



Intradialytic Parenteral Nutrition 3-in-1 Admixture vs. Separate Bags: Impact on Survival and Cost-related Outcomes

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Abstract

Background and Objectives: This is a secondary analysis of a previously published randomized study to assess the survival outcomes and costs of a 3-in-1 admixture of intradialytic parenteral nutrition (IDPN) and separate bags of IDPN in hemodialysis patients with end-stage renal disease (ESRD).

Methods and Study Design: Data were analyzed at 3 and 6 months for 26 patients. Survival outcomes, cost per bag, and preparation and administration time for treatment were analyzed.

Results: The separate-bag IDPN group had four deaths while the admixture IDPN group had one. The C-reactive protein was reduced by 10.14 mg/ dL in the admixture group ($p=0.0002$) compared to 0.47 mg/ dL ($p=0.73$) in the separate bag group. Interleukin-6 showed an increase in level by 1.02 pg/ mL in the separate bag group as compared to a decrease of 12.89 pg/ mL ($p=0.0002$) in the admixture group. The overall cost per session was lower in the admixture IDPN group compared with the separate-bag IDPN group (USD 72.07 vs. 74.08, respectively). The average time required for the preparation and administration per session was also significantly less in the admixture IDPN group compared with that of the separate-bag IDPN group (357.4 vs. 1335.6 seconds; $p = 0.0002$).

Conclusions: The 3-in-1 admixture of IDPN was more cost-effective and had a better survival outcome than separate bags of IDPN.

Keywords

End-Stage Renal Disease; Hemodialysis; IPN; 3-in-1 Admixture; Survival; Cost-Related Outcomes

Article Highlights

- Intradialytic parenteral nutrition (IDPN) improves the nutritional status and survival rate in patients on hemodialysis.
- An admixture IDPN was associated with a better survival rate than a separate bag IDPN.
- A significant reduction in inflammatory markers was demonstrated by the admixture IDPN group.
- The 3-in-1 admixture IDPN was more cost-effective and time-efficient than separate bag IDPN.
- In patients on hemodialysis, a 3-in-1 admixture proved to be a promising agent in improving health-related outcomes.

Introduction

Protein-energy malnutrition (PEM) is a risk factor for the poor quality of life in patients on maintenance dialysis¹. PEM may contribute to morbidity in patients on hemodialysis with one possible route via an effect on the immune system and in causing infection². The pathogenesis of PEM is multifactorial where the loss of appetite, decreased intake of nutrients, and altered lean body mass anabolism/catabolism play crucial roles³. Other factors that can lead to PEM in patients with kidney disease include excessive blood loss, insulin resistance, diminished metabolic functions of the kidney, loss of amino acids, proteins, peptides, and vitamins in the dialysate⁴. Patients with end-stage renal disease (ESRD) are prone to developing malnutrition⁵. The malnutrition rate is between 8% and 33% in patients with renal disease receiving hemodialysis⁶.

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Protein-energy malnutrition leads to increased morbidity and mortality in patients on maintenance dialysis¹. The mortality rate could be predicted based on different levels of factors in patients with PEM/ESRD/chronic renal impairment. Urea reduction ratio (URR), serum albumin, prealbumin, and interleukin-6 (IL-6) are factors that influence the survival rate. A URR value of <60% is associated with a higher risk of death in patients with ESRD compared with a URR value of 65–69%⁷. Serum albumin level is an important parameter for evaluating nutritional status⁸. Lower levels of serum albumin are associated with increased mortality in patients on dialysis⁸. Additionally, persistently low serum albumin levels for a period of 6 months or longer have been linked with all-cause and cardiovascular mortalities.⁹ The mortality rate is two-fold higher with serum albumin concentrations of <3.5 g/dL compared with ≥4.0 g/dL in patients on hemodialysis¹⁰. Serum levels of inflammatory markers, such as IL-6, are also powerful predictors of mortality in patients on hemodialysis, which increase as chronic kidney disease (CKD) progresses^{11,12}. A serum prealbumin increase of >30 mg/L from day 0 to month 3 is reported to be linked with a two-fold improvement in 2-year survival in malnourished patients on hemodialysis¹³.

Management of PEM in patients on hemodialysis typically includes increased oral nutritional intake and dietary supplements as oral/enteral feeding might be insufficient in meeting the daily nutrient requirements¹⁴. Parenteral nutrition (PN) is beneficial and essential for patients on hemodialysis^{14,15}. Intradialytic parenteral nutrition (IDPN), a cyclic PN, improves the nutritional status (increase in body weight, body mass index [BMI], serum albumin, and prealbumin concentrations)¹⁶. IDPN is reported to improve survival in patients on hemodialysis with increased URR, serum albumin, and prealbumin levels^{7,13,15}. The two ways for the administration of total PN therapy are separate bags and three-compartment bag admixture. The cost of PN includes therapy costs and supply-related costs, such as intravenous lines (i.e., IV tubing) and infusion pumps¹⁷. Since it is a potent therapy, it is relatively expensive; thus, it is important to select the therapy that is clinically effective and economically efficient.

The present secondary analysis is aimed at determining the survival outcomes of malnourished patients with ESRD on hemodialysis receiving 3-in-1 admixture of IDPN or separate bags of IDPN and comparing the relative costs in these patients.

Methods

Study Design

The present analysis is a secondary analysis of a previously published, prospective, controlled, open-label, randomized trial that involved outpatients (age range, 20–80 years) undergoing dialysis at a secondary care hospital in Thailand, between April and November 2017¹⁸. Twenty-six enrolled patients with ESRD, if they met any two of the four criteria for malnutrition; (1) Body mass index (BMI) <20 kg/m²; (2) Weight loss of >5 % within 1 month, >7% within 3 months, or >10% within 6 months; (3) Serum albumin <3.4 g/dL; and (4) Dietary protein intake of <0.8 g/kg and a dietary intake of <25 kcal/kg after nutritional recommendation based on dietary recall, were randomized (1:1) to receive PN either via a 3-in-1 admixture or via separate bags over multiple sessions spanning 28 days of the overall treatment period (4 weeks). The eligibility criteria and the study methodology have been published previously¹⁸. The patients were assigned to either the 3-in-1 admixture of IDPN (admixture IDPN group) or separate bags of IDPN (separate-bag IDPN group) treatment for 4 weeks and were treated in parallel in the duration of the study¹⁸. In this secondary analysis, we retrospectively analyzed the data of the patients included in the study and evaluated their survival outcomes and also analyzed the comparative cost of treatment of the two modes of IDPN.

Intradialytic Parenteral Nutrition

Admixture of IDPN

The all-in-one admixture of IDPN contained three types of nutrients in one bag and was infused through a venous port using

an infusion pump for around 3.5–4.0 hours, with a total volume not exceeding 1,000 mL. The admixture of IDPN (Oliclinomel® N7-1000E) was available as a ready-to-use product with a three-chamber bag (1L) comprising of a larger outer chamber that contained dextrose (D-glucose) solution with calcium, a middle chamber that contained a solution of 15 amino acids, and a smaller outer chamber that contained a lipid emulsion comprising 80% olive oil and 20% soybean oil. The admixture of IDPN was infused to all patients in the admixture IDPN group at a constant rate of 250 mL/h via infusion pumps at the venous port during the whole dialysis session¹⁸.

Separate Bags of IDPN

Each nutrient was separated from the other using separate bags of IDPN. There was a separate dextrose bag, an amino acid bag, and a fat emulsion bag through which IDPN was given via infusion pumps in the venous port. Separate bags of IDPN (50% dextrose, 7.2% Kidmin®, and 20% Intralipid®) were administered to all patients in the separate-bag IDPN group. The 50% dextrose was administered through an arterial port (predialyzer) during the whole dialysis session, whereas the 20% Intralipid® was transfused via infusion pumps during the first 3 hours at the venous port, followed by a 7.2% Kidmin® during the last hours of the dialysis session through the infusion pump¹⁸.

Study Assessment

Nutritional and dialysis parameters, such as plasma albumin, prealbumin, urea, creatinine, URR, sodium, and potassium, were assessed and mean values for each parameter were recorded pre- and post-treatment. Plasma albumin and prealbumin levels were assessed by immunonephelometric assays. Urea, creatinine, sodium, and potassium levels were assessed using standard methods. Mean values of inflammatory and immune parameters, such as IL-6 (measured by ECLIA [Elecsys® and cobas immunoassay analyzers: cobas®]) and high-sensitivity C-reactive protein (hs-CRP), were also assessed pre- and post-treatment. Data on the mortality of patients in both groups were captured at 3 months and then again at 6 months post treatment.

Cost Analysis

Resource utilization between the two groups was estimated and compared based on the following: (i) cost per bag of the admixture IDPN and the separate-bag IDPN group and (ii) time taken for the preparation and administration of each treatment. All values were recorded in Thai baht (฿) and subsequently converted and represented in USD.

Statistical Analyses

Change from baseline was analyzed using the Wilcoxon test. Fisher's exact test was done for categorical variables. The Wilcoxon signed-rank test was used for within-group comparison analysis. Logistic regression analysis was carried out to predict survival outcomes at 3 months (univariate) and at 6 months (multivariate) in the two groups, based on the levels of specific biomarkers (IL-6, albumin, prealbumin, and URR). The Wilcoxon test was done to analyze the time required for the preparation and administration of IDPN in each group and to calculate the volume of PN used per session in each group. R software (version 4.1.0) was used for statistical data analysis. A *p*-value of <0.05 represented statistical significance.

Ethics

The methodology and study design used in the original study were as per the Helsinki Declaration of 1975 as revised in 1983. The study protocol was approved by the Institutional Review Board. Written informed consent was obtained from all patients at the beginning of the study.

Results

Patient Disposition

A total of 26 patients who were randomized to receive the 3-in-

Characteristics		Admixture IDPN (n = 13) Mean (SD) (Min, Max)	Separate-Bag IDPN (n = 13) Mean (SD) (Min, Max)
hs-CRP (mg/dL)	Pre-treatment	15.10 (11.39)	9.73 (4.20)
		(2.3, 33.2)	(2.29, 17.18)
	Post-treatment	4.96 (4.51)	9.26 (4.79)
		(0.59, 16.5)	(1.09, 17.91)
	<i>p</i> -value	0.0002	0.7354
IL-6 (pg/mL)	Pre-treatment	22.59 (12.48)	11.37 (6.78)
		(5.9, 50)	(2.36, 26.9)
	Post-treatment	9.70 (8.89)	12.39 (6.79)
		(1.5, 30.8)	(2.56, 29.76)
	<i>p</i> -value	0.0002	0.281
Prealbumin (mg/dL)	Pre-treatment	15.94 (3.96)	15.79 (3.15)
		(8.8, 24.5)	(9.39, 19.3)
	Post-treatment	31.18 (8.23)	24.09 (6.79)
		(17.9, 47)	(17.2, 37)
	<i>p</i> -value	0.0002	0.0002
Albumin (g/dL)	Pre-treatment	3.18 (0.35)	2.86 (0.44)
		(2.3, 3.63)	(2.1, 3.5)
	Post-treatment	3.60 (0.38)	3.01 (0.48)
		(2.68, 4.3)	(2.3, 3.88)
	<i>p</i> -value	0.0002	0.0134
URR	Pre-treatment	69.54 (1.94)	70.54 (2.54)
		(66, 72)	(67, 75)
	Post-treatment	72.46 (1.56)	71.46 (2.93)
		(69, 75)	(68, 78)
	<i>p</i> -value	0.0002	0.2217
Potassium (mEq/L)	Pre-treatment	4.01 (0.59)	4.63 (0.55)
		(3.11, 5.1)	(3.88, 5.9)
	Post-treatment	4.36 (0.55)	4.53 (0.67)
		(3.5, 5.4)	(3.63, 5.5)
	<i>p</i> -value	0.0215	0.8926

Table 1: Nutritional, Dialysis, and Inflammatory Markers Before and After the Treatment

hs-CRP, high-sensitivity C-reactive protein; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; SD, standard deviation; URR, urea reduction ratio.

1 admixture of IDPN (admixture IDPN group [n=13]) and separate bags of IDPN (separate-bag IDPN group [n=13]) were included in this secondary analysis.¹⁸

Baseline Characteristics

The baseline characteristics of both groups are presented in **Supplementary Table 1**. The mean age ($\pm$ standard deviation) of the patients was 70 ($\pm$ 9.8) and 72 ($\pm$ 8.6) years in the admixture IDPN and separate-bag IDPN groups, respectively. Over 60% of the patients in both groups were males. The mean duration of hemodialysis was 5.7 $\pm$ 5.5 years and 3 $\pm$ 1.5 years in the admixture IDPN and separate-bag IDPN groups, respectively. The body weight of patients in both groups was comparable.

Nutritional, Dialysis, and Inflammatory Markers

The differences in nutritional, dialysis and inflammatory marker parameters in the admixture IDPN and separate-bag IDPN groups are presented in Table 1. Within-group comparison indicated that there was a significant improvement in URR ($p = 0.0002$), potassium ($p =$

0.02), serum albumin ($p = 0.0002$), and prealbumin levels ($p = 0.0002$) in the admixture IDPN group (Table 1). Moreover, serum albumin ($p = 0.01$) and prealbumin ($p = 0.0002$) levels improved in the separate-bag IDPN group as well. There was a significant reduction in hs-CRPs ($p = 0.0002$) and IL-6 ($p = 0.0002$) levels in the admixture IDPN group whereas no significant changes were observed in the separate-bag IDPN group (Table 1). Mean changes in the parameters are provided in Table 2.

Survival Analysis

A greater number of deaths were reported in the separate-bag IDPN group (Figure 1). At 3 months, one death was reported in the separate-bag IDPN group compared to no death in the admixture IDPN group (Figure 1). At 6 months, four deaths (due to sepsis and myocardial infarction [MI]) were reported in the separate-bag IDPN group compared with one death (due to sepsis) in the admixture IDPN group (Figure 1). The effect of IDPN, in the overall population and the two groups, on the prediction of survival outcomes is presented in Figure 2. Univariate logistic regression analysis of data on albumin

Characteristics	Admixture IDPN (n = 13) Mean Change (SD) (Min, Max)	Separate-Bag IDPN (n = 13) Mean Change (SD) (Min, Max)	p-Value
hs-CRPs (mg/L)	-10.14 (8.7)	-0.47 (3.92)	0.002
	(-26.3, -1.28)	(-9.49, 6.7)	
IL-6 (pg/mL)	-12.89 (8.58)	1.01 (7.45)	0.0002
	(-27, -1.6)	(-12.4, 18.27)	
Prealbumin (mg/dL)	15.24 (8.67)	8.3 (6.52)	0.03
	(5, 32)	(0.6, 21.1)	
Albumin (g/dL)	0.41 (0.18)	0.16 (0.22)	0.0047
	(0.14, 0.7)	(-0.2, 0.69)	
FPG	-6.95 (50.47)	6.85 (33.06)	0.5438
	(-109, 59.7)	(-50, 48)	
URR	2.92 (0.76)	0.75 (2.83)	0.0266
	(2, 4)	(-5, 5)	
Potassium	0.35 (0.50)	-0.10 (0.75)	0.1133
	(-0.65, 1.1)	(-1.9, 0.85)	

Table 2: Mean Change in Nutritional, Dialysis, and Inflammatory Markers Before and After the Treatment

FPG, fasting plasma glucose; hs-CRP, high-sensitivity C-reactive protein; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; SD, standard deviation; URR, urea reduction ratio.

Parameter	Mortality at 3 Months		Mortality at 6 Months	
	Odds Ratio (Lower CI, Upper CI)	p-Value	Odds Ratio (Lower CI, Upper CI)	p-Value
	(Alive vs. Dead)		(Alive vs. Dead)	
Albumin	228.7 (0.60, ND)	0.24	6.00 (0.37, 95.57)	0.2
Prealbumin	1.87 (0.93, 11.25)	0.2	0.97 (0.71, 1.32)	0.85
IL-6	1.22(0.91, 2.53)	0.42	1.00 (0.09, 1.16)	0.85
Potassium	1.14 (0.04, 40.15)	0.93	0.74 (0.09, 6.07)	0.78
URR	1.77 (0.63, 11.18)	0.38	1.50 (0.84, 2.69)	0.16

Table 3: Logistic Regression Analysis of Mortality at 3 and 6 Months

CI, confidence interval; IL-6, interleukin-6; ND, not detected; URR, urea reduction ratio.

	Admixture IDPN (n = 13) Mean (SD) (Min, Max)	Separate-Bag IDPN (n = 13) Mean (SD) (Min, Max)	p-Value
Time required per session (seconds)	357.48 (5.59)	1335.63 (69.44)	0.0002
	(349.16, 369.58)	(1256.25, 1451.58)	
Volume of IDPN per session, pre-treatment (mL)	1000 (0.0)	1250 (0.0)	<0.0001
	(1000, 1000)	(1250, 1250)	
Volume of IDPN per session, post-treatment (mL)	1000 (0.0)	1214.42 (9.10)	0.0001
	(1000, 1000)	(1200, 1229.16)	

Table 4: Summary of Resource Utilization in the Two Groups

IDPN, intradialytic parenteral nutrition; SD, standard deviation.

($p = 0.28$), prealbumin ($p = 0.23$), potassium ($p = 0.48$), IL-6 ($p = 0.56$), and URR ($p = 0.38$) indicated that the change in values of these parameters at 3 months could not strongly predict mortality under the purview of this study (Table 3; Figure 2).

When treatment was included as a factor while running the data analysis, the odds of survival in the separate-bag IDPN group was lesser compared with the admixture IDPN group (odds ratio [OR], 0.01; confidence interval: <0.001, 2.55; $p = 0.11$). Multivariate logistic

regression analysis of mortality at 6 months also did not contribute significantly to the prediction of survival outcomes (albumin, prealbumin, potassium, IL-6, and URR) in these patients (Table 3; Figure 3).

Cost of the Admixture of IDPN and Separate Bags of IDPN

The average time required for the preparation and administration per session was significantly lower in the admixture IDPN group

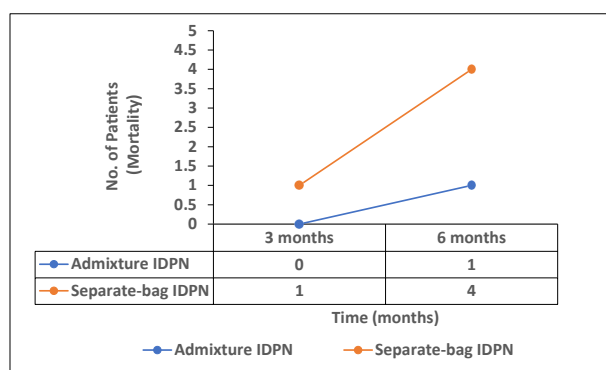


Figure 1: Effect of the admixture of IDPN vs. separate bags of IDPN on mortality.

IDPN, intradialytic parenteral nutrition.

Logistic regression analysis was carried out to predict survival outcomes at 3 months (univariate) and 6 months (multivariate) in the two groups. IDPN, intradialytic parenteral nutrition.

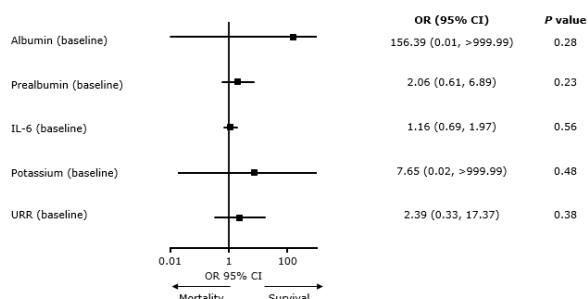


Figure 2: Univariate logistic regression analysis of mortality at 3 months in the separate-bag IDPN group.

CI, confidence interval; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; OR, odds ratio; URR, urea reduction ratio.

Univariate logistic regression analysis was carried out to predict survival outcomes at 3 months based on the levels of albumin, prealbumin, IL-6, URR, and potassium. CI, confidence interval; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; OR, odds ratio; URR, urea reduction ratio.

compared with that of the separate-bag IDPN group (357.4 vs. 1335.6 seconds; $p = 0.0002$; Table 4). The volume of IDPN used was significantly lower both pre- ($p < 0.0001$) and post-treatment ($p = 0.0001$) in the admixture IDPN group compared with the separate-bag IDPN group (Table 4; Supplementary Table 2). A detailed description of costs for the admixture of IDPN and separate bags of IDPN is provided in Table 5. The average cost of formulation for the admixture of IDPN and separate bags of IDPN was estimated to be USD 11.57 and USD 10.51 respectively. Personnel costs and costs for infusion pumps and infusion lines were lower in the admixture IDPN group compared with the separate-bag IDPN group (Table 5). The overall cost per session was lower in the admixture IDPN group compared with the separate-bag IDPN group (USD 72.07 vs. 74.08 respectively).

Discussion

The present secondary analysis was performed to determine survival outcomes in malnourished patients on hemodialysis receiving IDPN through separate bags or as a 3-in-1 admixture and to compare the treatment costs between the two methods. The results of the secondary analysis indicated a significantly greater improvement

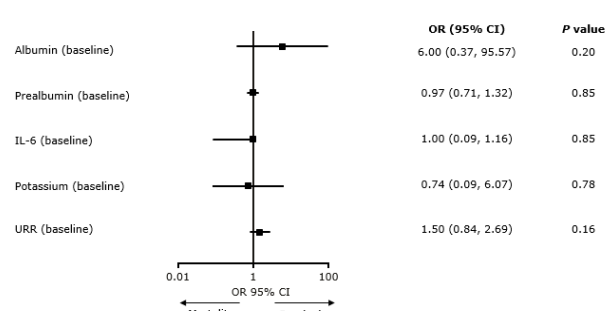


Figure 3: Multivariate logistic regression analysis of overall mortality at 6 months across both the groups.

CI, confidence interval; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; OR, odds ratio; URR, urea reduction ratio.

Multivariate logistic regression analysis was carried out to predict overall survival outcomes at 6 months based on the levels of albumin, prealbumin, IL-6, URR, and potassium. CI, confidence interval; IDPN, intradialytic parenteral nutrition; IL-6, interleukin-6; OR, odds ratio; URR: urea reduction ratio.

Parameters	Admixture IDPN (USD)	Separate-Bag IDPN (USD)
20% Intralipid® 250 mL	0	8.8
7.2% Kidmin® 500 mL	0	10.62
Oliclinomel® N7-1000E	50.38	0
50% DW 500 mL	0	2.68
Infusion pump	5.74	17.22
Infusion line	6.38	19.13
Personnel cost	9.57	15.94
Overall cost per session	72.07	74.08

Table 5: Cost of Items Used in USD

DW, dextrose in water; IDPN, intradialytic parenteral nutrition; USD, US dollar.

in URR, IL-6, serum albumin, and prealbumin levels along with a lower number of deaths in the admixture IDPN group compared with the separate-bag IDPN group. This may be because the admixture of IDPN contains 80% of olive oil which is rich in omega-9 fatty acids with recognized anti-inflammatory activity¹⁹.

On the contrary, separate bags of IDPN contain soybean, which may have procytokine effects¹⁹. The olive oil-based emulsion was characterized by a lower content of polyunsaturated fatty acids and n-6 fatty acids and a higher content of monounsaturated fatty acids and α -tocopherol compared with soybean oil-based emulsions¹⁸. These two types of intravenous lipid emulsions were reported to have similar oxidation rates and tolerance in healthy individuals and nonrenal malnourished individuals. Olive oil-based emulsions are associated with a lower peroxidation index compared with soybean oil-based emulsions²⁰. The findings from the present secondary analysis were comparable to previously published studies where lower URR, IL-6, serum albumin, and prealbumin levels were associated with a greater number of deaths²¹⁻²⁹. Although serum albumin levels significantly improved post-treatment and the number of deaths was lower in the admixture IDPN group, the regression analysis did not offer a significant correlation of this effect. Early serum albumin changes indicated a significant predictive power on mortality at 2 years in incident patients on hemodialysis where a higher mortality rate was reported with low serum albumin levels.²¹ Serum albumin levels below 2.5 g/dL (normal range, about 3.9–5.5 g/dL) were associated with a more than 20-fold increase in mortality rate in patients on

hemodialysis^{22,23}. However, in the current secondary analysis, we could not significantly draw a correlation between albumin levels and survival outcomes. This could be attributed to the very small sample size and lower number of deaths at 3 months and 6 months in the admixture IDPN group compared. Therefore, although intergroup variations in albumin levels were significant pre- and post-treatment, we could not correlate the mode of treatment to this effect.

Mortality in patients with ESRD occurred due to sepsis and MI with a greater number of deaths in the separate-bag IDPN group. Sepsis occurs frequently in patients receiving hemodialysis³⁰. A higher mortality rate due to sepsis is reported in patients with ESRD receiving dialysis compared with the general population³¹. Patients receiving dialysis are also at risk of sudden cardiac death with a high mortality rate due to MI^{32,33}. Inflammation, malnutrition, and cardiovascular complications are reported to be interrelated in patients with ESRD receiving hemodialysis^{34,35}. Hence, PEM, inflammation, and/or oxidative stress (together known as the “malnutrition–inflammation complex syndrome” [MICS]) might serve as another predictor of mortality in patients with ESRD³⁵.

This study also reported significantly improved serum prealbumin levels in the admixture IDPN group, though without any significant correlation to the prediction of survival outcomes in both groups. The adjusted relative risks of death were higher with lower prealbumin levels²⁴, and a low baseline serum prealbumin level is associated with a trend toward increased risk of death²⁵. Findings from the present secondary analysis were not comparable to previously published studies where an association between serum prealbumin levels and deaths in patients on hemodialysis has been reported.

Elevated circulating IL-6 level is reported to predict mortality in patients starting hemodialysis and is associated with all-cause mortality^{26,27}. The admixture of IDPN decreased IL-6 levels significantly in the present analysis compared with separate bags of IDPN. In advanced CKD, plasma levels of IL-6 are reported to increase and predict overall mortality, as well as cardiovascular mortality, in patients at different CKD stages¹². Although values were higher in the admixture IDPN group compared with the separate-bag IDPN group, the values were not significant regarding survival outcomes. The trend in survival outcomes appeared to be better in the admixture IDPN group even though the results were not significant.

The present analysis reported improved URR and potassium levels in the admixture IDPN group compared with the separate-bag IDPN group without any significant correlation with mortality prediction. Previously, it had been reported that patients with a URR of 60% had a greater risk of death compared with patients with a URR of 65–69%⁷. Patients on hemodialysis have a high risk of hyperkalemia where a potassium level of >5.7 mEq/L is reported to be associated with mortality^{28,29}. However, in the present analysis, improved potassium levels were observed in the admixture IDPN group. Post Dialysis potassium levels were not high enough to be classified as having hyperkalemia, indicating the beneficial effect of the admixture of IDPN.

The present analysis also compared the cost-effectiveness of the admixture of IDPN and separate bags of IDPN. The overall cost was lower in the admixture IDPN group. Notably, the overall resource utilization is greater for the separate-bag IDPN group. In this analysis, we found that while the cost of the formulation was higher for the admixture IDPN group, the overall cost of resource utilization was lower in the admixture IDPN group. Infusion pump, infusion line, and personnel costs were lower in the admixture IDPN group. Patients in the admixture IDPN group had an improvement in nutritional parameters and a reduction in inflammatory markers. In comparison with separate bags of IDPN, the admixture of IDPN would be easier to use as it only has one bag.

Factors such as preparation time, administration time, and duration of procedure all have a major impact on the cost. The

preparation time required per session and the volume of IDPN used was significantly lower in the admixture IDPN group. Due to the higher volume of IDPN used in the separate-bag IDPN group, there was greater water removal (ultrafiltration), which in turn caused a drop in the blood pressure (i.e., intradialytic hypotension), thereby leading to intradialytic complications requiring cessation of the administration of IDPN. Administration time and consistency in volume administered when taken individually and cumulatively over multiple PN sessions indicate greater cost-effectiveness of the admixture IDPN group. Our findings are comparable to those from earlier studies on the cost benefits of mixed-bag PN. Three-compartment bags (TCBs) have been reported to be less expensive compared with a separate bag/bottle system. Previously it had been reported that manpower cost has increased by 70% for customized bags compared with TCBs³⁷. Moreover, when total nutrient admixture is used, IV tubing, infusion pumps, and related supplies associated with the infusion can be spared compared with 2-in-1 PN bags¹⁷. The average time required per session was lower in the admixture IDPN group compared with the separate-bag IDPN group in the present analysis. Similar findings have been published by other studies as well with less time being consumed for TCBs³⁶. In addition, a survey has reported a higher preference among nursing staff towards the 3-in-1 admixture bag compared with the 2-in-1 bag. The risk of contamination and subsequent infections is also lower in patients receiving compounded PN. In comparison with the separate-bag IDPN group, fewer adverse events (AE) were reported in the admixture IDPN group with nausea/vomiting being the most common AE in both groups¹⁸. The common AEs caused by IDPN use include nausea, muscle pain, infections, hyperglycemia, and procedural complications^{38,39}.

The current secondary analysis has a number of limitations. Due to very small sample size of the study, we could not achieve a significant prediction of biomarkers tested. Moreover, owing to the short duration of the study, the overall survival outcomes of patients could not be analyzed in the long term. However, the present analysis showed a positive trend in surrogate markers of nutrition and inflammatory status within the study period although several studies were conducted for 12–16 weeks.

Conclusion

The administration of the 3-in-1 admixture of IDPN brought about a more pronounced effect than separate bags of IDPN in improving the levels of nutritional and inflammatory markers in malnourished patients on hemodialysis. However, there was no significant correlation between survival outcomes and different nutritional, dialysis, and inflammatory markers under the purview of this analysis. The 3-in-1 admixture is also a more cost-effective option when compared to separate bags of IDPN for malnourished patients with ESRD on hemodialysis.

Practical Applications

This study showed that the 3-in-1 admixture of IDPN is a more cost-effective option compared with separate bags of IDPN with lower overall cost and statistically better survival trends in malnourished patients on hemodialysis at 4 weeks. Additionally, the levels of nutritional and inflammatory markers also significantly improved following treatment with the 3-in-1 admixture of IDPN. A lower number of deaths were reported in the group of patients receiving the admixture of IDPN compared with separate bags of IDPN. The overall cost per hemodialysis session was less in the admixture IDPN group. Personnel costs and costs for infusion pumps and infusion lines were also lower in the admixture IDPN group which can help to provide enhanced support for patients within this group. This can reduce the workload burden, especially the workload at the nursing station, leading to potential improvements in both efficiency and productivity of treatment. In terms of efficiency and productivity, we suggest using the admixture of IDPN in daily clinical practice because it is cost-effective compared with separate bags of IDPN.

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