Evaluation of Measures against Exposure during Administration of Hazardous Drugs through a Feeding Tube

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INTRODUCTION

In the United States, the National Institute of Occupational Safety and Health (NIOSH) has warned of hazardous drugs (HD) exposure since 2004.1 The issue of healthcare worker antitumor agent exposure was initially reported in 1979.2 A recent study demonstrated the negative impact of HD at the gene level,3 and, thus, the health and safety of healthcare workers occupationally exposed to HD, even at very low concentrations, may be compromised. The U.S. Pharmacopeia Convention published standards (USP800)4 in 2016 to protect healthcare workers who handle HD with an implementation date of December 1, 2019. However, exposure countermeasures against HD were not seriously considered in Japan until approximately 10 years ago. In July 2015, guidelines for exposure countermeasures, namely, the “Joint Guidelines for the Safe Handling of Cancer Chemotherapy Drugs,”5 were initially published jointly in Japan by the following three societies: the Japanese Society of Cancer Nursing (JSCN), the Japanese Society of Medical Oncology (JSMO), and the Japanese Society of Pharmaceutical Oncology (JASPO) (Guidelines). Therefore, medical staff is now recognizing the importance of preventing HD exposure. The simple suspension method is a method employed in Japan by which drugs are administered via a feeding or gastrostomy tube; tablets or capsules for patients who have difficulty swallowing may be disintegrated and suspended in hot water (55°C) without crushing.6 This method is recommended by the guidelines as an administration method with less exposure because tablets and capsules do not need to be crushed.5 However, it currently remains unclear whether HD and the suspensions leak during their preparation and tube administration using this method. Specific exposure countermeasures need to be clarified for the safe handling of HD. In the present study, to establish effective countermeasures against HD exposure, we examined HD suspension leakage using a system in which contamination may be visualized during the simple suspension method.

MATERIALS AND METHODS

Comparison of the Contamination Status Using the Conventional and Exposure Countermeasures Methods

Subjects

Subjects were 16 nurses working in the neurology and neurological surgery ward at the Kitasato University Medical Center (Kitamoto, Japan) from whom consent for participation in the present study was obtained. This ward was selected because it has the largest number of tube feeding patients in our hospital. The protocol for the present study was reviewed and approved by the Research Ethics Committee at Kitasato University Medical Center (No. 29-13).

Administering a Suspension via a Feeding Tube Model

During the use of a nasogastric tubal feeding simulator (Sakamoto Nasogastric Tubal Feeding Trainer II, M190, Saka-
moto Model Corporation, Kyoto, Japan), the upper portion of the simulator was elevated by approximately 30° on a bed at a staff station in the Kitasato University Medical Center (Fig. 1). After each process, we exchanged the sheets (NS water-proof sheets, Nissho Sangyo Co., Ltd., Tokyo, Japan) and feeding tube (8 Fr catheter, external diameter 2.7 mm, external diameter of the weight 4.6 mm, length 120 cm, Kangaroo™ New Enteral Feeding Tube, Japan Covidien Corporation, Tokyo, Japan) to check the contamination status on the bedside and table during preparation. Nurses prepared the suspension using an alternative to HD, namely, 4 riboflavin butyrate tablets (MITAN® B2 Tablets 20mg, KYORIN Rimeido Co., Ltd., Ishikawa, Japan), which emit fluorescence upon UV ray irradiation, mixed with 20mL of tap water (approximately 55°C) at the staff station and suspended for 10 min. In a preliminary experiment, we examined the ease

Fig. 1. Experimental System for the Visual Evaluation of Contamination

Figure 1 shows the method for visually evaluating the contamination status using a nasogastric tubal feeding simulator. When nurses prepare the suspension using riboflavin butyrate tablets as an alternative to HD, this suspension is injected or flushed with water into a feeding tube, and contamination may be evaluated as fluorescence visualized by irradiating black light. (Color figure can be accessed in the online version.)

Fig. 2. Conventional Method

(Color figure can be accessed in the online version.)
of visual evaluation when 1, 2, and 4 tablets were suspended and administered, and found that the use of 4 tablets was the easiest for visual evaluation. After the suspension was drawn into an injector (Terumo catheter tip syringe, SS-20CA20P, 20 mL green, TERUMO CORPORATION, Tokyo, Japan), it was administered by connecting it to a feeding tube. The nurse flushed the tubes once with 20 mL of tap water and then wrapped the tubes using gauze and rubber bands (Fig. 1).

The Conventional Method

Figure 2 shows the conventional method. After a nurse put on personal protective equipment consisting of a pair of gloves (PURPLE NITRILE-XTRA, Halyard Health, Inc., Kanagawa, Japan), an isolation gown (No. 100, Taketora Holdings Co., Ltd., Kanagawa, Japan), and protective goggles (1653701JP, Bushnell Outdoor Products Japan Inc., Tokyo, Japan), the suspension was prepared. Four tablets of riboflavin butyric acid ester, an injector, a syringe cap (ED-CP, TERUMO CORPORATION, Tokyo, Japan), and a medicine cup (No. 3, 30 cc, blue scale, sterilized, MI CHEMICAL, Hyogo, Japan) were set on a table in advance. We explained to the nurse to suspend 4 tablets in 20 mL of hot water (55°C) while being aware of the handling of drugs that have a risk of occupational exposure. We also explained to the nurse to use the items on the table to prepare the suspension and administer the drugs as routinely performed. Hot water for the suspension and fresh water used for flushing were provided in an unsterilized cup with the lid removed (kendakun white, MI CHEMICAL, Hyogo, Japan). After receiving our explanation, each nurse prepared the suspension, administered it using the feeding tube model, and flushed the tube. All nurses suspended the drug using a medicine cup.

The Exposure Countermeasures Method

Figure 3 shows the exposure countermeasures method. After the experiment involving the conventional method, we explained exposure countermeasures in the following order (exposure countermeasures method): wear two layers of gloves, a gown, and goggles, prepare 20 mL of water for flushing, and use separate injectors for administration and cleaning of the tube (flushing). Drugs need to be handled on a tray, a cap is used with the injector, and the suspension needs to be injected while covering the connection site between the injector and the tube with gauze. Care needs to be taken to prevent the injector from pointing downward. After this explanation, a nurse performed the procedure under our instructions.

Checking the Contamination Status

We confirmed the contamination status (leakage of riboflavin butyrate to the preparation, administration instruments, and personal protective equipment) at each stage of the preparation, administration, and flushing of the suspension by observing fluorescence that appear under black light irradiation. The equipment was photographed using a digital single-lens reflex camera (EOS 8000D, Canon Marketing Japan Inc., Tokyo, Japan) in the manual shooting mode (exposure time 4 s, aperture value f/8 to 11, ISO 100). All experimenters wore protective goggles that cut UV rays by black light irradiation.

Questionnaire on Exposure

After the experiment using the conventional method, the first questionnaire on the simple suspension method of oral HD was conducted and imme-
Immediately collected. After the experiment using the exposure countermeasures method, a second questionnaire was distributed immediately and collected approximately one week later. In the first questionnaire, we asked whether nurses had experience administering oral HD using the simple suspension method and what they were paying attention to when preparing and administering the suspension using the conventional method (multiple answers allowed). In the second questionnaire, we asked what they were paying attention to when preparing and administering the suspension according to the exposure countermeasures method (multiple answers allowed) and whether implementing countermeasures against exposure are necessary.

RESULTS

Comparison of the Contamination Status with the Conventional and Exposure Countermeasures Methods

Table 1 shows subject backgrounds and the presence or absence of leakage in each process. Figure 4 shows the contamination status. In the conventional method, all nurses suspended oral HD using the medicine cup (Fig. 2). Contamination of
the gloves immediately after removing the drug from the press-through package (PTP) sheet was observed with the conventional and exposure countermeasures methods (gloves (1)). On the table for preparation, leakage was noted in 6 nurses with the conventional method, but only in 4 with the exposure countermeasures method (positive change: 5 nurses, negative: 3 nurses). With the medicine cup and unsterilized cup, leakage was noted in all 16 nurses with the conventional method; however, with the exposure countermeasures method, contamination was only noted in the unsterilized cup while drawing hot water into the injector for preparation in 4 nurses (positive change: 12 nurses, negative: none). On the bedside, the suspension frequently spilled when the injector was connected to the tube using the conventional method and leakage was noted in 14 nurses; however, there was no contamination with the exposure countermeasures method. Gloves were contaminated after administration (gloves (2)) in 11 nurses with the conventional method, but in only 2 with the exposure countermeasures method.

**Questionnaire on Exposure** Figure 5 shows the results of the first questionnaire (response rate: 100%). Only 2 nurses had experience of the tube administration of oral HD, and the drugs administered were Avolve® capsules (dutasteride) and unclear. Regarding issues nurses considered in the preparation of the suspension and tube administration using the conventional method, care was taken not to spill the suspension from the medicine cup (5 nurses), not to contaminate the instruments and work area (4 nurses), not to contaminate their hands (2 nurses), and tube obstruction and reflux (2 nurses).

Figure 6 shows the results of the second questionnaire (response rate: 75%), and descriptions about issues nurses considered in the preparation of the suspension and tube administration. Three or more nurses answered that they prevented leakage by using gauze (4 nurses), prepared the suspension in the injector (3 nurses), were careful to prevent contamination (3 nurses), and do procedures in the tray (3 nurses).

In all responders to the second questionnaire, awareness of the prevention of exposure during the handling of oral HD increased after the experiment. Furthermore, all responders answered that regulations for exposure countermeasures during
the tube administration of oral HD are necessary. The most frequent specific example of regulations for exposure countermeasures was a manual of the simple suspension method of oral HD (10 nurses).

**DISCUSSION**

Kurata et al. recommended careful injections leaving no residual drug in the injector in the tube administration of cytotoxic drugs, immediately discarding the injector, and drawing water into a new injector and flushing in the 6th Subcommittee, Committee on Academics, the Japanese Society of Hospital Pharmacists; however, the usefulness of these exposure countermeasures remains unclear, and the actual state of contamination has not yet been determined. In the present study, leakage of HD during the procedure usually performed by nurses in the clinical setting was investigated using the experimental tube administration system to evaluate the state of contamination. Furthermore, how HD leaked when our exposure countermeasures method was used was examined. The usefulness of exposure countermeasures needs to be confirmed by comparisons with the contamination state using the conventional method.

We found that gloves were contaminated during the process of drug removal from the PTP sheet in all nurses using the conventional and exposure countermeasures methods. Accordingly, preparation and administration using these gloves may contaminate subsequent processes. Thus, in the exposure countermeasures method, nurses were instructed to replace the outer layer of the gloves after removal of the drug, which may have reduced the subsequent degree of contamination.

A tray was used to reduce contamination, and if this prevented contamination of other areas, such contamination of the inside of the tray is considered to be acceptable. Thus, detailed data on contamination of the tray was not collected; however, in the exposure countermeasures method, contamination of the inside of the tray increased whereas contamination of the table for preparation and the bedside decreased compared with that in the conventional method. The exposure countermeasures method may have reduced leakage on the table and bedside by handling drugs on the tray and using caps.

However, 3 nurses who did not cause contamination using the conventional method caused contamination using the exposure countermeasures method because some nurses vent air from the injector before administration. Nurses need to be instructed to not vent air from the injector in the preparation of a HD suspension.

In our hospital, over-bed tables are frequently used for the preparation of tube administration. It is desirable not to contaminate over-bed tables because meals and the personal belongings of patients are placed on them. In addition to exposure countermeasures, it may be important to reduce exposure by setting an appropriate tray size, covering the entire table for preparation with a waterproof sheet, and changing the waterproof sheet each time.

In the conventional method, all nurses suspended the drug using a medicine cup, which contaminated the inside of the cup. An unsterilized cup was used to prepare water for flushing. The residual suspension in the injector used for administration spilled into the cup before drawing water into the injector in the conventional method. In contrast, in the exposure countermeasures method, the medicine cup was not used because the suspension was directly prepared in the injector. The unsterilized cup was used to draw hot water into the injector and also to draw water into a new injector for flushing. Four nurses spilled hot water into the cup when they drew into the injector, thereby contaminating the cup; however, 20 mL of hot water was accurately measured and completely drawn, which may have reduced contamination of the cup. Since water for flushing was drawn into an unused injector, the cup was not contaminated, in contrast to the conventional method, suggesting that exposure countermeasures using a separate injector for flushing from that used for preparation and administration are useful.

Regarding the procedure at the bedside, 14 nurses spilled the suspension using the conventional method, but not with the exposure countermeasures method. As the reason for this, when the feeding tube was detached for administration and flushing, the tips of the connected regions of the feeding tube and injector faced downward and the suspension spilled in many cases using the conventional method. Moreover, the suspension leaked while moving the used injector, and leakage also occurred from the connecting part when the plunger of the injector was pushed too fast for the injection, thereby forcing pressure in some cases. On the other hand, the exposure countermeasures method consisted of administration and flushing being performed on the tray, the tube tip not being turned downward, and the use of gauze during the injection and disconnecting the feeding tube. These steps may have reduced contamination. In addition, nurses were instructed to wrap the connection between the injector and feeding tube with gauze and inject at a speed of 20 mL per 10 s to prevent excessive pressure being loaded, which may also have reduced contamination. Careful pressurization is recommended for the injection, suggesting that exposure is preventable with appropriate instructions on the administration rate to prevent leakage from the connecting part during the injection.

Eleven nurses contaminated gloves when they removed the drug from the PTP sheet with the conventional method; however, this occurred in only 2 nurses with the exposure countermeasures method. Exposure countermeasures by applying gauze during the injection and flushing may have markedly reduced new contamination of the gloves. However, the cap touched the drug adhering to the tube tip when it was closed in one case. It is necessary to instruct nurses to be aware of the drug solution adhering to the tube tip and to carefully close the cap.

Our exposure countermeasures method may reduce leakage of the drug during the tube administration of HD by the simple suspension method more than the conventional method, and it is applicable to tube administration in consideration of exposure in the clinical setting.

In the present study, exposure countermeasures were performed with instructions after the experiment using the conventional method. Therefore, not only the execution of exposure countermeasures, but also the effects of these instructions may have contributed to the differences observed in contamination between the conventional and exposure countermeasures methods. In the second questionnaire, all responders answered that awareness of exposure during the handling of oral HD increased after the experiment. Furthermore, the con-
tent of answers regarding issues nurses considered during the preparation of the suspension and tube administration using the exposure countermeasures method became more specific and increased, suggesting that the effects of instructions on exposure countermeasures influenced the answers obtained.

Since the experiment with the conventional method was initially performed, nurses were familiar with the process and stages at which leakage occurs when the experiment with the exposure countermeasures method was subsequently conducted, and this may also have contributed to reductions in leakage. A workshop introducing the exposure countermeasures method may be effective.

All nurses who responded to the questionnaire after the experiment answered that the preparation of a manual on oral HD exposure countermeasures is needed, suggesting that exposure is reduced by education on the points at which leakage is likely to occur. Based on these results, our hospital has prepared a manual on tube administration using the simple suspension method that includes exposure countermeasures to oral HD, and its operation has been initiated.

The preparation of a suspension and tube administration using our exposure countermeasures method appears to reduce the leakage of oral HD, and, thus, is useful for safely performing tube administration. The preparation of a manual describing these exposure countermeasures in addition to education will facilitate the safe handling of oral HD.

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Conflict of Interest The authors declare no conflict of interest.

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