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Parenteral Nutrition Preparation Procedure: A Hazard Analysis and Critical Control Points Approach at a Pediatric Hospital in Vietnam

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ABSTRACT

Background: Hazard analysis and critical control points (HACCP) is a tool for food safety assurance, but the application of HACCP in healthcare facilities in Vietnam has been understudied and underregulated given a lack of governmental guidelines. This study aimed to explore the hazards and determine the critical control points related to the parenteral nutrition (PN) preparation procedures in a pediatric hospital in Vietnam.

Methods: A cross-sectional study was conducted at Children Hospital No. 2 in Ho Chi Minh City, Vietnam, from July to September 2019. The study subjects were eleven standard operating procedures for preparation of a PN product called Vaminolact 6.5%. The hazards were explored based on the probability of occurrence, the severity of consequence, and the quantity of influenced individuals. Each step in the PN procedure was determined by multiplying the points of three standards. A step with a point equal to or higher than 18 was considered a hazard. The critical control point (CCP) was determined by following the five-question decision tree.

Results: Eight hazards were explored via hazard analysis, including sanitation prior to compounding, measurement of basal solution, compounding, labeling, sanitation of preparation room, in-out control, air flow control, and primary filter system. Nine critical control points were determined as follows: sterilization by alcohol, glove change per every 10 vials, basal solution measurement, compounding, mini-spike change per every 10 vials, syringe change per every 10 vials, air flow control, primary filter system, and sterilization check-up.

Conclusion: The hospital manager should consider this study as support for an evidence-based adjustment to improve PN preparation procedure.

Keywords: contamination, HACCP, parenteral nutrition, pediatrics, safety, Vietnam

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INTRODUCTION

Parenteral nutrition (PN) is the intravenous administration of nutrition, which may include proteins, carbohydrates, lipids, minerals, electrolytes, vitamins, and other trace elements.[1] PN is widely used in healthcare settings to deliver critical nutrients to patients who are unable to tolerate enteral feeding.[2] Due to the requirements of careful titration and a combination of multiple components, PN has been considered to be one of the most complicated pharmaceutical products within the healthcare sectors.[3, 4]

As it is crucial to prepare PN in a sterile environment, most of the healthcare facilities in Vietnam purchase manufactured, premixed formulation of PN. Using PN on pediatric patients is complex given that children's nutrition needs from differ adults' needs, children have small vein diameters, and they under-absorb nutrients.[5] Some pediatric hospitals maintain their PN preparation procedure for special adjustment.

Hazard analysis and critical control points (HACCP) is a systematic preventive approach to food safety from biological, chemical, and physical hazards in production processes.[6] The HACCP was first suggested for widespread use at the Conference of Food Protection in the United State in 1971.[7] The Codex Alimentarius Commission recommended the application of HACCP in combination with the maintenance of good manufacturing practices (GMP) to ensure food safety and hygiene. HACCP is introduced in the standard coded 5603:2008 of Vietnam National Standard, which is similar to the standard coded CAC/RCP 1-1969, Rev.4-2003 of Codex.[8]

In its early stages, HACCP was applied to control quality and safety in the food manufacturing industry. Recently, the seven principles of HACCP have been applied in other fields,[9] including the pharmaceutical industry. Prior to the application of HACPP, GMP was considered to be the only tool for quality assurance. HACCP can be applied in the pharmaceutical manufacturing process to explore, assess, and control the hazards that influence drug safety, focusing on prevention rather than addressing incidents of the effects of hazards.[10]

Hospital management's support and commitment to HACCP application is vital. A PN safety management system based on HACCP principles in a hospital provides a method of achieving active managerial control of multiple risk factors, contributes to consistency in PN preparation, and enhances employee awareness and participation in safety procedures.[11]

The application of HACCP in healthcare facilities in Vietnam has been under-considered due to the lack of governmental guidelines. This study aimed to explore the hazards and determine the critical control points related to the PN preparation procedures in a pediatric hospital in Vietnam.

METHODS

Study design and study site

This was a cross-sectional study conducted at Children Hospital No. 2 in Ho Chi Minh City, Vietnam, from July to September 2019. This is one of the three largest healthcare facilities specializing in pediatrics in southern Vietnam.

Materials

The study subjects were 11 SOPs for PN preparation, including the following: i) designation of preparation room, ii) sanitation of preparation room, iii) preparation of ingredients and medical supplies, iv) monitoring the ultraviolet light, v) setting formulation and labeling, vi) preparation prior to compounding, vii) compounding, viii) unqualified product storage and demolition, ix) distribution, x) biological contamination control, and xi) sanitation of clothes and recycling equipment. These SOPs had been established for years and been adjusted several times, but not been assessed systemically yet.

The PN product called Vaminolact 6.5% was set for analysis. This is the most complicated PN product compounded in the hospital. The product contained 19 vital amino acids, supplying 240 kcal per liter.

Data analysis

The hazards were explored based on three standards: the probability of occurrence,[12] the severity of consequence,[13] and the quantity of influenced individuals.[14]

For each standard, there were three levels of assessment, rated from one to three (Table 1). Each step of PN procedure was rated by multiplying the points of three standards. The cut-off point was 18-that is, each step with a point total equal to or higher than 18 was considered to be a hazard.

The critical control point (CCP) was determined by following the decision tree as shown in Figure 2. There were five questions, with dichotomous choices for each one.[15]

Ethical consideration

This study protocol was approved by the Ethical Council of Children Hospital No. 2. There were no experiments or interventions on animals or humans.

RESULTS

Eight hazards were explored through hazard analysis, including sanitation prior to compounding, measuring basal solution, compounding, labeling, sanitation of preparation room, in-out control, air flow control, and primary filter system.

Nine critical control points were determined as follows: sterilization by alcohol, glove change per every 10 vials, basal solution measurement, compounding, mini-spike change per every 10 vials, syringe change per every 10 vials, air flow control, primary filter system, sterilization check-up.

Table 1. Hazard determination standard

Standard	Low	Intermediate	High
Probability of occurrence	≤3 aseptic units to compound the final PN ≤2 aspirations for each unit Simple technique Individual usage	≤4 aseptic units to compound the final PN Simple technique Time consuming Mass usage	Unqualified ingredient and/or equipment Septic, aquatic product, storage ≥6 hours prior to final sterilization Wrong clothes and/or gloves
Severity of consequence	Likely to have little or no effect on the patient	Likely to lead to an increase in level of care, e.g., review, investigations, or referral to another clinician	Likely to lead to permanent reduction in bodily functioning leading to, e.g., increased length of stay; surgical intervention Likely to lead to a major permanent loss of function Likely to lead to death
Quantity of influenced individuals	<1/1000	1/1000 to <1/100	≥1/100

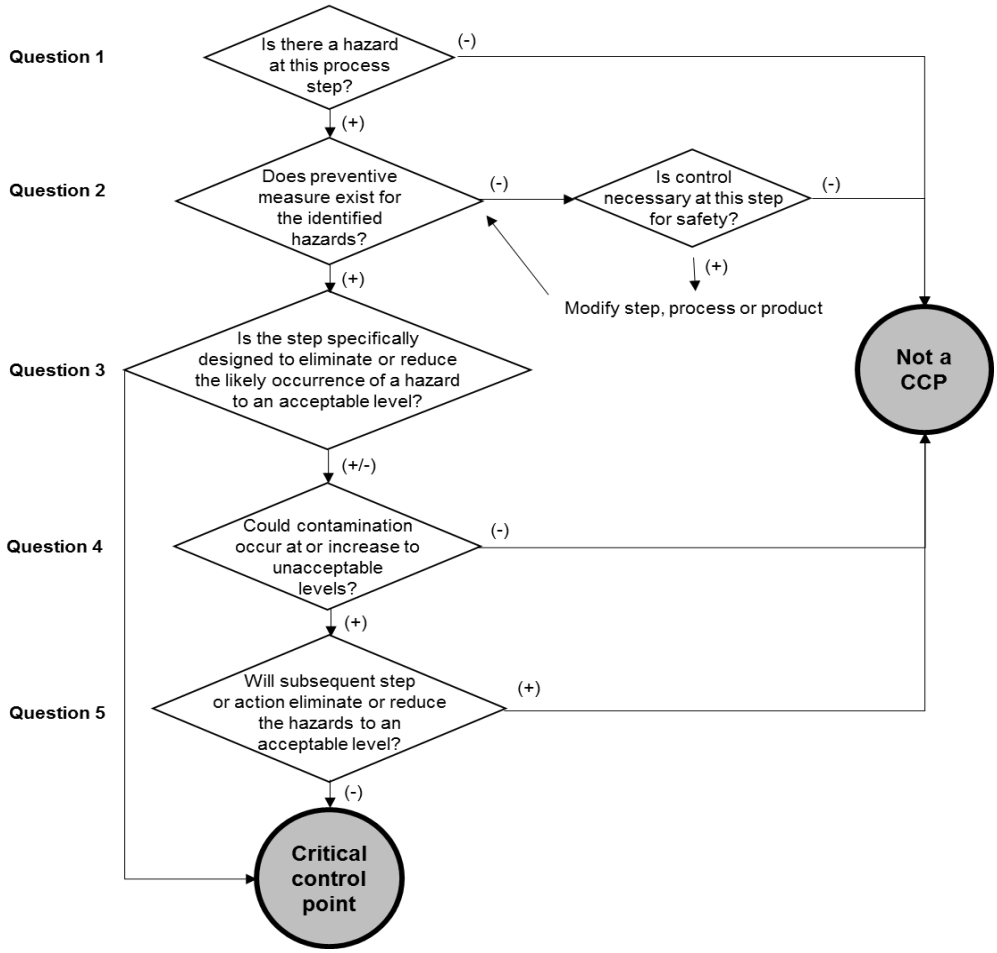

Figure 2. Decision tree for CCP determination

Table 2. Hazard determination of the parenteral nutrition preparation

Process step	Risk	Point				Is a hazard?
		Probability of occurrence	Severity of consequence	Quantity of influenced individuals	Total points	
BEFORE COMPOUNDING						
Prescription receipt	Wrong prescription leading to wrong ingredient preparation	1	3	3	9	No
Formulation	Wrong information leading to wrong ingredient preparation	1	3	3	9	No
Preparation of ingredients and medical supplies	NA	1	1	1	1	No
Sanitation prior to compounding	Biological contamination	3	3	3	**27**	**Yes**
COMPOUNDING						
Measuring basal solution	Biological contamination	3	3	3	**27**	**Yes**
Compounding	Biological contamination	3	3	3	**27**	**Yes**
PN products	Incompatibility	2	3	2	12	No
Labeling	Wrong label	2	3	3	**18**	**Yes**
Packaging	NA	1	1	3	3	No
AFTER COMPOUNDING						
Distribution	Wrong destination department	1	1	1	3	No
INFLUENT FACTORS						
Sanitation of preparation room	Biological, medical, physical contamination	3	3	3	**27**	**Yes**
In-out control	Biological, medical, physical contamination	3	2	3	**18**	**Yes**

Air flow control	Biological, medical, physical contamination	3	3	3	**27**	**Yes**
Primary filter system	Biological, medical, physical contamination	3	3	3	**27**	**Yes**

Table 3. Critical control points determination

Process step	Hazard	Question 1	Question 2	Question 3	Question 4	Question 5	Is a CCP?
Sanitation of preparation room	Biological contamination	Yes	Yes	No	No	-	No
Sterilization by nebulizer	NA	Yes	Yes	No	No	-	No
Sanitation of floor	NA	Yes	Yes	No	No	-	No
Sanitation of supplies and equipment	NA	Yes	Yes	No	No	-	No
Ingredient preparation	Inadequate	Yes	Yes	Yes	No	-	No
Supplies preparation	Inadequate	Yes	Yes	Yes	No	-	No
Formula preparation	Wrong information	Yes	Yes	Yes	No	-	No
Sterilization by alcohol	NA	Yes	Yes	Yes	Yes	No	Yes
Ultraviolet light turning on	Unqualified light	Yes	Yes	Yes	No	-	No
Special clothes change	NA	No	-	-	-	-	No
Hand washing	NA	No	-	-	-	-	No
Aseptic clothes change	NA	No	-	-	-	-	No
Hand washing prior surgery	NA	No	-	-	-	-	No
Clouting	NA	No	-	-	-	-	No
Wearing gloves	NA	No	-	-	-	-	No
Glove change per every 10 vials	Biological contamination	Yes	Yes	No	Yes	No	**Yes**
Basal solution measurement	Biological, chemical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Compounding	Biological, chemical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Mini-spike change per every 10 vials	Biological, chemical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Syringe change per every 10 vials	Biological, chemical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Final PN product	Incompatibility	Yes	Yes	No	No	-	No
Storage	NA	No	-	-	-	-	No
Distribution	Wrong destination department	No	-	-	-	-	No
Air flow control	Biological, medical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Primary filter system	Biological, medical, physical contamination	Yes	Yes	No	Yes	No	**Yes**
Sterilization check-up	Biological contamination	Yes	Yes	Yes	Yes	No	**Yes**

DISCUSSION

This is the first study in Vietnam that has applied HACCP to assess safety in PN preparation for pediatric patients. We explored eight hazards and nine critical control points that should be studied more closely to improve procedures.

Incidents due to the incorrect formulation of PN products may influence to 2-3/70 people in worldwide per day.[16] Case reports have shown that errors in prescription receipts can result in patient deaths.[17,18] Wrong formulation due to information could also potentially lead to comorbidity, economic burden, and mortality.[19] Incorrect labeling on final PN products has been reported to be one of the most common mistakes in laboratories, impacting 1-2/70 patients per day,[16] leading to medication error and influencing patients' health, knowledge, and pharmaceutical compliance.[19]

Physical and medical contamination easily occurred in severe patients with PN,[20,21] influencing approximately 1/260 patients per day.[16] This may pose negative effects on the sustainability of the products,[22,23] and patients' health.[24] Shortcoming on packaging as well as distribution to destination department has not been reported yet, but it is estimated to impact 2/70 people per day when errors occur.[19]

As shown in Tables 2 and 3, most of the hazards and critical control points are related to biological contamination. After checking the SOPs of PN preparation procedures, we found that the SOP for "unqualified product storage and demolition" was inappropriate. The SOP for "biological contamination control" was similar to the standards of United States Pharmacopeia (USP) and those of the National Association of Pharmacy Regulatory Authorities (NAPRA) in Canada. Therefore, it is acceptable to continue using this SOPs, but to specify each step.

At present, the PN preparation procedure requires a change of gloves, mini-spikes, and syringes every 10 vials. However, we

suggest given evidence-based appraisal that the frequency of change should be adjusted if appropriate. Document storage is one of the most important parts of HACCP. We recommend replacing the paper-based database with an electronic-based database, which requires less space and time to operate, in order to eliminate errors or lack of information.[25]

According to the World Health Organization, monitoring is the scheduled measurement or observation of a CCP relative to its critical limits. Monitoring should be recorded. The monitoring procedures used must be able to detect loss of control at the CCP, and this information should ideally be available in time to make adjustments to ensure control of the process and prevent violations of the critical limits. Data derived from monitoring must be evaluated by a designated person with the knowledge and authority to carry out corrective actions when indicated. The personnel conducting the monitoring of CCPs and control measures should be engaged in production (e.g., line supervisors and maintenance staff), and, where appropriate, staff from quality control department. The personnel should be trained in monitoring procedures. Statistically designed data collection or sampling systems should then be used. All records and documents associated with monitoring CCPs should be signed and dated by the person carrying out the monitoring and by a responsible reviewing official.

CONCLUSION

HACCP is a useful tool to ensure the quality and safety of parenteral nutrition compounding at pediatric hospitals. The hospital manager should consider this study for an evidence-based adjustment to improve preparation procedure.

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CONFLICT OF INTEREST

The authors have no conflicts of interests to declare.

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