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Platinum Contamination of Laparoscopic Instruments During Pressurized Intra Peritoneal Aerosol Chemotherapy (PIPAC)

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Research Article

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ABSTRACT

Background: Beside room and hardware surfaces in the operating room, instruments used during Hyperthermia Intra-Peritoneal Aerosol Chemotherapy (HIPEC) or Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) represent another potential source of contamination. Current regulations in Germany prohibit re-sterilization of medical devices used for distributing radioisotopes or cytotoxic drugs.

Methods: We examined the PIPAC process in order to identify which instruments can be potentially contaminated with chemotherapy and to determine the effective level of contamination of these instruments with platinum before and after sterilization. Analysis was blinded and performed by an external certification laboratory.

Results: During PIPAC, only the laparoscopic camera is exposed to chemotherapy and is not a single-use instrument. All other laparoscopic instruments, trocars, tubes, etc. are removed before chemotherapy application or are single-use instruments. Eleven cameras were examined for the presence of platinum traces. Three samples were wiped before sterilisation, eight samples afterwards. All samples showed no traces of platinum after sterilization. One out of 3 cameras wiped before sterilization exhibited a detectable amount of platinum, corresponding to 0.001 percent of the drug applied during PIPAC, or $1:10^{-6}$ of a usual systemic chemotherapy dose.

Conclusion: After PIPAC, minimal traces of platinum were present on the laparoscopic camera. After sterilization, no more traces of platinum were detected. We conclude that laparoscopic cameras can be safely reused after PIPAC:

INTRODUCTION

Hyperthermic intraperitoneal chemotherapy (HIPEC) appears to be a safe procedure for surgeons. In particular, skin wipe samples were demonstrated to be free of platinum contamination, and no platinum traces could be detected in air and urine samples in any tested source and session [1]. Also the theoretical risk of pulmonary contamination of hospital staff with aerosolized chemotherapy during HIPEC appears to be negligible [2,3]. In analogy, environmental analysis during pressurized intra-peritoneal aerosol chemotherapy (PIPAC) demonstrated that, for the drugs tested, PIPAC is in compliance with European Community working safety law and regulations. Workplace contamination remained below the tolerance margin [4,5].

However, Cisplatin contamination was detected on the surgical gloves after HIPEC [1,3], which does not appear surprising.

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Moreover, evaluation of hardware contamination by platinum drugs in the operating room during HIPEC showed that low surface loads are detectable, as documented by wipe samples. Sporadically, high platinum concentrations on surfaces of the HIPEC circulation pump and the operating room floor were detected [6].

Beside room and hardware surfaces in the OR, instruments used during HIPEC or PIPAC represent another potential source of platinum contamination. Current regulations in Germany prohibit re-sterilization of medical devices used for distributing radioisotopes or cytotoxic drugs [7]. Although a positive or negative list of the devices included in this definition is not provided, this directive concerns indeed all instruments used during a HIPEC or a PIPAC procedure that might be contaminated with chemotherapy. In the absence of a precise risk evaluation, the consequence might be that only single-used instruments should be used during HIPEC or PIPAC. For obvious cost reasons, such an extreme definition would be difficult to implement in everyday hospital practice. Thus, there is a need for assessing the risk of contamination of surgical instruments with chemotherapeutic drugs after HIPEC or PIPAC.

The aim of the present study was to examine the PIPAC process in order to identify which instruments are contaminated with chemotherapy and to determine the effective level of contamination of these instruments before and after sterilization.

METHODS

PIPAC Procedure

The PIPAC procedure consisted of 4 phases:

Access to the abdomen: After insufflation of a 12 mmHg capnoperitoneum (with open access or Veres needle), two trocars (5 and 12 mm, Kii®, Applied Medical, Düsseldorf, Germany) were inserted into the abdominal wall. Ascites was removed.

Staging laparoscopy: The extent of peritoneal carcinomatosis was determined. Peritoneal biopsies were taken in all 4 quadrants, and acentimetric local peritonectomy was performed to improve the accuracy of histopathology, in particular when biopsies remained negative.

Administration of chemotherapy: An aerosolizer (Capnopen®, Capnomed, and Villingendorf, Germany) was connected to an intravenous high-pressure injector (Arterion Mark 7®, Medrad, Germany) and inserted into the abdomen. The tightness of the abdomen was documented via a zero-flow of CO_2. The procedure was performed in a room equipped with laminar air flow. A pressurized aerosol containing doxorubicin at a dose of 1.5 mg/m^2 body surface in a 50 ml NaCl 0.9% followed by Cisplatin at a dose of 7.5 mg/m^2 in a 150 ml NaCl 0.9% was applied. Flow was 30 ml/min and upstream pressure was 200 psi. Injection was remote-controlled and nobody remained in the room during application. The therapeutic aerosol was maintained in the abdomen at 12 mmHg for 30 min at 37°C.

Exsufflation: The toxic aerosol was released via a Closed Aerosol Waste System (CAWS). Trocars were retracted and laparoscope ended. No drainage was applied.

Sampling Procedure

Eleven cameras were collected over the period 9 December 2015 to 8 January 2016. Wipe samples were taken from the cameras using Cyto Wipe Kits company (Exposure Control Sweden AB, Bohus-Björkö, Sweden). Three cameras were wiped before and eight after Sterilisation. This was not known by the lab when the analyses were performed (blinded assessment). The wipe samples were taken according to the instructions of the manufacturer with 2 tissues and 17 ml 0.05 M HCl solution. In addition, two blank samples were added at the laboratory. The wipe samples were stored at room temperature after sampling and during transport until analysis at the laboratory.

Platinum Determination

Analysis was performed by an independent certification company (Exposure Control Sweden AB, Bohus-Björkö, Sweden). The wipe samples were extracted after 140 ml 0.5 M HCl was added (total volume 157 ml). A part of the extract was destructed using UV-light in combination with hydrogen peroxide and hydrogen chloride. Platinum compounds such as cisplatin, carboplatin and oxaliplatin were transformed into platinum (PT) ions. Ultra traces of platinum were analysed using voltammetry in combination with a computrace [8]. The results were corrected for potential background values of platinum (compounds) in the environment not being platinum associated with chemotherapy drugs. The detection limit of the analytical method was 0.5 ng PT/ml HCl extract. Cisplatin contains 65% platinum. The platinum results were recalculated into cisplatin equivalents assuming all platinum detected was from cisplatin.

RESULTS

An exhaustive list of the instruments and devices used during PIPAC was determined **(Table 1).** Only a single device is exposed to chemotherapy and is not a single-use instrument: the videoscopic camera. All other laparoscopic instruments are exclusively used during staging laparoscopy before the application of chemotherapy so that a direct contamination with chemotherapy is not possible, or they are single-use instruments (for example, trocars and tubing).

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Table 1. List of the devices used during Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC). Only a single device is exposed to chemotherapy and is not single-use: the videoscopic camera. All other laparoscopic instruments are exclusively used during staging laparoscopy, before application of chemotherapy.

Instruments and devices	Contact with chemotherapy	Single-use	Multiple use
Trocars	X	X	
Veress Needle	-	X	
Biopsy forceps	-		X
Endoscopic scissors	-		X
Capnomed ® device including high-pressure line	X	X	
Close aerosol waste system (CAWS) including microparticles filters	X	X	
CO_2 tubing	-	X	
Op-drapes	X	X	
Videoscopic camera	X		X
Chemotherapy syringe	X	X	

The results of the wipe samples from the eleven cameras are presented in **Table 2.** Disclosure of the blinded data after analysis showed that the samples 1 to 8 were from cameras wiped after sterilization and the samples 9-11 were from cameras wiped before Sterilisation. On one camera a barely detectable amount of platinum was found. The amount was 0.001 percent of the drug applied during PIPAC. Since about 10% of a usual systemic dose of chemotherapy is applied during PIPAC, this represents an order of magnitude of $1:10^{-6}$ of such a systemic chemotherapeutic dose. The blank samples did not contain platinum.

Table 2. Platinum (PT) in wipe samples from eleven PIPAC cameras. The results show no platinum detected on the cameras after sterilization and almost no platinum present on the cameras before sterilization.

Sample	Drug	Camera ID	Time point	Total HCl (ml)	(PT) (ng/ml HCl)	(PT) (ng)	CisPT equivalents (ng)
1	Cisplatin 12.0 mg	1	Post	157	ND		
2	Cisplatin 12.0 mg	2	Post	157	ND		
3	Cisplatin 14.0 mg	3	Post	157	ND		
4	Cisplatin 13.0 mg	4	Post	157	ND		
5	Cisplatin 13.0 mg	1	Post	157	ND		
6	Cisplatin 12.5 mg	2	Post	157	ND		
7	Cisplatin 14.0 mg	3	Post	157	ND		
8	Cisplatin 14.5 mg	4	Post	157	ND		
9	Cisplatin 14.0 mg	4	Pre	157	0.71	111	171
10	Cisplatin 13.0 mg	3	Pre	157	ND		
11	Cisplatin 11.0 mg	2	Pre	157	ND		
12	No cisplatin	--	Blank		ND		
13	No cisplatin	--	Blank		ND		

Note: ND: Not Detected (PT<0.50 ng/Ml HCl); *CisPT equivalents=PT/0.65; Pre=before Sterilization; Post=after sterilization; Blank=negative control.

In summary, the results show no platinum detected on the cameras after Sterilisation and almost no platinum present on the cameras before sterilization.

DISCUSSION

This study was designed to determine a possible contamination of surgical instruments used during PIPAC with chemotherapeutic drugs. Platinum was used as a tracer substance for contamination with chemotherapeutic drugs (cisplatin and doxorubicin) delivered to the patient during the procedure.

The main result of our study is that only a single device, the videoscopic camera, is exposed to chemotherapy and is not a single-use instrument. Thus, the camera must be sterilized after each PIPAC procedure and there might be a potential risk of contamination of the next patient with platinum. In principle, such a re-sterilization procedure is not admissible in Germany according to the current regulatory guidelines [7].

Several approaches are possible to address this problem:

1) To discard the camera after each PIPAC procedure. This would be the ideal, but very costly, solution.

2) To remove the camera from the abdomen before administration of chemotherapy. This is possible but would imply that the chemotherapy administration and exsufflation phases cannot be video-monitored. Although no major intraoperative safety event was recorded so far in 970 consecutive PIPAC and 20 PIPAC procedures (Reference for this?), a blind phase of 40-45 min during a surgical procedure does not appear advisable.

3) To protect the camera with a sterile single-use disposable-sheath. This cover sheath could be discarded after each PIPAC procedure and would prevent the contamination of the camera with chemotherapy. This solution appears practicable. Such disposable sheets are available for endoscopes [9] but not for laparoscopes (to our knowledge) and would require regulatory certification.

4) To use single-use cameras. Low-price cameras with sufficient optical characteristics and image definition are available, are already integrated in CE-certified single-use endoscopes [10] and could be implemented for monitoring the chemotherapy administration phase during PIPAC.

However, the results obtained in the present study suggest that current practice, namely to monitor chemotherapy administration during PIPAC with conventional reusable video-laparoscopic equipment, is perfectly safe. Clearly, there is no platinum contamination detectable after sterilization of the camera after PIPAC, and even contamination of the camera before sterilization appears to be minimal.

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