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Evaluation of exposures to healthcare personnel from cisplatin during a mock demonstration of intra-operative intraperitoneal chemotherapy administration

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HIGHLIGHTS

- Using personal protection equipment, administration of intraperitoneal cisplatin during optimal debulking surgery is safe to involved healthcare personnel.
- This is the first report of its kind to evaluate the safety of healthcare personnel during debulking surgery.

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ABSTRACT

Ovarian cancer is the leading cause of death from gynecologic malignancies in the United States. In 2006, the National Cancer Institute released an announcement supporting the use of intraperitoneal (IP) chemotherapy in advanced ovarian cancer. It remains unanswered how many cycles of IP chemotherapy are required to maintain a survival advantage. There may be a benefit with as few as three IP cycles and possibly as few as one IP chemotherapy cycle.

Objective. In preparation for a clinical trial in which chemotherapy would be administered intra-operatively, the question of exposure to healthcare personnel arose, therefore, the purpose of this study was to perform an evaluation of healthcare personnel exposure to cisplatin during a mock demonstration of intraperitoneal chemotherapy administration.

Materials and methods. The National Institute of Occupational Safety and Health (NIOSH), the Women's Cancer Center of Nevada, and the staff of the University Medical Center, Las Vegas, participated in this mock demonstration. Employees wore personal protective equipment recommended by NIOSH. Wipe, area, and breathing zone air samples were taken from the pharmacy and operating room, and during sterilization of equipment.

Results. All samples were negative for cisplatin, except for one surface wipe from the floor of the operating room (OR) after the mock procedure. Upon sanitization of the OR, no cisplatin was detected on the floor.

Conclusion. This was the first study evaluating the exposure of healthcare personnel to the administration of cisplatin intra-operatively. NIOSH endorsed this practice so long as the employees adhere to using the recommended personal protective equipment.

Introduction

Ovarian cancer is the leading cause of death from gynecologic malignancies in the United States with an estimated 21,990 new cases and 15,460 new deaths in 2011 [1]. A paradigm shift has taken place after the completion of multiple, large, randomized clinical trials by the Gynecologic Oncology Group (GOG), a National Cancer Institute (NCI)-sponsored co-operative group, all showing improved median survival when intra-peritoneal (IP) chemotherapy was added to standard intravenous (IV) chemotherapy in optimally debulked stage III epithelial ovarian cancer [2–6]. After the completion of the latest of these trials, the NCI released a clinical announcement supporting the use of IP chemotherapy in advanced ovarian cancer patients who were optimally debulked [7]. This announcement recognized the improved survival associated with the use of IP chemotherapy and should have in and of itself harkened a change in the standard of care in the treatment of advanced ovarian cancer from optimal cytoreductive surgery followed by intravenous chemotherapy to surgery followed by combined IV and IP chemotherapy [8]. However, it has been found that only 37% of ovarian cancer patients are offered

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intraperitoneal chemotherapy after optimal cytoreductive therapy [9]. One possible explanation for this is physician concern regarding exposure to themselves and healthcare personnel when administering chemotherapy, particularly in the intraoperative setting.

For a variety of well-documented reasons, the percentage of patients with advanced stage ovarian cancer able to complete six cycles of IP in combination with IV chemotherapy continues to be low, yet the advantage as expressed in terms of median survival remains significant. An analysis of IP catheter outcomes was undertaken by Walker et al. [10] in optimal stage III ovarian and primary peritoneal cancer. Of the 205 patients that were randomized to the IP arm, 119 (58%) patients did not complete six cycles of IP chemotherapy. Of the 119, 40 (34%) discontinued IP chemotherapy due to catheter complications. 34 (29%) patients discontinued IP chemotherapy secondary to unrelated reasons. Of the 205 patients that were randomized to the IP arm, 86 (42%) completed six cycles of IP chemotherapy, 11 (5%) completed five cycles, 10 (5%) completed four cycles, 14 (7%) completed three cycles, 30 (15%) completed two cycles, 38 (19%) completed one cycle, and 16 (8%) were unable to complete a single cycle of IP chemotherapy. It remains unanswered just how few cycles of IP chemotherapy are required to maintain the survival advantage observed in the GOG trials. It appears that there may be an advantage associated with as few as three cycles of IP chemotherapy and this advantage may extend to those receiving as little as one cycle of IP chemotherapy. This is very much consistent with the hyperthermic intraperitoneal chemotherapy (HIPEC) literature in the treatment of patients with pseudomyxoma and colorectal malignancies [11]. Assuming that one cycle of IP chemotherapy confers an equivalent survival advantage as does 3–6 cycles of IP chemotherapy, it could be argued that the best time to administer chemotherapy, is at the time of optimal cytoreductive surgery. Intra-operatively, the surgeon can guarantee optimal distribution of the chemotherapy and dwell times can be controlled. In attempting to design a trial to be undertaken at the University Medical Center of Southern Nevada questions arose to the safety of delivering IP chemotherapy in this setting. Specifically, the risks of contamination of staff and facilities were unknown and needed to be assessed prior to initiating such treatment at that institution.

To that end and prior to initiating any IP chemotherapy at the time of optimal cytoreductive surgery, the University Medical Center of Southern Nevada requested that the National Institute for Occupational Safety and Health (NIOSH) perform a health hazard evaluation (HHE) of potential healthcare personnel exposures to cisplatin during a mock IP procedure.

Methods

A mock demonstration of intra-operative IP chemotherapy was performed on May 11–12, 2009, in the operating room at University Medical Center, Las Vegas, Nevada, to determine the potential chemotherapy drug exposures to healthcare personnel. This evaluation included those individuals (MDs, RNs and surgical technicians) administering the pre-mixed chemotherapy in the operating room as well as the pharmacy, environmental services, and sterile processing staff. Pharmacy personnel were evaluated in their role in preparing the drug for intra-operative administration. Cisplatin (Platinol®) was the chemotherapeutic agent that was chosen as the intraperitoneal drug administered during this mock procedure [12].

Cisplatin is an antineoplastic drug that has been approved by the Food and Drug Association in the treatment of ovarian cancer [13]. Cisplatin is categorized, as a probable human carcinogen by the International Agency for Research on Cancer [14]. This drug is an alkylating agent that prevents deoxyribonucleic acid synthesis. Cisplatin is cell cycle nonspecific [10].

All employees involved in this procedure (employees in the pharmacy, OR staff, environmental services staff, and sterile processing staff) with the exception of the surgeon, wore loose fitting powered air purifying respirators with high efficiency particulate air filters, a chemotherapy protective gown over scrubs, and disposable coverings over shoes. Employees were asked to wear two pairs of gloves. 100% cotton gloves (Lab Safety Supply, Janesville Wisconsin) were worn beneath Biogel® (Cardinal Health, Dublin, Ohio) surgical gloves or nitrile chemotherapy protective gloves. The surgeon wore a surgical mask, and Biogel® gloves as his only personal protective equipment.

Wipe samples, area air samples, and personal breathing zone air samples were taken from the inpatient pharmacy during chemotherapy solution preparation; from the operating room; before, during, and after the mock procedure; during the cleaning of the operating room, and during the sterilization of the surgical equipment. Fig. 1 illustrates a NIOSH employee collecting a wipe sample from the OR floor prior to the mock procedure. In addition, protective gloves worn by employees were tested for cisplatin to evaluate the potential for dermal exposure from permeation or leakage through the gloves.

The procedure

An employee in the inpatient pharmacy prepared the 5% cisplatin solution (100 mL of cisplatin in 1900 mL of saline) in a ventilated laboratory hood, wearing the recommended personal protective equipment (a surgical mask, two pairs of chemotherapy gloves, chemotherapy protective covering and hairnet). Cisplatin was injected into an IV bag of saline and a nurse delivered the IV bag to the operating room.

We then place Ioban™ on the patient, to protect the skin from exposure. Additionally, we use a standard cesarean drape to also prevent spillage. The surgeon emptied the IV bag via plastic tubing into a metal pan, which represented an open abdominal cavity. The solution and the metal pan were both at room temperature. The solution remained in the metal pan for 25 min, while the surgeon intermittently swirled the solution with his gloved hand to simulate manual manipulation of the drug. After 25 min, the solution was suctioned out of the metal basin into a closed container that was labeled “chemotherapy waste”. While using a basin was done in this mock procedure, in an in-vivo procedure, an abdominopelvic reservoir would be constructed using a self-retaining retractor, a cv balfour (double-bladed with martin arms). Prior to administration of intraperitoneal chemotherapy, all surgical instruments are removed from the abdominal cavity so that exposure is minimized. The balfour retractor remains in the cavity during the administration of chemotherapy. Once the procedure is complete, the balfour is removed and immediately placed in a yellow chemotherapy waste bag, as to minimize exposure. As to exposure to others, the primary surgeon remains at the immediate bedside, as to periodically manipulate the

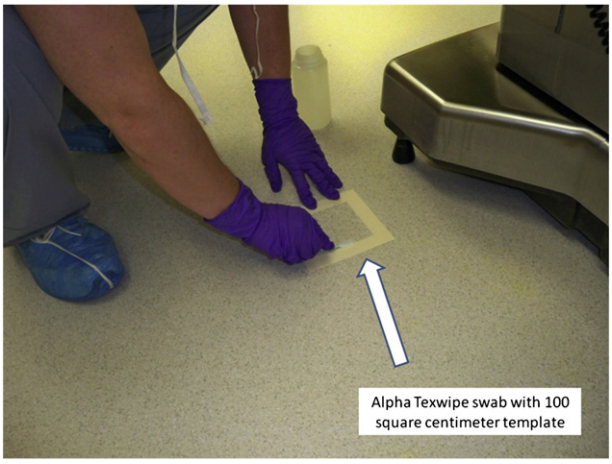

Fig. 1. Collection of wipe sample with Alpha TexWipe® swabs with a 100 cm^2 template.

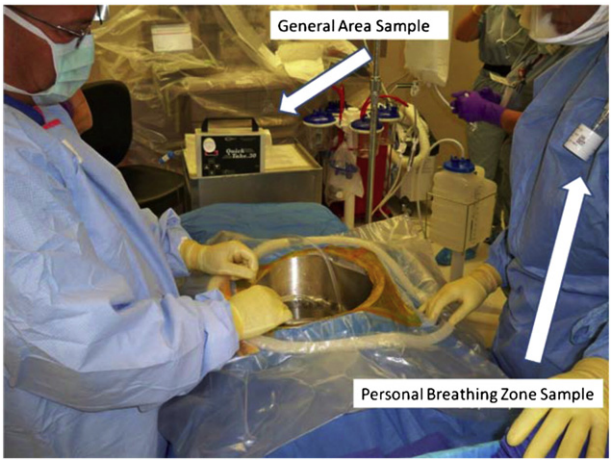

Fig. 2. General area and personal breathing zone samples collected during the cisplatin interperitoneal mock procedure.

intraperitoneal solution. Additional operating room personnel are asked to keep their distance from the patient during the procedure. We then remove just enough cisplatin solution in order to close the abdomen, as the cisplatin solution is absorbed systemically in less than 30 min.

Disposable items were placed into waste containers labeled "chemotherapy waste". Reusable surgical equipment and other items were placed in yellow chemotherapy waste bags and sent to sterile processing.

When the surgical equipment was received in sterile processing, the equipment was first rinsed with water, to remove gross contamination; then washed with a 10% bleach/water solution to neutralize any remaining cisplatin; and finally rinsed with a 1% sodium thiosulfate/water solution (to neutralize any residual chlorine).

The environmental services staff sterilized the operating room by using a 10% bleach solution, followed by a 1% sodium thiosulfate solution. These solutions were used on the walls, floors, and any other accessible surface.

Results

Airborne cisplatin was not detected in any area or personal breathing zone samples (limit of detection was 0.009 μg of cisplatin per sample) (Fig. 2). All wipe samples (Table 1) were negative for cisplatin (limit of detection was 0.007 μg of cisplatin per sample) except for one surface wipe sample (0.08 μg per 100 cm^2) that was collected on the floor of the OR after the mock procedure, but prior to the sanitization procedure. After the sanitization procedure, no cisplatin was detected from this location. No cisplatin was detected on any of the cotton gloves worn beneath the chemotherapy gloves.

Discussion

This is the first reported study to evaluate the safety of healthcare personnel administering normothermic intraperitoneal chemotherapy at the time of optimal cytoreductive surgery. In this study, potential exposures to employees were identified, and use of the advised personal protective equipment (surgical mask, two pairs of chemotherapy protective gloves, chemotherapy protective covering, and hairnet) was used to reduce potential employee exposures to cisplatin.

As this was a mock procedure, several weaknesses that must be addressed during an in-vivo procedure such as actual exposures and the appropriate level of protective equipment exist; the degree of manipulation of the cisplatin solution is surgeon dependent, and will affect exposure potential especially when administered into an open abdominal cavity containing bowel, and other abdominal organs. In this study, the metal basin that the solution was manipulated in was at room temperature, which is cooler than that of a human abdominal cavity. This lower temperature may have lessened the volatilization of cisplatin. However, cisplatin in a saline solution has a relatively low vaporization pressure of 25 °C, and a boiling point of 100 °C, suggesting that the solution will not readily vaporize at room temperature [15]. As 100 mg of cisplatin is usually diluted in 1000–2000 cm^3 of normal saline, the solution given during this procedure contained 100 mg of cisplatin/1900 cm^3 of normal saline and this could have affected the detection and exposure rates found in this study.

Because cisplatin is a platinum-based drug, sampling methods analyze for platinum, a conversion factor is used to convert results to cisplatin concentrations. This allows for very small concentrations to be identified during the exposure assessment. Since no other platinum-based drugs were used in the areas during sampling and no platinum was found in samples collected prior to the procedure, we assumed that all platinum detected on the one positive sample was from the cisplatin used during the mock procedure.

Table 1
Cisplatin wipe sample results using Alpha TexWipe swabs on May 11–12, 2009.

Sample location	Sample description	Result (μg/sample)[a]
Inpatient pharmacy	Surface of chemotherapy mixing hood after cisplatin solution was prepared	ND[b]
Operating room (before mock interperitoneal procedure)	On the floor away from cisplatin	ND[b]
	On the floor nearside to cisplatin	ND[b]
	On the floor, at the head of the operating table	ND[b]
	Hand wipe from registered nurse	ND[b]
	Hand wipe from environmental services manager	ND[b]
Operating room (after mock interperitoneal procedure but before sanitization)	On the floor away from cisplatin	ND[b]
	On the floor nearside to cisplatin	0.08
	On the floor, at the head of the operating table	ND[b]
Sterile processing	Surface of stainless steel decontamination sink (sink contained 10% bleach solution)	ND[b]
	Surface of stainless steel rinse sink	ND[b]
	On the cart used to transport surgical instruments from the operating room to sterile processing	ND[b]
Operating room (after sanitization)	On the floor away from cisplatin	ND[b]
	On the floor nearside from cisplatin	ND[b]
	On the floor at the head of the operating table[c]	ND[b]

TexWipe moistened with deionized water. A disposable template was not used for these samples.
[a] A 10 cm × 10 cm^2 disposable template was used to define the sampling area.
[b] ND = not detected (below the LOD of 0.007 μg of cisplatin per sample).
[c] The hand wipe samples were collected by swabbing both hands of the employee with an Alpha.

NIOSH recommended the following administrative controls: (1) minimize splashing and spilling of cisplatin by gently manipulating the solution within the cavity; (2) punctually clean and dispose any cisplatin that may have spilled during the procedure; (3) use two pairs of chemotherapy protective gloves when handling cisplatin; (4) wear chemotherapy protective gowns composed of polyethylene-coated polypropylene; and (5) provide an educational program to the employees regarding cisplatin and how to protect themselves from potential exposure.

The results of this initial hazard evaluation suggest that administering intraperitoneal chemotherapy at the time of optimal cytoreductive surgery can be performed safely with regard to occupational exposures to healthcare personnel. All healthcare personnel handling chemotherapy drugs or potentially contaminated items should be educated to the potential hazards and health effects of these drugs, adhere to using the recommended personal protective equipment, and follow all safety protocols to prevent exposure.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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