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Professional risks when carrying out cytoreductive surgery for peritoneal malignancy with hyperthermic intraperitoneal chemotherapy (HIPEC): A French multicentric survey

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Abstract

Background: Over the last two decades, many surgical teams have developed programs to treat peritoneal carcinomatosis with extensive cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). Currently, there are no specific recommendations for HIPEC procedures concerning environmental contamination risk management, personal protective equipment (PPE), or occupational health supervision.
Methods: A survey of the institutional practices among all French teams currently performing HIPEC procedures was carried out via the French network for the treatment of rare peritoneal malignancies (RENAPE).
Results: Thirty three surgical teams responded, 14 (42.4%) which reported more than 10 years of HIPEC experience. Some practices were widespread, such as using HIPEC machine approved by the European Community (100%), individualized or centralized smoke evacuation (81.8%), "open" abdominal coverage during perfusion (75.8%), and maintaining the same surgeon throughout the procedure (69.7%). Others were more heterogeneous, including laminar flow air circulation (54.5%) and the provision of safety protocols in the event of perfusate spills (51.5%). The use of specialized personal protective equipment is ubiquitous (93.9%) but widely variable between programs.
Conclusion: Protocols regarding cytoreductive surgery/HIPEC and the associated professional risks in France lack standardization and should be established.

Keywords: HIPEC; Professional risks; Peritoneal carcinomatosis; Practices survey; Intraperitoneal chemotherapy; Personal protective equipment

Introduction

Following pioneering efforts in the 1990's, many other French programs have emerged to treat peritoneal carcinomatosis (PC) with extensive cytoreductive surgery (CS) and hyperthermic intraperitoneal chemotherapy (HIPEC).[1,2] However, despite the increase in popularity of these complex procedures there are no specific recommendations concerning either environmental contamination risk management or personal protective equipment (PPE) of the staff. In particular, surgical smoke poses a potential hazard for the operating room staff,[3–6] and the handling of concentrated doses of chemotherapeutic agents is unusual and its consequent risks unknown. To address the need for standardised practices, we began by using the French network for the treatment of rare peritoneal malignancies and peritoneal carcinomatosis (BIG-RENAPE)[7] to administer a survey regarding the operating and organisational methods of all French teams currently performing HIPEC procedures.

Materials and methods

The questionnaire was created by an operating room nurse specialising in HIPEC with additional experience in professional risk management[8] in collaboration with several physicians with similar experience. Throughout 2013, we solicited participation from all member teams of the RENAPE network (n = 27) as well as those not in the network but who perform CS/HIPEC procedures (n = 7). The questionnaire was sent to both the lead surgeon and the operating room staff for each team, with a maximum of three follow-up requests if there was no answer. Incongruous answers were common between these two entities, but all replies were weighted equally thus producing more than 33 answers for several items. The questionnaire concerned both the HIPEC technique itself as well as PPE practices, environmental risk management, waste management, and the training and supervision of team members.

Results

Survey participants

All French teams currently performing HIPEC procedures were successfully contacted and 33/34 (97%) responded to this survey. Half (n = 17) responded after the first request with joint answers from both the lead surgeon and the operating room staff.

Several of the teams (42.4%) have a large HIPEC experience (>10 years) including two pioneering teams with more than 20 years, 13 (39.4%) between 5 and 10 years, and 6 (18.2%) with less than 5 years (Table 1).

HIPEC procedure

The open abdomen "coliseum" technique[9] is used in 76% in favour of the closed abdomen procedure.[10] With an open abdomen technique, a covering system is used (n = 15) either by means of a specific kit (n = 5) or a transparent adhesive drape (n = 5), a plastic ring drape (n = 3), a bowel bag (n = 3), a cytotoxic extractor (n = 3) and, in just three cases, two of these systems. There are ten teams which do not use any special protection at all.

Table 1
HIPEC team and technique used.

		N	%
Number of years HIPEC practice	>20 years	2	6
	>10 and ≤20 years	12	36.4
	≥5 and ≤10 years	13	39.4
	<5 years	6	18.2
HIPEC procedure	Open abdomen	25	76
	Closed abdomen	8	24
Covering in open abdomen cases	Specific devices	16	48.5
	With aerosol extraction	3	9
	No specific protection	10	30.3
HIPEC system	Performer LRT (Rand®)	14 (O: 12; C:2)	45.2
	SunCHIP (Gamida®)	11 (O: 10; C:1)	35.5
	Cavitherm (Soframedical®)	6 (O: 1; C:5)	19.3
	Home-made system	0	0
Who manages the HIPEC machine?	Operating room nurse	23	69.7
	Biomedical engineer	11	33.3
	Surgeon	7	21.2
	Anaesthetist	3	9
HIPEC team	Always the same surgeon	23	70
	Always the same operating theatre nurse	10	30.3
	Always the same anaesthetist	3	9
Restriction of access during the HIPEC procedure	Fewer than 3 people	11	33.3
	Fewer than 5	22	66.6
	Pregnant women	31	93.9
	Refusal to take part	11	33.3

*O: Open abdomen HIPEC procedure; C: Closed abdomen HIPEC procedure.

HIPEC system used

Only European Community-approved HIPEC machine are used – either Performer LRT (Rand®) (n = 14); Sunchip (Gamida®) (n = 11); or Cavitherm (Soframedical®) (n = 6). At the present time, none of the teams reported using a "homemade" HIPEC system. The preparation and use of the system is handled by a biomedical engineer (n = 11), by an operating room nurse (n = 23), by an anaesthetist (n = 3), or by the surgeon (n = 7).

HIPEC team

Regarding CS/HIPEC, a single surgeon performs the entire procedure in most teams (n = 23), while the similar use of a single operating room nurse (n = 10) or a single anaesthetist (n = 3) is less common. All teams are deliberately kept small after the chemotherapy injection with fewer than three participants in the theatre in some programs (n = 11) and fewer than five in the remainder (n = 22). In 31 teams, pregnant women or those who wish to become pregnant are excluded from the operating room during both CS and HIPEC. Some staff members refuse to take part in the actual HIPEC procedure in 11 teams for various reasons, including a fear of chemotherapy or smoke toxicity, the complexity of the surgery, and the risk of spillage.

Table 2
Procedures for the use of chemotherapy.

		N	%
Concomitant IV injection	Yes	25	76
	No	8	24
Who prescribes the chemotherapy?	Surgeon	21	63.6
	Medical oncologist	17	51.5
	Anaesthetist	1	3
Who checks the dose once prepared?	Pharmacist	14	42.4
	Medical oncologist	7	21.2
	Surgeon	9	27.3
	Operating room nurse	3	9
	Anaesthetist	3	9
	Not checked	1	3
Packaging of waste	Specific bin for potentially infectious clinical waste	26	78.8
	Specific cytotoxic bin	3	9
	Container for potentially infectious clinical waste	3	9
Waste disposal	Cytotoxic circuit (1200 °C)	13	39.4
	Circuit for potentially infectious clinical waste (850 °C)	13	39.4
	No awareness of the circuit	10	30.3

Intraperitoneal chemotherapy

Various intraperitoneal drugs are administered depending upon the pathology: oxaliplatin (n = 32), cisplatin (n = 24), mitomycin C (n = 25), doxorubicin (n = 11) and irinotecan (n = 10). In most of the teams (n = 25), an IV chemotherapy injection is performed simultaneously (Table 2).

Chemotherapy is usually prescribed by the surgeon (n = 21) but less frequently by a medical oncologist (n = 17), and in one case by an anaesthetist. The prescribed dose is checked by a medical oncologist (n = 7), hospital pharmacist (n = 14), surgeon (n = 9), operating room nurse (n = 3), or anaesthetist (n = 3). There is no post-prescription checking in just one team.

Air conditioning in operating theatres

The operating theatre is ventilated by means of a laminar flow system in most programs (n = 18). Fourteen of 33 teams report awareness and monitoring of the standards hourly air change rate (between 15 and 60 volumes/h, Table 3). For the destruction of tumour implants, the majority of teams use high voltage electrocautery (n = 30), and more rarely an Argon system (n = 11, 3 plasma) or bipolar electrode (n = 4). The smoke generated by these techniques are removed by centralized (n = 11) or individual (n = 16) extraction system with a 0.1 micron filter (high efficiency particulate air [HEPA]). However, no extraction system is used in 7 teams.

Personal protective equipment (PPE)

Answers regarding PPE are highly variable. The majority of teams primarily employ a reinforced sterile gown (n = 27) while tear-away disposable garments (n = 9) and plastic aprons (n = 4) are less common. The use of a surgical mask with FFP (Filtering Face Pieces) protection is reported by the majority of the teams (n = 30, Table 3). Filtering Face Pieces-1 devices are used by 13 teams (6/13 in closed abdomen procedure). Shoe covers are worn in 17 teams (3/17 in closed abdomen procedure). Eye protection via goggles is reported by most teams (n = 27, 7/27 in closed abdomen procedure) and/or masks with a protective face shield (n = 10), glasses (n = 16), or leaded glasses (n = 1); in 2 cases, the surgeon does not report using any eye protection. The most commonly used gloves are made of latex (n = 29) and, more rarely, of neoprene (n = 3) or vinyl (n = 1). Double-gloving is reported in 21 teams (6/21 in closed abdomen procedure). Those teams reporting the use of long-sleeve NBC (nuclear, biologic, and chemical) protective gloves are used during the mixing of the chemotherapy (n = 25) also report systematic glove changes at 20- (n = 2) or 30-min (n = 9) intervals, while the remainder (n = 14) does not change gloves at this stage.

Table 3
Protection and personal protective equipment (PPE).

		N	%
Surgical smokes	Operating theatre with laminar flow system	18	54.5
	Individual smoke evacuator	16	48.5
	Centralized smoke extractor	11	33.3
	No extraction	7	21.2
Surgical clothing	Reinforced gown	27	81.8
	Shoe covers	17	51.5
Surgical mask	FFP3	6	18.2
	FFP2	14	42.4
	FFP1	13	39.4
Protection for the eyes	Protective goggles	27	81.2
	Mask with protective face shield	10	30.3
	Glasses	16	48.5
	No protection	2	6
Gloves	Latex	29	87.9
	Neoprene	3	9
	Double pair	21	63.6
	NBC long-sleeved double pairs	25	75.7
	Change every 30 min	11	33.3
	No change	14	42.4
Protection in the event of spillage or splashing	Written procedure	16	48.5
	Spillage kit	17	51.5

Protective procedure for staff in operating theatres

In the event of splashing or spillage of chemotherapeutic agents, a written safety protocol of which all team members are aware is available to 16 teams (3 specific to closed abdomen procedures). Seventeen teams also possess an emergency spill kit (n = 17) including absorbent devices, mild soap, bleach and/or an eye wash kit. Spillages are deemed exceptional in 20 programs and non-existent in 13 (6 and 6, respectively, among programs referring specifically to closed abdomen procedures).

Waste management

At the end of the HIPEC procedure, the dialysate and surgical equipment (tubes, temperature probes, etc.) are commonly stored in a permanently sealed plastic container specifically designed for potentially infectious clinical waste (n = 26). These are then disposed either by a specific circuit for “cytotoxic waste” with incineration at 1200 °C (n = 13) or “potentially infectious clinical waste” with incineration at 850 °C (n = 13). The remaining teams (n = 7) are not aware of specific disposal methods (Table 2).

Specific technical training

Initial HIPEC training was performed by experienced outside surgical teams (n = 21), by representatives of the HIPEC system manufacturer (n = 23), by a biomedical engineer (n = 3) or by a qualified perfusionist (n = 2). Continuing training is managed by periodic conferences (n = 20), individual research (n = 14), and regular

Table 4
Training and monitoring of members of staff.

		N	%
Initial training	Company selling the recirculator	23	69.7
	Experienced team	21	63.6
	Biomedical engineer	3	9
	Perfusionist	3	9
Continuing training	Conference	20	60.6
	Sharing of experience	16	48.5
	Individual training	14	42.4
	No training	5	15.1
Specific medical supervision	Specific identification	17	51.5
	Exactly the same rate as for medical oncology	16	48.5
	Annual blood and urine test	11	33.3
	Staff register	10	30.3

discourse with other CS/HIPEC teams (n = 16). Five teams report a lack of continuous training (Table 4).

In most programs, HIPEC team members are specifically identified by their institution's occupational health department (n = 17) or by a departmental register that tracks team membership and exposure incidents (n = 10). Some teams also report annual direct observation and critique of team members (n = 16), with associated blood and/or urine toxicology tests (n = 11).

Discussion

The centres participating in this survey represent a particular French "school" of HIPEC, comprised of pioneering programs and others that were trained in and adopted many of the original protocols.[11] With 19 of 33 teams reporting fewer than 10 years of experience, they are often still comprised of original members from their program's inception. Furthermore, the advanced training necessary for both recirculator operation and surgical dissection as well as the universal voluntary restriction of team size serve to keep staff turnover low. As such, there is considerable homogeneity regarding team membership and CS/HIPEC procedures seen in this survey.

However HIPEC remains a nascent therapy as reflected by the stark differences in safety protocols and team training. Operating room staffs are usually familiar with the risks of exposure to various infectious agents, solvents, anaesthetic gases, and X-rays. But the management of PC poses additional hazards of surgical smoke and cytotoxic drugs that require further training and contingency planning. This study was therefore designed to address the Paucity of data on the operative and safety practices of teams specifically trained in CS/HIPEC.

The wearing of PPE varies considerably – probably reflecting individual differences between surgeons despite the availability of contrary evidence in the literature. The wearing of two pairs of gloves, for instance, is important in order to reduce contact with the chemotherapeutic agent as far as possible[12–14] but reported in only 21 of 33 teams. Various articles have listed the "essential" PPE[8,30,31]: two pairs of gloves, one of them with long sleeves and NBC treated, the wearing of protection for the eyes, the use of high level filtering masks (FFP2 or 3) although there remains no evidence-based proof of superiority.

A few publications have also reported possible drug contamination of the workplace surface, especially around the operating table.[15,16] Several reports have identified chemotherapy metabolites in the urine of health care workers, and measured the associated genotoxic responses.[17] Other studies demonstrate no detectable levels of the cytotoxic agent in any of the samples.[18–21] A residual risk is mainly due to the possibility of direct or indirect skin exposure and can be prevented by the correct use of PPE.[20] The failure to detect chemotherapy residues depends on the measuring techniques used, taking on board the chosen detection threshold.[20,22,23]

Many of the antineoplastic agents are known or suspected human carcinogens, and effects on fertility and reproduction are documented.[24,25] Chromosomal aberrations, micronuclei induction, DNA damage represent the most frequent abnormalities from occupational exposure.[26] Although limited, some publications demonstrate a relationship of occupational exposure to cytotoxic agents with cancer in health care workers.[27,28] Data are missing concerning the real impact to HIPEC exposure. There are not currently any formal European Guidelines about the type of PPE to be used for the HIPEC procedure. Some teams follow the recommendations made by the National Institute for Occupational Safety and Health (NIOSH).[29]

One specific feature of PC surgery is the production of toxic surgical smoke, especially when using high power ball electrode or Argon system. This amounts to the same exposure risk as smoking six cigarettes.[32] The potentially carcinogenic components of surgical smoke are sufficiently small to be breathable.[3,33] The electrocautery smokes with fine particles exposure increases the average cancer risk for surgeons.[33] Carrying out this type of surgery in an operating theatre equipped with a laminar flow system (with an air change rate of 15–60 volumes per hour) helps to reduce the risk of inhalation injury to staff members. The use of a smoke extractor with a HEPA filter has become widespread. The extraction needs to be carried out in immediate proximity to the place of production (less than 5 cm away). The wearing of FF3 masks which can filter particles as small as 0.07 µm is strongly recommended during procedures with high smoke production.

A chemotherapy procedure cannot be introduced into an operating room without stress upon the teams involved. Because of recommended practices are not always followed, training and education for health care workers are required.[34,35] Training is essential both in terms of risk awareness and the appropriate response to exposure.[36] Perhaps most importantly, spills must be considered exceptional events, and constant vigilance is required to

Table 5
HIPEC main safety guidelines.

Protective equipment – conditions – procedures	Main risks	Recommended
Personal protective equipment (PPE)		★★★★★
Two pairs of gloves	Skin exposure	★★★★★
Wearing of protection for the eyes	Splashing or spillage of chemotherapeutic agents	
Use of high level filtering masks (FFP2 or 3)	Surgical smokes	
Protective procedure for staff in operating theatres		
Emergency spill standard operating procedure	Splashing or spillage of chemotherapeutic agents	★★★★★
Air conditioning in operating theatres		
Laminar flow system	Surgical smokes	★★★★
Extraction system [HEPA]		★★★★
HIPEC procedure		
Closed abdomen procedure	Skin exposure, splashing or spillage of chemotherapeutic agents	★★★★
Waste management		
Specific infectious clinical waste and circuit with incineration (850 °C, 1200 °C)	Contamination	★★★
Specific technical training	Dysfunction	★★★
Registry by the occupational health office	Non-reporting of exposure incidents	★★★

prevent them. In addition, written procedures are essential in the event of spills, as are emergency kits providing quick absorption of HIPEC solution and first aid (especially eye wash).[37] Notably, the voluntary exclusion of women who are or may become pregnant a precaution of all teams and a practice that should be continued. Supervision of staff members is essential to provide appropriate follow-up, and a register of accidents and incidents should be created where they do not already exist, including a list of staff members who come into contact with chemotherapy (during the HIPEC procedure or disposal of the waste).[36,37]

Finally, the disposal of waste material is an at-risk phase for members of staff who are usually unaware of the basic rules for handling products of this kind. It is important that waste be stored in a rigid, sealed container and that staff members be trained to minimize the risk of exposure. If these cytotoxic materials have been metabolized, they must be disposed of as potentially infectious clinical waste and incinerated at 850 °C, unlike pure cytotoxic materials which are incinerated at 1200 °C in order to reduce the risk of producing biologically active metabolites.

Conclusion

The increasing number of teams employing PC with CS/HIPEC procedures and the lack of practical guidelines lead to a disparity in the protection of staff members regarding PPE, the prevention of environmental contamination, staff monitoring, and waste disposal.

We need to create and distribute good practice guidelines and to organize training programs especially via the BIG-RENAPE network, which includes the majority of teams performing HIPEC procedures in France (Table 5). Literature regarding the risks of staff member contamination and regulatory aspects of CS/HIPEC need to be adopted. Specific studies are also needed to evaluate the short and long term mutagenic effects of HIPEC for operating room staff.

Conflict of interest statement

The authors have declared no conflicts of interest.

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References

1. Glehen O, Kwiatkowski F, Sugarbaker PH, et al. Cytoreductive surgery combined with perioperative intraperitoneal chemotherapy for the management of peritoneal carcinomatosis from colorectal cancer: a multi-institutional study. *J Clin Oncol* 2004;**22**:3284–92.
2. Glehen O, Mohamed F, Gilly FN. Peritoneal carcinomatosis from digestive tract cancer: new management by cytoreductive surgery and intraperitoneal chemohyperthermia. *Lancet Oncol* 2004;**5**:219–28.
3. Mowbray N, Ansell J, Warren N, et al. Is surgical smoke harmful to theater staff? A systematic review. *Surg Endosc* 2013;**27**:3100–7.
4. Smith JP, Moss CE, Bryant CJ, Fleeger AK. Evaluation of a smoke evacuator used for laser surgery. *Lasers Surg Med* 1989;**9**:276–81.
5. *Health hazard evaluation and technical assistance reports*;. NIOSH Publication; 1988.
6. *Health hazard evaluation and technical assistance reports*;. NIOSH Publication; 1990.
7. Villeneuve L, Isaac S, Glehen O, et al. The RENAPE network: towards a new healthcare organization for the treatment of rare tumors of the peritoneum. Description of the network and role of the pathologists. *Ann Pathol* 2014;**34**:4–8.
8. Simon L, Halilou MC, Gladieff L, et al. Hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC): evaluation, prevention and

policies to avoid occupational exposure for operating room personnel. *Bull Cancer* 2009;**96**:971–7.

9. Fujimura T, Yonemura Y, Fujita H, et al. Chemohyperthermic peritoneal perfusion for peritoneal dissemination in various intra-abdominal malignancies. *Int Surg* 1999;**84**:60–6.
10. Glehen O, Cotte E, Kusamura S, et al. Hyperthermic intraperitoneal chemotherapy: nomenclature and modalities of perfusion. *J Surg Oncol* 2008;**98**:242–6.
11. Glehen O, Gilly FN, Boutitie F, et al. Toward curative treatment of peritoneal carcinomatosis from nonovarian origin by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy: a multi-institutional study of 1,290 patients. *Cancer* 2010;**116**: 5608–18.
12. Caneparo A, Massucco P, Vaira M, et al. Contamination risk for operators performing semi-closed HIPEC procedure using cisplatin. *Eur J Surg Oncol* 2014;**40**:925–9.
13. Konate A, Poupon J, Villa A, et al. Evaluation of environmental contamination by platinum and exposure risks for healthcare workers during a heated intraperitoneal perioperative chemotherapy (HIPEC) procedure. *J Surg Oncol* 2011;**103**:6–9.
14. Capron A, Destree J, Jacobs P, Wallemacq P. Permeability of gloves to selected chemotherapeutic agents after treatment with alcohol or isopropyl alcohol. *Am J Health Syst Pharm* 2012;**69**:1665–70.
15. Schierl R, Novotna J, Piso P, et al. Low surface contamination by cis/oxaliplatin during hyperthermic intraperitoneal chemotherapy (HIPEC). *Eur J Surg Oncol* 2012;**38**:88–94.
16. Kushnir CL, Fleury AC, Couch J, et al. Evaluation of exposures to healthcare personnel from cisplatin during a mock demonstration of intra-operative intraperitoneal chemotherapy administration. *Gynecol Oncol* 2013;**130**:350–3.
17. Connor TH, McDiarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. *CA Cancer J Clin* 2006; **56**:354–65.
18. Naslund Andreasson S, Anundi H, Thoren SB, et al. Is platinum present in blood and urine from treatment givers during hyperthermic intraperitoneal chemotherapy? *J Oncol* 2010;**2010**:649719.
19. Stuart OA, Stephens AD, Welch L, Sugarbaker PH. Safety monitoring of the coliseum technique for heated intraoperative intraperitoneal chemotherapy with mitomycin C. *Ann Surg Oncol* 2002;**9**: 186–91.
20. Villa AF, El Balkhi S, Aboura R, et al. Evaluation of oxaliplatin exposure of healthcare workers during heated intraperitoneal perioperative chemotherapy (HIPEC). *Ind Health* 2015;**53**:28–37.
21. Schmid K, Boettcher MI, Pelz JO, et al. Investigations on safety of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) with mitomycin C. *Eur J Surg Oncol* 2006;**32**:1222–5.
22. Guerbet M, Goulle JP, Lubrano J. Evaluation of the risk of contamination of surgical personnel by vaporization of oxaliplatin during the intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC). *Eur J Surg Oncol* 2007;**33**:623–6.
23. Pretty JR, Connor TH, Spasojevic I, et al. Sampling and mass spectrometric analytical methods for five antineoplastic drugs in the healthcare environment. *J Oncol Pharm Pract* 2012;**18**:23–36.
24. Dranitsaris G, Johnston M, Poirier S, et al. Are health care providers who work with cancer drugs at an increased risk for toxic events? A systematic review and meta-analysis of the literature. *J Oncol Pharm Pract* 2005;**11**:69–78.
25. Fransman W, Roeleveld N, Peelen S, et al. Nurses with dermal exposure to antineoplastic drugs: reproductive outcomes. *Epidemiology* 2007;**18**:112–9.
26. Testa A, Giachelia M, Palma S, et al. Occupational exposure to antineoplastic agents induces a high level of chromosome damage. Lack of an effect of GST polymorphisms. *Toxicol Appl Pharmacol* 2007; **223**:46–55.
27. Barle EL, Winkler GC, Ulrich P, et al. Cancer risk of immunosuppressants in manufacturing. *Regul Toxicol Pharmacol* 2014;**70**:122–4.
28. Hansen J, Olsen JH. Cancer morbidity among Danish female pharmacy technicians. *Scand J Work Environ Health* 1994;**20**:22–6.
29. *Preventing occupational exposures to antineoplastic sand other hazardous drugs in health care settings*;. NIOSH Publication; 2004.
30. Gonzalez-Bayon L, Gonzalez-Moreno S, Ortega-Perez G. Safety considerations for operating room personnel during hyperthermic intraoperative intraperitoneal chemotherapy perfusion. *Eur J Surg Oncol* 2006;**32**:619–24.
31. Mischke C, Verbeek JH, Saarto A, et al. Gloves, extra gloves or special types of gloves for preventing percutaneous exposure injuries in healthcare personnel. *Cochrane Database Syst Rev* 2014;**3**:CD009573.
32. Andreasson SN, Anundi H, Sahlberg B, et al. Peritonectomy with high voltage electrocautery generates higher levels of ultrafine smoke particles. *Eur J Surg Oncol* 2009;**35**:780–4.
33. Tseng HS, Liu SP, Uang SN, et al. Cancer risk of incremental exposure to polycyclic aromatic hydrocarbons in electrocautery smoke for mastectomy personnel. *World J Surg Oncol* 2014;**12**:31.
34. Boiano JM, Steege AL, Sweeney MH. Adherence to safe handling guidelines by health care workers who administer antineoplastic drugs. *J Occup Environ Hyg* 2014;**11**:728–40.
35. Kieffer C, Verhaeghe P, Lagrassa S, et al. Preventing the contamination of hospital personnel by cytotoxic agents: evaluation and training of the para-professional healthcare workers in oncology units. *Eur J Cancer Care (Engl)* 2015 May;**24**(3):404–10.
36. Nygren O, Lundgren C. Determination of platinum in workroom air and in blood and urine from nursing staff attending patients receiving cisplatin chemotherapy. *Int Arch Occup Environ Health* 1997;**70**:209–14.
37. Steege AL, Boiano JM, Sweeney MH. NIOSH health and safety practices survey of healthcare workers: training and awareness of employer safety procedures. *Am J Ind Med* 2014;**57**:640–52.