Standardized Versus Individually Customized Parenteral Nutrition Solutions: A Comparison of Serum Electrolyte Values

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Purpose: Many healthcare facilities that take a multidisciplinary approach to the provision of parenteral nutrition solutions use both standardized and customized formulations, which are administered at the discretion of the physician and have their own benefits and drawbacks.

Objective: To assess the cost savings and the effect that customized and standardized parenteral nutrition solutions have on nutritional parameters.

Design: Standardized formulations for peripheral use, central use, high stress, and fluid restriction use were compared to customized formulations. A total of 1298 patient days of parenteral nutrition were studied during a 4-month period. Patients received either facility-developed standardized formulations or customized formulations at the discretion of the physician. The levels of 6 serum electrolytes—sodium, potassium, carbon dioxide, magnesium, phosphorus, and chloride—were monitored and the number of results within normal limits or abnormal results for each of the formulations was tabulated.

Setting: A 496-bed tertiary care/trauma center located on Long Island, New York.

Results: There was a higher percentage of results within normal limits in the patients receiving standardized formulations than in the patients receiving customized formulations (73% vs 67%, respectively). Using a chi-square test, it was determined that there was a significant increase in the number of serum electrolytes within normal limits in the group receiving standardized formulations than the group receiving customized formulations.

Conclusions: The use of standardized parenteral nutrition solutions is cost effective and may provide better control of serum electrolytes.

There has been much controversy over the years as to whether or not standardized parenteral nutrition solutions (SPNS) have a place in the management of the acute, severely ill, or metabolically challenged patient.[1] Opponents of SPNS claim that individualized parenteral nutrition (PN) solutions are needed, because the only way to meet the ever-changing needs of patients who are in a state of metabolic flux is to custom design PN solutions on a daily basis. Proponents of SPNS claim it reduces the costs of maintaining a patient on PN while meeting the nutritional needs of patients.[1]

SPNS are less expensive than custom-designed or customized parenteral nutrition solutions (CPNS). This is mainly because it can be easily made in a bulk manufacturing process and stored for later use.[2] Manufacturing in bulk inherently saves time, therefore reducing labor costs involved in the preparation of PN solutions. The price of the components of PN solutions has dropped drastically over the years.[3] In addition, the cost of services provided by pharmacy personnel has increased.[4] Any measure that reduces the number of hours to prepare PN solutions would likely impact overall costs.

Another reason that the cost of PN solution preparation would decrease is that most states allow only pharmacists to compound prescription medications.[5] On the other hand, pharmacy technicians are permitted to manufacture prescription medications, provided there are explicit policies, procedures, and quality control measures in place.[6] Preparing SPNS in bulk is a manufacturing, not compounding, process, because the solutions are not being prepared for any one specific patient. Because of this difference, a pharmacy techni-

cian or nonpharmacist is permitted to prepare SPNS. Using pharmacy technicians in place of pharmacists inherently saves money due to the difference in salary between the two professions.

Background

University Hospital and Medical Center (UHMC), which is part of the State University of New York at Stony Brook, is a 496-bed tertiary care/trauma center located on Long Island, New York. Of the 496 beds, 103 are for the critical care center, which comprises the surgical intensive care unit, the medical intensive care unit, the cardiac care unit, the burn center, the cardiac surgery intensive care unit, and a pediatric and neonatal intensive care unit.

At any one time, approximately 5% (25 patients) of the total patient population are maintained on PN. Of this number, approximately 17 to 20 patients are admitted to one of the adult care services. The rest of the patients receiving PN are pediatric or neonatal patients.

Prior to starting PN, all patients at UHMC receive a consultation from the nutritional support service (NSS). The NSS is made up of representatives from the medical, surgical, and pediatric services as well as the pharmacy and dietary departments. If the NSS determines that PN is the appropriate method of providing nutritional support, a written recommendation is made on a patient's chart detailing the exact formulation that should be used. At no time does any patient start PN without formal consultation with the NSS.

On average, patients remain on PN approximately 5 to 7 days, depending on the service to which the patient has been admitted. To reduce the financial burden to the institution, the pharmacy department (via the NSS) determined that it is prudent to examine the feasibility of using SPNS on adult patients who needed PN. The method to determine whether or not SPNS should be used is described below.

Study Design

After performing a literature search from 1980 to the present, no journal articles were found comparing the efficacy of SPNS with CPNS. Because of this lack of data on SPNS efficacy, the authors undertook a 3-phase project.

Phase 1

The first phase of the project was to design a small number of SPNS. To do this, PN orders over the last several years were examined and placed into categories. The authors looked at protein, carbohydrate, and lipid content as well as the amounts of electrolytes added to the solutions. A total of 4 different formulas were developed for peripheral use, for central-line use, for high-stress, and for fluid-restricted patients. Each formula was made as a 3-in-1 solution in a single container that was designed to hang for 24 hours.

In developing the formulas, the authors remained cognizant of commercially-available container sizes and selected quantities of the various components that maximized the yield of product manufactured while minimizing waste. The authors chose to examine electrolyte

Table 1 **Types of Parenteral Formulations Developed**

Solution	Peripheral PN Formula	Central PN Formula	High-Stress PN Formula	Fluid-Restricted PN Formula
Amino Acid	85 g	85 g	128 g	75 g
Dextrose	200 g	250 g	350 g	250 g
Lipid	100 g	100 g	100 g	50 g
Na	150 mEq	150 mEq	155 mEq	80 mEq
K	80 mEq	80 mEq	80 mEq	40 mEq
Ca	360 mg	360 mg	360 mg	180 mg
Mg	240 mg	240 mg	240 mg	120 mg
Acetate	72 mEq	72 mEq	226 mEq	134 mEq
Cl	143 mEq	143 mEq	145 mEq	70 mEq
P	310 mg	310 mg	465 mg	233 mg
MVI-12	10 mL	10 mL	10 mL	10 mL
Trace Elements	5 mL	5 mL	5 mL	5 mL

PN = parenteral nutrition; Na = sodium; K = potassium; Ca = calcium; Mg = magnesium; Cl = chloride; P = phosphorous; MVI-12 = multivitamin infusion.

values that could be achieved using commercially-available multielectrolyte cocktails, such as Lypholyte, for ease of use and reduction of costs. Table 1 shows the formulas developed.

Phase 2

The second phase of the study was to develop a system for practitioners that would facilitate ordering these SPNS formulas without having to memorize the values in each formula. To do this, the authors developed an electronic PN ordering system. This eliminated problems such as unclear physician handwriting and physically transporting paper orders from the nursing units to the pharmacy. The authors also wanted to provide a link to the laboratory database so physicians could easily view laboratory test results while accessing the PN ordering system. Also designed into the system was a method of sending nonemergent communications or messages from the pharmacy to the practitioner that would be viewed the next time a PN solution was ordered.

With the help of the Information System Department, a computerized PN ordering system was developed. Physicians were able to select 1 of the 4 SPNS or choose a custom screen to order any combination of the components of the PN solution from any computer terminal located in the nursing units. The practitioner ordering a SPNS was not able to change any of the values on the SPNS ordering screen. If that practitioner determined that the SPNS could not be used, he or she would have to enter the order via the custom menu.

Because all quantities of substrates were fixed in these formulas, the rate at which the SPNS was run was determined by the protein needs of the patient. For example, if the patient was placed on the standard peripheral formula, and it was calculated that the patient needed 85 g of protein, the entire volume was run in over the 24-hour period. If it was determined that the patient required 64 g of protein, then the rate was set so that 75% of the bag's contents was run in over the 24-hour period. Excess quantities of solution were discarded. After determining which solution to order and at what rate it would be run, the practitioner approved the order. A copy of the order was printed at the nursing station where the patient was located as well as in the pharmacy. All PN orders were electronically signed via the log on process at the terminal.

Phase 3

The third and final phase of this study was to compare certain metabolic parameters of patients on SPNS with those of patients who were placed on CPNS.

Although protein requirements were approximately equal in both groups, there was no routine laboratory test for quickly determining differences in outcomes with different caloric contents (ie, fat and carbohydrate). The authors, therefore, decided not to examine these components. Instead, standard laboratory tests that were used in daily PN ordering were considered. This was applicable because opponents of the system were not as concerned with protein and caloric content as much as with the need to alter electrolyte concentration.

A decision was made to compare the incidence of normal and abnormal laboratory values of 6 electrolytes—sodium (Na), potassium (K), carbon dioxide (CO_2), magnesium (Mg), phosphorous (P), and chlo-

Table 2 **Laboratory Test Results I**

	Na		K		CO_2		Mg		P		Cl		Totals	
	S	C	S	C	S	C	S	C	S	C	S	C	S	C
No. of lab tests	469	283	460	281	465	282	195	137	179	125	466	283	2234	1391
No. of normal lab tests	341	187	417	241	337	166	135	88	129	90	288	159	1647	931
No. of abnormal lab tests	128	96	43	40	128	116	60	49	50	35	178	124	587	460
No. of low lab values	104	82	27	36	92	81	40	12	38	12	41	59	342	282
No. of high lab values	24	14	16	4	36	35	20	37	12	23	137	65	245	178
% of normal lab tests	72.7	66.1	90.7	85.8	72.5	58.9	69.2	64.2	72.1	72.0	61.1	56.2	73.7	67.0
% of abnormal lab tests	27.3	33.9	9.4	14.2	27.5	41.1	30.8	35.8	27.9	28.0	38.2	43.8	26.3	33.0
% of low lab values	22.2	29.0	5.9	12.8	19.8	28.7	20.5	8.8	21.2	9.6	8.8	20.9	15.3	20.3
% of high lab values	5.1	5.0	3.5	1.4	7.7	12.4	10.3	27.0	6.7	18.4	29.4	23.0	11.0	12.8

Na = sodium; K = potassium; Ca = calcium; Mg = magnesium; Cl = chloride; P = phosphorous; S = standardized parenteral nutrition solution; C = customized parenteral nutrition solution.

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ride (Cl)—in patients receiving either standardized or customized formulations.

Because the major goal of this study was to determine if SPNS were as efficacious as CPNS, the authors decided to examine the electrolyte values for both groups to determine if they had the same distribution around facility-accepted normal values.

The laboratory results of all adult patients on both SPNS and CPNS for a period of 4 months were examined. All patients who were to be placed on PN were assessed by the nutritional support team, and an appropriate solution was suggested. If the medical team caring for the patient was opposed to the suggestion, they were permitted to change to any of the other solutions at the onset of initiation of PN as well as at anytime during the patient's need for PN. The results of the laboratory tests are listed in Table 2.

Table 3 **Laboratory Test Results II**

Test Results	SPNS	CPNS	Total
Tests WNL	1647	931	2578
Tests ABN	587	460	1047
Total	2234	1391	3625

SPNS = standardized parenteral nutrition solution; CPNS = customized parenteral nutrition solution; WNL = within normal limits; ABN = abnormal.

Results

During the 4-month period in which patients on PN were monitored, there was a total of 1298 patient days of PN. Exactly 992 patient days of SPNS were given, and 306 patient days of CPNS were given. During this time, patients in both groups had 3625 laboratory determinations of the following serum electrolytes: Na, K, CO_2, Mg, P, and Cl. In the SPNS group, 2234 total laboratory determinations were performed; in the CPNS group, 1391 laboratory determinations were performed.

Interpretation of Results

The initial purpose of this study was to determine if the SPNS formulations were equivalent to CPNS formulations with regard to generating electrolyte levels within normal limits. However, upon examination of the results, it became clear that the performance of the standardized formulations may have been superior to that of the customized formulations. The incidence of levels within normal limits for patients on standardized formulations was 73%, whereas the incidence of levels within normal limits for patients on customized formulations was 67%. Because of the relatively large sample size, there was a need to analyze the data statistically to determine if these results were meaningful.

A chi-square test was selected to analyze the data. The hypotheses were revised to reflect the following:

- independent variable = type of formulation (SPNS or CPNS)
- dependent variable = electrolyte laboratory test results (within normal limits or abnormal) including Na, K, CO_2, Mg, P, and Cl
- H_0 (null hypothesis) = there is no difference in the occurrence of abnormal or within normal limits laboratory test results whether the independent variable is SPNS or CPNS formulation
- H_1 (alternate hypothesis) = there is a difference in the occurrence of abnormal or within normal limits laboratory test results whether the independent variable is SPNS or CPNS.

Developing the Chi Square

Based on the observed data, the chi square was developed as seen in Table 3.

The chi-square test was performed at a *P* value of 0.005. This means that the alpha is less than 0.1. Another way of stating this is that the probability that the null hypothesis has been erroneously rejected (a type-1 error) is stated as alpha. In this case, the *P* value (or level of significance of 0.005) used has guaranteed that the risk is less than 1% that a type-1 error has been made in the study analysis (ie, the risk is less than 1% that the null hypothesis has been erroneously rejected).

The next step was to determine the number of degrees of freedom in this analysis.

The number of degrees of freedom (*df*) was calculated as follows:

df = (number of rows - 1) x (number of columns - 1) in the chi square

df = (2-1) x (2-1) = 1

The expected frequencies were then calculated from the chi square, as shown in Figure 1. Chi square now contains both the observed and expected frequencies, as seen in Table 4.

Calculation of Chi Square

The final step was to calculate chi square, which is shown in Figure 2.

The calculated chi square is compared to the chart value at 1 *df* and *P* = 0.005. The chart value is 7.88. The calculated chi square value is greater than the chart value.

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$$E = \frac{(\text{Total for Row}) \times (\text{Total for Column})}{(\text{Grand Total})}$$

$E1 = \frac{2578 \times 2234}{3625} = 1589$ $E3 = \frac{1047 \times 2234}{3625} = 989$

$E2 = \frac{2578 \times 1391}{3625} = 645$ $E4 = \frac{1047 \times 1397}{3625} = 402$

Figure 1 Calculation of expected frequencies.

Table 4 **Laboratory Test Results III**

		SPNS	CPNS
Labs WNL	Observed	1647	931
	Expected	1589	989
Labs ABN	Observed	587	460
	Expected	645	40

SPNS = standardized parenteral nutrition solution; CPNS = customized parenteral nutrition solution; WNL = within normal limits; ABN = abnormal.

$$\chi^2 = \text{Sum of } \left[\frac{(\text{Observed} - \text{Expected})^2}{\text{Expected}}\right]$$

$$\chi^2 = \frac{(1647-1589)^2}{1589} + \frac{(931 - 989)^2}{989} + \frac{(587 - 645)^2}{645} + \frac{(460 - 402)^2}{402}$$

$$\chi^2 = 19.1$$

Figure 2 Calculation of chi square.

Therefore, there is a 99% probability that one can reject the null hypothesis and accept the alternate hypothesis. The alternate hypothesis states that if patients receive standardized formulations of electrolytes in their PN solutions, they will more than likely have laboratory serum electrolyte values within normal limits.

Conclusions

The issue of adjustment of PN formulations to address variances in serum electrolyte values has been discussed in many forums. This study examined a large number of patients receiving PN for a wide variety of disease states. The initial research question was to determine if patients could receive benefits from the use of SPNS equivalent to that which they receive from patient-specific CPNS.

This study required an adjustment to the research question. The question became: Is the increase in serum electrolyte values found within normal limits in patients receiving facility-developed SPNS statistically significant? Another question is: Do constant adjustments made to the PN formulations hamper efforts to stabilize serum electrolyte concentrations? It seems clear from this study that the use of standardized formulations that have been developed in concert by the medical, nursing, nutrition, and pharmacy services in many cases leads to better control of serum electrolyte levels.

The authors conclude that the use of SPNS is cost effective and may provide better control of serum electrolytes.

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