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End-Stage Renal Disease Hemodialysis Patients Malnutrition Treatment Using Intradialytic Parenteral Nutrition (IDPN); Prospective Effectiveness and Potential Adverse Effects

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Abstract— Intradialytic parenteral nutrition is a complementary route of nutritional administration to treat the 5th renal stage hemodialytic malnourished cases. Multiple clinical studies have elucidated contradictory suggestions regarding Intradialytic parenteral nutrition efficacy and validity. This review displays a comprehensive assessment for the use of Intradialytic parenteral nutrition, the controversy over indications, benefits, and risks, as well as summarizes the current recommendations for Intradialytic parenteral nutrition indication and variable health outcomes.

Keywords— Hemodialysis, End-stage renal failure (ESRD), Intradialytic parenteral nutrition (IDPN).

1. Introduction

End-stage renal disease (ESRD) is recognized as total kidney failure, while hemodialysis is a valid treatment. Morbidity and mortality among hemodialysis patients are predicted due to malnutrition which affects 20-60% of patients and results in protein loss, energy store loss, and metabolic alteration [1].Nutritional counseling is recommended as a first-line treatment for malnutrition in hemodialysis, which involves a registered dietician assessment for the patient, disease-specific nutrient, energy needs, and monitoring of intake and indicators of nutritional status (Figure 1). Guidelines commonly recommend the oral route of feeding primarily with some oral supplementation to aid in meeting patient nutrient and energy requirements intake. When this failed due to several barriers such as taste, nausea, diarrhea, and limited food access, guidelines recommend enteral tube feeding. Oral and enteral supplementation are recommended because they maintain the usual physiological mechanisms of the GI tract [2].

Intradialytic parenteral nutrition (IDPN) is parenteral nutrition partially administered during regularly scheduled hemodialysis as a supplement (commonly 3 times per week) and requires the patients to have their meals, not in hemodialysis session [3]. This critical review aims to provide an updated assessment of nutritional and health outcomes, disadvantageous risk factors, and advantages of IDPN in ESRD malnourished hemodialysis patients. To identify the relevant studies with validity and strength in describing the major concepts of this critical review; an exhaustive literature search was performed using PubMed, Google Scholar, Science Direct, and Springer. For research, keywords were used as follows: “end-stage renal disease”, “hemodialysis”, “intradialytic parenteral nutrition”. Studies were conducted between (1998-2020).

2. IDPN formulation recommendations

IDPN is given by IV infusion during hemodialysis, with a total of 800–1200 kcal intake, in a composition of glucose, lipids, and amino acids. Amino acids can be lost during dialysis due to the hemodialysis filter. Accordingly, not more than 3000 kcal of energy including 150 g of amino acids can be added via IDPN /3 sessions of hemodialysis /week, [4].Thus, in a 70-kg patient, approximately 6 kcal/kg/day of energy and 0.30 g/kg/day of amino acids are provided by IDPN.

3. Health society recommendations on IDPN

The European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines suggest employing IDPN in malnourished dialysis patients suffering from oral nutrition intolerance. ESPEN recommends IDPN as it

develops nutrition status in undernourished hemodialytic patients. In contrast, the American Society of Parenteral and Enteral Nutrition does not suggest IDPN due to the lack of supporting data [4]. The variations in suggestions among societies come from the lack of valid clinical experiments, which makes primarily opinion-based recommendations.

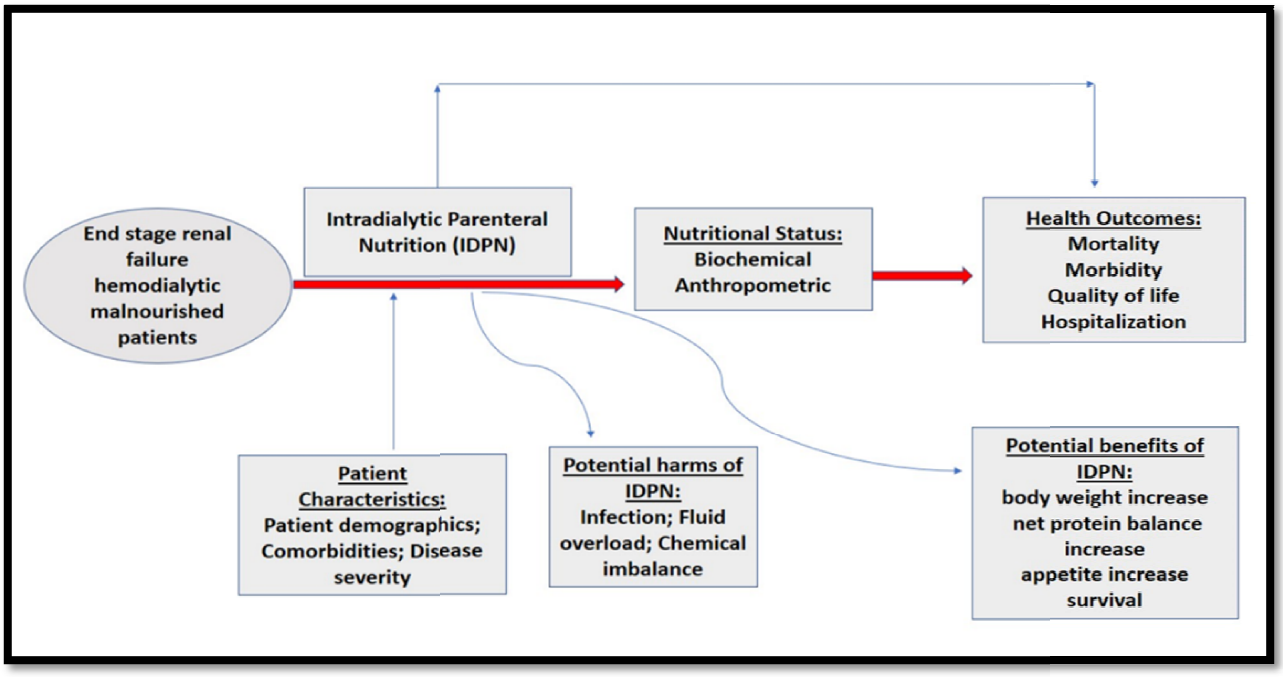
Figure 1. Analytic Framework of IDPN for Malnutrition in ESRD hemodialytic patients

4. IDPN effectiveness and potential advantages

Multiple clinical studies have elucidated a major developing in patient's nutritional condition and outcomes; increase in body weight, net protein balance, appetite, and survival [5,6]. Studies on the impact of IDPN with protein metabolism have elucidated an enhancement of whole-body protein synthesis, lowering proteolysis, and a positive net protein balance [3,7]. IDPN generally decrease mortality and enhance scores on various nutritional outcomes but not consistently in comparison with oral supplementation [8,9].IDPN can't provide larger than 25 % of nutrient intake goals in patients who aren't taking daily nutrition targets, so placement of a feeding tube to enteral nutrition (EN) or parenteral nutrition (PN) use can be the suitable next process [10, 11]. IDPN advantages are summarized as: unnecessity for an enteral feeding tube or parenteral nutrition administration, minimal risk of fluid overload due to ultrafiltration during dialysis, and less time and efforts. IDPN is safe with fewer complications in ESRD patients and does not promote a proatherogenic lipid status or hepatic dysfunction. Table 1 summarizes a group of studies that examined IDPN hemodialytic patients'clinical - nutritional statusand outcomes.

5. IDPN risks and critical disadvantages

Inadequate data are available on IDPN side effects, which lead to discontinuation of IDPN. No variations in adverse events among intervention and control groups were documented in most studies [12]. On the



contrary, other studies demonstrated risks such as hyperglycemia, hypokalemia, hypophosphatemia, and hyperlipidemia[13]. However, explaining these outcomes as consistent evidence of side effects is restricted by heterogeneity in findings, duration, and follow-up duration too. Hyperglycemia happens in IDPN as a result of extra glucose infusion, as a response to physiological stress. The maximum glucose infusion rate in IDPN is 9 mg/kg/min within the American Society for Parenteral and Enteral Nutrition guidelines. And vice versa, patients may suffer from post-infusion reactive hypoglycemia as a result of the lag action of endogenous insulin [14]. Hypertriglyceridemia occurs when the solution of IDPN includes lipids and fast

infusion rate, while IDPN free- lipids formula can be employed instead. During IDPN; blood lipids and liver enzymes must be observed monthly, while serum potassium and phosphate monitoring are desired weekly to avoid their deficiency. As hypoglycemia, hyperglycemia, and hypertriglyceridemia can be surely prevented via regular laboratory monitoring, no observed adverse reactions have been shown compared to the oral dosage forms. IDPN disadvantages could be concluded as IDPN supplies inadequate protein to support daily long-term needs, it leads to metabolic and electrolyte abnormalities with extremely time-consuming, and its high-cost procedures[15,16].

Table 1. Summary of studies for IDPN clinical and nutritional outcomes

Author, Year N= sample size	Study Design Follow-up	Intervention	Comparator	Outcomes
Cano et al., 2007 N=186	Prospective, randomized control trial (RCT) 2 years	IDPN + oral/usual dialysis	Oral sup.	No definite advantages
Marsen et al.,2017 N= 107	RCT 16 weeks	Standardized nutritional counseling +IDPN X4/week	Standardized nutritional counseling	Minor Improvements in clinically relevant critical markers
Thabet et al., 2017 N= 40	Prospective randomized study 6 months	IDPN	No IDPN infusion	Improving refractory anemia Increasing hemoglobin levels, body weight, and serum albumin levels
Rytter, 2014 N= 25	Randomized, controlled study	Fasting, intradialytic enteral intervention	Parenteral intervention	Greater retained in enterally administered amino acids than parenterally
Joannidis et al., 2008 N=12	Prospective cohort study 6 months	IDPN Per usual dialysis	Usual recommended diet	Increase body weight No pro-atherogenic induction (lipid composition) IDPN is safe and effective
Lanzi et al., 2016 N= 31	RCT 3 months	Personalized IDPN bags of carbs 70-130gr, proteins 40-50gr, lipids 20-40gr	No IDPN	IDPN provides nutritional status support, linked with enhanced oral nutrients intake
Eminsoy and Eminsoy, 2019 N= 20	RCT 1 month	IDPN: amino acid solution and dextrose	No IDPN	IDPN enhanced patients‘ nutritional status
Hiroshige et al., 1998 N=28	Prospective cohort 6 months	IDPN 3x/week	Usual recommended diet	IDPN avoids muscle protein catabolism and stimulates body protein-sparing (balance)

Dezfuli et al., 2009 N= 196	A prospective cohort study 5 years	IDPN 3-12 months	Usual recommended diet	enhancement of nutritional condition, decreasing mortality and morbidity
Pupim et al., 2002 N= 7	Randomized crossover study	IDPN 3 weeks	Usual recommended diet	Increase in whole-body protein Decrease in proteolysis

6. Limitations

There are important limitations such as limited observation of clinically significant findings involving life-quality, and cost-effectiveness. The meaningfulness and reliability of outcomes are restricted by small sample size, short follow-up duration, and indirect outcomes.

7. Future research

Further studies comparing IDPN to dietary counseling are warranted. Additional studies comparing IDPN to oral supplementation and comparison studies between IDPN and enteral tube feeding are strongly required to justify the initiation of IDPN. On the other hand, the conflicting recommendations highlight the clinical judgment requirements via strong studies in defining which patients may avail from IDPN.

8. Conclusion

IDPN has not been elucidated to enhance patient health or clinically significant nutritional findings over the present guideline recommending therapies of nutritional counseling. Therefore, the usage of IDPN before other nutritional therapy choices does not show ensured. However, because of its potential enhancement in dietary indicators, IDPN is a reasonable therapy with patients who are unsuccessful to respond to primary treatments or are incapable to take initial treatments. Fewer data are available onIDPN side effects; therefore, future research should focus on comparing IDPN with enteral tube feeding, oral feeding, and dietary counseling with larger sample sizes, longer follow-up duration, and better-characterized control groups.

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