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Original Article

Suitability in compounding sterile preparations: An observational study in a referral hospital

[Idoneidad para elaborar preparaciones estériles: Un estudio observacional en un hospital de referencia]

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Abstract

Context: Compounding sterile preparations in hospitals requires special attention because the process is more complex. Errors that occur when compounding sterile preparations can cause contamination of the prepared preparations.

Aims: To evaluate the compounding of sterile preparations in a referral hospital.

Methods: This research was conducted by observing nine critical aspects in the compounding of sterile preparations. The research instrument used was a checklist, as regulated in USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations. After that, the most mixed preparations were tested for sterility using a fluid thioglycollate medium and soybean casein digest medium.

Results: Of the 36 compounding sterile preparations, discrepancies were found in the aspects of compounding personnel (100%), building (100%), equipment (100%), aseptic procedures (100%), packaging (0%), labels (100%), storage (2.78%), distribution (2.78%) and quality assurance (100%). Furthermore, sterile preparations prepared in the cleanroom in this referral hospital indicate the occurrence of microbial contamination.

Conclusions: Most of the critical aspects in compounding sterile preparations at this referral hospital have not met the recommendations of the USP <797> Guidelines and the Basic Guidelines for the Dispensing of Sterile Preparations, except for the packaging aspect. Improvements in several critical aspects need to be made to ensure the quality of the prepared preparations from microbial contamination.

Keywords: compounding; dispensing; sterility; USP.

Resumen

Contexto: La elaboración de preparados estériles en hospitales requiere una atención especial porque el proceso es más complejo. Los errores que ocurren cuando se elaboran preparaciones estériles pueden causar contaminación dichas preparaciones.

Objetivos: Evaluar la elaboración de preparados estériles en un hospital de referencia.

Métodos: Esta investigación se llevó a cabo observando nueve aspectos críticos en la elaboración de preparaciones estériles. El instrumento de investigación utilizado fue una lista de verificación, según lo regulado en las pautas de la USP <797> y las pautas básicas para dispensar preparaciones estériles. Después de eso, se ensayó la esterilidad de las preparaciones más mezcladas utilizando un medio fluido de tioglicolato y un medio de digestión de caseína de soja.

Resultados: De las 36 preparaciones estériles elaboradas, se encontraron discrepancias en los aspectos de personal de elaboración (100%), construcción (100%), equipo (100%), procedimientos asépticos (100%), empaque (0%), etiquetas (100%), almacenamiento (2,78%), distribución (2,78%) y garantía de calidad (100%). Además, las preparaciones estériles preparadas en la sala blanca de este hospital de referencia indican la existencia de contaminación microbiana.

Conclusiones: La mayoría de los aspectos críticos en la elaboración de preparados estériles en este hospital de referencia no han cumplido con las recomendaciones de las guías USP <797> y las guías básicas para la dispensación de preparaciones estériles, excepto en el aspecto de empaque. Es necesario realizar mejoras en varios aspectos críticos para garantizar la calidad de las preparaciones elaboradas a partir de la contaminación microbiana.

Palabras Clave: dispensación; elaboración; esterilidad; USP.

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INTRODUCTION

The process of compounding sterile preparations is one of the stages that require special attention to not affect the quality of the preparations produced. Sterile preparations that are of poor quality or contaminated with microbes are known to cause the patient's health to deteriorate or even death (Myers, 2013; Suvikas-Peltonen et al., 2017).

Guidelines that can use to compound of sterile preparations in hospitals are United States Pharmacopeia (USP) chapter 797, which contains various requirements for compounding personnel, buildings, equipment, aseptic procedures, packaging, labeling, storage, distribution to quality assurance (USP, 2019). In Indonesia, there are also basic guidelines for dispensing sterile preparations in 2009, which contain various aspects that must consider in the compounding of sterile preparations, including human resources, room and equipment, aseptic techniques, storage, distribution and documentation (Depkes, 2009). These guidelines should be followed to produce a sterile and high-quality concoction product. Nevertheless, the compounding error in Germany and the UK is still quite large, which is estimated at around 34-48% (Melviya et al., 2019).

The same thing happened at the referral hospital in Purwokerto, where this research was conducted. In addition to being a referral hospital, this hospital is also a teaching hospital. But unfortunately, there are still limitations in the implementation of compounding sterile preparations. In the last five years, there has been a compounding error of 3%, which causes incompatibility of preparations. This encourages researchers to observe and evaluate the activities of compounding sterile preparations at the referral hospital in Purwokerto city. The results of this study are expected to be an evaluation material for the hospital to improve various critical aspects in the compounding of sterile preparations that are not appropriate and maintain things that are in accordance with the guidelines for compounding sterile preparations.

MATERIAL AND METHODS

Study design

The study was conducted in a government-owned hospital, which is one of the referral hospitals in Purwokerto, Indonesia. This study followed ethical research principles, and ethical approval was obtained from the Ethics and Medical Research Committee (approval number: 420/09770/IX/2020).

This study observed every sterile preparation prepared in a clean room during the period June-August 2020, except for cytostatic preparations. The number of samples was determined using a saturated sampling technique (Sugiyono, 2019). During the study period, it was found that only 36 names of sterile preparations were prepared in this hospital.

Data collection procedure

Data collection was carried out prospectively at a referral hospital in Purwokerto city, Indonesia, with a permit number 420/09769/IX/2020. Researchers made a vague observation of several critical aspects that must be met in the compounding of sterile preparations. Observations were made during the compounding process and recorded every incident during the observation using a checklist sheet.

Research instrument

The research instrument was in the form of a checklist sheet consisting of several critical aspects that must be met in the compounding of sterile preparations based on the USP <797> Guidelines and the Basic Guidelines for Dispensing Sterile Preparations. These critical aspects include personnel, buildings, equipment, procedures, packaging, labeling, storage, distribution, and quality assurance. Every critical aspect in the compounding of pharmaceutical preparations is under the scrutiny of researchers. The checklist sheet was validated before being used for observation. Validation was carried out by five health workers consisting of two lecturers from the pharmacy faculty and three pharmacists from the hospital where the research took place. The validated checklist sheet is in Appendix 1.

Sterility test

This test was carried out on one of the most widely prepared sterile preparations in a clean room during the study period. The test method used was adapted from the Indonesian Pharmacopoeia, which used fluid thioglycollate medium to grow anaerobic and aerobic bacteria, then soybean casein digest medium for the growth of aerobic bacteria and fungi. The samples were planted in the medium, then incubated at a temperature of 30-35°C and 22-25°C for 14 days each and replicated 3 times. The same treatment was also carried out for the negative control (without sample). If for 14 days there was microbial growth in the planting media sample and no growth occurred in the negative control, then contamination had occurred during the compounding of sterile preparations (Kemenkes, 2014).

Statistical analysis

Data from observations of compounding sterile preparations obtained in this study were analyzed descriptively and presented in the form of tables or figures. Furthermore, the sterility test data was carried out by paired T-test using SPSS version 26.0 (IBM Corporation, USA).

RESULTS

Characteristic of sterile preparations

Observations during the study period involved 36 drugs prepared in a cleanroom at the referral hospital. Based on Table 1, it was known that compounding personnel carries out repackaging or transfer from primary packaging to injection syringes as many as 22 names of drugs (61.1%), and about fourteen other names of drugs were only dissolved (38.9%). Furthermore, it can be seen that ranitidine injection was the most widely prepared sterile preparation in the cleanroom at this referral hospital.

Critical aspects in compounding sterile preparations

The observations on the critical aspects required in the compounding of sterile preparations are described in Table 2.

The presentation of the discrepancy of each critical aspect during the compounding process of sterile preparations (n = 36) can be seen in Fig. 1.

Compounding personnel, buildings, equipment, procedures, labeling, and quality assurance were critical aspects that are 100 percent not in accordance with the USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations recommendations. Furthermore, it was known that aspects of storage and distribution did not meet the guidelines, each of which was 2.78%. Meanwhile, for the packaging aspect, it was in accordance with the USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations.

Sterility test

Sterile preparations prepared in a cleanroom that did not meet the recommendations of USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations showed that there was microbial growth on the test medium, which can be seen in Fig. 2. The amount of microbial growth there was a difference on day 0 with day 14 ($p<0.05$), which can be seen in Table 3.

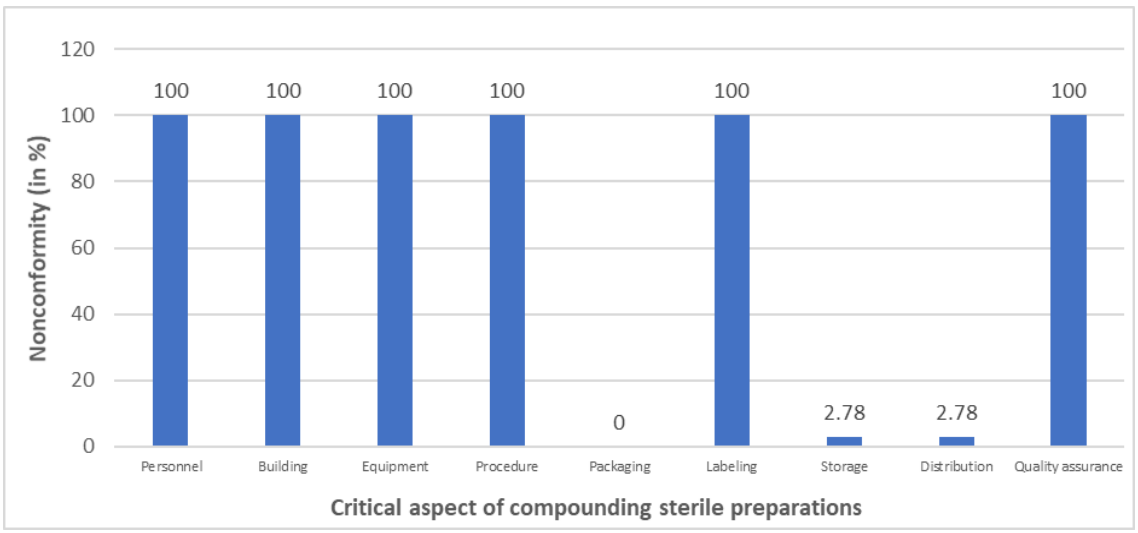

Figure 1. Percentage of non-conformance of each critical aspect in the compounding of sterile preparations at a referral hospital (n = 36).

Table 1. Characteristic of sterile preparations (n = 36).

Generic name	Dosage form	Compounding type	Σ	Storage	
				Observation result	Literature study (Trissel, 2009)
Carbamazochrome	Ampoule	Repackaging	16	Room temperature in a clean room and in a refrigerator if in the ward	Refrigerator
Amikacin	Vial, liquid	Repackaging	14	Room temperature	Room temperature
Ampicillin	Vial, powder	Reconstitution	43	Room temperature	Below 30°C or room temperature
Azithromycin	Vial, powder	Reconstitution	37	Room temperature	Below 30°C or room temperature
Hyoscine butylbromide	Ampoule	Repackaging	292	Room temperature	Room temperature between 20 and 25°C
Ampicillin-sulbactam	Vial, powder	Reconstitution	173	Room temperature	Room temperature
Ceftriaxone	Vial, powder	Reconstitution	1135	Room temperature	Below 30°C or room temperature
Cefotaxime	Vial, powder	Reconstitution	76	Room temperature	Below 30°C or room temperature
Cefoperazone	Vial, powder	Reconstitution	44	Room temperature	Room temperature not exceeding 25°C
Ceftazidime	Vial, powder	Reconstitution	409	Room temperature	Room temperature
Cefazolin	Vial, powder	Reconstitution	10	Room temperature	Room temperature
Citicoline	Ampoule	Repackaging	73	Room temperature	Room temperature
Dexamethasone	Ampoule	Repackaging	220	Room temperature	Room temperature
Diphenhydramine HCl	Ampoule	Repackaging	32	Room temperature	Room temperature
Diazepam	Ampoule	Repackaging	469	Room temperature	Room temperature
Furosemide	Ampoule	Repackaging	993	Room temperature	Room temperature
Hydrocortisone	Vial, powder	Reconstitution	15	Room temperature	Below 30°C
Fursultiamine HCl	Ampoule	Repackaging	84	Room temperature	Room temperature not exceeding 25°C
Gentamicin	Ampoule	Repackaging	111	Room temperature	Room temperature
Ketorolac	Ampoule	Repackaging	751	Room temperature	Room temperature
Methyl prednisolone	Vial, powder	Reconstitution	372	Room temperature	Room temperature
Metamizole	Ampoule	Repackaging	197	Room temperature	Below 30°C or room temperature
Mecobalamin	Ampoule	Repackaging	316	Room temperature	Room temperature
Meropenem	Vial, powder	Reconstitution	97	Room temperature	Room temperature between 20 and 25°C
Metoclopramide	Ampoule	Repackaging	177	Room temperature	Room temperature
Omeprazole	Vial, powder	Reconstitution	870	Room temperature	Room temperature not exceeding 25°C
Ondansetron	Ampoule	Repackaging	960	Room temperature	Room temperature
Phenytoin	Ampoule	Repackaging	149	Room temperature	Room temperature
Ranitidine	Ampoule	Repackaging	1619	Room temperature	Between 4 and 30°C
SNMC	Ampoule	Repackaging	22	Room temperature	Room temperature not exceeding 25°C
Streptomycin	Vial, powder	Reconstitution	254	Room temperature	Room temperature
Tranexamic acid	Ampoule	Repackaging	670	Room temperature	Room temperature not Exceeding 25°C
Tramadol	Ampoule	Repackaging	111	Room temperature	Below 30°C or room temperature
Ampicillin	Vial, powder	Reconstitution	90	Room temperature	Below 30°C or room temperature
Vit K	Ampoule	Repackaging	182	Room temperature	Room temperature
Vit C	Ampoule	Repackaging	17	Room temperature in a clean room and in a refrigerator if in the ward	Refrigerator

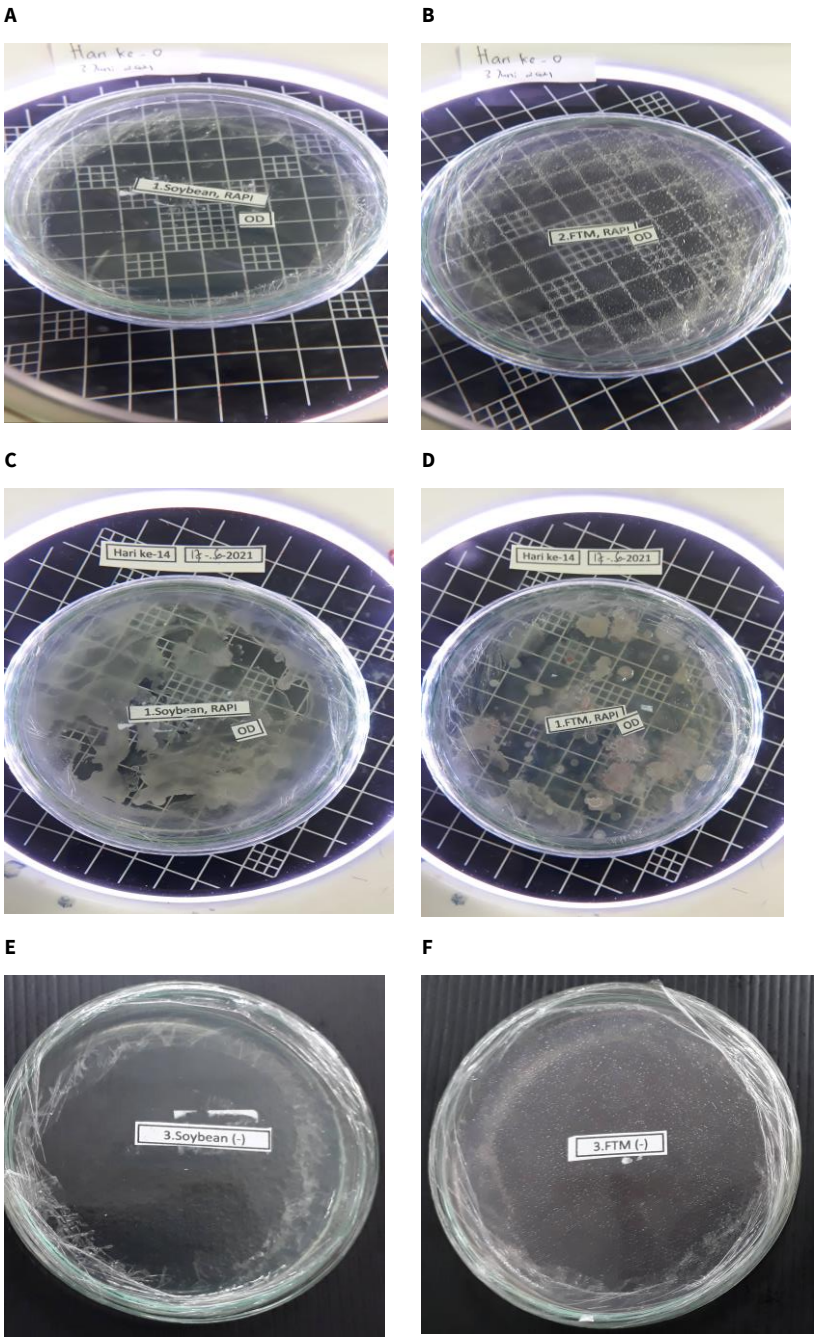

Figure 2. Sterility test result of sterile preparations (1st replication).

(A) Day 0 using soybean casein digest medium; **(B)** Day 0 using fluid thioglycollate medium; **(C)** Day 14 using soybean casein digest medium; **(D)** Day 14 using fluid thioglycollate medium; **(E)** Day 0 until day 14, negative control using soybean casein digest medium; and **(F)** Day 0 until day 14, negative control using fluid thioglycollate medium.

Table 2. Observation results on critical aspects of compounding sterile preparations.

Critical aspect	Requirements[a]	Observation result
Personnel	Pharmacists, pharmacy technicians, or personnel trained in compounding sterile preparations	Nurses who had never attended training
Building	Sterile compounding facilities must be prepared in an ISO Class 5, which has temperature (18-22°C) and humidity (35-50%). Sterile room is divided into preparation room, raw material room, product administration room, hand washing and changing room, anteroom, and clean room	The compounding room was divided into a preparation room, changing and raw materials room, anteroom and cleanroom. However, the cleanroom does not meet the requirements of ISO class 5, and the Laminar Air Flow (LAF) is in a state of disrepair
Equipment	Gowning, headgear, gloves, disposable mask, shoe cover, LAF, underpad and alcohol	Disposable mask, headgear, and gowning
Procedure	Aseptic technique	Aseptic technique has not been carried out properly
Packaging	Primary packaging that is not easily damaged	Syringes, infusion bottles
Labeling	Internal identification number (prescription number, patient name, prescription date, etc.), active ingredient and quantity, storage conditions, beyond used date (BUD), route of administration, volume of administration	Hospital identity, patient name, medical record number, name of ward, name of drug, date of compounding
Storage	Protected from direct light and in accordance with the recommended storage temperature for each name of drug	In the compounding room, it was placed at room temperature. After being distributed to the wards, the storage was adjusted to the recommended temperature (carbazochrome and vitamin C)
Distribution	Containers that are tightly closed and protected from light. If for a drug that must be maintained its stability at a certain temperature, it is placed in a container that is able to maintain its temperature consistency	Container/container that was tightly closed, but has not used a container that was able to maintain temperature consistency (carbazochrome and vitamin C)
Quality assurance	Adherence to procedures (SOP document, personnel training records, temperature logs, compounding records, sterile preparation handover document), information related to complaints and adverse events, quality records periodically to prevent errors and other quality problems	Document of the flow of sterile preparations compounding services, injection drug compounding protocol recording the name, type and quantity of drugs prepared in the compounding room

[a]USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations.

Table 3. Colony number and paired t-test results.

Medium	Observation day	Number of colonies				p-value
Fluid thioglycollate medium (FTM)	Day 0	Sample	0	0	0	0.038
		Negative control	0	0	0	
	Day 14	Sample	77	38	76	
		Negative control	0	0	0	
Soybean casein digest medium (SCDM)	Day 0	Sample	0	0	0	0.033
		Negative control	0	0	0	
	Day 14	Sample	69	132	93	
		Negative control	0	0	0	

DISCUSSION

The researcher made a vague and direct observation of the compounding of 36 names of drugs. Most of the sterile preparations at this referral hospital have primary packaging in ampoules (58.3%) and vials (41.7%). Therefore, the most commonly found compounding activity for sterile preparations was in the form of reconstitution (61.1%) and transferring the drug from the primary packaging to the injection syringe (38.9%).

The vial packaging is a double dose container used for injection containers in both liquid and powder forms. Vials containing the drug in powder form require reconstitution with a solvent before being administered to the patient. The solvent that is often

used to reconstitute sterile preparations is water for injection (WFI). WFI is a solvent that is free of endotoxin content and is easily compatible with sterile preparations (Gupta, 2016), and the direct observation on sterile preparations diluted with WFI did not find any incompatibility. Therefore, this WFI is most often used to compound sterile preparations in hospitals.

Compounding sterile preparations for patients in the inpatient ward of a referral hospital is known to be still prepared by nurses (100%; n = 36). Compounding sterile preparations is carried out based on experience and without attending training on compounding sterile preparations. There are three nurses on duty in the compounding room with 20-23 years of work experience. The same thing happened in the previous study. It was found that nurses who did the compounding of sterile preparations in hospitals in Istanbul and Indonesia did not receive special training for compounding sterile preparations (Maharani et al., 2013; Bulbul et al., 2015; Putri and Yuliani, 2018).

Compounding performed by non-pharmaceutical personnel or untrained technicians results in more contaminated preparations than preparations prepared by pharmaceutical personnel (Thomas et al., 2005). The same thing also happened to a study conducted by Austin, where the compounding of sterile preparations carried out by nurses resulted in a higher level of bacterial contamination than those carried out by pharmacists (Austin and Elia, 2013). Therefore, it is necessary to provide training programs for compounding personnel, especially for nurses at referral hospitals, in order to increase knowledge and skills in compounding sterile preparations. This is in line with several studies that education given to nurses or non-pharmaceutical compounding personnel can increase understanding of compounding sterile preparations (Maharani et al., 2013; Bulbul et al., 2015).

Furthermore, regarding the aspects of the building and equipment used for compounding sterile preparations in this referral hospital, it is still 100 percent not in accordance with what is required in the USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations (Depkes, 2009; USP, 2019). In addition, referral hospitals also do not have standard operating procedures for compounding sterile preparations in detail, starting from the preparation stage to evaluating the results of compound preparations. It is proven that in the process of compounding sterile preparations, the compounding personnel has not carried out comprehensive aseptic techniques (100%; n = 36).

Aseptic technique is a work procedure that can minimize the occurrence of microbial contamination (Austin and Elia, 2013; Austin et al., 2015). The procedures that have been carried out correctly by the compounding personnel include: 1) performing a 6-step hand washing procedure, 2) taking sterile preparations and removing them through a pass box, and 3) disposing of used drug waste into a garbage bag. Meanwhile, the work procedures that have not been carried out by the compounding personnel include: 1) not removing watches/jewelry and carrying mobile phones during work 2); not using headgear, gloves, and shoe covers when mixing; 3) not disinfecting the preparation table and the primary packaging of the drug; 4) the underpad is never replaced; 5) the compounding is carried out under and or beside the damaged LAF; 6) the gowning is removed and placed in the compounding room. Factors that trigger non-compliance are due to the absence of supervision from the Hospital Occupational Health and Safety (K3RS) officer, lack of self-awareness, and insufficient facilities available (Hendra et al., 2011).

The non-compliance behavior of compounding personnel is feared to increase the risk of microbial contamination during the injection drug compounding process. Compounding sterile preparations carried out at LAF in a cleanroom or in a compounding room in accordance with appropriate aseptic procedures can prevent significant microbial contamination compared to preparations prepared outside the criteria required by USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations (Allen and Okeke, 2009; Stucki et al., 2009; Austin and Elia, 2013; Austin et al., 2015). Research conducted by Dewi et al. (2018) showed that the frequency of bacterial contamination was higher in preparations prepared in the treatment ward than those prepared in clean rooms that met the guidelines.

Sterile preparations must be labeled with complete and clear information to reduce the risk of errors in therapy (Cohen and Smetzer, 2008). The label on the sterile compound preparation at the referral hospital does not meet the provisions of the USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations. Where the label does not include appropriate storage conditions (100%; n = 36), does not include the route of administration (100%; n = 36), and does not include the Beyond Use Date (BUD) of the preparation (100%; n = 36). It is crucial to include BUD on the label to ensure that sterile preparations are used at the right time (Allen, 2012). In addition, the storage conditions should also be written on the label so that the stability of the mixture is maintained. Based on Table 1, it is known that carbamazochrome and vitamin C during the compounding and distribution process did not match the required storage temperature (2.78%; n = 36). Vitamin C is a powerful an-

tioxidant that is easily unstable at warm to hot temperatures and is easily damaged when exposed to sunlight (Alvarado and Palacios Viteri, 1989; Caritá et al., 2020).

Compounding sterile preparations at this referral hospital has not met good quality assurance (requirements in Table 2). Compliance with procedures has not been carried out correctly (100%; n = 36). Compounding sterile preparations has not followed the existing SOP, and there is no good documentation process. All sterile preparations are prepared, only recorded on the handover sheet. The guidelines for compounding sterile preparations recommend always complying with SOPs, evaluating critical aspects or results of preparations on a regular basis, and keeping good records so that the quality of the resulting compounded preparations can be guaranteed (Depkes, 2009; USP, 2019). The quality of good preparation will certainly affect the possibility of medication errors.

In our study, it can be concluded that sterile preparations prepared in hospitals with aspects that do not meet the recommendations of the USP <797> Guidelines and Basic Guidelines for Dispensing Sterile Preparations can cause microbial contamination ($p<0.05$).

A validated research instrument is a strength in our study. However, there are limitations to this study. This research is observational, so the results of the study depend on the experience of the researcher. In addition, there is also the possibility of changes in the behavior of the object of research after knowing that research is being carried out. Therefore, the results of our study are limited to the reported findings.

CONCLUSION

Most of the critical aspects in compounding sterile preparations at this Referral Hospital have not met the recommendations of the USP <797> Guidelines and the Basic Guidelines for the Dispensing of Sterile Preparations, except for the packaging aspect. Improvements in several critical aspects need to be made to ensure the quality of the prepared preparations from microbial contamination.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Genatrika E	Puspitasari I	Kristina SA	Sulaiman TNS
Concepts or ideas	x	x	x	x
Design	x	x		
Definition of intellectual content	x	x	x	x
Literature search	x			x
Experimental studies	x			
Data acquisition	x			
Data analysis	x		x	
Statistical analysis	x			
Manuscript preparation	x			
Manuscript editing	x	x	x	x
Manuscript review	x	x	x	x

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Appendix 1. Checklist sheet on aspects of compounding sterile preparations.

Observation variable		Result*	
GENERAL			
1.	Have standard operating procedures (SOP) related to compounding sterile preparations (if any, attach)	Yes	No
COMPOUNDING PERSONNEL			
1.	Conducted by pharmacist	Yes	No
2.	Conducted by pharmaceutical technical personnel	Yes	No
3.	Conducted by nurses	Yes	No
4.	Conducted by other health workers (if any, please specify)	Yes	No
5.	Compounding personnel have at least attended in-house training on compounding sterile preparations	Yes	No
BUILDING			
1.	There is a preparation room that can be used to remove shoes from the outside and watches	Yes	No
2.	There is a raw material room	Yes	No
3.	There is a product administration room that can be used to prepare administrative completeness of medical equipment and medicinal materials	Yes	No
4.	There is a room for washing hands and changing clothes before entering the anteroom	Yes	No
5.	There is an anteroom that must be passed by compounding personnel who will enter the cleanroom	Yes	No
6.	There is an cleanroom	Yes	No
7.	The temperature in the cleanroom is around 18-22°C	Yes	No
8.	Humidity in cleanroom is around 35-50%	Yes	No
9.	The number of particles in the cleanroom is not more than 350,000 particles	Yes	No
10.	There is a pass box located between the product administration room and the cleanroom	Yes	No
EQUIPMENT			
1.	Have personal protective equipment (PPE)/gowning, which includes regular protective clothing, head cover, gloves (powder free), disposable mask, shoe cover	Yes	No
2.	There is laminar air flow (LAF) (if any, state the type of LAF)	Yes	No
3.	There is alcohol to disinfect products, hands and others	Yes	No
4.	There is literature on drug stability, hardcopy is stored in the product preparation/administration room	Yes	No
5.	There is literature on drug incompatibility, hardcopy is stored in the product preparation/administration room	Yes	No
ASEPTIC PROCEDURE			
1.	Perform 6 steps of hand washing (upper and lower palms, between fingers and nails) using soap	Yes	No
2.	Personnel remove watches and jewelery while working with aseptic technique	Yes	No
3.	Personnel use PPE/gowning correctly (head covering should cover all hair and tucked into the neck of overalls, masks cover beards, cover feet to toe, pants/overalls should be tucked into leg covers, sleeves tucked into gloves)	Yes	No
4.	Disinfect using 70% alcohol on gloves, medical equipment, containers and work tables in the same direction	Yes	No
5.	All materials needed during the mixing process are taken through the pass box	Yes	No
6.	The mixing process is carried out in LAF	Yes	No
7.	Prepare the liquid absorbent mat in LAF	Yes	No
8.	Prepare garbage disposal bags in LAF and issue them through pass through	Yes	No
9.	Clean the work area after finishing work	Yes	No
10.	Removing the container that already contains the sterile preparation product through a different pass box	Yes	No
11.	Personnel must remove PPE/gowning after leaving the sterile room and place it in the specified container	Yes	No

Appendix 1. Checklist sheet on aspects of compounding sterile preparations (continued...)

Observation variable		Result*	
## SPECIAL CONDITIONS (If there is no LAF facility)			
1.	Compounding is done in a clean room, only for sterile preparations	Yes	No
2.	Doors and windows must always be closed	Yes	No
3.	There are no permanent hand washing stations and shelves	Yes	No
4.	Walls are easy to clean	Yes	No
5.	The workbench should be away from the door	Yes	No
6.	Using personal protective equipment/gowning, which includes regular protective clothing, headgear, gloves (powder free), disposable mask, shoe cover	Yes	No
7.	Clean the workbench with 70% alcohol and cover the surface of the workbench with a liquid-absorbing mat	Yes	No
8.	Clean all medical equipment and medicine containers before and after use with 70% alcohol	Yes	No
9.	Clean the work area by washing with detergent and rinsing with distilled water, then finally with alcohol	Yes	No
10.	Compounding personnel remove PPE after completion of the compounding process	Yes	No
11.	Dispose of tools and materials that are not used in a closed bag and routinely disposed of every day	Yes	No
PACKAGING AND LABELING			
1.	Give appropriate labels for each sterile preparation product	Yes	No
2.	Packaging (bags, vials etc.)	Yes	No
3.	Product label (patient name, rm number, treatment room, drug name, dose, route of administration, storage conditions, date of manufacture, expiration date of the mixture)	Yes	No
4.	Shipping label (patient name, medical record number, treatment room, package contents)	Yes	No
STORAGE			
1.	Storage conditions are adjusted to the stability of each drug	Yes	No
2.	There is a refrigerator for medicines that need to be stored under special conditions (temperature 2-8°C)	Yes	No
3.	There is a storage area protected from direct light for drugs whose stability is affected by light	Yes	No
4.	There is temperature monitoring in the storage area	Yes	No
DISTRIBUTION			
1.	Use a tightly closed container and protected from light	Yes	No
2.	For drugs that must be stabilized at a certain temperature, they are placed in a container that is able to maintain a consistent temperature	Yes	No
3.	There is a handover book for sterile preparation products	Yes	No
QUALITY ASSURANCE			
1.	There is a record of compounding sterile preparations including master formulas, implementation documents, etc	Yes	No
2.	Preparation of the room before use for compounding sterile preparations	Yes	No
3.	There is monitoring of temperature, humidity and the number of particles in the cleanroom	Yes	No
4.	Conducted periodic microbiological tests of preparations and rooms	Yes	No

* Circle the appropriate hospital condition