Malays. Appl. Biol. (2018) 47(3): 1–11

ENABLING INTRADIALYTIC PARENTERAL NUTRITION IN MAINTENANCE HAEMODIALYSIS PATIENTS IN MALAYSIA: THE WHAT, WHO AND HOW SCENARIOS OF IMPLEMENTATION?

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Accepted 22 June 2018, Published online 30 June 2018

ABSTRACT

In Malaysia, prevalence of end stage renal disease patients on haemodialysis has risen exponentially over the last 2 decades and malnutrition is significant in this population. In particular, protein energy wasting (PEW) is highly prevalent and associated with increased mortality and complications. Inadequate oral intake and poor appetite are implicated issues in the etiology of PEW. Intradialytic Parenteral Nutrition (IDPN) has been recommended by the International Society of Renal Nutrition and Metabolism as a treatment modality when dietary counselling and oral nutrition supplements fail to treat PEW in dialysis patients. IDPN does not require an additional infusion access and allows the delivery of nutrients during haemodialysis. IDPN practice protocols are now placed at different regions in the world. However, despite improved patient metabolic and nutritional status with IDPN, evidence linking IDPN with reduction in hospitalisation rates and mortality risk is limited. This review discusses IDPN composition and prescription, IDPN patient selection criteria, current available IDPN practice guidelines and the delivery of IDPN to haemodialysis patients. We conclude that IDPN is a potential adjunctive treatment strategy in the outpatient setting which is safe and efficacious for malnourished haemodialysis patients, when intensive dietary counselling and oral supplementation are compromised.

Key words: Haemodialysis, protein energy wasting, intradialytic parenteral nutrition

INTRODUCTION

Intradialytic parenteral nutrition (IDPN) is an intravenous adjunct approach to nutritional feeding with an admixture solution containing dextrose, amino acids, lipids, electrolytes, trace elements and vitamins. IDPN contrasts with the parenteral feeding associated with the critical care setting in that the target patient group is free living (Ikizler *et al*., 2009; Worthington *et al*., 2017). According to the Kidney Disease Outcomes Quality Initiative (NKF K-DOQI, 2000) guideline, IDPN may be beneficial to malnourished Stage 5 chronic kidney disease (CKD) patients on dialysis whose anorexia affects sufficiency of energy and protein intakes to optimise recommended nutritional goals whether orally or through tube feeding (Kopple *et al*., 2001). It is estimated that a minimum 10% of dialysis patients in the United States who are severely malnourished meet the criteria for IDPN prescription (Mehrotra *et al*., 2001). Based on the 23rd Report of the Malaysian Dialysis and Transplant Registry 2015 (Abdul Gafor *et al*., 2015) the total number of haemodialysis (HD) patients in Malaysia, had increased almost 2.5 fold from 13,770 to 33,456 over 10 years (2006-2015) with a significant

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proportion malnourished as defined by serum albumin below 35 g/L and BMI below 18.5. Therefore, IDPN may be considered as a therapeutic option to treat severe malnutrition for 5-10% of this HD population in Malaysia.

IDPN use during HD was first explored in 1975 by Heidland and Kult who reported improved serum proteins including total protein, albumin, transferrin, complement levels, in 18 HD patients who received 60 weeks of intravenous essential amino acids plus histidine at the end of HD (Goldsterin *et al*., 1991). IDPN became an established therapy to replete malnourished CKD patients on HD from the early 1990s (How *et al*., 2004). An old concern is that the IDPN option has the potential for introducing infection (Mortelmans *et al*., 1999) but now with expert recommendations (Sabatino *et al*., 2014), its application as adjunct nutritional feeding for malnourished HD patients needs to be critically examined. However, its use is only considered after intensive nutrition counselling, oral or tube feeding supplementation approaches have been unsuccessful (Cano *et al*., 2009; Mactier *et al*., 2011; Ikizler *et al*., 2013).

IDPN gained traction as an intensive treatment modality for potential outpatient use when the International Society of Renal Nutrition and Metabolism (ISRNM) recognised that chronic HD patients with protein energy wasting (PEW) were usually unable to tolerate oral or enteral nutrition supplementation because these patients were anorexic. The prevalence rate of PEW in end-stage renal disease (ESRD) patients globally varies between 18-70% (Corbello *et al*., 2009). In Malaysia, a limited cross-sectional study has reported 38.5% of HD patients in the Klang Valley had PEW using the diagnostic criteria set by ISRNM (Sahathevan *et al*., 2015).

PEW in ESRD patients is a complex and putative face of malnutrition (Ikizler *et al*., 2013) defined as a state of metabolic and nutritional derangements originating from the primary and chronic failure of the kidneys characterised by the uremic state (Fouque *et al*., 2008). Multiple factors affecting the nutritional and metabolic status of CKD patients are known to be dietary protein and energy intake inadequacy, metabolic disturbances arising from metabolic acidosis, systemic inflammation, dialysis inadequacy or hormonal deficiencies (Carrero *et al*., 2013). Inadequate oral intake is a recognised major causative factor for PEW. Poor oral intake from chronic poor appetites arise from altered adaptive mechanisms developing in PEW patients. Indeed, in a Malaysian CKD population, poorer appetite has been noted in PEW-diagnosed patients (Sahathevan *et al*., 2015). A significant decline in measures of muscle mass as well as reduced energy and protein intake were correlated with poorer appetite in these HD patients (Sahathevan *et al*., 2015). Carrero *et al.* (2013) hypothesized that in PEW patients the energy regulation system fails to induce hunger feelings with a resultant lowering of resting energy expenditure. Furthermore, additional nutrient losses during the dialysis procedure such as amino acids, some peptides, blood, vitamins, trace elements and glucose may further predispose these patients to increased risk of PEW (Ikizler *et al*., 1994; Combarnous *et al*., 2002).

Today, IDPN is being practised as a treatment modality for malnourished HD patients either at in-patients or out-patient settings in different regions globally (British Columbia Provincial Renal Agency, 2014; Tan *et al*., 2015; Mafrici & Wilcox, 2016). IDPN treatment at Malaysian hospitals are traditionally reserved for critically ill patients with multiple co-morbidities, where intensive care management plays a critical role (Cano *et al*., 2009). However, IDPN use as proposed by ISRNM to address PEW in the outpatient setting where patients come in for dialysis 3 times a week, calls for IDPN practice to be optimized at the early stages of PEW before patients become severely ill. Given this different environment for IDPN practice, a transformation is required for patient benefits and improvement in nutritional status. The change in practice requires governance in three major areas, namely the caregivers, the nature of the product and duration of use, and the target group of patients.

Therefore, the present review aims to discuss the potential role of IDPN as a nutritional modality in ESRD patients on maintenance HD with PEW. Questions pertaining to "what", "who" and "how" on IDPN treatment will be used to define IDPN's role as a treatment modality based on available evidence in literature.

What is IDPN?

Indication for IDPN

An indication for treatment is usually defined for any medical condition and in the context of PEW, the proposed treatment as defined in this review is IDPN (Ikizler *et al*., 2013). Until today, indications for IDPN are not well-defined as per expert guidelines (Brown & Compher, 2010; Wright & Jones, 2011). This is because IDPN only provides 25% of total targeted nutrient intake of a patient with the remaining gained from the patient's diet orally, outside of dialysis time (Ikizler *et al*., 2009; Sabatino *et al*., 2017). The ESPEN (2009) guidelines have proposed if oral consumption is lower than 20 kcal/kg/day (and/or lower than 0.8 g/kg/day of proteins) conventional enteral or parenteral nutrition is recommended instead of IDPN (Cano *et al*., 2009). Evidence on benefits of IDPN include improve-

ments in nutritional status (Cano *et al*., 2007) and appetite (Wolfson *et al*., 1996) as well as possibly reduced mortality (Cano *et al*., 2007) of patients with ESRD on maintenance HD. However, IDPN as an intensive mode of therapy cannot be initiated until dietary counselling and oral nutrition supplementation are indicated to have failed to support nutrition optimization in this group of patients (NKF K-DOQI 2000; Cano *et al*., 2009).

Although IDPN is indicated for treating PEW in HD patients, there are some situations where IDPN is contraindicated. IDPN should not be prescribed in patients who are allergic to eggs, corn and sulphites; palliative patients with no anticipated increase in quality of life; patients with fluid gain above 4% of dry weight; severe hyperglycemia with random blood glucose above 20 mmol/l); patients receiving blood transfusion on dialysis day; deranged liver function tests; septic and chronic infection patients (with elevated CRP) (British Columbia Provincial Renal Agency, 2014).

IDPN composition and prescription

The composition of IDPN solutions generally enable feeding of essential and non-essential amino acids, glucose and lipid emulsions through the parenteral route via the venous chamber of the dialysis circuit, each time a patient attends a dialysis session (Cano *et al*., 2004; Sabatino *et al*., 2014). Thus, taking into account, that 4 to 8 g of amino acids are lost through the filtrate of each dialysis session and that dialysis is performed 3 times weekly, the maximum weekly amount of nutrients provided by IDPN cannot exceed 3,000 kcal and 150 g of amino acids, 6 kcal/kg/day and 0.30 g/kg/day of amino acids in a 70 kg patient (Sabatino *et al*., 2014). IDPN allows optimising nutritional requirements for HD patients only if the patient's spontaneous feeding is equal to or above 20 kcal/kg/day and 0.8 g protein/kg/day (Cano *et al*., 2004; 2009). The maximum energy and protein dosage from IDPN per dialysis session provided is thus aimed to be 15 kcal/kg/dialysis and protein to be 0.8 g/kg/dialysis (Sabatino *et al*., 2014).

Initiating IDPN

IDPN is indicated when neither dietary counselling to motivate patient self-efficacy for increased food consumption (Fuhrman *et al*., 2009) nor oral nutrition feeding with commercial nutrition products (Stratton *et al*., 2005; Lacson *et al*., 2012) are able to sustain the nutrition intervention plan to treat PEW in malnourished HD patients. Figure 1 is an algorithm for the management of PEW in non-acutely ill malnourished HD patients based on the ESPEN Guidelines for the management of adult renal failure patients (Cano *et al*., 2009). In patients presenting with PEW as defined by ISRNM criteria presenting with spontaneous intake at least 20 kcal/kg/day or more, dietary counselling and oral nutrition supplements should be primarily prescribed. However, where patients fail to

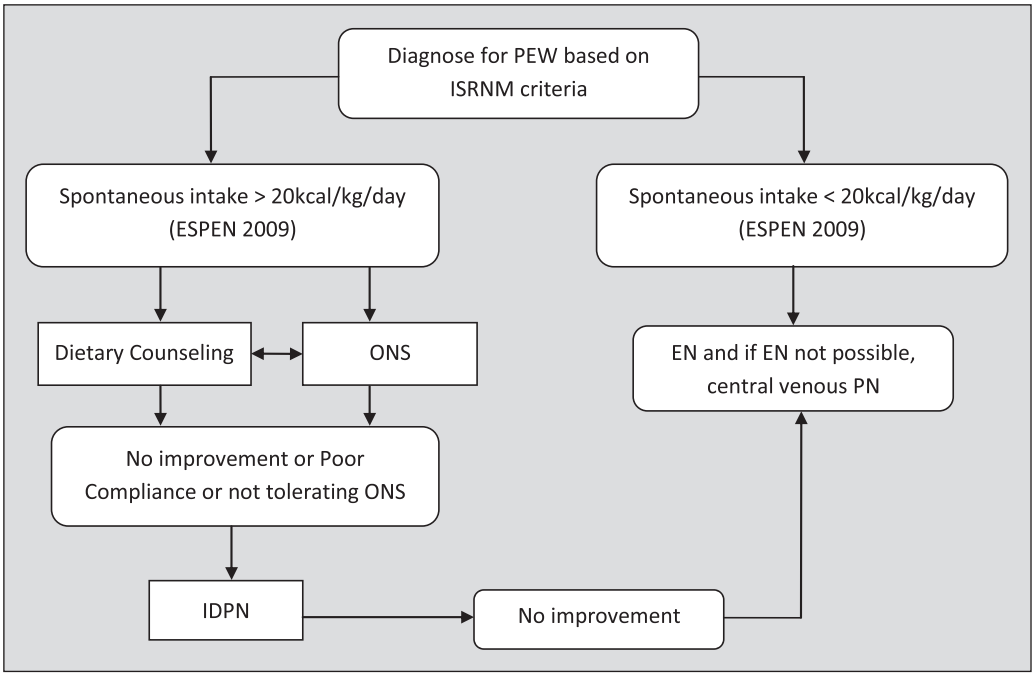

Fig. 1. Algorithm on Initiating IDPN in ESRD patients on Haemodialysis.
PEW = Protein Energy Wasting; ISRNM = International Society Renal Nutrition and Metabolism; ESPEN = European Society of Clinical Nutirion and Metabolism; ONS = Oral Nutrition Supplements; EN = Enteral Nutrition; PN = Parenteral Nutrition; IDPN = Intradialytic Parenteral Nutrition.

satisfactorily comply to oral supplementation, then IDPN is indicated (Corbello *et al*., 2009). Sometimes, enteral nutrition which necessitates a nasogastric tube insertion in the patient may be deemed necessary when either oral supplementation or IDPN fail to improve nutritional status (Cano *et al*., 2009). However in PEW patients with spontaneous intakes falling below 20 kcal/day or in severe stress conditions with illness requiring hospitalisation, both feeding options are generally unable to provide satisfactory nutritional supply and therefore contraindicated (Sabatino *et al*., 2017). Daily nutritional support is necessary and preferably achieved through enteral rather than parenteral feeding (Cano *et al*., 2009). As a last resort, the central venous parenteral route is indicated when the enteral route is impossible or insufficient (Cano *et al*., 2009).

IDPN practice

Various caregivers are involved in the management of IDPN patients (Moore *et al*., 2007). The uncertainties in practice for these caregivers include the initiation of IDPN, delivery process, managing complications from patients, timely monitoring and administration protocols, intravenous access, advantages and disadvantages of IDPN (Moore *et al*., 2008). The core aspect for IDPN initiation would be nutritional assessment of the patient, which calls for dietitian skills. In the current state, the use of IDPN in Malaysia is based on medical opinion (Ghazali *et al*., 2009) but there is lack of practice guidelines to guide care givers in the delivery of IDPN intervention to HD patients (Chan *et al*., 1994). In Malaysia, IDPN is prescribed and monitored by nephrologists in collaboration with the dialysis unit's managers and pharmacists at local hospitals (personal communication). To date there is no available data on policies or procedures on practice of IDPN in the country established by the Ministry of Health (Ghazali *et al*., 2009; Nephrology Services Operational Policy, 2010). Thus IDPN practice in Malaysia is not an organised interventional nutrition service nationwide, nor do any standards of operations exist within individual hospital institutions. It appears then that IDPN practice is individualised.

Internationally the only best practice guidelines were published in 2014 in Canada (British Columbia Provincial Renal Agency, 2014). The British Columbia practice guidelines describe the rationale for IDPN use, initiation criteria, composition and administra-tion of IDPN, discontinuation criteria for IDPN, potential complications and monitoring suggestions. In contrast, ESPEN (2009) suggests to initiate IDPN with 8 ml/kg of dry body weight at each dialysis session for the first week followed by progressive increase to a maximum of 16 ml/kg on second week onwards. Hospitals in Singapore and the United Kingdom have adopted the ESPEN (2009) guidelines. Details on IDPN protocols adopted by various countries are listed in Table 1. Available literature agree that total fluid provision through IDPN should not exceed 1,000 ml which should be enough to provide at least 1,000 kcal and 50 g of amino acids per dialysis session (Wolfson *et al*., 1982; Ikizler *et al*., 1994).

Table 1. Intradialytic Parenteral Nutrition Protocols from Different Countries

IDPN Prescription	Changi General Hospital, Singapore	Nottingham University Hospital, United Kingdom	British Columbia Network Hospitals	Vancouver Coastal Health Hospital
Total Energy	800–1200kcal, 3x weekly (7–8 kcal/kg/day)	800–1100 kcal 3x weekly	480-648 kcal 3x weekly	997-1125kcal 3x weekly
Protein	30–60g, (0.3–04 g/kg/day)	25–50gm	35–56g	35–50gm
Carbohydrate	63–125gm	63–125gm	Lipid free	50gm
Lipid	19–38gm	19–38gm	Per request	105–125gm
Volume	500–960ml, 125–240ml/hr	First week: 8ml/kg (500ml) Subsequent week: 16ml/kg (max 1000ml)	500–750ml in 3–4 hours infusion	750–1000ml in 3.5–4 hours infusion
Electrolytes	Electrolyte free	phosphate (2.8mmol/l)	Can be added per request	Electrolyte free
Type of bag	Standard	Standard	Compounded	Compounded

Reference: British Columbia Provincial Renal Agency IDPN Practice Guidelines, 2014; Tan *et al.,* 2015; Mafrici & Wilcox, 2016.

Summary of IDPN studies

Studies on the effects of IDPN in ESRD patients on maintenance HD have been cited through randomized and non-randomized studies. Improvement in nutritional status (Cherry *et al*., 2002; Czekalski *et al*., 2004), whole body-net protein accretion (Pupim *et al*., 2002), appetite (Wolfson *et al*., 1996) and survival (Chertow *et al.*, 1994) have been indicated. Table 2 lists randomised controlled trials (RCT)s with IDPN provided as intervention and with either dietary counselling or oral supplementation or no treatment at all as control in maintenance HD patients with overt PEW. Notably some studies report improvements in nutritional parameters (Guarnieri *et al*., 1980; Cano *et al*., 1990; Navarro *et al*., 2000; Cano *et al*., 2006; Cano *et al*., 2007; Abdi Metin *et al*., 2012; Marsen *et al*., 2017; Thabet *et al*., 2017). Some retrospective and non-randomized prospective studies have also addressed the nutritional effects of IDPN in malnourished HD patients (Capelli *et al*., 1994; Chertow *et al*., 1994; Foulks *et al*., 1994; Hiroshige *et al.*, 1998). However, these studies are very heterogenous in relation to the number of subjects, the nutritional status of patients at baseline, the composition of IDPN solutions, the treatment duration and the criteria considered for evaluating IDPN outcomes (Sigrist *et al*., 2010).

Table 2. Randomised Controlled Trials with IDPN as intervention

Authors	Number of patients (n)	Intervention	Days	Nutritional Significant Effects
Guarnieri *et al.* (1980)	18	IG: 2 groups with different AA solutions CG: no IDPN	60	– ↑ Body weight in IG.
Cano *et al.* (1990)	16	IG: IDPN CG: no IDPN	90	– ↑ DEI, Body weight, AMC, TSF, serum albumin, pre-albumin, creatinine in IG.
Navarro *et al.* (2000)	17	IG: IDPN CG: no IDPN	90	– ↑ TSF, serum albumin and nPCR in IG.
Cano *et al.* (2006)	35	IG: Olive oil lipid emulsion with IDPN CG: Soybean oil lipid emulsion with IDPN	35	– Both groups ↑ nPCR, serum albumin, prealbumin and creatinine.
Cano *et al.* (2007)	186	IG: IDPN + ONS CG: ONS only	365	– No advantage of adding ONS to IDPN group, ↑ nPNA, BMI, serum albumin, prealbumin in both groups
Abdi Metin *et al.* (2012)	20	IG: IDPN plus 100 mg of nandrolone IM once every 2 weeks. CG: IDPN composition of 1000 mL, AA 42.5 g, glucose 125 g, lipid 50 g, and total non-protein calories 925 kcal.	180	– ↑ serum albumin, total protein and body weight from baseline for both groups.
Marsen *et al.* (2017)	83	IG: IDPN (617 ml/day, 40.8 gm AA/day and 815 kcal/day) with DC CG: DC 3x/week	120	– 41.0% of patients on IDPN had ↑ in prealbumin from baseline to week 4 compared to 20.5% of CG. – More patients in IG achieved an increment of prealbumin >30 mg/L at week 16 (48.7% vs. 31.8%). – Prealbumin in IG was more prominent in moderate malnutrition (SGA score B) compared to patients with severe malnutrition (SGA score C).
Thabet *et al.* (2017)	40	IG: IDPN (8ml/kg initial dose increase to 16 ml/kg, 500–1000 ml) 3x/week CG: No IDPN	180	– Mean Hemoglobin, BMI and serum albumin were significantly ↑ in IG and MIS significantly ↓ after the 3rd and 6th months of IDPN in IG.

Abbreviation: IG = Intervention Group; CG = Control Group; AA = Amino Acids; IDPN = Intradialytic Parenteral Nutrition; DEI = Dietary Energy Intake; AMC = Arm Mid Circumference; TSF = Triceps Skinfold; nPCR = normalised protein catabolic rate; IM = Intramuscular; ONS = Oral Nutrition Supplements; nPNA = normalised protein nitrogen appearance; BMI = Body Mass Index; DC = Dietary Counseling; SGA = Subjective Global Assessment; MIS = Malnutrition Inflammation Score; ↑ = increase; ↓ = decrease.

Who are the PEW patients?

PEW diagnosis and patient selection

Guidelines (Ikizler *et al*., 2013) recommend that nutritional status assessment should be performed in CKD/ESRD patients and focused towards an integrated approach combining the evaluation of body mass and anthropometrics, biochemistry and dietary intake assessment. In fact, the ISRNM has provided specific criteria for diagnosing PEW (Fouque *et al*., 2008; Ikizler *et al*., 2013). These criteria focus on 4 main components to diagnose PEW which include several clinical, nutritional, and biochemical parameters as shown in Table 3. Based on the ISRNM (2013) guidelines, patients are diagnosed with PEW if they meet any 3 of the 4 main components which are low serum levels of albumin, transthyretin or cholesterol, reduced body mass (low or reduced body mass or fat mass or weight loss), reduced muscle mass (muscle wasting or sarcopenia, reduced mid-arm-muscle circumference) and reduced dietary intake (<0.8 g/kg/day of dietary protein and <25 kcal/kg/day of dietary energy intake for at least 2 months) (Fouque *et al*., 2008; Cano *et al*., 2009).

IDPN recommendation from guidelines

IDPN is recommended for a dialysis patient with spontaneous intake above 20 kcal/kg/day and 0.8–0.9 g/kg/day of dietary protein (Ikizler *et al*., 2013; Sabatino *et al*., 2014). However, depending on only IDPN, provided thrice weekly, is insufficient to maintain good protein-energy nutritional status or correct PEW. It is only suggested as adjunct therapy to other sources of nutritional intake which provide at least 50–80% of a patient's protein and energy needs (Dukkipati *et al*., 2010). However, current practice in Malaysia is only prescription of PN for renal compromised patients who are critically ill and presenting with severe malnutrition and hypoalbuminemia. At this stage, total parenteral nutrition which provides total energy and protein requirements is usually indicated as per ESPEN (2009) guidelines which is protein intake dosed at 1.5 g/kg/day and total energy targeted at 30–35 kcal/kg/day similar to acute renal failure patients (Cano *et al*., 2009). The patient group expected to benefit from IDPN are suggested to be those at high risk for PEW but not yet severely malnourished, where development of PEW can be prevented with an early nutritional support intervention (Sabatino *et al*., 2014).

IDPN can be discontinued upon improvement in the patient's PEW criteria. Improvement in nutritional status should be evident by weight gain, increase in serum albumin to 38 g/L or greater, increased oral intake (calories above 30 kcal/kg/day) and protein intake more than 1.0 g/kg, respectively (How *et al*., 2004). Oral nutritional supplementation will then be sufficient for

Table 3. Diagnostic Criteria for Protein Energy Wasting (PEW) in Malnourished Chronic Kidney Disease Patients

Nutrition Markers	NKF KDOQI 2000	ESPEN 2009	ISRNM 2013
Laboratory	Albumin < 4.0 g/dL	Albumin <35 g/L Transthyretin <300mg/L	Albumin <3.8 g/dL Prealbumin <30 mg/dL Serum cholesterol <100mg per 100 ml
Body fat mass and weight	>6% edema-free usual BW loss or <90% of IBW in <6 months	BMI <20kg/m2 Loss of BW ≥10% in 6 months	BMI <23 Unintentional weight loss over time: 5% over 3 months or 10% over 6 months Total body fat percentage <10%
Dietary Intake	DPI <1.0g/kg/d	NR	DPI <0.8g/kg/d for at least 2 months DEI < 25 Kcal/kg/d for at least 2 months
Anthropometry	NR	NR	Reduced muscle mass 5% over 3 months or 10% over 6 months Reduced MAMC area (reduction >10% inrelation to 50th percentile of reference population)
Nutrition Assessment	SGA malnourished	NR	NR
Appetite	Poor appetite/poor oral intake	NR	NR

Reference: National Kidney Foundation (2000) K/DOQI clinical practice guidelines for nutrition in chronic renal failure; Cano *et al*., 2009; Ikizler *et al*., 2013.
Abbreviations: BW = Body Weight; IBW = Ideal Body Weight; BMI = Body Mass Index; DPI = Dietary Protein Intake; DEI = Dietary Energy Intake; NR = Not Reported; MAMC = Mid-Arm Muscle Circumference; SGA = Subjective Global Assessment.

maintenance. However, if improvement is not seen after several months on IDPN or if significant adverse effects or complications are apparent, IDPN should be discontinued.

How to deliver IDPN?

For safe administration of IDPN, infusion should be managed by trained dialysis nurses or medical assistants who are both competent and confident in administering the admixture along with strict aseptic procedures in place (How *et al*., 2004). An infusion pump is required to establish a consistent flow rate. IDPN infusion can be started after 15 min of dialysis, when dialysis machine pressures and patient parameters are stable (Sabatino *et al*., 2014). There are no definitive guidelines on how to initiate IDPN currently. However, infusion should be initiated slowly and titrated up to a level that provides maximum nutrients without causing adverse effects such as nausea, muscle pain, infections, hyperglycemia, and procedural complications (Anderson *et al*., 2018). The total IDPN volume infused into a patient is a critical consideration requiring adjustment with the total ultrafiltration volume to be removed from the patient.

Type of IDPN bags

There are basically two main types of IDPN bags available in Malaysia, i.e. compounded admixture-based IDPN, which is formulated at hospital pharmacies and commercial admixture-based provided by pharmaceutical manufacturers (Sabatino *et al*., 2014). The hospital compounded formulations allow for specific tailoring of the admixture composition to the patient's requirements (Druml *et al*., 2009). However, availability of an aseptic compounding facility and storage space adds to the cost of preparation. Further, the short interval time between compounding and administration increases patient safety risk and wastage (Sabatino *et al*., 2014) . Usually, concentrated solutions are preferred (Sabatino *et al*., 2014), due to fluid restriction in ESRD patients and the need to maximize calories during the standard 4-hour HD sessions. In some patients electrolyte-free admixtures may be indicated if there is high intradialytic weight gain, hyperkalemia or hyperphosphatemia (Sabatino *et al*., 2014; Sabatino *et al.,* 2017). Therefore, a commercial admixture is preferred compared to a compounded IDPN bag due to reduced preparation time and cost-effectiveness (Druml *et al*., 2009). A summary of standard IDPN admixtures available in Malaysia is listed in Table 4.

Advantages and disadvantages of IDPN

IDPN has been shown to be a safe and convenient therapy (Ikizler *et al*., 2013), with a low complication rate in ESRD patients, without inducing liver function impairment or proatherogenic lipid status (Cano *et al*., 1990; Cano *et al*., 2006; Cano *et al*., 2007; Joannidis *et al*., 2008). Some of the advantages of IDPN includes administration of concentrated or hyperosmolar admixtures supplying calories and proteins during

Table 4. Standard All-in-One Admixtures for Intradialytic Parenteral Nutrition in ESRD patients on Haemodialysis in Malaysia

Manufacturer	Bbraun®		Fresenius Kabi®	
Regime	Nutriflex Lipid Special	Nutriflex Lipid Plus	SMOF Kabiven EF	SMOF Kabiven
Total Volume (ml)	625-1250	1250	493-986	986
Protein(g/L)	57.6	38.4	50	50
Total energy (kcal/L)	1180	1012	1100	1100
Non-protein (kcal/L)	936	840	900	900
Nitrogen (g/L)	8	5.6	8	8
Glucose (g/L)	144	120	125	125
Lipid(g/L)	40	40	38	38
Fish oil (g)	0	0	5.6	5.6
Type of Lipid	PUFA+MCT	PUFA+MCT	PUFA(omega 3) +OO+MCT	PUFA(omega 3) +OO+MCT
Osmolarity(mOsm/L)	1545	1215	1300	1500
Sodium	53.6	40	0	40
Potassium	37.6	28	0	30
Phosphate	16	12	0	12
Available without electrolytes?	Yes	Yes	Yes	No

Reference: Product Inserts from Bbraun (Malaysia) Sdn. Bhd. and Fresenius Kabi (Malaysia).
Abbreviations: ESRD = End-Stage Renal Disease; EF = electrolyte free; PUFA = Polyunsaturated Fatty Acids; MCT = Medium Chain Triglycerides; OO = Olive Oil.

Table 5. Potential Metabolic Complications of IDPN administration

Observation	Possible Cause	Management
Fluid Overload	Inadequate dialysis (Kt/V<1.2)	– To include IDPN volume infused over 4 hours into the total ultrafiltration volume
Hyperglycemia	– Pre-existing diabetes – Infection – Rapid infusion of dextrose – Concurrent steroid therapy	– Sliding scale insulin subcutaneously – Observe for signs and symptoms of infection – Routine blood glucose monitoring (dextrostix) – Do not speed up infusion to compensate for lost time
Hypoglycemia	– Hyperinsulinemia can persist if concentrated dextrose solution is discontinued abruptly	– Monitor blood glucose post IDPN – Provide and encourage a snack of 15-30g of carbohydrate 20-30 minutes prior to discontinuing IDPN – Adjustment of insulin as required
Electrolyte Abnormalities Associated with Refeeding	– Infusion of dextrose can cause an intracellular shift of electrolytes – Increased demand for electrolytes due to anabolism	– Routine monitoring of potassium, magnesium and phosphorus
Respiratory Distress	– Excessive dextrose load resulting in increased CO_2 production – Too rapid infusion of IDPN	– Observation and evaluation of pulmonary status – Provide dextrose and lipid in a 50:50 energy ratio – Ensure patient's "dry" weight is obtained by the end of the dialysis session
Abnormal Liver Function (Elevated Liver Enzymes, Hypertriglyceridemia, Hepatic Steatosis	– Hyperglycemia – Excessive lipid and/or dextrose intake	– Mandatory testing of ALT, Alk Phos, total bilirubin, TG – Controlling blood glucose – Prescribing appropriate amounts and infusion rates of macronutrients

Adapted from British Columbia Provincial Renal Agency standards and practice guidelines in IDPN, 2014.
Abbreviations: ALT = Alanine Aminotransferase; Alk Phos = Alkaline phosphatise; TG = Triglycerides.

HD treatment without the need to establish a central venous line (Bossola *et al*., 2010) through pre-existing vascular access. Although patient's compliance to dietary counseling and oral supplementation may vary, gastrointestinal complications generally do not influence the parenteral nutrient intake (Fuhrmann *et al*., 2009). Table 5 describes potential metabolic complications associated with IDPN infusion and suggested management.

It must be noted that since nutrient infusion in IDPN is provided as fluids, it is critical that if this additional volume is not optimally removed during the ongoing dialysis session, then there is added risk for overhydration (Fuhrman *et al*., 2009). As IDPN is only administered during the HD session, 3 times weekly, there is limited potential to enable micronutrient optimisation (Cano *et al*., 2009). Thus the short duration of IDPN administration is considered as only a nonphysiologic adjunct therapy, circumventing the normal nutrient-gut interactions (Sabatino *et al*., 2014). Additionally, IDPN is expensive, and requires nursing time and commitment (Dukkipati *et al*., 2010).

Education and training

IDPN delivery involves a team effort comprising the physician, nurse, pharmacist, and dietitian. Collaboration from these health care members requires additional time, work and effort for effective and safe delivery of IDPN to HD patients (Moore & Celano, 2005). Physicians awareness on nutrition support particularly related to physical and clinical responses to IDPN (Moore *et al*., 2008) and fluid-removal determination from sound nursing assessment are important for initiation of IDPN therapy at outpatient setting (Moore & Celano, 2005). Additionally, anticipation of metabolic consequences and monitoring of substrate provision during IDPN administration also need to be addressed (Moore *et al*., 2008). Therefore time investment on education and training provided by those experienced with IDPN on proper handling and storage procedures of IDPN bags, IDPN bag and solution inspection for evidence of particulate matter or discolouration, use of the infusion pump, and administrative procedures with vitamins and medications is needed for HD unit staff to ensure

effective administration and monitoring of IDPN (Moore & Celano, 2005).

CONCLUSION

Malnourished ESRD patients, particularly those with PEW, undergoing HD three times weekly are at high risk for increased mortality and serious complications. IDPN is a safe and efficacious method of providing nutrient supplementation for vulnerable patients who do not respond to intensive dietary counselling and oral nutrition supplementation. However, IDPN treatment is only efficacious when adequate spontaneous oral intake is present in the patient. Evidence and guidelines are now available to guide the use of IDPN in this population. Capacity building of health care team members, nurses, pharmacists and dietitians, is called for in order to deliver IDPN with optimal care and safety. However, the readiness to use IDPN to treat PEW patients in the outpatient setting is still nascent. This stems from a need to establish effectiveness or lack of benefit of IDPN. Large well-designed trials are required to establish the efficacy of IDPN in preventing long-term poor outcomes in ESRD patients on dialysis, as well as demonstrating cost-benefits in terms of reduced morbidity and improvement in quality of life. As well, standard operating protocols for ease of practice in the outpatient dialysis setting which incorporates safe practice is urgently needed in Malaysia.

ACKNOWLEDGEMENT

The author has received a PhD scholarship from University Kebangsaan Malaysia Medical Centre, Kuala Lumpur.

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