals for acute and chronic symptoms in relation to mixture exposure variables. When the GENMOD models did not converge, Fischer's exact test was used to compare symptom prevalence among the exposure categories. Age, gender, and smoking status were initially included in the GENMOD log-binomial regression models, however, the models did not converge. The LOGISTIC procedure in SAS was used to examine associations of age, gender, or smoking status with upper and lower airway symptoms. The LOGISTIC procedure in SAS was also used to analyze associations between asthmagen product use, each individual chemical constituent in the TM (HP, PAA, or AA), and upper and lower airway symptoms in the 50 post-shift survey and 35 extended questionnaire participants.

Results

Exposure assessment

Overall, full-shift TWA exposure levels for HP, PAA, and AA ranged from <11.0 to 511.4 parts per billion (ppb), <2.2 to 48.0 ppb, and <8.8 to 319.4 ppb, respectively (Fig. 1). Nine HP, 11 PAA, and 5 AA samples were below their respective LODs and were spread out across different locations. One TWA full-shift sample could not be analyzed because of error in sampling time duration. The arithmetic mean, geometric mean, and 95th percentile for full-shift TWA exposure to HP, PAA, AA, and total summed ppb exposures for each hospital area are reported in Table 1. The highest HP, PAA, AA, OM (HP + PAA), and TM (HP + PAA + AA) exposures were observed in the birth center, birth center triage, birth center operating rooms, and the medical-surgical areas.

Product A was the main cleaning product used for all surfaces except floors. Participants dispensed Product A into a bottle that they then used to pour the product into a container with submerged disposable wipes. All surface cleaning tasks were performed using Product A saturated wipes. Participants occasionally used other cleaning products containing ethanolamines (n = 3/50), bleach (n = 2/50), or quaternary ammonium compounds (n = 16/50) when cleaning glass, general surfaces, or bathroom surfaces, respectively. Nitrile gloves were used routinely when working with cleaning products. Staff occasionally chose to also wear goggles when working with cleaning products. We also observed cleaning staff who chose to wear a surgical mask when working with cleaning products; we informed them that a surgical mask does not mitigate exposure to cleaning chemical vapors.

Air sampling, acute symptom survey, and extended questionnaire participants

Demographic information for cleaning staff who participated in the air sampling, post-shift survey, and extended questionnaire can be seen in Supplementary Table 1 (available at *Annals of Work Exposures and Health* online). The median age of participants was 40 years and ranged from 20 to 67 years (Supplementary Table S1, available at *Annals of Work Exposures and Health* online). Fifty-seven percent were female (Supplementary Table S1, available at *Annals of Work Exposures and Health* online). Median tenure was 3.5 years and ranged from 0.21 to 26.2 years. Current, former, and never smokers accounted for 23%, 6%, and 71% of participants, respectively.

Work-related acute upper and lower airway symptoms

Prevalence of work-related acute eye and upper and lower airway symptoms among all post-shift survey participants is reported in Table 2. Work-related nasal and eye irritation were the most commonly reported acute symptoms. Approximately half of participants reported work-related nasal (52%) and eye irritation (44%) (Table 2). Sneeze and burning, dry, or sore throat were reported by 22% and 18% of post-shift survey participants, respectively.

Symptom prevalence in low, medium, and high TM and OM exposure groups can be seen in Table 2. Work-related nasal irritation, eye irritation, sneeze, and burning, dry or sore throat was reported by 29.4%, 17.7%, 11.8%, and 17.7%, respectively, of participants in the lowest TM exposure group. The same eye and upper airway symptoms were reported by 1.4–4.6 fold more participants in the highest TM exposure group (87.5%, 81.3%, 37.5%, and 25.0%, respectively). Prevalence of work-related acute eye and upper airway symptoms were similar in the TM and OM exposure groups (Table 2). No workers in the lowest TM or OM exposure groups reported acute work-related wheeze, chest tightness, shortness of breath, or difficulty breathing. In comparison, workers exposed to mixture levels in the medium and highest TM and OM exposure groups ($n = 33$) reported wheeze ($n = 3$, 9%), chest tightness ($n = 2$, 6%), shortness of breath ($n = 3$, 9%), and difficulty breathing ($n = 2$, 6%) (Table 2). Despite these trends, Fisher's exact test did not indicate any significant associations.

Age, smoking status, gender, and use of other cleaning products containing asthmagens were not significantly associated with acute eye, upper airway, or lower airway symptoms reported in the post-shift survey and were not included in multiple regression models. No single individual chemical constituent in the TM of HP, PAA, and AA was consistently associated with work-related acute symptoms (Supplementary Table 2, available at *Annals of Work Exposures and Health* online). Work-related nasal and eye irritation were significantly positively associated with increased exposure to the TM as well as the OM. The highest TM and OM exposure groups had 3.0 ($P = 0.005$) and 3.5 ($P = 0.005$) fold higher prevalence of nasal irritation symptoms when compared to the lowest TM and OM exposure groups (Fig. 2 and Table 3). Eye irritation prevalence in the highest TM and OM exposure groups was 4.6 ($P = 0.005$) and 6.4 ($P = 0.006$) fold higher, respectively, when compared to the lowest TM and OM exposure groups (Fig. 2 and Table 3). Although not significant, an exposure-response was observed for sneeze and throat symptoms as well. Workers in the highest TM mixture exposure group had 3.2 ($P = 0.12$) and 1.4 ($P = 0.61$) fold higher prevalence of sneeze and burning, dry, or sore throat, respectively, when compared to the lowest exposure group (Fig. 2). Workers in the highest OM mixture exposure group had 5.3 ($P = 0.11$) and 1.4 ($P = 0.6$) fold higher prevalence of sneeze and burning throat, respectively, when compared to the lowest exposure group. The number of workers that reported lower airway symptoms during their shift was too small to calculate prevalence ratios using the GENMOD log-binomial procedure in SAS.

Chronic upper and lower airway symptoms

Chronic nasal problems and watery eyes in the last 12 months were reported by 57.1% and 51.4% of participants in the extended questionnaire ($n = 35$; Table 2). Chronic lower airway symptoms of usual cough, shortness of breath when hurrying on level ground, wheeze in the

previous 12 months, and awaken from chest tightness in the previous 12 months were reported by 5.7%, 22.9%, 14.3%, and 17.1% of the 35 extended questionnaire participants, respectively.

No single individual chemical constituent in the TM of HP, PAA, and AA was consistently associated with the chronic upper and lower airway symptoms (Supplementary Table 3, available at *Annals of Work Exposures and Health* online). The highest TM and OM exposure group had 3.4 and 3.7 fold higher prevalence of shortness of breath on level ground when compared to the lowest OM and TM exposure groups, respectively (Table 3). Shortness of breath on level ground was significantly associated with increased TM ($P = 0.022$) and OM exposure ($P = 0.017$). Prevalence of wheeze in the last 12 months was 2.5–2.8 fold higher in the highest TM and OM exposure groups, when compared to the lowest exposure group (Table 3). Age, smoking status, gender, and use of other cleaning products containing asthmagens were not significantly associated with chronic eye, upper airway, or lower airway symptoms reported in the extended questionnaire and were not included in the analyses presented here.

Discussion

Few studies have evaluated occupational exposure to HP, PAA, and AA and health outcomes in a health care setting (Cristofari-Marquand *et al.,* 2007; Casey *et al.,* 2017). In this study, work-related acute eye and nasal symptoms and chronic airway symptoms were reported by hospital workers using a sporicidal product containing HP, PAA, and AA. We observed significant associations between work-related acute eye and nasal symptoms and chronic airway symptoms and increases in exposure to the total exposure mixture (TM), as well as when AA was not included in the exposure mixture variable (OM). The highest TM (HP + PAA + AA) and OM (HP + PAA) exposure groups were both associated with a 3.0–3.5 and 4.6–6.4 fold increase in acute nasal and eye irritation, respectively (Fig. 2). Our observation of increases in acute nasal and eye irritation was not surprising given that HP and AA have OELs based on eye, upper respiratory tract, and skin irritation in exposed subjects, however, no full-shift exposures measured in our study exceeded the OELs of 1 ppm for HP or 10 ppm for AA, respectively. Further, increases in exposure to the TM and OM were also significantly associated with chronic shortness of breath on level ground. The highest TM and OM exposure groups had 3.4- and 3.7-fold higher prevalence of shortness of breath, and 2.5- and 2.8-fold higher prevalence of wheeze in the last 12 months, when compared to the lowest TM and OM exposure groups, respectively, albeit these increases were not significant (Table 3).

HP and PAA are both strong oxidants and are associated with biological effects at much lower concentrations than AA, as evidenced by the lower established and suggested exposure limits for HP and PAA (Pacenti *et al.,* 2010; ACGIH 2016). Previous work by Gagnaire et al. observed responses in mice exposed to either HP, PAA, or AA and noted that the irritant potency of PA was the strongest of the three chemicals. The authors noted that PAA's irritant potency was similar to other powerful irritants to include formaldehyde, allylic compounds, chloropicrine, and chlorine or nitrogen trichloride (Gagnaire *et al.,* 2002). Gagnaire et al. also highlighted that HP had an irritant potency similar to strongly

irritating amines to include propylamine, n-butylamine, or n-pentyl amine (Gagnaire *et al.,* 2002). Because HP and PAA are strong irritants and oxidants, exposure to the mixture of HP and PAA vapors may have contributed to the acute eye and upper airway irritation symptoms, as well as shortness of breath, reported by hospital cleaning workers using Product A.

We note that although ACGIH established a 15-min exposure TLV of 0.4 ppm for PAA, no full-shift TWA OEL currently exists in the United States for exposure to PAA. Multiple researchers have proposed a TWA OEL of 0.2 ppm for PAA based on observed respiratory irritation in rodents and humans (Gagnaire *et al.,* 2002; Pacenti *et al.,* 2010; Pechacek *et al.,* 2015).The Institut National de Recherche et Sècuritè in France also proposed a full-shift OEL for PAA of 0.2 ppm (Pacenti *et al.,* 2010). Air concentrations of PAA observed in our study were well below the suggested TWA OEL for PAA. Maximum levels of PAA in our study approached one-quarter the proposed 0.2 ppm TWA OEL (Gagnaire *et al.,* 2002; Pacenti *et al.,* 2010; Pechacek *et al.,* 2015). We observed significant positive associations with eye and airway irritation symptoms at exposures below the existing or suggested exposure limits for HP or PAA, respectively. Because HP and PAA are both strong oxidants and may have a similar mode of action on the respiratory tract, we consider our approach of using the ACGIH additive mixture formula to sum concentrations of HP and PAA, normalized to their respective established and suggested OELs, to be a potentially biologically relevant exposure metric. We observed significant positive associations with eye and airway symptoms at additive mixture exposure levels (OM) that were below the ACGIH additive mixture equation TLV of one (ACGIH, 2016).

A 2007 case study reported occupational asthma in two nurses exposed daily to HP, PAA, and AA vapors when sterilizing endoscopy equipment and documented work-related rhinorrhea, conjunctivitis, cough, wheeze, and shortness of breath (Cristofari-Marquand *et al.,* 2007). Work-related symptoms were reported by each worker as beginning after 5 months or 3 years of daily exposure to HP, PAA, and AA vapors. Although Cristofari-Marquand *et al.* did not quantify exposure to HP and PAA, they used AA area air concentrations as a surrogate for exposure to HP and PAA. They reported that the highest area AA exposures measured ranged from 1.6 to 9.7 ppm, and in the highest case, approached the NIOSH REL and OSHA PEL of 10 ppm for AA. The maximum AA concentrations observed in our study here were 5- to 30-fold less than maximum area AA concentrations reported in the case study. However, we observed increases in many of the same eye, upper airway, and lower airways symptoms reported by Christofari-Marquand *et al.,* despite lower air concentrations measured in our survey. No full-shift TWA samples in our survey exceeded the NIOSH REL or OSHA PEL of 1 ppm for HP or 10 ppm for AA (Fig. 1). Maximum HP and AA levels observed in our study were approximately one-half and one-twentieth of the NIOSH REL and OSHA PEL of 1 ppm for HP, and 10 ppm for AA, respectively.

Cleaning staff are often exposed to a complex mixture of irritants and sensitizers (Bessonneau *et al.,* 2013; Gonzalez *et al.,* 2014; Melchior Gerster *et al.,* 2014). Exposure to cleaning agents with sporicidal activity such as glutaraldehyde, formaldehyde, and chlorine compounds is associated with adverse health outcomes which include upper airway irritation

and irritant or sensitizer induced asthma (AOEC, 2015). The Association of Occupational and Environmental Clinicians (AOEC) recently listed the mixture of HP and PAA as an asthmagen. However, the mechanism by which HP and PAA induce asthma has yet to be characterized (Rideout *et al.,* 2005; Cristofari-Marquand *et al.,* 2007; AOEC, 2015). Cristofari-Marquand *et al.* (2007) hypothesize that both the irritant and sensitizer pathways to asthma may be possible after exposure to HP and PAA. Regardless of the mechanism, the prognosis for workers who develop occupational asthma and continue to be exposed to the irritant or sensitizing agent is poor (Ortega *et al.,* 2002). Additionally, we note that when OELs do exist, the exposure limits may not be protective for a worker that has become sensitized. Previous studies highlight that sensitizer induced asthma may have greater socio-economic consequences for a worker that develops occupational asthma beyond the health effects alone. Vandenplas *et al.* (2003) highlight that 25–38% of workers diagnosed with occupational asthma will experience prolonged work disruption and 42–78% will report a substantial loss in income. For cleaning staff that develop asthma related to exposure to HP and peroxy acids, removal from cleaning duties that require the use of sporicidal agents may be warranted; however, these decisions should be discussed carefully with their physician (Mapp *et al.,* 2005; Smith and Bernstein, 2009).

The Healthcare Infection Control Practices Advisory Committee (HICPAC) provides recommendations for when and where sterilization with sporicides, versus disinfection with high- and low-level disinfectants, should occur in health care facilities (Rutala and Weber, 2008). HICPAC states that at higher concentrations, HP, and PAA mixtures are used as high-level disinfectants for semicritical items that come into contact with mucus membranes or non-intact skin like respiratory therapy and anesthesia equipment, and some endoscopes (Rutala and Weber, 2008). In the 2007 case study, the nurses who developed work-related rhinorrhea, conjunctivitis, cough, wheeze, and shortness of breath were exposed to HP, PAA, and AA vapors while sterilizing endoscopy equipment (Cristofari-Marquand *et al.,* 2007). Recently, the mixture of HP and PAA at lower concentrations has shown promise as a novel sporicidal agent that can be used on a wide variety of surfaces (Deshpande *et al.,* 2016). We note that the at-use concentrations for HP and PAA in Product A are lower than concentrations of HP and PAA used for high-level disinfection. However, we observed acute symptoms in cleaning staff exposed to HP, PAA, and AA vapors even with a lower at-use concentration of HP and PAA. We observed cleaning staff using the sporicidal agent, Product A, on surfaces throughout the hospital, including surfaces in patient rooms and in nonpatient care areas. Substitution with a low-level disinfectant for routine cleaning of surfaces in non-patient areas is one option for reducing exposures, though this may not be possible for surfaces in areas with isolation precautions in place. Additionally, substitution with another low-level disinfectant such as phenolic, iodophors, alcohols, or chlorine compounds may also cause upper airway irritation and irritant or sensitizer induced asthma in some workers. A combination of engineering controls such as increased ventilation, administrative controls such as removal from cleaning duties, and PPE controls can be used in areas where substitution with less hazardous chemicals may not be possible.

Our study was small and this may have affected our ability to detect significant associations. The small sample size impaired our ability to calculate prevalence ratios for the acute lower airway symptoms. Furthermore, our health assessment was limited to symptoms; we did not

include objective health measurements such as lung function testing. However, we used questions from standardized instruments whenever possible. In particular, we defined asthma-like symptoms based on a set of questions that had been validated by reference to clinical diagnosis of asthma (Grassi *et al.,* 2003). Nonetheless, we were unable to assess potential limitations associated with self-report such as recall bias. We did not assess the severity of acute symptoms reported by cleaning staff in our post-shift survey. Future studies that utilize a survey of acute symptoms could be designed to include questions about the severity and duration of acute symptoms experienced by the workers during their shift as well as objective health measurements. Another limitation of our study is that we only collected full-shift TWA samples for the three chemical constituents, HP, PAA, and AA, found in Product A. Sampling and analytical limitations hindered our ability to assess short-term exposures and compare short-term exposures with the established short-term exposure limits established by the ACGIH. Additionally, we did not sample for other irritants or sensitizers. However, we were able to observe and record cleaning workers' use of other asthmagen-containing products, and did not find any significant associations between symptoms and use of products containing bleach, ethanolamine, quaternary ammonium compounds, or any combination of the three other asthmagens observed in use by cleaning staff as they performed their regular cleaning duties.

Occupational exposure to PAA has been largely undocumented due to previous sampling and analytical method limitations. The sampling method we used to collect HP and PAA relies upon a sampling train that simultaneously collects HP and PAA (Hecht *et al.,* 2004). Manning *et al.* (2016) observed that because HP and PAA share similar reactivity, almost any reagent that reacts with HP will react with PAA, and they noted the potential for some PAA to be collected on the quartz filter used for collection and analysis of HP. The results presented by Manning *et al.* (2016) suggest that given the range of PAA concentrations measured in our study (<2.2–48 ppb), the actual concentrations of PAA could have been twice as high as what we measured, and some of the PAA may have been misclassified as HP on the quartz filter. We attempted to address this potential limitation by summing the values of HP and PAA to generate the OM and TM exposure variables used for all analyses.

Our study here measured occupational exposure to HP, PAA, and AA in a hospital facility; however, workers may be exposed to HP, PAA, and AA in occupational settings outside of health care settings such as childcare, food service, agricultural, and food production industries (Straus and Meinelt 2009). Further study is warranted to develop an improved sampling method for HP and PAA collection and analysis, and characterize the potential health effects from occupational exposure to HP, PAA, and AA across a wide range of possible exposures in different occupational settings.

Conclusions

Hospital workers using a sporicidal product containing HP, PAA, and AA reported work-related acute eye and upper airway symptoms, as well as chronic airway symptoms at low levels of measured exposures. Increased exposure to the mixture of the two oxidants: HP and PAA, as well as the total mixture of HP, PAA, and AA, were significantly associated with increases in work-related acute nasal irritation and eye irritation, as well as chronic shortness

of breath. All full-shift TWA air samples for HP and AA were below established US OELs. To date, no full-shift TWA OEL for PAA has been established in the United States, although a TWA OEL of 0.2 ppm for PAA has been proposed by several groups. All TWA air samples for PAA were below the proposed TWA OEL of 0.2 ppm for PAA. Because both HP and PAA are strong oxidants, the mixture of HP and PAA potentially contributed to the airway symptoms reported by cleaning staff, at the low levels of measured exposures. Our observations of respiratory symptoms in hospital workers using a sporicidal product containing HP, PAA, and AA, indicate a need for engineering, administrative, and/or PPE controls to reduce exposure. Follow-up monitoring of respiratory and eye symptoms in hospital cleaning staff using cleaning products containing HP, PAA, and AA, can be used to evaluate the effectiveness of controls used to reduce exposure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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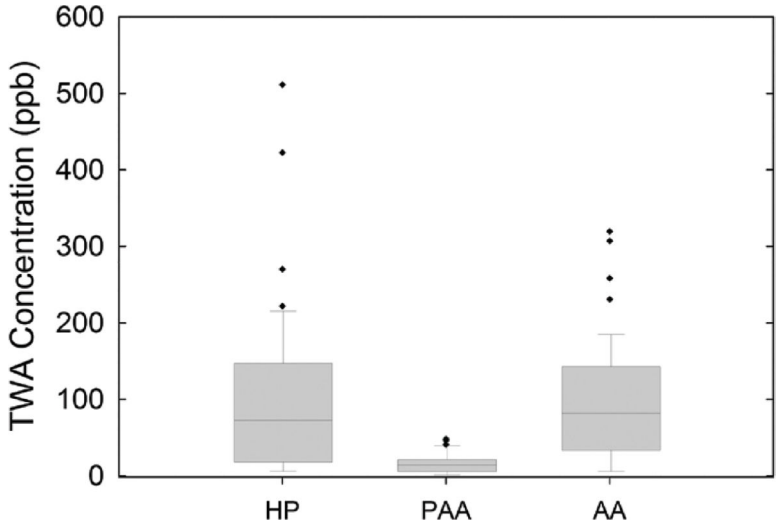

Figure 1.

Box-whisker plots of time-weighted average (TWA) concentrations for hydrogen peroxide (HP), peracetic acid (PAA), and acetic acid (AA). Outliers are indicated by single points. Each box shows the 25th to 75th percentile range for HP, PAA, and AA, respectively, with the median value marked as the horizontal line inside the box. The NIOSH REL and OSHA PEL is 1000 ppb for HP and 10 000 ppb for AA.

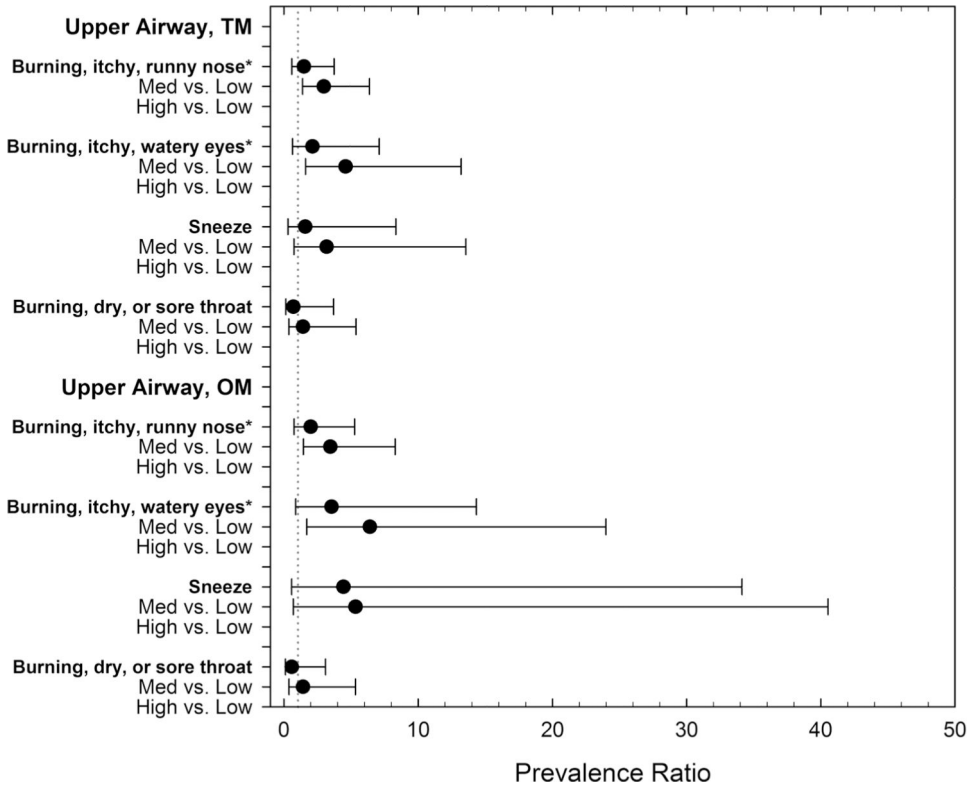

Figure 2.

Prevalence ratios and 95% confidence intervals for eye and upper airway symptoms reported during work-shift in the medium and high total mixture and oxidant mixture exposure groups. *P < 0.05.

Table 1.

Arithmetic mean, geometric mean, and 95th percentile of time-weighted average (ppb) exposures to hydrogen peroxide, peracetic acid, acetic acid, total mixture, and oxidant mixture by hospital area.

Hospital area (*n* = 49)	Hydrogen peroxide (HP)			Peracetic acid (PAA)			Acetic acid (AA)			HP+PAA+AA (ppb)			HP+PAA (ppb)		
	Mean (± SD)	GM	95%ile	Mean (± SD)	GM	95%ile	Mean (± SD)	GM	95%ile	Mean (± SD)	GM	95%ile	Mean (± SD)	GM	95%ile
Main OR (*n* = 3)	13 (± 11)	10	26	3 (± 4)	2	7	26 (± 35)	13	67	42 (± 51)	26	101	16 (± 15)	12	33
Birth center (*n* = 10)	186 (± 132)	144	511	23 (± 12)	20	46	159 (± 75)	145	307	368 (± 183)	327	701	208 (± 132)	173	522
Birth center triage (*n* = 3)	90 (± 42)	85	138	32 (± 14)	30	48	81 (± 41)	75	129	203 (± 56)	197	248	122 (± 42)	117	166
Birth center OR (*n* = 3)	175 (± 59)	167	222	26 (± 20)	21	48	150 (± 49)	143	185	350 (± 119)	335	455	200 (± 72)	191	270
Ante- and postpartum (*n* = 6)	64 (± 30)	55	94	18 (± 12)	15	41	122 (± 36)	117	167	204 (± 65)	193	270	82 (± 36)	73	117
Medical-surgical (*n* = 2)	113 (± 52)	106	149	21 (± 8)	21	27	158 (± 104)	140	231	292 (± 148)	272	396	134 (± 44)	130	165
Surgery, orthopedics (*n* = 3)	32 (± 36)	19	72	5 (± 7)	2	13	47 (± 63)	22	119	84 (± 105)	48	204	37 (± 42)	22	85
ICU (*n* = 2)	62 (± 15)	61	73	15 (± 1)	15	15	84 (± 3)	84	86	161 (± 12)	161	170	77 (± 15)	76	88
Oncology (*n* = 3)	97 (± 107)	45	215	9 (± 10)	5	21	40 (± 20)	37	64	147 (± 110)	110	253	106 (± 108)	52	222
NICU (*n* = 5)	133 (± 168)	60	423	11 (± 9)	5	22	32 (± 27)	24	73	175 (± 197)	100	510	143 (± 172)	67	437
Outpatient clinic (*n* = 3)	14 (± 7)	12	19	7 (± 6)	5	12	30 (± 13)	27	39	51 (± 26)	45	70	21 (± 13)	18	31
Public bathrooms (*n* = 1)	25	–	–	5	–	–	122	–	–	151	–	–	29	–	–
Float (*n* = 4)	69 (± 92)	26	202	12 (± 16)	5	34	128 (± 135)	63	319	210 (± 238)	107	555	81 (± 108)	31	236
Floors (*n* = 1)	6	–	–	1	–	–	6	–	–	13	–	–	7	–	–

SD indicates one standard, deviation, ± one standard, deviation shown in parentheses. GM indicates geometric mean. 95%ile indicates 95th percentile. Float = employees assigned, to cover cleaning duties in multiple units; NICU = neonatal intensive care unit; OR = operating room. The symbol '—' indicates too few samples from location to calculate GM or %ile.

Table 2.

Acute and chronic symptom prevalence, by total mixture and oxidant mixture exposure group

Work-related acute symptom	Overall prevalence (%)	TM prevalence (%)			OM prevalence (%)		
	(*n* = 50)	Low	Medium	High	Low	Medium	High
Nasal irritation[ab]	52.0	29.4	43.8	87.5	25.0	50.0	86.7
Eye irritation[ab]	44.0	17.7	37.5	81.3	12.5	44.4	80.0
Sneeze	22.0	11.8	18.8	37.5	6.3	27.8	33.3
Burning, dry, sore throat	18.0	17.7	12.5	25.0	18.8	11.1	26.7
Cough	20.0	23.5	18.8	18.8	18.8	22.2	20.0
Wheeze	6.0	0	12.5	6.3	0	11.1	6.7
Chest tightness	4.0	0	6.3	6.3	0	5.6	6.7
Shortness of breath	6.0	0	6.3	12.5	0	5.6	13.3
Difficulty breathing	4.0	0	12.5	0	0	11.1	0
Dizziness	6.0	5.9	6.3	6.3	6.3	5.6	6.7
Chronic symptom	(*n* = 35)	Low	Medium	High	Low	Medium	High
Nasal problems, previous 12 months	57.1	45.5	45.5	76.9	45.5	50.0	75.0
Watery eyes, previous 12 months	51.4	45.5	36.4	69.2	45.5	41.7	66.7
Usual cough	5.7	9.1	0	7.7	9.1	0	8.3
Shortness of breath on level ground[a,b]	22.9	9.1	27.3	30.8	9.1	25.0	33.3
Wheeze, previous 12 months	14.3	9.1	9.1	23.1	9.1	8.3	25.0
Awaken from chest tightness, previous 12 months	17.1	27.3	0	23.1	27.3	8.3	16.7
Asthma medication use	8.6	9.1	0	15.4	9.1	0	16.7
Asthma-like symptoms	28.6	36.4	9.1	38.5	36.4	16.7	33.3

[a]Indicates symptoms significantly positively associated with increased exposure to the total mixture of HP, PAA, and AA ($P < 0.05$).

[b]Indicates symptoms significantly positively associated with increased exposure to the oxidant mixture of HP and PAA ($P < 0.05$).

Table 3.

Acute and chronic symptom prevalence ratios, by total mixture and oxidant mixture exposure group[a]

Acute symptom	TM prevalence ratio (95% CI)		OM prevalence ratio (95% CI)	
	Medium	**High**	**Medium**	**High**
Nasal irritation[bc]	1.49 (0.59–3.74)	2.98 (1.39–6.36)	2.00 (0.76–5.26)	3.47 (1.45–8.29)
Eye irritation[bc]	2.13 (0.64–7.10)	4.60 (1.61–13.20)	3.56 (0.88–14.35)	6.40 (1.71–23.98)
Sneeze	1.59 (0.30–8.33)	3.19 (0.75–13.55)	4.44 (0.58–34.14)	5.33 (0.70–40.54)
Burning, dry, sore throat	0.71 (0.14–3.70)	1.42 (0.37–5.37)	0.59 (0.11–3.11)	1.42 (0.38–5.33)
Cough	–	–	–	–
Wheeze	–	–	–	–
Chest tightness	–	–	–	–
Shortness of breath	–	–	–	–
Difficulty breathing	–	–	–	–
Dizziness	–	–	–	–
Chronic symptom	Medium	High	Medium	High
Nasal problems, previous 12 months	1.0 (0.4–2.5)	1.69 (0.83–3.45)	1.10 (0.47–2.60)	1.65 (0.80–3.41)
Watery eyes, previous 12 months	0.8 (0.29–2.21)	1.52 (0.73–3.2)	0.92 (0.36–2.33)	1.47 (0.69–3.14)
Usual cough	–	0.84 (0.06–12.01)	–	0.92 (0.06–12.95)
Shortness of breath on level ground[b,c]	3.0 (0.36–24.6)	3.38 (0.44–26.0)	2.75 (0.33–22.69)	3.67 (0.48–28.00)
Wheeze, previous 12 months	1.0 (0.07–14.05)	2.54 (0.31–21.06)	0.92 (0.06–12.95)	2.75 (0.33–22.69)
Awaken from chest tightness, previous 12 months	–	0.85 (0.21–3.38)	0.31 (0.04–2.52)	0.61 (0.12–3.00)
Asthma medication use	–	1.69 (0.18–16.3)	–	1.83 (0.19–17.51)
Asthma-like symptoms	0.25 (0.03–1.90)	1.06 (0.37–3.0)	0.46 (0.10–2.03)	0.92 (0.30–2.81)

The symbol '—' denotes the number of workers that reported symptoms was too small to calculate prevalence ratios using the GENMOD log-binomial procedure in SAS.

[a] Compared to those in the low exposure group.

[b] Indicates symptoms significantly positively associated with increased exposure to the total mixture of HP, PAA, and AA ($P < 0.05$).

[c] Indicates symptoms significantly positively associated with increased exposure to the oxidant mixture of HP and PAA ($P < 0.05$).