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Protective Equipment Applicable to a Centralized Cytostatic Preparation Unit

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Abstract

Occupational exposure to cytotoxic agents has been recognized as a potential danger to the health of handlers. However, collective and individual protection equipment has been developed for use by professionals. This article aims to identify and describe the protection equipment applicable to a centralized unit of cytostatics preparation, using a qualitative and quantitative descriptive analysis. A questionnaire survey yielded 83 responses, covering 18 centralized cytostatic preparation units. The results show some weaknesses detected in some institutions such as the absence of a shower and eyewash fountain, the lack of knowledge about the procedures manual, and the use of a surgical mask. However, the results point to awareness by the general manipulators regarding the use of some personal protective equipment. This study contributes to the investigation of the use of equipment for the protection of cytostatic manipulators at work in centralized cytostatic preparation units.

Keywords: Centralized cytostatic preparation unit; Individual and collective protective equipment; cytostatic drugs, guidelines

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1. Introduction

The anticancer drugs also referred to as cytostatic (CTX), cytotoxic or antitumor, are increasingly used both in the treatment of malignancies, either with prophylactic intentions (adjuvant therapy). As well, in a growing spectrum of benign pathology (autoimmune diseases, chronic inflammatory diseases of the gastroenterological or rheumatologically, among others). However, its genotoxicity is proven in experimental models and patients treated with chemotherapy. Ideally, these should only affect cancer cells, but the available drugs, although preferentially affect malignant cells, are relatively specific, also affecting the genome of normal cells and thus conditioning the adverse health effects either of treated patients as well of health professionals exposed to them [1]. CTX is prepared through a specialized and complex process by healthcare professionals. However, those responsible for their preparation and administration are at risk of adverse effects on their own health. Several studies have confirmed the existence of widespread contamination of the environment and in work surfaces [2]. Due to occupational risks that may result from exposure to the involved pharmacy professionals are subject, high concern is necessary as the handling of these drugs. Risks of a chemical nature can manifest themselves through systematic contact with potentially dangerous antineoplastic drugs through teratogenic, mutagenic and carcinogenic manifestations [1].

Since occupational exposure to cytotoxic drugs has been perceived as a potential health hazard, guidelines and safety recommendations have been issued in several countries to try to improve procedures, set standards and minimize exposure. In Portugal, Infarmed licenses the opening of the centralized cytostatic preparation unit (CCPU), but there is no uniform procedure manual for all hospitals or in oncology centres. Currently, each hospital has its their own manual which is based on international guidelines. Nationally, there is no specific legislation regarding compliance with standards for the handling of CTX, using only guidelines indicated as the best working standards to be followed in some countries whose application is not required by law. National regulations are more focused on the good manufacturing of non-sterile (handled) preparations or sterile preparations, not highlighting the specifications and care related to cytotoxic manipulation. Only in the Hospital Pharmacy Manual makes some reference to this matter, although in a very scarce and little specific way.

Because of this national situation, this article is designed to answer the following research question: "Under what working conditions does the preparation of cytotoxic drugs take place and which are the main protective equipment applicable in the CCPU?" In order to answer this question, this paper aims to identify and describe the protection equipment applicable to a centralized unit of cytostatics preparation. This article is structured as follows. After this brief introduction, in section 2 and 3 is elaborated a literature review on centralized units of preparation of cytostatic and on protective equipment, both collective and individual. In the following section 4, the method used the research is described. In section 5, the results are presented and discussed. In section 6, it will be presenting the main conclusions of this study, and the limitations, future research and recommendations are suggested.

2. Centralized cytostatic preparation unit

The preparation of CTX involves several activities tasks and proceedings. In hospital settings, cytotoxic manipulation is considered the set of operations involving reception, storage and transport, preparation from a commercial package, administration to the patient, collection and disposal of wastes from the two previous operations, as well the collection and elimination of patients' excretions [3]. The preparation of injectable CTX should be centralized in a hospital area designed for this purpose. The centralization of CTX preparation has as its main objective the protection of patients, manipulator, environment and medicine. The preparation area should be located near of patients' administration area. The ideal facilities for the preparation of cytotoxic drugs should be constituted by three distinct areas (see Figure 1), called dirty, semi-clean and clean, physically separated zones [3]:

- Room dirty or black - where is the dressing room; the hand wash basin; emergency shower;
- Semi-clean or grey room - also called an antechamber, where personal protective equipment is worn for handling, accident prevention equipment; there is also a running bench that physically separates this area from the dirty area;
- Clean or white room - in this room the CTX is prepared, under aseptic conditions and with a minimum risk of contamination; there is the laminar flow chamber, class II, type B, and stainless steel workbenches, smooth, washable, waterproof and resistant to disinfection.

Fig. 1. Facilities of the CCPU production area, for the 3 different areas. Source [4].

In the cleanroom, there are mechanisms for extracting and filtering the circulating air, which maintains the required asepsis and eliminates the aerosols that can be released during the handling of these toxic products. Furthermore, this room is under negative pressure rap prevent potentially contaminated air streams to circulate outside the handling room, thus preventing environmental pollution of adjacent areas. There are pressure control devices at the entrance to the cleanroom, with a daily record of pressures [5]. The cleanroom should be kept at a lower pressure than adjacent rooms. The antechamber should have pressure higher than the preparation room and slightly higher than the other areas. Hazardous substances will therefore not be allowed to enter the antechamber and pathogens do not move from neighbouring rooms into the preparation room. The basic standards for each cytotoxic drug (forms of storage, stability, composition and special precautions) should be posted in the room.

Lastly, the cleanroom must have a grey room communication system, embedded on both sides, for the entrance of the trays with the drugs to be prepared and their exit from the trays with the drugs already handled, sealed and labelled so that the nursing team can administer to the patient [6]. In the cleanroom, it is forbidden to drink, eat, smoke, or that manipulators use cosmetics and accessories because they can be a source of infection [6].

The CCPU presents the following support processes: Environmental control, microbiological control, protocol/cleaning plan, cleaning material, waste and garbage collection.

3. Protection equipment

The CTX s substances are administered in patients weakened states, there can be no risk of contamination of the products and the health professionals who deal with this kind of material must be adequately protected from the harmful effects that may arise for your health. Therefore, there should be a strict protocol control of safety procedures that must be taken and recorded to guarantee the existence of failures that could jeopardize both the quality of the medicine and the health of the professionals. For this purpose, both collective and individual protective equipment have been developed.

3.1. Collective Protection Equipment

The CPE are equipment that is intended to maintain the safety of the collective of people, whether employees or not, but who frequent that place and deal with the materials in question. In addition, and feathers When the use of CPE is not sufficient to avoid/remove/mitigate the risk, they should be used PPE suitable individually protecting each worker, so the prosthesis rears the health and safety, avoiding accidents at work and potential occupational diseases [7]. The general principle of prevention points to the priority to respect CPE to PPE. In this particular work environment may stand out as CPE:

- **Shower and eyewash**: They are intended to eliminate or minimize damage caused by accidents in the eyes and/or face and in any part of the body, and there must be preventive maintenance [8].

- **Flow chamber** vertical laminar class II, type B: Preparation of CTX should occur within a vertical laminar flow chamber (VLFC) class II, type B, in order to ensure effective protection of the operator concerning the contact with the medicament all the microbial contamination of the solution, which constitutes a great danger. In the VLFC, a barrier is created between the operator and the work area. This barrier consists of a flow in which all the air located in a defined space is displaced at a defined speed through parallel and oriented lines (flow lines) with a minimum of turbulence [9]. The chambers must have a protective glass for the worker. All these chambers must be equipped to show pressure differences and must present audible alarms that can be activated if the optimum airflow velocity is not reached, indicating a failure in the safety of the chamber [8].
- **Before each work session**, and after the placement of PPE, the VLFC should be cleaned with an appropriate antiseptic solution such as alcohol at 70º. For VLFC that works for 24 hours, it is recommended to be cleaned 2 to 3 times per day. Disinfection should include all surfaces of the chamber and should be performed from top to bottom (in the direction of airflow) starting from the back wall in parallel passages. The work surface is the last part to be disinfected. After disinfection, wait 5 minutes. All material placed inside the VLFC should be sprayed with alcohol at 70 °C.
- **It is also important to point out that decontamination should be carried out whenever**: drugs of different nature are handled to avoid cross-contamination; at the end of the working day; the run a stroke; and complete in maintenance operations.
- **However, a deeper cleaning of the VLFC** (removal of the surface grille or lower worktop) should be done once a week. This procedure should also occur whenever contamination occurs, or when major changes are observed (e.g., camera maintenance) [2].
- **Sterile Working Field**: The preparation of cytotoxic agents should be performed on a sterile working field with absorbent and impermeable (double-sided) characteristics. This should be changed at the end of each session (according to the supplier's specifications) and whenever there is a cytotoxic effusion [2].
- **High-Efficiency Particulate Air Filters**: VLFC s are equipped with HEPA Filters or Absolute Filters, they are a filter surface characterized by having a 99.7% efficacy on particles with a diameter equal to or greater than 0.3 μm. They are absolute filters with a degree of resolution of 99.7% and have the capacity to capture submicron particles. The particles are retained by HEPA filters by the following phenomena: sedimentation, inertia (impact); intersection and diffusion [10]. To the company with which the maintenance of the equipment is contracted the takes responsibility for the cleaning and maintenance of these filters.
- **Cytotoxic drug spill kit**: Should exist a stroke kit cytotoxic all handling areas, an access zone and always ready for use. Each institution must have the policy to cope with an accidental spill/exposure of cytotoxic agents. It is essential that all healthcare professionals know how to handle the kit. Removal and disposal of cytotoxic agents may only be performed by appropriately trained and trained personnel. Spill and accidental exposure procedures should be part of the standard work and periodic training [11]. Generally, this is constituted by manual of instructions, handling information leaflet, low permeability protection gown, two pairs of gloves (one of them cytotoxic), self-filtration respirator P3, one pair of goggles, one pair of gloves footwear guards, two emergency signs, a Group IV bag for waste disposal, absorbent material, alkaline detergent (decontamination agents), a short-piercing waste container, a sealing wire, irrigation saline, a spade a tape to signal the contaminated area [2]. After use, it should be replaced or replaced as soon as possible and must be sealed to ensure the integrity of the same [2].

3.2. Equipment's for individual safety

From an individual perspective, PPE serves to protect the professional who handles this kind of delicate and dangerous substances. The use of PPE is fundamental and should be appropriate to the task performed by each element. All PPE shall bear the CE marking and, if applicable, a specific indication for the preparation of cytotoxic substances. A question very pertinent is when in your selection and the theme of comfort that must be taken into consideration and weighted in the face of cost. Pharmaceutical Services should be involved in the selection of this type of equipment [12]. In this particular environment it can be considered as PPE:

- **Fighter surgery**: the use of surgical uniform is recommended ("fact" operating room) of cotton or cotton/polyester to reduce the microbiological load on the room environment and limit contamination by cytostatic [12].

- **Footwear: According to WorkSafe BC** [13], workers' footwear must comply with the following rule: "The design, construction and material of footwear must be adequate for the protection required." It must be reserved exclusively for the CCPU. In addition, its constitution must have material that is easily washable and allows its disinfection. Sometimes it is necessary to wear 2 PPE of shoes.
- **Disposable feet cover**: disposable plastic device to completely cover the foot, it should be sturdy, non-slip and waterproof with elastics to ensure their grip. In the preparation area, two pairs of feet should be used and should be of single-use, thus helping to ensure the asepsis of the preparation room, while protecting the operator. Ideally, they should be non-slip [14].
- **Cap**: It should be disposable, with the purpose of avoiding the "fall" of hair, to protect the operator and to reduce contamination [14].
- **Mask**: Mask should be disposable. It serves to prevent contamination of the solutions and to prevent the inhalation of CTX aerosols by the operator. According to DIN EN 149, there are three classes of masks P1, P2 and P3. The use of a P2 or P3 type mask is recommended for handling cytotoxic agents. The greater the effectiveness of a mask, the greater the resistance it offers to breathe, which, in turn, interferes with the comfort of the user. When the mask is used improperly, it contributes to the increased risk of exposure. The shift mask should always be made to feel a lot of resistance in breathing, or the end of a no more than eight-hour shift [2].
- **Grips**: They should be disposable and sterile, made of material of poor permeability so that if there is splashing or spilling, the liquid will flow instead of being absorbed. The gown should be closed at the front with an opening at the back and the cuffs should be elastic so that they tighten around the wrists. As regards the time of use the recommendations are: immediately change equipment in the event of contamination or accident and remove the equipment when leaving the cytotoxic preparation area, having the stability of eight hours [2].
- **Gloves**: Gloves are the first protective barrier used against a possible exposure of workers also serving to protect the integrity of the product to be prepared. The ideal for a protective glove is a good impermeability to harmful substances versus comfort/sensitivity. Although some gloves refer to their specific use for the preparation of cytotoxic agents, all gloves on the market are permeable to these medicaments, and permeability is found to increase with contact time. For this reason, the specific indications of each supplier must be followed. As a general rule, the change from hour to an hour of use and/or whenever a spill or contamination occurs, unless the manufacturer's specification indicates a different period. Each supplier must provide documentation with the results of different tests of resistance, penetration and permeability to different cytotoxic agents. It is recommended to use a double coat of gloves (cytotoxic gloves plus sterile gloves). The use of two pairs of gloves at the same time is highly recommended, ensuring greater efficiency in operator protection. It should be noted that the second pair of (outer) gloves should be regularly replaced, for reasons already expressed above. At least the pair of outer gloves will have to be sterile [11]. Gloves without powder are preferable, due to dust particles can contaminate the sterile area to absorb contaminants, increasing skin contact potential [11].
- **Protective Goggles**: Goggles should be worn, these should allow lateral and frontal protection, and should prevent particulate contamination without reducing the visual field. They must be of light and malleable material and conform to the contours of the operator's face. They must be neutral and the model to be selected should allow the simultaneous use of the graduation glasses if necessary [12].

All PPE are disposable and disposed of as Group IV hospital waste (hazardous waste) [11].

4. Methods

It was used both qualitative and quantitative research, of a descriptive and exploratory nature. In order to achieve the main objective of this study, a detailed and systematic review on the subject was carried out, which allowed the construction of a questionnaire as a data collection instrument. This questionnaire was developed and applies to professionals working in the area of CTX manipulation, who were approached about the procedures verified in the hospital where they carry out the professional activity. Of the 36 institutions contacted, 18 gave authorization, 6 gave a negative opinion and 12 did not respond. This study includes 18 hospital institutions out of 36 from the National Program for Oncological Diseases - 2015, from the National Health Service [15]. The time horizon of the survey was between June and September 2017. The sample consists of 83 cytostatic manipulators. The manipulators are mostly female, have an average of 35 years of age and a large part performs functions in hospitals that are located in Lisbon. Most are pharmacy technicians and, on average, have 8 years of service as handlers. In general, these respondents

attended specific courses to be CTX handlers, and most of them took short courses, which were mostly provided by the institutions where they work.

5. Results and discussion

5.1. Field of work and shower/eyewash

Concerning safety and procedures in the CCPU and specifically to the CPE, all manipulators are aware of the existence of a cytostatic effusion kit in the units. Most manipulators (89.2%, n=74) exerts functions in a double-sided working area, and of these, 78.4% (n=58) who refer this field is permeable, waterproof referring field 20 only, 3% (n=15) and one of the manipulators did not indicate the nature of the field. Regarding the presence of showerhead/eyewash, 67.5% (n=56) of affirmative responses were obtained, and 83.9% of these (n=47) were made and recorded periodic maintenance. It is important to note that 27 handlers report that there is no shower/eye-wash in the CCPU where they work. However, according to ASHP [2], the manipulation of CTX must be performed in a sterile labour field, but there are 9 professionals who do not use it. It should also be pointed out that 27 professionals refer to the lack of showers at the CCPU. According to Garcia [8], these are intended to eliminate or minimize damage caused by accidents in the eyes and/or face and in any part of the body. Revealing this equipment as an CPE of great relevance for intervention in case of an accident. In addition, according to Canastro [5], the use of facilities with inadequate maintenance and equipment can lead to risks for the professional, such as the inhalation of aerosols that may have allergic reactions; infertility or birth defects. If we take into account the distribution of showers and eyewash by district, it is verified that all refer to the existence of showers and eyewash in the districts of Lisbon, Braga and Porto. In addition, most manipulators in the district of Vila Real also refer to the existence of this CPE. The totality of the manipulators of the district of *Viseu*, *Évora* and the totality of the manipulators of the district of *Setúbal* and *Guarda* mention that this CPE does not exist in the unit where they carry out functions.

5.2. Characterization of the laminar flow chamber and aseptic room

With regard to the chamber and laminar flow, the great majority is vertical of class II and type B (86.7%; n=72) and the rest are vertical of class II and type A. As for the moment in which the chamber is connected, most refer that it is always on (n=51, 61.4%); in 31.3% of the cases (n=26) the chamber is turned on 30 minutes before the beginning of the work and turned off 30 minutes after the end of the work. There were still 6 respondents who answered none of the options. Regarding disinfection of the laminar flow chamber, 97.6% (n=81) refer before the beginning and at the end of the work. Only two respondents mention disinfection before the commencement of work. Disinfection is mostly done using alcohol at 70 degrees. The majority of handlers (n=67; 80.7%) also reported performing interim cleanings throughout the day, the main reasons being: after manipulation of Bacillus Calmette-Guérin (BCG) or intrathecal CTX (n=25; 37.3%); after manipulation of BCG, intrathecal CTX or with each new entry into the aseptic room (n=13, 19.4%) and after ophthalmic preparations (n= 10, 14.9%). All manipulators refer to performing weekly laminar flow chamber cleanings. Preventive maintenance is performed every six months (n=41, 49.4%) or annually (n=39, 47%), these being the most common periodicities. HEPA filters are replaced in most situations (n=77, 92.8%) by technicians qualified for this purpose. With regard to the aseptic room (see Table 1), all CCPUs have air extraction and filtration mechanism for circulating air and pressure control, and all control the temperature. According to Canastro [5], this device has a dual purpose. On the one hand, this device allows the room to maintain the required asepsis, eliminated aerosols that can be released during the handling of these products. On the other hand, this device prevents that the potentially contaminated airflow flows out of the handling room, thus avoiding environmental contamination of adjacent areas. Regarding VLFC, most handlers do what is recommended by the ASHP guidelines [2], such as cleaning the chamber with an appropriate antiseptic solution such as alcohol at 70º; it is recommended to be cleaned 2 to 3 times a day or whenever drugs of different nature are handled to avoid cross-contamination and weekly cleaning. Finally, the exchange of HEPA filters is carried out by qualified and specialized technicians as mentioned by Nunes [10].

Table 1. Characterization of the laminar flow chamber and aseptic room.

			n	%
Laminarflow chamber	Type			
	Is turned on	30 minutes before work starts and is left on for 30 minutes after finished work		
		It remains continuously connected		
		None of the options		
	Disinfection is performed	Only before starting work		
		Before the beginning and at the end of work		
	The disinfection is done with	Alcohol at 70º		
		water and detergent at neutral pH		
		Alcohol at 70º+ hypochlorite solution		
		Alcohol at 70º+ other		
		Other		
		Alcohol at 70º+ water and detergent at neutral pH + other		
	During the day performs interleaved cleaning	Yes		
		No		
	Situations leading to interleaved cleaning (n=67)	After manipulating CTX for intrathecal administration		
		entry into the aseptic room		
		During the work activities		
		After manipulation of BCG or after manipulation of CTX for intrathecal administration		
		After manipulation of BCG or after manipulating CTX for intrathecal administration or with each new entry into the aseptic room		
		Other: When handling bendamustine		
		Other: Ophthalmic preparations		
		Other: Before the handling of non-CTX drugs		
	Weekly cleaning	Yes		
		No		
	Preventive maintenance	Quarterly		
		Semi-annually		
		Annually		47.0
		Other (Unknown)		2.4
	Exchange HEPA filters by qualified technicians	Yes		92.8
		Do not know	6	7.2
Aseptic room	There is an air extraction/filtration mechanism and pressure control	Yes		
		No		
	Temperature and pressure control	Yes		
		No		

5.3. Characterization of UCPC for cleanliness, safety data sheets and signalling

Most manipulators report that the CCPU where they perform functions is cleaned daily (n=80, 96.4%), there are 2 handlers that report 2 cleanings per day and 1 that they do not know. Regarding the existence of safety data sheets of products handled, most refer to their existence (n=71; 85.5%), but there are 7 manipulators who do not know about their existence and 5 reports that there are no such files. As to the existence of local signs for compulsory use of PPE, only half report their existence (n=42, 50.6%). Respondents report the presence of hazard signs in 66.3% (n=55) of the CCPU where they work and emergency only 24.1% (n=20). In the CCPU, 5 professionals there are no safety data sheets and 7 professionals are unaware of their existence. A safety data sheet is available for all hazardous agents in the workplace, according to ASHP [2]. The correct cleaning of the CCPU is done daily. In the different areas of the CCPU, the working instructions must be clearly visible, as well as signs of compulsory use of PPE [5], as with most of the manipulators who participated in this study.

5.4. Characterization of PPE and degree of importance

Concerning the characterization of PPE, only 1 of the 83 CTX manipulators believes that PPE does not reduce exposure to chemical risk and only 2 indicate that the PPE they use does not have the CE marking. However, the use of PPE is fundamental and should be appropriate to the task performed by each element. All PPE must bear the CE marking and, if applicable, specific indication for the preparation of cytotoxic agents [12]. In addition, a positive factor is that most professionals are aware and sensitized of the use of PPE, as it reduces the chemical risk.

It analysed the degree of importance given by CTX manipulators using a scale type Likert of 5 points, where 1 corresponds to no important and 5 is extremely important. For each PPE, the absolute and relative frequencies recorded in each degree of importance, the mean and the standard deviation are presented. The average varies from 1 to 5 according to the attribution of the answers given the importance and the higher the average, the greater the importance attributed by the manipulators to this PPE.

The respondents stated that the use of disposable plastic feet (84.3%; n=70) and cape use (81.9%; n=68) is extremely important, which leads to mean values close to 5 and its standard deviation, namely 4.74 ± 0.72 and 4.80 ± 0.48. In addition, during the manipulation of CTX, the most used mask is the P3 class, since 97.6% (n=81) responded extremely important. Following, the class mask P2 with 54.2% (n=45) of handlers considered very important and 21.7% (n=18) extremely important. Regarding the surgical mask, most manipulators consider that their use is not relevant (60.2%, n=50), and as far as the activated carbon filter mask is concerned, most do not know or have no information (57.8%, n=48). The majority of respondents considered the use of frontally closed dressing gown nothing or insignificant (72.2%, n=60), the mean being 2.04 ± 1.13. However, the use of closed-back, long sleeve, elastic and disposable wrists is considered extremely important by 78 of the 83 manipulators surveyed, which translates into an average of 4.94 ± 0.37 what is attested to the importance attributed to this PPE.

As for the use of disposable gloves such as clown gloves and non-sterile latex gloves, the manipulators are not consensual about their importance, since the answers are distributed from nothing important to extremely important. The average value registered in the former was 2.97 ± 1.20 and in the remaining 3.00 ± 1.18. On the other hand, the use of sterile latex gloves is of the utmost importance for most manipulators (85.5%, n=71), with an average value of 4.72 ± 0.77. Non-sterile nitrile gloves are considered very important by 42.2% (n=35) of the manipulators and extremely important by 28.9% (n=24), which leads to an average of 3.90 ± 0.98. The use of sterile nitrile gloves (78.3%; n=65), as well as the use of thick latex gloves (57.8%; n=48) and the use of thick gloves of non-sterile latex (78.3%, n=65). Finally, the use of goggles is not of the most important PPE for the manipulators, since most of the answers fall into nothing important or insignificant (13.3% and 45.8%, n=11 and n=38, respectively), with an average of 2.58 ± 1.21. It should also be pointed out that the importance attributed by the manipulators to the following PPE: feet, cap, P2 and P3 masks, Bata closed-back, long sleeve, elastic and disposable cuff, sterile latex gloves, sterile nitrile gloves, gloves of latex and non-sterile gloves (‘blue glove’).

5.5. Hand hygiene and use of PPE during the manipulation of cytostatics

The information detailed on the handwashing and the use of PPE during handling CTX demonstrates that T anodes handlers proceed to hand hygiene before and after CTX manipulation. Most use disposable feet (83.1%, n=69) and, of these, a large part uses two pairs (55.1%; n=38), and most of them use non-slip feet (79.7%; n=55). As for the type of mask used, most manipulators indicate P3 class (67.5%; n=56) or P2 class (21.7%; n=18). It should be noted that eight manipulators (9.6%) mention that they manipulate with a surgical mask. In addition, the material constituting the gowns is impermeable in almost all manipulators (97.6%, n=81).

Regarding the number of pairs of gloves used, all the manipulators indicate two pairs, the material of which is latex and nitrile rubber in 76 of the 83 manipulators. As for the frequency with which the gloves are changed, most handlers report from hour to hour (65.1%, n=54) or every two hours (19.3%, n=16). Almost all respondents changed gloves in a situation of stroke (98.8%, n=82). In addition, most handlers do not use protective devices (89.2%, n=74). All PPE used by the manipulators are disposable and 59% (n=49) report that they reuse some of them. The gown and mask are the most commonly reused PPE (46.9%, n=23), and there are, also, 12.2% (n=6) who recycle the cap. There is still 16.3% (n=8) that recycles only the sacks, while 14.3% (n=7) recycle the robe. The manufacturer's guaranteed stability and savings are the two main reasons justifying the re-use of these PPE. It should be noted that all wash hands before

and after, while some do not use plastic feet, but according to Beaney [14] should use, in order to ensure aseptic. A very important note is the use of a surgical mask by some professionals, which is incorrect because according to ASHP [2], the mask to be used must be of type P2 or P3. The surgical mask, also called the P1 mask, has a low filtration efficiency and should not be used in CTX manipulation. As far as the dressing is concerned, most use a waterproof jacket, so that if there is splashing or spilling, the liquid will flow instead of being absorbed. As for gloves, most practitioners follow recommendations [11], change each hour to an hour of use and/or whenever a stroke or contamination occurs, the use of two pairs of gloves at the same time is strongly recommended.

5.6. Manipulators' opinion: Comfort, choices and costs knowledge of PPE

Most of the manipulators report that the PPE are comfortable (61.4%; n=51), that pharmaceutical services are involved in their choice (83.1%; n=69) and in the last, they have not received any new PPE (72.3%; n=60).

Addressing finally the knowledge of the handlers about the cost of PPE, most CTX handlers that integrate this study reported having an idea of the costs of PPE (57.8%; n=48) and 60.4% (n=29) of these says that its cost is high. 80.7% (n=67) of the manipulators associate this high cost with the expected duration of its effectiveness. The quality of PPE is another factor that justifies their costs (83.1%; n=69) and of these, 94.2% (n=65) consider that the most expensive PPE are better. Most of the manipulators surveyed in this study also report that the most ergonomic PPE are better (92.8%; n=77). As for the reduction of PPE costs, the majority of respondents (79.5%, n=66) believe that this is not possible. Of those who consider that it is possible to lower these costs, the ways to achieve this goal are: use of reusable materials, greater stability of PPE and greater competition between suppliers.

6. Conclusions and Limitations and scope for further studies

In Portugal, there is no uniform procedures manual for all the Centralized Cytotoxic Preparation Units (UCPC), Infarmed is based on international guidelines and recommendations for their opening and inspection.

The use of CPE should be a priority for the Institutions. Due to their relevance, the manipulators' perception of the procedures and the use of this equipment is indispensable. All manipulators are aware of the existence of a cytostatic spill kit in the units. In general, the manipulators perform functions in a double-sided and largely permeable working field. About 70% of the 18 institutions have an easy-to-use shower and eyewash, which is indispensable for trying to reduce or even eliminate damages caused by accidents. However, as far as its distribution by district, the districts of Lisbon, *Braga* and *Porto* are distinguished with institutions in which all mention the existence of showerhead and eyewash. In addition, not all have preventive maintenance and written record of them.

Most of the laminar flow chambers are vertical class II, type B and almost always their disinfection is carried out before the beginning and at the end of the work, mainly with alcohol. During the day, several intercalations are performed, mainly after the manipulation of BCG or CTX for intrathecal administration. In total, cleaning to the camera is done on a daily basis, generally being biannual or annual maintenance. In addition, 92.8% of HEPA filters are exchanged by qualified technicians. In all aseptic rooms, there is an air extraction/filtration mechanism and pressure control, and in addition, there is a daily manual recording of temperature and pressure.

Given the importance of the use of PPE, the manipulators must be aware of them and their importance. By the analysis, it is verified that almost everybody realizes that the use of the same translates in the reduction of the exposure to the chemical risk. Despite the mandatory CE marking, not all of these devices present it. There is a concern of the totality of manipulators in the hygiene of the hands, before and after the manipulation. Most manipulators use disposable plastic feet, one or two pairs. However, few shoe protectors are non-slip. The most frequently used masks are of the P3 class and almost all wear impermeable gowns. All respondents use two pairs of gloves and most of them exchange them hour by hour, most of them in latex and nitrile rubber. In general, whenever there is a stroke, the gloves are replaced. All PPE are disposable and some are reused, namely the gown and the mask, with stability and savings being the major reasons for reuse. It turns out that most of these professionals do not wear goggles. Most manipulators consider PPE to be comfortable, most of them have not received any new PPE in the last 6 months, and their choice is usually made by the pharmaceutical services.

In general, the results point to an awareness on the part of the manipulators of the use of some PPE, namely the use of mask P3, the closed jacket behind long sleeves and elastic cuffs and thick latex gloves, non-sterile ("blue glove"),

which evidence a safe practice of CTX manipulation. According to the ESOP guidelines [12], this equipment is of great importance in the protection of the professional that manipulates this type of substance, and their use is fundamental and must be adapted to the task performed by each element. More than half of these professionals have a notion of the cost of PPE, considering it high, they know that the duration of their effectiveness and quality is related to costs, the most expensive and ergonomic being the best. For the most part, they understand that the cost of PPE cannot be reduced, believing that through greater stability and materials reuse is possible.

The results obtained are following the guidelines used in the clinical practice of handling cytostatics. This research has established the essential about the equipment used for the protection of cytostatic manipulators at work in centralized cytostatic preparation units. The results obtained through the surveys allow us to identify some of the strengths and weaknesses that the institutions have. As strengths are identified the knowledge of PPE, all institutions present in the aseptic room pressure control and the existence of a spill kit. The weaknesses detected in some institutions were the lack of shower and washes/eyes, the lack of knowledge of the procedures manual and the use of a surgical mask, although statistically low. Some limitations were identified in this study. The main limitation of this study was the difficulty in obtaining answers. The nature of this work is only exploratory and descriptive. This study was performed only in Portuguese hospitals. The present study can be extended in different aspects in the future. It would be interesting and in future research to conduct this study in other countries to compare results. To conduct an empirical study to test the impact of the use of protective equipment on the health of the manipulator and the impact of the lack of equipment on occupational risk.

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