VALUE IN HEALTH ▮ (2014) ▮▮▮–▮▮▮

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

A Retrospective, Observational Study of Patient Outcomes for Critically Ill Patients Receiving Parenteral Nutrition

Glenn Magee, MBA[1], *Gary P. Zaloga, MD*[2], *Robin S. Turpin, PhD*[3,4,5], *Myrlene Sanon, MPH*[3,*]

[1]*Premier, Inc., Philadelphia, PA, USA;* [2]*Global Medical Affairs, Baxter Healthcare, Deerfield, IL, USA;* [3]*Global Health Economics and Outcomes Research, Deerfield, IL, USA;* [4]*Health Delivery Systems and Pharmacoeconomics, Takeda Pharmaceuticals, Deerfield, IL, USA;* [5]*Jefferson School of Population Health, Thomas Jefferson University, Philadelphia, PA*

ABSTRACT

Objective: To evaluate health care–related utilization for critically ill patients receiving parenteral nutrition (PN) administered via a premixed multichamber bag (MCB) or compounded solutions (COM). **Design:** A retrospective database analysis of critically ill patients (intensive care unit stay ≥ 3 days) receiving PN and discharged between January 1, 2010, and June 30, 2011, using the Premier Hospital Database. Patients were identified as receiving MCB or COM on the basis of product description codes. Primary outcomes were length of stay (LOS) and total costs. Comorbidities and clinical outcomes were identified using *International Classificaion of Diseases, Ninth Revision* diagnosis codes. All costs reported were for inpatient services only. Patients receiving MCB and COM were matched on key patient and hospital characteristics using a propensity score methodology. Multivariate regression models for cost and LOS used generalized linear models with a log link and gamma distribution. **Results:** A total of 42,631 patients met the inclusion criteria (MCB = 5,679; COM = 36,952), and the final matched population included 3,559 patients from each cohort. Baseline patient and hospital characteristics were well matched between groups. Adjusted multivariate models demonstrated a small difference between groups for LOS (MCB = 9.40 days vs. COM = 9.65 days; $P = 0.014$). In addition, patients receiving MCB incurred approximately 9.1% less in total costs (MCB = $37,790 vs. COM = $41,569; $P < 0.001$). **Conclusions:** Overall, patients receiving MCB and COM experienced similar LOS, though patients receiving MCB had significantly lower overall costs. Interpretation of the study findings is subject to several limitations, and additional studies that include explicit identification of the method for compounding are needed.

Keywords: hospital compounded bag, infection, multichamber bag, parenteral nutrition, ready-to-use, total cost.

Introduction

Parenteral nutrition (PN) has been established as the standard of care for critically ill patients with dysfunctional gastrointestinal tracts since the 1960s [1–3]. Although PN is a common treatment in this population, there is uncertainty regarding optimal clinical practices for its use. PN may be administered through various techniques, which include premixed multichamber formulations and compounded formulations.

During the PN compounding process, there is an associated 4.4% to 6.7% contamination rate [4,5]. Techniques leading to fewer manipulations of infusion containers, sets, syringes, needles, and so forth, thereby minimizing the potential for contamination during PN preparation and administration, are highly favored. Premixed and ready-to-use products, for which sterility is guaranteed by the manufacturing process, are industrially manufactured all-in-one admixtures provided as multichamber bags (MCBs). Compounding processes in hospital pharmacies vary extensively from using manual methods to automated compounding devices. Significant advances in automated technology have led to a shift from manual compounding procedures, and most PN today in the United States is prepared using automated techniques. The American Society of Health-System Pharmacists estimated that in 2000 approximately 65% of US hospitals used automated compounding devices for parenteral admixtures in their daily practice [6]. Moreover, changing health care pressures demand that admixture compounding be as safe and efficient as possible. The decision around PN choice can be complex, and there are no specific guidelines advising the appropriate circumstances under which premixed, standardized, or custom PN should be used for various patient populations [6].

Several studies have evaluated the cost of different PN compounding methods [7–9]. A few studies evaluated the cost of care for patients on PN, but most evaluated only small, select populations that are not easily generalizable to other patient populations or hospitals. Of most recent, we analyzed the acquisition costs associated with compounded PN versus premixed MCB PN [10]. Clinical and economic outcomes were evaluated for hospitalized patients between January 2005 and December 2007. Patients receiving compounded PN compared with those receiving premixed PN were at a higher risk for bloodstream infections (odds ratio = 1.56; 95% confidence interval 1.37–1.79; $P < 0.0001$).

Conflict of Interest: Robin S. Turpin participated in and contributed to the study while at Baxter Healthcare.

* *Address correspondence to:* Myrlene Sanon, Baxter Healthcare, DF5-3W, One Baxter Parkway, Deerfield, IL 60015.
E-mail: myrlene.sanon@gmail.com.

1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2014.02.009

Moreover, the acquisition cost of PN for premixed MCBs in this study was lower than that of compounded PN (US $164 vs. US $239). Although acquisition costs are important to hospitals as they attempt to constrain the cost of care, the more relevant parameter for researchers to investigate is total costs associated with patients during hospitalization.

This analysis is an update to our previous analysis [11], using a later time period for the catchment population and evaluation of updated codes for infection identification. The goal was to compare two PN delivery techniques (premixed MCBs vs. compounded PN) as it relates to total costs, length of stay (LOS), infectious complications, and hospital readmission rates. This retrospective study assesses a large number of critically ill adult patients who received PN. The sample includes a large number of hospitals from across the United States. The study tested the hypothesis that patients receiving PN via MCBs have lower total costs than do patients treated with compounded solutions (COM). The clinical effectiveness of MCB versus COM was assessed through the evaluation of a number of infection-related outcomes, LOS, and hospital readmission rates.

Methods

Data Source

Premier's Hospital Database is the largest US hospital clinical and economic database developed for quality and utilization benchmarking. It contains a total of 2.5 billion patient daily service records, and about 45 million records are added each month. Annually, more than 5 million inpatient discharges and 35 million hospital outpatient visits are recorded in the database. In addition to the data elements available in most of the standard hospital discharge files, the Premier Hospital Database contains a date-stamped log of all billed items including procedures, medications, laboratory, and diagnostic and therapeutic services at the individual patient level.

The Premier Hospital Database is a complete census of all inpatients and hospital-based outpatients from more than 600 geographically diverse hospitals. It is not a random sample; information on all patients treated from all therapeutic areas is collected and retained in the database.

Data exist from calendar year 2000 forward. Patients can be tracked across the inpatient and hospital outpatient settings, as well as across visits with a unique person identifier. All procedures and diagnoses are captured for each patient, as well as all drugs and devices received. There is no limit to any of the aforementioned elements on the number recorded in the database. Patients can be identified as to whether they were treated in the intensive care unit (ICU) or ward bed by day of service on the basis of the data from the hospital charge master. Drug utilization information is available by day of stay and includes quantity, dosing, strength used, and cost. Costs are as reported in hospital charge masters and include room and board, pharmacy, laboratory, imaging, central supply, and all costs incurred by the hospital including general and administrative (overhead). This does not represent hospital charge or reimbursement.

The All Patient Refined (APR) diagnosis-related group and APR Severity Level are proprietary to 3M Health Information Systems. This methodology assigns a severity of illness (minor, moderate, severe, or extreme) on the basis of patient-specific information and is used by several states for reimbursement purposes [11]. All data within the Premier database are compliant with regulations defined in the 1996 Health Insurance Portability and Accountability Act and subsequent revisions. Data deliverables contain limited Protected Health Information. Therefore, the time of admission and discharge is provided as month and year. Day-of-service level details are reported using chronological days (e.g., day 1, day 2). The age of patients older than 89 years is reported as 89 years.

Patient Selection and Matching

The study population included all adult (age $\geq$ 18 years) critically ill inpatients who received PN, were in the ICU for 3 days or more, and were discharged between January 1, 2010, and June 30, 2011. Patients were then categorized as receiving MCB or COM. MCB PN was defined as patients receiving PN with a description including Clinimix (manufactured PN in a dual-chamber bag with glucose and amino acids, which may have included additions of minerals, vitamins, and/or electrolytes), whereas COM was identified as PN with a description of Admix or Compound. These patients constituted the primary study population.

Patients' demographic characteristics and hospital characteristics were identified for all patients. Specific comorbidities (pancreatitis, liver impairment, renal failure, diabetes, malnutrition, gastrointestinal disorders, and malabsorption) were identified using *International Classificaion of Diseases, Ninth Revision* (*ICD-9*) diagnosis codes (see Appendix A in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.02.009).

Patients were matched using a propensity score method with a greedy match algorithm. Patients were matched to reduce any selection bias and confounding of PN method indication [12]. The propensity model included patients' demographic variables (age, race, sex, and admission type), patients' clinical covariates (malabsorption, pancreatitis, liver impairment, renal failure, diabetes, malnutrition, gastrointestinal disorder, number of days in ICU, and first day of parenteral feeding), and hospital characteristics (geographic region, teaching status, and urban/rural status). The likelihood-ratio test, Hosmer-Lemshow goodness of fit, and concordance *c* statistics (0.84) were utilized to assess the goodness of fit of the models.

Outcome Measures and Statistical Analyses

The primary outcomes for analysis included total hospitalization costs (inclusive of inpatient stay, professional care, and medications), total LOS, and ICU LOS. Secondary outcomes of interest were urogenital candidiasis, disseminated candidemia, bloodstream infection, composite infection measure, any infection complication, inpatient death, 30-day all-cause readmission, and 90-day all-cause readmission. For infection-related outcomes, a patient was identified as possibly being infected if he or she had a discharge *ICD-9* code present for a specific infection (see Appendix B in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.02.009). If patients, however, had a discharge *ICD-9* code of infection yet did not receive any antibiotic or antifungal during their hospitalization, they were not considered infected; to be considered infected, a patient had to have both a diagnosis of infection and be treated with antimicrobial agents. Patients with infection codes noted as present on admission (i.e., before the institution of PN) were not evaluated because we were interested in nosocomial infection cases that may be associated with PN.

Univariate descriptive statistics were calculated for all patient and hospital covariates. Univariate analysis utilized chi-square tests for categorical data and Student *t* tests or Wilcoxon sign rank test for continuous variables.

Multivariate analysis of outcome measures utilized generalized linear models. LOS and cost outcomes were analyzed using multivariate regression with a gamma distribution and a log link due to the skewed nature of the data. Binary outcomes were analyzed using multivariate logistic regression. The analysis accounted for potential confounding factors by inclusion of relevant clinical and demographic covariates. Final models were