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Original Article

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Airborne and surface contamination after rotational intraperitoneal pressurized aerosol chemotherapy using cisplatin

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ABSTRACT

Objective: We evaluated the occupational exposure levels of healthcare workers while conducting rotational pressurized intraperitoneal aerosol chemotherapy (RIPAC) using cisplatin in a large animal model.
Methods: We performed RIPAC using cisplatin in 6 female pigs and collected surface and air samples during the procedure. Surface samples were obtained from RIPAC devices and personal protective equipment (PPE) by wiping, and air samples were collected around the operating table. All samples were analyzed by inductively coupled plasma–mass spectrometry to detect platinum.
Results: Among all surface samples (n=44), platinum was detected in 41 samples (93.2%) but not in all air samples (n=16). Among samples collected from RIPAC devices (n=23), minimum and maximum cisplatin levels of 0.08 and 235.09 ng/cm^2 were detected, mainly because of direct aerosol exposure in the abdominal cavity. Among samples collected from healthcare workers' PPE (n=21), 18 samples (85.7%) showed contamination levels below the detection limit, with a maximum of 0.23 ng/cm^2. There was no significant contamination among samples collected from masks, shoes, or gloves.
Conclusion: During the RIPAC procedures, there is a potential risk of dermal exposure, as platinum, a surrogate material for cisplatin, was detected at low concentration levels in some surface samples. However, the respiratory exposure risk was not identified, as platinum was not detected in the airborne samples in this study.

Keywords: Antineoplastic Agents; Carcinogens; Cisplatin; Surgical Procedures; Occupational Exposure

Synopsis

We assessed the occupational exposure of healthcare workers performing rotational intraperitoneal pressurized aerosol chemotherapy (RIPAC) using cisplatin. Although RIPAC devices and personal protective equipment might have surface contamination at low concentration levels, traces of cisplatin were not detected in the air. Despite the low risk of inhalation, safety measures are necessary.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Data Sharing Statement
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions
Conceptualization: K.H.S., Y.C.; Data curation: P.M., Y.C.; Formal analysis: K.S., J.W.; Funding acquisition: K.H.S., Y.C.; Investigation: P.S.J., L.E.J., K.H.S, J.W., P.M.; Methodology: P.M., Y.C.; Project administration: P.M., Y.C.; Resources: Y.C.; Software: J.W., P.M.; Validation: P.M., K.H.S., Y.C.; Writing - original draft: J.W., P.M., P.S.J., L.E.J., K.H.S., K.S., Y.C.

INTRODUCTION

Peritoneal metastasis (PM) is a therapeutic challenge because its treatment is difficult, and the prognosis is poor. To increase the average life expectancy of affected patients and improve their quality of life, the current treatment is multimodal therapy that combines cytoreductive surgery, which eliminates cancer tissues in the peritoneum, with hyperthermic intraperitoneal chemotherapy (HIPEC) to remove residual cancer cells through the distribution and penetration of liquid anti-neoplastic drugs [1,2].

The aerosolization of anti-neoplastic drugs was introduced to treat PM because of its greater feasibility, safety, and efficacy compared to treatment that combines cytoreductive surgery and HIPEC [3]. Anti-neoplastic drugs sprayed in aerosol form penetrate tissues more deeply than do drugs administered via conventional injection. This novel pressurized intraperitoneal aerosol chemotherapy (PIPAC) technique was introduced in 2012 [4]. Typically, PIPAC process comprises several steps, including the insufflation of carbon dioxide (CO_2) into the peritoneum and the application of anti-neoplastic drugs from a syringe into the peritoneum under high pressure [5]. Various types of anti-neoplastic drugs are administered using PIPAC, including the platinum compound cisplatin. However, cisplatin has been classified as likely carcinogenic to humans (group 2A) by the International Agency for Research on Cancer [6]. Thus, anti-neoplastic drugs used in PIPAC could have serious health effects such as carcinogenicity, teratogenicity, reproductive toxicity, and other organ toxicity even at low doses [7,8].

Concerns have been raised about occupational exposure during PIPAC procedures, and several studies have conducted exposure assessments of surface and air contamination levels in preclinical stages for PIPAC. The greatest potential risk comprises surface contamination during the handling, injection, and disposal of anti-neoplastic drugs used in PIPAC treatment [9]. Platinum, which is present in cisplatin in trace amounts, has been detected in syringes used to inject anti-neoplastic drugs, on the floor near the operating table, and on gloves used by healthcare workers [10-12]. The particle size of aerosols sprayed from the PIPAC nozzle is approximately 3–15 μm; this poses a potential inhalation risk related to injection trocar leakage [5]. Studies that measured platinum for the analysis of platinum compound drugs (e.g., cisplatin and oxaliplatin) reported that it was below the limit of detection (LOD) in the air during PIPAC [13,14].

The aerosolization of anti-neoplastic drugs increases the depth of their penetration into cells [5]. In addition, the conical pendulum motion can be applied in PIPAC to improve the efficiency, distribution, and penetration of aerosols. Recently, the Korean Rotational Intraperitoneal pressurized Aerosol chemotherapy Trial Group reported the efficacy and safety of rotational intraperitoneal pressurized aerosol chemotherapy (RIPAC) in a preclinical setting, but it might increase the risk of aerosols leakage from the abdominal cavity [15]. To our knowledge, no studies have examined the risks of RIPAC procedures; therefore, it is necessary to assess the risk of occupational exposure to healthcare workers by during RIPAC. The objective of this study was to evaluate surface and air contamination with cisplatin by measuring its surrogate, platinum concentrations during RIPAC procedures.

MATERIALS AND METHODS

1. RIPAC using cisplatin

This study was approved by the Institutional Animal Care and Use Committee (IACUC) of Seoul National University Hospital before study initiation (No. 18-0051-S1A0), and the investigators complied with the protocol of IACUC. Thereafter, we performed RIPAC using cisplatin in 6 female pigs weighing 40–50 kg, which was diluted with 14.7 mg in 70 mL of 0.9% sodium chloride. Then, 50 mL of the mixture was injected into a RIPAC syringe for administration via spraying. The 7 healthcare workers who performed RIPAC included a veterinarian who provided anesthesia to the swine, a surgeon, a nursing assistant, three nurses who prepared the anti-neoplastic drug, and an engineer who controlled RIPAC devices.

RIPAC procedures involved the insertion of two 12-mm trocars (Eagle-Port®; Dalim Medical Corp., Seoul, Korea) into the abdominal cavity to ensure tightness. CO_2 insufflation was then conducted using the second trocar to maintain a constant pressure of 12 mmHg in the abdominal cavity. Then, 50 mL of the prepared cisplatin drug was injected into the syringe, and the drug was transferred from the syringe to DreamPen® (Dreampac Corp., Wonju, Korea), a stainless-steel spraying nozzle developed for RIPAC [16]. The spraying nozzle was inserted into the first trocar for spraying cisplatin; a laparoscope was inserted into the second trocar with a CO_2 hose to observe the interior of the abdominal cavity. After the procedural equipment had been prepared, healthcare workers exited the operating room, and the drug was sprayed automatically at a flow rate of 30 mL/min. After spraying had been completed, the healthcare workers waited outside the operating room for approximately 35 minutes to allow drug dispersal and penetration of the peritoneum. Next, the healthcare workers entered the operating room and relieved the air pressure within the abdominal cavity through an air waste system equipped with a glass microfiber filter that had been impregnated with a carbon layer (Laparo Clear Smoke Filtration Kit; pore size, 0.027 μm; diameter, 50 mm; GVS Filter Technology, Bologna, Italy) (**Fig. 1**).

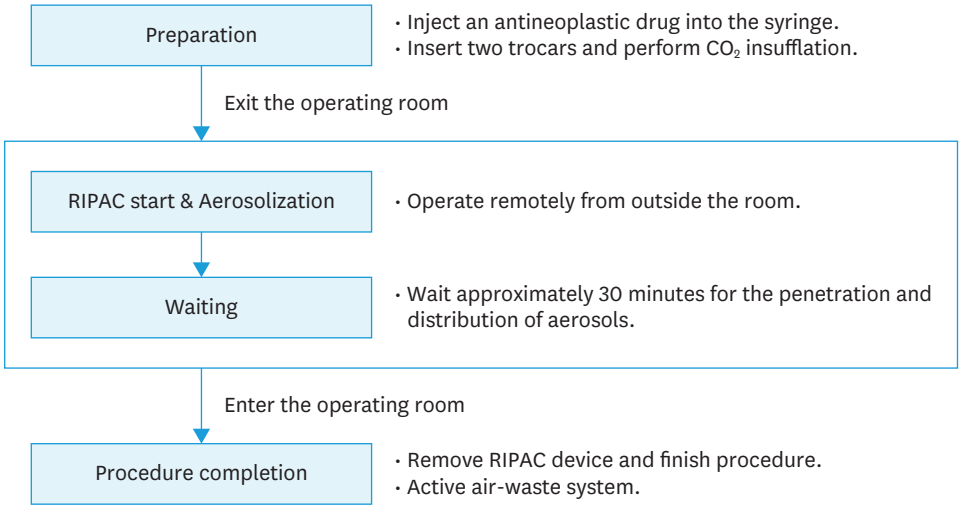

Fig. 1. Flowchart of RIPAC procedures.
RIPAC, rotational intraperitoneal pressurized aerosol chemotherapy.

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2. Sampling and analysis

Operating room conditions

The volume of air within the operating room was approximately 98.1 $m^3$with a downward airflow ventilation (i.e., laminar flow). The airflow ventilation system contained 2 air supply vents in the ceiling and one air exhaust vent in each of the 4 corners. The flow rate (m^3/min) was measured using a direct-reading balometer (Alnor EBT-731; TSI Inc., Shoreview, MN, USA). For air supply vents where direct reading equipment could not be used, the flow rate was calculated by multiplying the area by the flow rate measured using an air velocity meter (Veloci-CALC 9545; TSI Inc.). The average flow rates of the air supply and exhaust were 30.2 and 15.1 m^3/min, respectively. A smoke test was performed at the entrance of the operating room and at the site of trocar insertion to evaluate the air pressure status (positive or negative). It showed that the operating room maintained positive pressure relative to the corridor. Because the pressure in the abdominal cavity was maintained by insufflation, we measured the velocity around the 2 trocar insertion sites to check for possible leakage. The measured velocity was zero, indicating no airflow. The temperature and relative humidity of the building were controlled using a centralized system. Temperature and relative humidity data were measured using a thermohygrometer (TR-72Ui; T & D Corp., Matsumoto, Japan). The average relative humidity was 40.5%, and the average temperature was 22.7°C. The temperature was similar to the set value of 22°C, whereas the relative humidity was below the set value of 50% (**Table 1**, **Fig. S1**).

Surface sampling of RIPAC devices and protective equipment

Surface sampling was conducted by wiping surfaces with ashless filter paper (Whatman 42; diameter, 55 mm; GE Healthcare Life Science, Chicago, IL, USA), as described previously [15]. The filter papers were pretreated prior to sampling. The papers were wetted with a wiping solution that consisted of 10% acetonitrile, 25% methanol, and 65% Milli-Q water, and the solution was buffered to pH 6.0 [16]. The selected sites were wiped along the maximum area (cm^2) on uneven surfaces [17]. As the first step of the sampling strategy, the whole wetted filter was used to wipe over the target area, folded in half to wipe in the opposite direction, and then folded in half again to wipe in the original direction. To prevent sample loss through evaporation, the filter was folded again and placed in a 50-mL vial, stored at approximately −4°C, and transported to the laboratory.

Sample collection targets were primarily selected from equipment used in RIPAC (e.g., RIPAC devices such as the trocars, laparoscope, and spraying nozzle) and personal protective equipment (PPE) worn by individuals, where high exposure was anticipated (**Fig. S2**).

Table 1. Items present in the operating room for the RIPAC procedure

Antineoplastic drug	No.	No. of swine	No. of samples air/wipe (all)	Temperature* (°C)	Relative humidity* (%)	Air supply† (m^3/min)	Air exhaust† (m^3/min)
Cisplatin	1	1	4/7 (11)	22.8±0.5	40.9±5.1	30.2	15.1
	2	1	4/10 (14)				
	3	2	4/13 (17)				
	4	2	4/14 (18)				
	Total	6	16/44 (60)				

Values are presented as mean±standard deviation.
The air velocity of a slit around the closed entrance doors was approximately 1.7 m/s.
RIPAC, rotational intraperitoneal pressurized aerosol chemotherapy.
*The temperature and relative humidity of the building were controlled by a centralized management system; the settings were 22°C and 50%, respectively; †The air supply and exhaust rate were measured separately after the RIPAC procedures had been completed.

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After use, the spraying nozzle was cleaned 4 to 5 times with cotton soaked in 70% ethanol, and the nozzle was sampled before and after cleaning. Cleaning was conducted after the RIPAC procedure had been completed. To evaluate surface contamination on the PPE, we obtained the masks, gloves, and shoes of the surgeon and nurses. The anesthesiologist was excluded from equipment analysis because the pig had been anesthetized prior to the start of the RIPAC procedure.

Air sampling

Air samples were collected using a mixed cellulose ester membrane filter (diameter, 37 mm; pore size, 0.8 μm; SKC Inc., Eighty Four, PA, USA), which is recommended for trace platinum sampling according to the National Institute for Occupational Health and Safety Manual of Analytical Methods, protocol 7300 [17]. For air sampling, a high-flow pump sampler (SARA-5100; KEMIK Corp., Seoul, Korea) was used at a flow rate of approximately 17–18 L/min, calibrated using an airflow calibrator (Bios Drycal; Mesa Laboratories, Lakewood, CO, USA) before and after measurement. These measurements were conducted at locations where healthcare workers were stationed during the procedure (**Fig. 2**). Individuals working around the operating table (the surgeon, nurses, and the anesthesiologist) were selected for sampling on the basis of their task relationship with the RIPAC surgical procedure. Samples were also collected at the left corner of the entrance to the operating room at the height of approximately 1.5 m, which was regarded as the breathing zone of the healthcare workers. Sampling was conducted throughout the procedure (93.3±30.4 minutes), including drug preparation, syringe injection, and air waste management.

Analytical methods

We analyzed platinum as a surrogate for cisplatin, as described in the Manual of Analytical Methods, protocol 7300. A microwave (MARS 6; CEM Corp., Matthews, NC, USA) was used

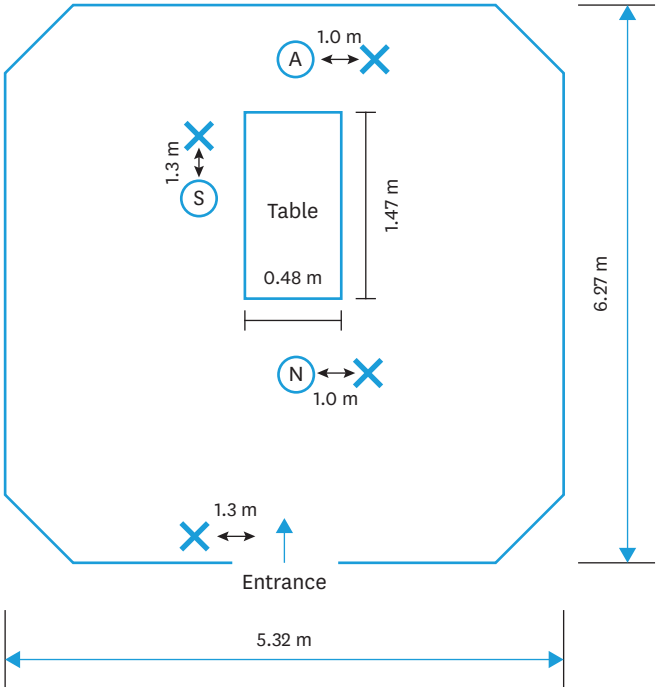

Fig. 2. Plan of air sampling locations.
A, anesthesiologist; N, nurse; S, surgeon.

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for preprocessing. Air samples were placed in a microwave vessel containing 3 mL of 70% nitric acid (Sigma-Aldrich, St. Louis, MO, USA). The temperature of the microwave was gradually increased to 200°C for 15 minutes, then maintained for 15 minutes. The pressure was set to 800 psi, while the power was set to 900–1050 W. For surface samples, 5 mL of nitric acid were injected into the microwave vessel; the temperature was gradually increased to 180°C for 15 minutes, then maintained for 10 minutes. The pressure and power were the same as the settings for air samples. Distilled water was added to the extracted samples for a final volume of 40 mL, and analysis was performed using an inductively coupled plasma mass spectrometer (NexION 350D ICP–MS; PerkinElmer Inc., Houston, TX, USA).

The LOD of the platinum in the cisplatin solution was calculated by multiplying 3 standard deviations from 7 replicate measurements at the lowest level (1 ng/mL) of the standard solution. This relationship was linear, with a correlation coefficient (r^2) for platinum of 0.9999–1.0000. The LOD of the platinum was 0.37 ng/sample.

3. Data analyses

Descriptive statistics were calculated using SPSS software, version 25 (IBM Corp., Armonk, NY, USA). Normality was assessed using the Shapiro–Wilk test; the data showed a lognormal distribution. To calculate the geometric mean (GM) and geometric standard deviation, non-detection values were set to 1/2 LOD divided by the average air volume sampled for data analysis [18]. The Kruskal–Wallis rank test was used to compare surface concentrations among PPE types (masks, gloves, and shoes) and to compare air locations.

RESULTS

Samples collected from the surfaces of RIPAC devices, including the trocars, laparoscope, and spraying nozzle (before and after cleaning) showed contamination (**Table 2**). Platinum was measured above the LOD in all surface samples (n=23), at levels of 0.02–235.09 ng/cm^2. Surprisingly, the location with the highest measured level of platinum was the second trocar (GM, 5.55 ng/cm^2). The GMs of the first trocar, laparoscope, and nozzle before and after cleaning were 4.80, 3.90, 2.43, and 0.31 ng/cm^2, respectively. The contamination level of the second trocar was 0.08–235.09 ng/cm^2. The mean was influenced by a single sample that measured 235.09 ng/cm^2. Platinum levels were higher in both trocars, which had been inserted into the abdomen, than in the laparoscope and spraying nozzle, which had been inserted into the abdominal cavity and exposed directly to the drug.

Table 2. Surface concentrations on devices used during the RIPAC procedure

Sampling location	Platinum concentration (ng/cm^2)		
	Proportion of samples measuring <LOD	GM±GSD	Min–max
Trocar 1*	0/3	4.80±1.42	3.21–6.00
Trocar 2†	0/3	5.55±55.07	0.08–235.09
Laparoscope	0/6	3.90±3.14	1.68–35.90
Nozzle (before cleaning)	0/6	2.43±2.00	1.19–8.94
Nozzle (after cleaning)	0/5	0.31±12.18	0.02–5.12
Total	0/23	2.14±7.73	0.02–235.1

The LOD of platinum was 0.37 ng/sample; GM and GSD were calculated using 1/2 LOD.
GM, geometric mean; GSD, geometric standard deviation; LOD, limit of detection; Min, minimum; Max, maximum; –, no measurement; RIPAC, rotational intraperitoneal pressurized aerosol chemotherapy.
*Trocar 1 was used to insert the spraying nozzle; †Trocar 2 was used to insert the laparoscope and CO_2 insufflation nozzle.

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Table 3. Surface concentrations on personal protective equipment used during RIPAC procedures for the administration of 3 antineoplastic drugs

Role	Type	Platinum concentration (ng/cm^2)			
		No. of samples measuring <LOD	GM±GSD	Min–Max	p-value*
Surgeon	Masks	1/4	0.05±9.20	<LOD–0.22	0.123
	Gloves	0/4	0.06±3.14	0.02–0.23	
	Shoes	1/4	<0.01±5.90	<LOD–0.02	
Nurse	Masks	0/3	0.06±1.63	0.03–0.08	0.067
	Gloves	0/3	0.04±2.04	0.02–0.09	
	Shoes	1/3	<0.01±5.56	<LOD–0.01	
Total		3/21	0.02±6.81	<LOD–0.23	

The LOD of platinum was 0.37 ng/sample; GM and GSD were calculated using 1/2 LOD.
GM, geometric mean; GSD, geometric standard deviation; LOD, limit of detection; Max, maximum; Min, minimum; –, no data; RIPAC, rotational intraperitoneal pressurized aerosol chemotherapy.
*Kruskal–Wallis rank test.

Moreover, platinum was detected in 18 of 21 (approximately 86%) samples collected from PPE. The Kruskal–Wallis rank test was used to compare concentrations among the 3 equipment types. No significant differences in platinum levels were observed among the 3 equipment types used by the surgeon (p=0.123). The platinum concentration on equipment was lowest on shoes (GM, <0.01 ng/cm^2), whereas masks (GM, 0.05 ng/cm^2) and gloves (GM, 0.06 ng/cm^2) had similar concentrations. When cisplatin was used in the procedure, the platinum concentration levels on nurses' PPE were similar to the levels on the surgeon's PPE, and no significant differences were detected among equipment types (p=0.067) (**Table 3**).

In terms of airborne contamination during RIPAC, cisplatin levels were below the LOD in all samples that had been collected in accordance with RIPAC procedures (n=16).

DISCUSSION

To evaluate the risk of occupational exposure to cisplatin through the surface and airborne contamination, we examined its concentration levels in accordance with RIPAC procedures. Occupational exposure during RIPAC administration has rarely been reported outside of preclinical and clinical studies; however, a few studies have reported air and surface contamination (**Table 4**). Notably, air concentrations below the LOD have been reported for platinum compounds since the development of the PIPAC in Europe [13]. However, low levels of surface contamination have been reported on objects surrounding the operating table, such as the floor of the operating room, PPE, and PIPAC devices. Similarly, we detected contamination in some surface samples but not in air samples.

In this study, we used pigs as the treatment target for RIPAC procedures. However, our procedure standards (e.g., CO_2 pneumoperitoneum pressure) were the same as the standards in previous studies that involved actual patients [5,19]. We conducted this study under higher risk conditions than other studies because we adopted precessional motion and excluded measures to prevent aerosol leaks such as disposable protective surgical drapes and laminar flow in the operating room; our approach ensured conservative contamination detection levels. In addition, the administration and injection of anti-neoplastic drugs into the syringe were performed in the operating room in this study, whereas in a real RIPAC procedure, the drugs would be provided to healthcare workers in a finished form after mixing, dilution, and injection into the syringe. Each step of the RIPAC procedure carries a risk of dermal contact, including drug preparation, RIPAC device operation, and aerosol dispersion into the abdominal cavity [9].

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Table 4. Summary of previous studies regarding air and surface contamination during PIPAC procedures

Authors(yr)	Ref.	AD used	Participants	Objective	Key finding(s)
Solass et al. (2013)	[13]	DX, CP (Pt)	Patients	Identify and evaluate potential hazards concerning occupational exposure during PIPAC procedures under real clinical conditions that involve human patients.	*Airborne contamination* All cisplatin samples were detected below the LOD at the working positions of the surgeon and anesthesiologist under real PIPAC conditions.
Graversen et al. (2016)	[14]	DX, CP (Pt)	Patients	Measure the presence of airborne platinum particles in the OR during PIPAC procedures.	*Airborne contamination* Filters showed no traces of platinum. Chemotherapy particles in the air were probably limited. Data were consistent with safety data from other PIPAC studies.
Willaert et al. (2017)	[20]	DX, CP (Pt), OX (Pt)	Patients	Comprehensive toxicological analysis including air and surface samples collected in accordance with clinical PIPAC procedures using CP/DX and OX.	*Surface and airborne contamination* Platinum contamination was undetectable in surface, air, or material samples collected during or after clinical PIPAC procedures. Toxicological analysis is recommended prior to starting a clinical PIPAC program to ensure the adequacy of protective measures.
Ndaw et al. (2018)	[11]	CP (Pt)	Patients	Investigate exposure to platinum compounds among medical staff during HIPEC and PIPAC procedures.	*Surface contamination* Substantial contamination of PIPAC devices. Heavy contamination of the floor within 2 m of the operating table during a leak after trocar removal. The outer surface of the surgeon's gloves was contaminated during trocar removal and laparoscopic incision closure. The surgeon's hands were not contaminated after glove removal.
Ametsbichler et al. (2018)	[10]	CP (Pt)	Patients	Evaluate contamination levels under real clinical conditions to minimize and control occupational exposure risk.	*Airborne contamination* Unless accidental leakage occurs, the inhalation of AD aerosols by OR personnel is unlikely. *Surface contamination* Platinum was detected on all surface types (floor, injector, trocar). Head ends of trocars and parts of injection devices (e.g., syringe holder) were heavily and frequently contaminated. Platinum traces on the OR floor were comparatively low. Careful cleaning and disposal of used equipment are critical for avoiding cross-contamination.
Delhorme et al. (2019)	[21]	DX, CP (Pt)	Patients	Ensure surgeon and co-worker safety during PIPAC procedures in an OR without laminar airflow.	*Airborne contamination* CP and DX levels in all air samples were <0.02 μg/m^3. *Surface contamination* 25 samples (96%) contained <2.5 ng CP. Only one sample (4%) collected from the outer surface of surgeon's first pair of gloves was positive for CP.
Roussin et al. (2021)	[12]	DX, CP (Pt)	Patients	Toxicological analyses of air and surface samples collected in accordance with e-PIPAC procedures using CP and/or DX.	*Airborne contamination* No trace of CP found in air samples. *Surface contamination* CP and DX were detected on the OR floor, surfaces, devices, and PPE, regardless of cleaning.
Larroque et al. (2021)	[22]	OX (Pt)	NA	Evaluate the risk of exposure for medical and non-medical staff during PIPAC procedures using OX.	*Surface contamination* Platinum levels were <LOD in all surface samples collected from 6 surfaces.

AD, anti-neoplastic drugs ; CP, cisplatin; DX, doxorubicin; HIPEC, hyperthermic intraperitoneal chemotherapy; LOD, limit of detection; NA, not available; OR, operation room; OX, oxaliplatin ; PIPAC, pressurized intraperitoneal aerosol chemotherapy; PPE, personal protective equipment.

Previous studies have investigated occupational exposure and safety during the PIPAC procedure, generally by evaluating platinum contaminations on surfaces and in the air. Most such studies reported contamination of the surfaces of PIPAC devices such as injectors, syringes, and trocars. One study reported surface contamination of the floors (≥0.01 pg/cm^2) and trocars (≤1.7 ng/cm^2) [10]. The contamination of PIPAC injector syringe holders, handles, and nozzle heads have also been reported [11,12]. In a 2017 study, the use of 2 clinical PIPAC procedures revealed no platinum on the floor around the operating table [20]. Similar to the findings in previous studies, we detected higher contamination levels on trocars (0.02–235.1 ng/cm^2) than on other devices used in the RIPAC procedure. Trocars and laparoscopic devices can be contaminated by droplets while they are inserted into an abdominal cavity

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that contains aerosols. Therefore, devices such as trocars, spraying nozzles, and laparoscopes should be cleaned or disposed of immediately after use to reduce cross-contamination.

Surface contamination of healthcare workers' PPE was detected in this study. Platinum was detected mainly on the outer pair of gloves. One study reported a maximum platinum concentration on the gloves of a nurse who cleaned the PIPAC injector; other studies have shown higher glove contamination rates for drug container removal [10,12]. However, some previous studies have found no or trace levels of platinum on gloves [11,20]. In this study, we detected platinum contamination of gloves, masks, and shoes, although all concentrations were low. Nevertheless, there remains a risk of dermal exposure during device handling; precautions are needed for workers who operate RIPAC devices related to drug administration.

Assessments of airborne contamination during the PIPAC procedure were first conducted in 2013. In that study, cisplatin levels were below the LOD in all samples that had been collected at working positions under real PIPAC conditions [13]. Subsequent studies have detected no traces of cisplatin in air samples [12,20-22], indicating a low risk of airborne contamination during PIPAC. Some reports have supported the safety of the PIPAC procedure if no specific event (e.g., leakage) occurs [10,14]. Similarly, we found that platinum levels were below the LOD in all airborne samples (n=16).

Occupational exposure to cisplatin has also been reported in HIPEC and other anti-neoplastic drug related work. Most studies reported below the limit of quantification or detection in air during HIPEC procedures, but one studies reported 0.014 ng/m^3 and 0.05 ng/m^3 in the anesthetist and nurse's position around the operating table, respectively [23]. In addition, for surface contamination, most studies evaluated the external or internal gloves of healthcare workers and the surrounding tables, and reported concentrations below the limit of quantification or similar to this study. One study reported a maximum of 7.94 ug/L outside of gloves during HIPEC procedures. Occupational exposure surveys in hospitals handling platinum based anti-neoplastic drugs, not HIPEC and PIPAC procedures, have reported concentrations as high as 3.75 pg/cm^2 on a drug mixing table in a gastroenterology ward [24].

Cisplatin is a cytotoxic drug that reportedly has carcinogenic, mutagenic, and teratogenic effects in animals [25]. The oral half-lethal doses of cisplatin are 32 mg/kg in mice and 20 mg/kg in rats [13]. It is difficult to directly compare the present results with these values; however, our surface contamination findings indicate that specific safety and health protocols for the procedure should be established and followed to minimize occupational exposure to anti-neoplastic drugs. Inhalation toxicity data for humans are difficult to find for cisplatin, although several countries have established occupational exposure limits. In the United States, the Occupational Safety and Health Administration, National Institute for Occupational Safety and Health, and American Conference of Governmental Industrial Hygienists have limited the time-weighted average of platinum as cisplatin to 0.002 mg/m^3 [26]. In the Netherlands, an additional lifetime cancer risk level of 4×10^{-5} for 40 years of occupational exposure was set at 0.05 μg/m^3, whereas no standard for cisplatin in PIPAC has been established in Germany [27]. In Korea, a time-weighted average of 0.002 mg/m^3, proposed by the American Conference of Governmental Industrial Hygienists, has been applied. Thus, although toxicological data are limited, we suggest the possibility of exposure through certain routes and the need for preventive measures.

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The operating room conditions in this study were similar to those in the real operating room where RIPAC is performed on real patients, specifically in a laminar flow condition to reduce the airborne contamination. Initially, operating room with negative pressure systems were recommended to be safe for occupational exposure, but recently, one study have reported to be of low risk without negative pressure system or laminar flow condition [28]. Therefore, most operating room where RIPAC procedures will be performed in Korea have been identified as having laminar flow, which is likely to have a lower risk than the results of this study.

This study had 2 limitations. First, we could not evaluate contamination of the floor and the area around the operating table, which have been reported in previous occupational exposure assessments related to RIPAC procedures. However, we selected and evaluated representative points where high exposure levels were expected (e.g., trocars, laparoscopes, and PPE). Concentration levels on the surfaces of devices inserted into the abdominal cavity, which are directly exposed to antineoplastic drug aerosols, were evaluated; the results suggest potential exposure among healthcare workers. The methodology for selecting surface or airborne locations with greater probabilities of detection must be improved. Second, the exposure assessment was performed for only one or 2 procedures per day. Contamination levels may be higher when procedures are performed multiple times per day under clinical conditions, particularly if contaminants accumulate over time. Future studies should evaluate whether exposure levels change under such circumstances to determine the appropriate number and intensity of RIPAC procedures in clinical practice.

In conclusion, there was no or very low risk of air exposure when using RIPAC, a new treatment method using cisplatin as an anti-neoplastic drug, but the possibility of surface exposure could not be ruled out. We detected platinum, in the form of trace cisplatin levels, on samples collected from the surfaces of RIPAC devices and PPE; our findings indicate a risk to healthcare workers through potential dermal exposure when handling drugs and RIPAC devices. Although the concentration levels measured in this study are considered safe, we cannot eliminate the possibility of such risks. We recommend that trocars and spraying nozzles are considered disposable items and that the laparoscope is cleaned several times after each use. Because platinum was detected in healthcare workers' PPE, disposable gloves, shoes, masks, and safety gowns should be selected for these procedures. Consistent with previous studies, we detected no traces of platinum in air samples. Therefore, the likelihood of respiratory exposure is low. Although the RIPAC procedure is a safe chemotherapy administration method, we conclude that safety checklists and measures remain necessary to avoid healthcare worker exposure to antineoplastic drugs.

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SUPPLEMENTARY MATERIALS

Fig. S1

The operating room and devices. The operating room used for RIPAC procedures, including (A) 1 operating table, 2 preparation tables, 3 laparoscopic monitors, 4 operation lamps, and 5 RIPAC devices (device details in panel B). (B) Syringe, 2 syringe pumps, and 3 RIPAC device consoles.

Fig. S2

Diagram of the RIPAC procedure performed on swine in this study. Surface sampling sites included 2 trocars, a laparoscope, and a spraying nozzle.

REFERENCES

1. Facchiano E, Scaringi S, Kianmanesh R, Sabate JM, Castel B, Flamant Y, et al. Laparoscopic hyperthermic intraperitoneal chemotherapy (HIPEC) for the treatment of malignant ascites secondary to unresectable peritoneal carcinomatosis from advanced gastric cancer. Eur J Surg Oncol 2008;34:154-8. PUBMED | CROSSREF
2. Verwaal VJ, Bruin S, Boot H, van Slooten G, van Tinteren H. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. Ann Surg Oncol 2008;15:2426-32. PUBMED | CROSSREF
3. Reymond L, Solass W, Tempfer C. Pressurized intraperitoneal aerosol chemotherapy (PIPAC). In: Berhardt LV, editor. Advances in medicine and biology, volume 87. New York, NY: Nova Science Publishers; 2015. p. 159-180.
4. Solaß W, Hetzel A, Nadiradze G, Sagynaliev E, Reymond MA. Description of a novel approach for intraperitoneal drug delivery and the related device. Surg Endosc 2012;26:1849-55. PUBMED | CROSSREF
5. Khosrawipour V, Khosrawipour T, Kern AJP, Osma A, Kabakci B, Diaz-Carballo D, et al. Distribution pattern and penetration depth of doxorubicin after pressurized intraperitoneal aerosol chemotherapy (PIPAC) in a postmortem swine model. J Cancer Res Clin Oncol 2016;142:2275-80. PUBMED | CROSSREF
6. International Agency for Research on Cancer. IARC monographs on the identification of carcinogenic hazards to humans [Internet]. Lyon: International Agency for Research on Cancer; 2021 [cited 2021 Oct 31]. Available from: https://monographs.iarc.who.int/list-of-classifications.
7. National Institute for Occupational Safety and Health. Preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings (publication No. 2004-165) [Internet]. Cincinnati, OH: DHHS (NIOSH); 2004 [cited 2021 Oct 31]. Available from: https://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf?id=10.26616/NIOSHPUB2004165.
8. National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings (publication No. 2012-150) [Internet]. Cincinnati, OH: DHHS (NIOSH); 2012 [cited 2021 Oct 31]. Available from: https://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf.
9. Giger-Pabst U, Tempfer CB. How to perform safe and technically optimized pressurized intraperitoneal aerosol chemotherapy (PIPAC): experience after a consecutive series of 1200 procedures. J Gastrointest Surg 2018;22:2187-93. PUBMED | CROSSREF

10. Ametsbichler P, Böhlandt A, Nowak D, Schierl R. Occupational exposure to cisplatin/oxaliplatin during pressurized intraperitoneal aerosol chemotherapy (PIPAC)? Eur J Surg Oncol 2018;44:1793-9. PUBMED | CROSSREF
11. Ndaw S, Hanser O, Kenepekian V, Vidal M, Melczer M, Remy A, et al. Occupational exposure to platinum drugs during intraperitoneal chemotherapy. Biomonitoring and surface contamination. Toxicol Lett 2018;298:171-6. PUBMED | CROSSREF
12. Roussin F, Taibi A, Canal-Raffin M, Cantournet L, Durand-Fontanier S, Druet-Cabanac M, et al. Assessment of workplace environmental contamination and occupational exposure to cisplatin and doxorubicin aerosols during electrostatic pressurized intraperitoneal aerosol chemotherapy. Eur J Surg Oncol 2021;47:2939-47. PUBMED | CROSSREF
13. Solass W, Giger-Pabst U, Zieren J, Reymond MA. Pressurized intraperitoneal aerosol chemotherapy (PIPAC): occupational health and safety aspects. Ann Surg Oncol 2013;20:3504-11. PUBMED | CROSSREF
14. Graversen M, Pedersen PB, Mortensen MB. Environmental safety during the administration of pressurized intraperitoneal aerosol chemotherapy (PIPAC). Pleura Peritoneum 2016;1:203-8. PUBMED | CROSSREF
15. Park SJ, Lee EJ, Lee HS, Kim J, Park S, Ham J, et al. Development of rotational intraperitoneal pressurized aerosol chemotherapy to enhance drug delivery into the peritoneum. Drug Deliv 2021;28:1179-87. PUBMED | CROSSREF
16. Lee HS, Kim J, Lee EJ, Park SJ, Mun J, Paik H, et al. Evaluation of a novel prototype for pressurized intraperitoneal aerosol chemotherapy. Cancers (Basel) 2020;12:633. PUBMED | CROSSREF
17. Turci R, Sottani C, Spagnoli G, Minoia C. Biological and environmental monitoring of hospital personnel exposed to antineoplastic agents: a review of analytical methods. J Chromatogr B Analyt Technol Biomed Life Sci 2003;789:169-209. PUBMED | CROSSREF
18. Hornung RW, Reed LD. Estimation of average concentration in the presence of nondetectable values. Appl Occup Environ Hyg 1990;5:46-51. CROSSREF
19. Tempfer CB, Celik I, Solass W, Buerkle B, Pabst UG, Zieren J, et al. Activity of pressurized intraperitoneal aerosol chemotherapy (PIPAC) with cisplatin and doxorubicin in women with recurrent, platinum-resistant ovarian cancer: preliminary clinical experience. Gynecol Oncol 2014;132:307-11. PUBMED | CROSSREF
20. Willaert W, Sessink P, Ceelen W. Occupational safety of pressurized intraperitoneal aerosol chemotherapy (PIPAC). Pleura Peritoneum 2017;2:121-8. PUBMED | CROSSREF
21. Delhorme JB, Klipfel A, D'Antonio F, Greget MC, Diemunsch P, Rohr S, et al. Occupational safety of pressurized intraperitoneal aerosol chemotherapy (PIPAC) in an operating room without laminar airflow. J Visc Surg 2019;156:485-8. PUBMED | CROSSREF
22. Larroque M, Arnaudguilhem C, Bouyssiere B, Quenet F, Bouazza N, Jarlier M, et al. Evaluation of the environmental contamination and exposure risk in medical/non-medical staff after oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy. Toxicol Appl Pharmacol 2021;429:115694. PUBMED | CROSSREF
23. Rodier S, Saint-Lorant G, Guilloit JM, Palix A, Divanon F, Sichel F, et al. Is hyperthermic intraperitoneal chemotherapy (HIPEC) safe for healthcare workers? Surg Oncol 2017;26:242-51. PUBMED | CROSSREF
24. Hori A, Shimura M, Iida Y, Yamada K, Nohara K, Ichinose T, et al. Occupational exposure of platinum-based anti-cancer drugs: five-year monitoring of hair and environmental samples in a single hospital. J Occup Med Toxicol 2020;15:29. PUBMED | CROSSREF
25. Pan American Health Organization. Safe handling of hazardous chemotherapy drugs in limited-resource settings [Internet]. Washington, D.C.: Pan American Health Organization; 2013 [cited 2021 Nov 6]. Available from: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=24983&Itemid=&lang=en.
26. Murff SJ. United States consensus occupational exposure level(s)/limits for cytotoxic drugs. In: Murff SJ, editor. Safety and health handbook for cytotoxic drugs. Lanham, MD: Government Institutes An imprint of The Scarecrow Press; 2012. p 244.
27. Dutch Expert Committee on Occupational Standards (DECOS), A Committee of the Health Council of the Netherlands. Cisplatin; health-based calculated occupational cancer risk values (publication No. 2005/03OSH) [Internet]. The Hague: Health Council of the Netherlands; 2005 [cited 2021 Nov 6]. Available from: https://www.healthcouncil.nl/documents/advisory-reports/2005/04/19/cisplatin.
28. Girardot-Miglierina A, Clerc D, Alyami M, Villeneuve L, Sgarbura O, Reymond MA, et al. Consensus statement on safety measures for pressurized intraperitoneal aerosol chemotherapy. Pleura Peritoneum 2021;6:139-49. PUBMED | CROSSREF