CHAPTER I

INTRODUCTION

1.1 Background and Significance of the Study

Malnutrition is commonly found in hospitalized patients. It contributes to poor prognosis, immune function impairment, increased length of hospital stay, hospital cost, morbidity, mortality, and the rate of readmission to the hospital (Kyle, Genton and Pichard, 2005; Matarase and Hamilton, 1998; Therny, 1996). Nutrition support may be indicated as a primary therapy or considered adjunctive therapy to avoid malnutrition and its consequences for hospitalized patients (Matarase and Hamilton, 1998). There are two routes of nutrition support including enteral and parenteral administration. The functional capacity of the gastrointestinal tract is a key determinant in the selection of enteral versus parenteral administration. In general, the enteral route is always preferred as long as nutrient requirements can be consistently met. Patients with nutrient needs greater than that, which can be provided enterally, should be considered for parenteral supplementation. If the gastrointestinal tract is nonfunctional, parenteral nutrition (PN) shall be used to meet the patient's total nutrition need (Teasley-Strausberg, 1992).

Intravenous hyper-alimentation or total parenteral nutrition (TPN) is the intravenous administration of hypertonic solution of amino acid and a non-nitrogen caloric sources (dextrose, lipid or both), together with appropriate amounts of electrolytes, vitamins and minerals (Swenson, et al., 1977). Although PN represents a major advancement of the nutritional care of patients, there are many complications from this administration route. Septicemia is one of the most common and serious

complications. The solution used, catheters and management of the PN systems all represent sources for introduction of infectious agents (Wershil, 1986).

Llop et al (1993) reported an outbreak of sepsis related to contamination of TPN admixtures with *Staphylococcus saprophyticus*, a common environmental microorganism. In this occurrence, TPN admixtures prepared under laminar air flow hood (LAFH) located in the aseptic room of the TPN unit. They found that four of forty-five patients receiving the TPN admixtures showed clinical signs of sepsis, and ten of sixty-nine TPN admixtures from the TPN unit appeared positive in the microbiological control for *S. saprophyticus* along with positive cultures for *S. saprophyticus* in tips, hubs and blood cultures. They attributed the idea of an outbreak caused by TPN contamination to an accidental breakdown of the aseptic elaboration procedure used in preparing the admixtures. The PN solutions were probably contaminated during the preparation, although the exact source of contamination could not be identified. Septicemia is the complicated cause which increases morbidity and, sometimes, mortality as a consequence of infusing contaminated PN admixture. Hence, the introduction of pharmacy compounding services has made a major impact on reducing infection risk in patients receiving PN. It is clearly determined to pharmacists to provide continuously review, monitor and improve their aseptic processes and quality assurance systems to minimize and if possible, eliminate the contamination of PN admixtures during the compounding process (Allwood, 1997).

Consequently, continuous improvement has been introduced in many compounding units to reduce contamination risk. It must be realized that environmental control in the PN admixture area is one of the most important factors for minimizing the

contamination risk in PN solutions. Because it is unreasonable to believe that proper aseptic technique alone can control the contamination when LAFH is placed in uncontrolled area (Kastango, 2005). LAFH located in uncontrolled environment is the least safe system (Allwood, 1997). With this manner, cleanroom technology is introduced to assure that the bioburden of the environment should be appropriate for aseptic processing, and be a mandate requirement for the preparation of sterile admixtures in the hospital.

Cleanroom is a room designed for proper sterile compounding and required a strict design system. Thus, the process area, the interactions with surrounding areas and the movement of people, materials and equipment should not be compromised to this aseptic condition. Engineering control and associated controlled environments are designed to prevent, reduce, and control potential nonviable (e.g. dust, pollen, skin) and viable (e.g. mold, fungus, bacteria) contaminants in compounding sterile products. A properly designed, constructed, and maintained cleanroom is contributed to the quality of compounding sterile products (Kastango, 2005).

In Thailand, PN admixing unit at Pharmacy Department is still in the early stages. Sinthawat (1994) set up the Parenteral Nutrition Admixing Center (PNAC). PN solutions from this center were prepared under LAFH located in a separated room situated in the preparation area of the Pharmacy Department at Ramathibodi Hospital. It was found that microorganisms did not contaminate PN solutions from PNAC. In addition, the estimated cost of PN solution from PNAC was lower than that from nursing units about 3.64%. Leewiriya (1996) established Parenteral Nutrition Preparation Unit (PNPU) at Lopburi Hospital. PN solutions were prepared under LAFH located in a separated room

situated in the sterile product production area of Pharmacy Department. It was revealed that there was no microorganism in PN solutions prepared from PNPU but the cost of them was 1.2-1.5 times higher than PN solution cost of pre-PNPU period. Ingcharoensunthorn (2000) implemented Parenteral Nutrition Admixing Unit (PNAU) designed as a cleanroom and situated in the sterile production area of the Pharmacy Department at Queen Sirikit National Institute of Child Health. It was found that all PNAU-prepared PN solutions were free from microorganisms. Sakpanich (2002) established Siriraj Parenteral Nutrition Admixing Center (SPNAC). PN solutions were prepared under LAFH located in a separated room of Sterile Production Building in the Pharmacy Department. It showed that 99.1% of prepared PN solutions passed the sterility test and the remaining was not assured; however, none of the patients receiving those PN bags with uncertain sterility results developed septic complication. According to the cost analysis, PN prepared from SPNAC showed 32.2% lower cost compared with PN prepared on ward and there was 9.5% cheaper when the cost of quality assurance and others were included. PN-prepared Unit in each hospital was designed in different environment (e.g. separated room or cleanroom) depending on their respect guidelines, budget and the limitation area in the hospital. However, none of researchers has directly compared the contamination rates of cleanroom with the traditional compounding environment.

As the benefit of nutrition support for hospitalized patient has been well-known, the PNAC in Pharmacy Department at Ramathibodi Hospital has been set up since 1994 and the rate of PNs usage has increased more than 10% every year. The statistical data from the Ramathibodi PN preparation unit showed that there were only 4,787 bottles of

PN solutions prepared from this unit and they earned 3,242,966 Baht to the hospital in 1998. In addition, the recent data recorded in 2006, showed that 20,487 PN bottles prepared from this unit made hospital incomes about 13,078,381 Baht. The PN from this unit has augmented coinciding with the idea of expanding the sterile compounding production lines (e.g. IV admixtures) in order to meet the Hospital Accreditation standard surveillance and to be the leader in pharmacy service. The hospital policies have focused on construction a new cleanroom center for preparing non-harmful sterile products including parenteral nutrition. In relevance to an idea of the influence of the environmental condition on the quality of PN solutions, the aim of this research was to study the influence of environment on contamination of PN admixtures by comparing contamination rates of PN solutions prepared from the traditional separated room with those from the new cleanroom at Ramathibodi Hospital.

1.2 Objectives of the Study

1.2.1 To investigate the contamination rate of PN solutions prepared from the cleanroom compared with the traditional separated room

1.2.2 To calculate the unit cost of PN solution prepared from the cleanroom compared with the traditional separated room

1.3 Benefits of the Study

The information provided from this study is beneficial for pharmacists or hospital administrators in planning to set up or renovate the PN admixing center for the best quality of PN solutions.

Glossary

Aseptic processing: A mode of processing pharmaceutical and medical products in transferring the product into the container and its closure under microbiologic critically controlled conditions.

Cleanroom: A room in which the concentration of airborne particles is controlled to meet a specified airborne particulate Cleanliness Class. In addition, the concentration of microorganisms in the environment is also monitored to be appropriate for aseptic processing system.

Performance test: Procedure to demonstrate that media used in the microbiological environment monitoring program are capable of supporting growth of indicator microorganisms and of environmental isolates from samples obtained through the monitoring program.

Production environment: Areas and surfaces in a controlled environment designed for preparing PN admixtures that are in direct contact with either products, containers, or closures and the microbiological status of which can result in potential microbial contamination of the product/container/closure system.

Separated room: A room separated from other uncontrolled environment.

Sterility: Within the strictest definition of sterility, an article is deemed sterile when there is complete absence of viable organisms.