Evaluation of the ceiling levels of ortho-phthalaldehyde exposure among health care workers engaged in endoscope disinfection: A new methodology using video-exposure monitoring

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Abstract

Objectives: The present study aimed to develop a method for measuring the ceiling level of ortho-phthalaldehyde (OPA) exposure and evaluate the ceiling levels of OPA exposure among health care workers who handle disinfectant solutions containing OPA for the disinfection of endoscopes.

Methods: The study consisted of a preliminary survey and main survey. In the preliminary survey, processes involving high-concentration exposure to OPA were identified by video-exposure monitoring (VEM). In the main survey, the ceiling levels of OPA exposure for high-concentration exposure processes identified from the results of the preliminary survey were determined using a measuring method combining sampling using a 2,4-dinitrophenylhydrazine-silica cartridge and analysis by high-performance liquid chromatography tandem mass spectrometry.

Results: In the preliminary survey, seven processes involving high-concentration exposure to OPA were identified by VEM. The duration of each process was short, lasting from 20 seconds to a few minutes. In the main survey, the OPA concentrations for the identified high-concentration exposure processes ranged from 1.18 to 4.49 ppb, which markedly exceeded the threshold limit value ceiling (TLV-C) of 0.1 ppb recommended by the American Conference of Governmental Industrial Hygienists.

Conclusions: The method for measuring the ceiling level of OPA exposure was established using VEM and the highly sensitive method of chemical analysis; and we successfully evaluated the ceiling levels of OPA exposure among health care workers engaged in endoscope disinfection. This approach can also be applied to other chemical substances with recommended TLV-Cs, and important information for reducing exposure can thus be obtained.

Keywords
endoscope, measurement method, ortho-phthalaldehyde, threshold limit value-ceiling, video exposure monitoring
1 | INTRODUCTION

The molecular structure of ortho-phthalaldehyde (OPA) consists of two aldehyde groups bound to carbon atoms in a benzene ring, and it is solid at room temperature. OPA is used as a raw material or intermediate to manufacture of disinfectants, enzyme-inhibitors, indicators, drugs, and organic compounds. In medical institutions, OPA is used widely in sterilizing agents and disinfectants for endoscopes and other medical equipment. In humans, OPA has been reported to have the potential to induce irritation of the eyes and respiratory organs, dermatitis, respiratory sensitization, etc. There have also been reports of adverse health effects among health care workers who handle OPA disinfectant solutions. Therefore, in 2019, the American Conference of Governmental Industrial Hygienists (ACGIH) recommended an extremely low concentration, 0.1 ppb, as the threshold limit value ceiling (TLV-C) for OPA.

The ACGIH defines the TLV-C as “the concentration that should not be exceeded during any part of the working exposure”, and also makes the following stipulation about sampling for measuring the ceiling level: “If instantaneous measurements are not available, sampling should be conducted for the minimum period of time sufficient to detect exposures at or above the ceiling value”. However, to our best knowledge, there are no reports on the ceiling levels of OPA exposure because no methods currently exist for instantaneous measurement of OPA in air. Therefore, measuring the ceiling level of OPA exposure requires (a) identification of high-concentration exposure works; and (b) measurement methods that can detect OPA at 0.1 ppb with very short-term sampling. To meet these requirements, previously, we developed a highly sensitive measuring method combining sampling using a 2,4-dinitrophenylhydrazine (DNPH)-silica cartridge and analysis by high-performance liquid chromatography tandem mass spectrometry (DNPH-HPLC). This method can detect OPA at 0.1 ppb with a sampling duration of 18 seconds.

The objective of this study was to develop a method for measuring the ceiling level of OPA exposure and to evaluate the ceiling levels of OPA exposure for health care workers who handle OPA disinfectant solutions for disinfection of endoscopes. To achieve this goal, we identified high-concentration exposure processes during the washing and disinfection of endoscopes by video-exposure monitoring (VEM) and we also evaluated the ceiling levels of OPA exposure for the identified high-concentration exposure processes using the DNPH-HPLC method developed. VEM is a tool that was developed in Sweden in the mid-1980s for visualization of exposure of a worker to chemical substances. After a worker, fitted with a real-time monitor and a wearable video camera, finishes his/her work, the data from the real-time monitor and the video from the wearable camera are exported and synchronized. Therefore, visual confirmation of the exposure level during his/her work becomes possible. VEM is used as an analysis tool for works involving exposure, to support training in communication of risks, and to promote participation and motivation of workers in improving the workplace environment. In this study, as a new way of utilizing VEM, the high-concentration exposure processes were identified using VEM to assess the ceiling values with high accuracy.

2 | MATERIALS AND METHODS

2.1 | Field surveys

2.1.1 | Outline of endoscope washing and disinfection procedures

The subjects were one or two health care workers who handle OPA disinfectant solution for washing and disinfection of endoscope. The workers used DISOPA Solution 0.55% (ASP Japan, LLC) containing OPA as a disinfectant solution. Figure 1 is a floor plan of the endoscope washing room. Four endoscope washing and disinfection apparatuses (Endoclens-D; Amano Co. Ltd) were set up in the room separated (automatic disinfection apparatus room) within the endoscope washing room. The volume of DISOPA Solution used in each endoscope washing and disinfection apparatus was 15.2 L. A general ventilation system was installed at the lower part of the automatic disinfection apparatus room, and was in operation, with an actual exhaust capacity of 842 m³/h (specified exhaust capacity of 1500 m³/h). At the time of the survey, no chemical substances other than OPA were used in the endoscope washing room.

The workers mainly carried out the following operations: (a) automatic washing using the endoscope washing and disinfection apparatus; and (b) manual washing of endoscope parts by immersion in DISOPA Solution. The automatic washing process for the endoscope using the endoscope washing and disinfection apparatus consisted of the following sequence of operations: (a) washing for 2 minutes using a neutral enzymatic cleaning agent (specified cleaning agent for EndoPure/Endoclens; ASP Japan LLC); (b) immersion in DISOPA Solution for 10 minutes; (c) rinsing in water for 2 minutes; and (d) passage of air for 1 minute. The total duration of a single washing cycle, including the time needed for liquid replacement in each operation, was 26 minutes. The manual washing process for endoscope parts involved immersing the endoscope parts (which had been washed with water) in an immersion tray containing DISOPA Solution for 10 minutes, picking them up, and rinsing the DISOPA Solution off with water. Automatic and manual washing processes were carried out irregularly, but consecutively. The total duration of the processes was approximately 60 minutes.
2.1.2 Preliminary survey

A preliminary survey was carried out using VEM to identify high-concentration exposure processes in the washing and disinfection of endoscopes. TIGER (Riken Keiki Co. Ltd.) was used as a real-time monitor equipped with a photoionization detector. The ionization energy of the photoionization detector lamp was 11.7 eV, and the data-recording interval was 1 second. The real-time monitor was calibrated using volatile organic compound-free gas (pure air or nitrogen) and 100 ppm isobutylene gas. The indicated values were then converted from isobutylene equivalent concentrations to total volatile organic compounds (TVOC) equivalent concentrations using a correction factor. Therefore, values in ppm indicated by the real-time monitor were converted to TVOC equivalent concentrations. A wearable video camera (HX-A1H; Panasonic Corporation) was fixed at the eye level on the worker’s temporal region. To collect data, the real-time monitor was placed close to the breathing zone of the workers by the investigators, and it was moved so as to follow the worker’s movements. Risk viewer (Japan High Soft Corporation) was used as a data-handling software for VEM.

2.1.3 Main survey

In the main survey, the ceiling levels of OPA exposure for the high-concentration exposure processes identified in the preliminary survey were measured by VEM and DNPH-HPLC. The equipment for VEM was the same as that used at the preliminary survey, except for the real-time monitor. To obtain accurate information than monitor by an investigator who follows the worker, CUB (Riken Keiki Co., Ltd.) which was small enough to be attached to the worker’s chest was used as the real-time monitor used for VEM. The ionization energy of the photoionization detector lamp in the CUB was 10.6 eV, and the data-recording interval was 1 second. The real-time monitor was calibrated in the same way as the equipment used in the preliminary survey. The sampling duration for DNPH-HPLC was 30 seconds from the start of the identified high-concentration exposure processes.
exposure processes because the duration of high-concentration exposure processes shown by VEM in the preliminary survey was 20 seconds to 2 minutes. Therefore, the OPA concentrations were expressed as an average over 30 seconds.

2.2 Procedure of DNPH-HPLC

The procedure of sampling and analysis for OPA in workplace air was carried out using the method developed by Yamamoto et al.⁷ OPA vapor was introduced into the DNPH-silica cartridge (DNPH815H; Komyo Rikagaku Kogyo Co. Ltd.) using an automatic gas-sampler (GSP-400FT; Gastec Corporation), with a flow rate of 1.0 L/min.

After sampling, OPA-DNPH was extracted by passing 5 mL of acetonitrile through the DNPH-silica cartridge. To complete the reaction between OPA and DNPH, a 50 µL aliquot of phosphoric acid/acetonitrile solution (2%, v/v) was added to 950 µL of the extraction solution and the sample was allowed to stand at room temperature for 30 minutes. Aliquots were subsequently analyzed by HPLC-tandem mass spectrometry.

High-performance liquid chromatography separation was performed using a Shimadzu Nexera UHPLC/HPLC system consisting of a DGU-20AR degasser, two LC-30AD pumps, an SIL-30AC autosampler, and a CTO-30A column oven (Shimadzu Scientific Instruments). An InertSustain C18 column (2.1 mm × 150 mm; 2 µm; GL Sciences Inc) was used and the column temperature was 40°C. The mobile phase consisted of a 70/30 (v/v) mixture of acetonitrile and 0.1 vol% formic acid in water. The flow rate was 0.2 mL/min and the injection volume was 2 µL.

Qualitative and quantitative determination of the target compounds was performed using an LCMS-8030 triple quadrupole mass spectrometer with an electrospray ionization source (Shimadzu) in negative ion mode. The analysis parameters were as follows: interface voltage = 4.5 kV, interface temperature = 350°C, resolution line temperature = 250°C, nebulizer gas flow rate = 3.00 L/min, block heater temperature = 400°C, and drying gas flow rate = 15.00 L/min. Collision-induced dissociation was performed with argon gas. Multiple reaction monitoring, optimized using OPA bis-DNPH standard solutions, was used in the analysis of the OPA bis-DNPH-derived fragment combination. The precursor ion peak and product ion peak were m/z 493 and m/z 182, respectively.

3 RESULTS

3.1 Preliminary survey

A screenshot of the data-handling software for VEM is shown in Figure 2. The values indicated by the real-time monitoring of seven high-concentration exposure processes identified from the results of VEM are shown in Table 1. The durations of these processes ranged from 19 to 87 seconds. Among the seven processes, those for which the values indicated by the real-time monitoring were particularly high include (a) opening the door to the automatic disinfection apparatus room (2.884 ppm, process 1); (b) picking up the washed endoscope from the endoscope washing and disinfection apparatus (1.419 ppm, process 2); and (c) handling the trash bags containing the waste containers of DISOPA Solution (2.295 ppm, process 5) (Table 1).

3.2 Main survey

For the identified high-concentration exposure processes, the values indicated by the real-time monitoring and the OPA concentrations measured by the DNPH-HPLC are shown in Table 2. Among these processes, the three with the highest values indicated by the real-time monitoring were the same as those identified in the preliminary survey, and the durations of these processes ranged from 20 to 190 seconds. The OPA concentrations measured by DNPH-HPLC ranged from 1.18 to 4.49 ppb, which greatly exceeded the TLV-C recommended by the ACGIH (0.1 ppb). The highest OPA concentration was recorded when picking up the endoscope from the endoscope washing and disinfection apparatus after completing the automatic washing process and was 4.49 ppb.

4 DISCUSSION

The aims of this study were to develop the measuring method for the ceiling level of OPA exposure and to evaluate those levels among health care workers engaged in endoscope disinfection using OPA disinfectant solution. For measuring the ceiling level of OPA exposure, it seemed appropriate to use a device that enabled instantaneous measurement such as a real-time monitor. However, real-time monitors currently on the market cannot measure OPA concentrations accurately because they are not calibrated for OPA. In addition, because these real-time monitors have low selectivity, the values indicated by these real-time monitors could potentially be affected by coexisting substances. In order to overcome these difficulties, we tried a combination of VEM and DNPH-HPLC.

No chemical substances other than OPA were used at the time of measurement in the endoscope washing room, so the values indicated by the real-time monitor were taken to be due to OPA. From the results of VEM, seven high-concentration exposure processes were identified (Tables 1 and 2). Among them, those with high-exposure concentrations were (a) opening the door to the automatic disinfection apparatus room; (b) picking up the washed endoscope from the endoscope washing and disinfection apparatus; and (c) handling the trash bags containing the waste containers of DISOPA Solution.
containing the waste containers of DISOPA Solution. The high OPA concentration at the time of removing the washed endoscope from the endoscope washing and disinfection apparatus suggests that there was residual OPA in the endoscope despite it having been washed. The process of handling the trash bags containing the waste containers of DISOPA Solution had no

**TABLE 1** Details and durations of high-concentration exposure processes shown by VEM, and values indicated by TIGER, in the preliminary survey

| Process | Process duration (min:s)
|---------|--------------------------|
| 1. Opening the door to the automatic disinfection apparatus room | Max | Mean |
| 2. Picking up washed and disinfected endoscope from washing and disinfection apparatus | 21 s (23:08-23:29) | 1.419 | 0.549 |
| 3. Pouring the DISOPA Solution (four containers per apparatus) | 87 s (24:35-26:02) | 0.481 | 0.355 |
| 4. Crushing the waste containers of DISOPA Solution | 58 s (26:04-27;02) | 0.424 | 0.243 |
| 5. Handling the trash bags containing the waste containers of DISOPA Solution | 22 s (27:08-27:30) | 2.295 | 0.384 |
| 6. Transfer of washed and disinfected endoscope parts from the drying rack | 19 s (28:36-28:55) | 0.555 | 0.228 |
| 7. Picking up immersed endoscope parts from immersion tray, and rinsing in water | 81 s (29:57-31:18) | 0.274 | 0.053 |

Abbreviation: VEM, video-exposure monitoring

a(min:s) indicated the elapsed time of work displayed on the video exposure monitoring

bValues as the concentrations of total volatile organic compounds indicated by TIGER during the processes
direct connection with the endoscope washing operation, so the high OPA concentration was unexpected. *Ortho*-phthalaldehyde is used widely in Japanese medical institutions, and numerous field reports have been published by Japanese researchers. OPA concentration measurements for endoscope washing processes in previous studies were carried out by the working environment measurement method or the personal exposure monitoring method. Fujita et al measured the OPA concentrations at the time of opening the cover of the immersion tray during manual washing processes. Miyajima et al measured those at the times of sterilizing the endoscope scoop in the endoscope washing and disinfection apparatus, replacing the disinfection solution of the endoscope washing and disinfection apparatus, and sterilizing accessory parts in the immersion tray. The researchers used a personal exposure monitoring method. Similarly, Honma et al measured the OPA concentrations at the times of the manual and automatic washing processes using B-sampling according to the Working Environment Measurement Standards. The high-concentration exposure processes identified by the VEM in this study were consistent with those estimated in previous studies because the endoscope washing protocols at this medical institute were the standard protocols in use in Japan, and were similar to those in previous studies. However, the VEM results in this study also identified other high-concentration exposure processes. It is probable that this discrepancy was because in the previous studies the high-concentration exposure processes were not objectively identified, in that the investigator observed a sequence of processes, and subjectively estimated high-concentration exposure processes. Therefore, VEM is considered to be useful and helpful for measuring the ceiling level of OPA exposure.

In the main survey, the OPA concentrations of the identified high-concentration exposure processes measured by DNPH-HPLC ranged from 1.18 to 4.49 ppb (Table 2). In the previous studies, the sampling duration for measuring the OPA concentration and the OPA concentration were reported as 5 minutes and 2.01 ppb, 3-22 minutes and not detected (0.2 ppb) to 10.0 ppb, and 10 minutes and not detected (3.0 ppb) to 10 ppb, respectively. Although the OPA concentrations in this study were similar to those used in previous studies, it is considered that the results of the previous studies were due to the combination of some high-concentration exposure processes because the endoscope washing procedures were carried out as diverse, consecutive, and short. In addition, as our developed DNPH-HPLC method could detect concentrations as low as 0.1 ppb with a sampling duration of 18 seconds, Miyajima et al required a sampling duration of 6 minutes to detect 0.1 ppb. Therefore, it was difficult to obtain accurate ceiling levels with the methods used in previous studies.

However, our study had limitations. (a) VEM was carried out twice in this study, in the preliminary and main surveys, and the order of the high-concentration exposure processes with respect to the indicated value of real-time monitor differed between the preliminary and main surveys. We could not use the same real-time monitor in the two surveys. Therefore, difference in the real-time monitors used and their setting position may have influenced the order of the high-concentration exposure processes. Additionally, the VEM videos showed differences in the order of the high-concentration exposure processes; this may be due

| Process | Process duration (mins)$^a$ | Values indicated by CUB (ppm)$^b$ | OPA concentration (ppb) |
|---------|-----------------------------|----------------------------------|-------------------------|
| 1. Opening the door to the automatic disinfection apparatus room | 79 s (6:01-7:20) | 0.464 | 0.052 | 2.11 |
| 2. Pouring the DISOPA Solution (four containers per apparatus) | 190 s (26:30-29:40) | 0.173 | 0.129 | 1.43 |
| 3. Crushing the waste containers of DISOPA Solution | 92 s (31:29-33:01) | 0.111 | 0.097 | 1.39 |
| 4. Transfer of washed and disinfected endoscope parts from the drying rack | 20 s (39:23-39:43) | 0.206 | 0.155 | 1.18 |
| 5. Picking up immersed endoscope parts from immersion tray, and rinsing in water | 172 s (40:50-43:42) | 0.136 | 0.098 | 1.82 |
| 6. Picking up washed and disinfected endoscope from washing and disinfection apparatus | 53 s (50:40-51:33) | 11.920 | 4.461 | 4.49 |
| 7. Handling the trash bags containing the waste containers of DISOPA Solution | 80 s (52:55-54:15) | 5.693 | 1.167 | 4.43 |

Abbreviations: OPA, *ortho*-phthalaldehyde; VEM, video-exposure monitoring.

$^a$(min:s) indicated the elapsed time of work displayed on the video exposure monitoring

$^b$Values as the concentrations of total volatile organic compounds indicated by CUB during the processes

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TABLE 2 Details and durations of high-concentration exposure processes shown by VEM, values indicated by CUB, and OPA concentrations, in the main survey.
to differences in the frequency of endoscopic washing between the two surveys. It seemed that the amount of DISOPA Solution used was different because the frequency of endoscope washing depended on its frequency of use. Therefore, if measurement of the ceiling level by DNPH-HPLC is performed according to our proposed method, it must be carried out on as many of the identified high-concentration exposure processes as possible. (b) At the field in this study, we successfully identified high-concentration exposure processes because the OPA concentrations of those processes markedly exceeded the TLV-C of 0.1 ppb recommended by the ACGIH. However, if the OPA concentrations are lower than those in this study, it may be necessary to use the real-time monitor which is more sensitive than that used in this study. Therefore, it is desirable to test real-time monitors with different sensitivity at the preliminary survey.

5 | CONCLUSION

We developed a measurement method for the ceiling level of OPA exposure using VEM and the highly sensitive method of chemical analysis and successfully assessed the ceiling levels of OPA exposure among health care workers engaged in endoscope disinfection. By using VEM, it was possible to identify high-concentration exposure, and thus determine beforehand the timing for measuring the ceiling level. We believe that our approach to measuring the ceiling level is a new approach to utilizing VEM and that this study is the first report to accurately measure the ceiling level of OPA exposure among workers. Our approach could be applied to other chemical substances for which TLV-Cs have been recommended. This method could be used to obtain important information for reducing exposure, and is thus expected to lead to a simple, efficient, and accurate approach to reducing exposure.

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AUTHOR CONTRIBUTIONS

SY and AT designed the research; SY, YH, EY, TI, and YT collected the data; SY, MI, and MM analyzed the data; SY wrote the manuscript; MI and HH led the writing.

DISCLOSURE

Approval of research protocol: N/A
Informed consent: N/A
Registry and the registration no. of the study/trial: N/A
Animal studies: N/A
Conflict of interest: N/A.

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