Intradialytic Parenteral Nutrition in Hemodialysis Patients

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Disclosure Information

Intradialytic Parenteral Nutrition in Hemodialysis Patients

Hamdy Amin

I have no financial relationship to disclose.

AND

I will not discuss off label use and/or investigational use in my presentation.
Outline

• Introduction
• Protein Energy Wasting (PEW)
• Intradialytic Parenteral Nutrition (IDPN)
• Eligible for IDPN
• Components of IDPN
• Outcomes of IDPN
• Conclusion
Protein-energy wasting (PEW) is highly prevalent in patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis.

Prevalence in the ESRD population varies from 20% to 70%.

Clinical Nutrition (2009)

The severity of PEW increases with the number of years on dialysis and the older patients.
Protein Energy Malnutrition

• Presence of PEM is one of the strongest predictors of mortality and morbidity, albumin and transthyretin showing the strongest predictive value.

• Those with a serum albumin near the normal range (35-39 g/L) have a mortality rate twice as high as those with albumin greater than 40 g/L.

• The risk of death is increased more than 10-fold in those whose serum albumin levels are less than 25 g/L.
Protein losses during repeated dialysis are between 8-16 grams.

The kidney guidelines recommend a dietary protein intake:

- Not less than 1.2 gm/kg/day for patients under dialysis
- Not less than 1.3 gm/kg/day for patients undergoing peritoneal dialysis
## Diagnostic Criteria for PEW

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laboratory</strong></td>
<td>Sr. Albumin &lt;3.8 g/dl</td>
</tr>
<tr>
<td></td>
<td>Transythyretin &lt;30 mg/dl</td>
</tr>
<tr>
<td></td>
<td>Cholesterol &lt;100 mg/dl</td>
</tr>
<tr>
<td><strong>Body fat mass and weight</strong></td>
<td>Body mass index &lt; 23 kg/m²</td>
</tr>
<tr>
<td></td>
<td>Total body fat mass &lt;10%</td>
</tr>
<tr>
<td></td>
<td>Weight loss 5% over 3 months or 10% over 6 months</td>
</tr>
<tr>
<td><strong>Dietary intake</strong></td>
<td>&lt;0.8 gm/kg/day protein</td>
</tr>
<tr>
<td></td>
<td>&lt;25 kcal/kg/day</td>
</tr>
<tr>
<td><strong>Muscle mass</strong></td>
<td>Muscle mass loss 5% over 3 months or &gt;10% over 6 months</td>
</tr>
<tr>
<td></td>
<td>Mid-arm muscle circumference decreased 10% compared to 50th percentile of reference population</td>
</tr>
</tbody>
</table>

Fuhrman T, Support line. 2015
Causes and Sequences of Protein Energy Wasting

- Nutrients losses during dialysis
- Increase resting energy expenditure
- Anorexia
- Inadequate dialysis dose
- Multiple medications
- Dialysis-induced catabolism
- Metabolic acidosis
- Hormonal derangements

Figure 1: The conceptual model for etiology and consequences of protein energy wasting (PEW) in chronic kidney disease. IR: Insulin resistance; HPT: Hyperparathyroidism; GH: Growth hormone; CVD: Cardiovascular Disease
Historical Aspects of Intradialytic Parenteral Nutrition (IDPN)

- 1937 Elman’s use of protein hydrolysates with glucose infused into a peripheral vein
- 1962 Wretlind’s use of balanced intravenous nutrition that included lipids in a peripheral vein
- 1967 Demonstration of successful PN infusion in a central vein by Dudrick and his colleagues
- 1970 The idea of introducing IDPN
- 1990 IDPN as an established therapy for malnourished with chronic kidney disease
Intradialytic Parenteral Nutrition (IDPN)

- An intravenous nutrition support given to patients undergoing hemodialysis for end-stage renal disease (ESRD)

- Not commonly used in patients undergoing hemodialysis for ESRD

- Infused at the same venous drip chamber of dialysis
Parenteral Nutrition

- Water
- Dextrose
- Electrolytes
- Trace Elements
- Amino Acids 19
- Fatty Acids 20
- Vitamins 13
- Other Additives 5
## PN vs IDPN

<table>
<thead>
<tr>
<th>PN</th>
<th>IDPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administered through central or peripheral intravenous access</td>
<td>Administered through central venous access only</td>
</tr>
<tr>
<td>Infused as a continuous or Cyclic e.g. 8-22 hours)</td>
<td>Infused over 3 or 4 hours while the patient is receiving dialysis</td>
</tr>
<tr>
<td>Nutrient doses are variable</td>
<td>Mostly “one-size-fits-all)</td>
</tr>
<tr>
<td>Electrolytes are mostly added</td>
<td>Electrolytes: Not generally added</td>
</tr>
<tr>
<td>Vitamins and trace elements are mostly added</td>
<td>Vitamins and Trace elements: Not routinely added</td>
</tr>
<tr>
<td>Water is a part of PN</td>
<td>No additional water</td>
</tr>
</tbody>
</table>
How to Administer IDPN

The most common and preferred type of access for IDPN is internal arterio-venous fistula (AV fistula)

- Done by a surgeon (connecting an artery to a vein in patient arm)
- The procedure may take between 30-60 minutes
- Patient has to do some exercises to help the AV fistula to “mature”
Consider IDPN if patient meets any three of the following criteria:

- 3-month average serum albumin < 34 g/l
- Unintentional weight loss of > 10% of usual body weight or current body weight < 90% of ideal body weight
- A decrease in the intake of protein to < 1 g/kg/day or calories < 25 kcal/kg/day
- Subjective Global Assessment (SGA) yields a B or C rating, indicating moderate to severe malnutrition
- Protein intake < 1 g/kg/day and calories < 25 kcal/kg/day
- Documented diagnosis of a gastrointestinal disorder (e.g. malabsorption syndrome)
AND

• Failed attempts to increase nutritional status with oral nutritional supplements (ONS)
• Not a candidate for enteral tube feeding
• All possible attempts have been made to achieve adequate daily
Common Compositions of IDPN

- Concentrated macronutrient formula is highly advised
  - Amino acids
    - Concentration: 10%, 15%
    - Dose: 50-60 grams
    - Reduce in patient with hepatic encephalopathy
  - Dextrose
    - Concentration: 50%, 70%
    - Dose: 125 grams
- IV lipids
  - Concentration: 20%
  - Dose: 50 grams
### IDPN Formula and Infusion Rate

<table>
<thead>
<tr>
<th>Total Volume 750 mL</th>
<th>Total Volume 1000 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino Acid 10% w/o Lytes 250 mL</td>
<td>Amino Acid 10% w/o Lytes 500 mL</td>
</tr>
<tr>
<td>Dextrose 50% 250 mL</td>
<td>Dextrose 50% 250 mL</td>
</tr>
<tr>
<td>500 mL</td>
<td>750 mL</td>
</tr>
<tr>
<td>Fat Emulsion 20% 250 mL</td>
<td>Fat Emulsion 20% 250 mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dialysis Run Time (check box)</th>
<th>Infusion Rate</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 hr</td>
<td>150 mL/hr</td>
<td>225 mL/hr</td>
</tr>
<tr>
<td>4.0 hr</td>
<td>130 mL/hr</td>
<td>196 mL/hr</td>
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</tbody>
</table>

"Total nonprotein calories = 835 kcal/100 mL
Ten minutes total start-up/take-off time has been considered in rate calculations.

### IDPN Schedule

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Schedule</th>
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</thead>
<tbody>
<tr>
<td>Laboratory Tests (Predialysis)</td>
<td>Initial treatment, weekly x 2 weeks, then every 6 weeks</td>
</tr>
<tr>
<td>CBC</td>
<td></td>
</tr>
<tr>
<td>Electrolytes (K⁺, Ca⁺⁺, PO₄⁻, Mg⁺⁺)</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>Initial treatment, then every 6 weeks</td>
</tr>
<tr>
<td>Liver-function tests (alkaline phosphatase, AST, total bilirubin)</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td></td>
</tr>
<tr>
<td>Monitoring During Run(s)</td>
<td>Pre and post IDPN Non diabetic: pre, mid, and 30-min post for first 3 IDPN runs Diabetic: pre, mid, and 30-min post for first 6 IDPN runs, then weekly</td>
</tr>
<tr>
<td>Weight, BP, heart rate, temperature</td>
<td></td>
</tr>
<tr>
<td>Blood glucose via glucometer*</td>
<td></td>
</tr>
<tr>
<td>*CONTACT MD if glucose &lt;6 or &gt;18 mmol/L</td>
<td></td>
</tr>
<tr>
<td>PROVIDE snack/juice 30 minutes prior to discontinuing dialysis</td>
<td></td>
</tr>
</tbody>
</table>

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**Source:** Am J Health-Syst Pharm © 2002 American Society of Health-System Pharmacists
IDPN Monitoring

- **Vital signs and weight**
  - Pre and post each IDPN

- **Laboratory test**
  - Initial treatment, then 4-6 weeks
  - CBC
  - Electrolytes
  - Urea
  - Serum creatinine
  - Liver function tests
IDPN Monitoring

- **Amino acids**
  Response to any adverse event

- **Dextrose**
  - Blood glucose should be monitored before, during, and at the end of hemodialysis
  - First week of IDPN
  - Week after change in dextrose rate
  - Consider insulin if serum glucose level exceeds 16.5 mmol/l by adding 4-6 units of regular insulin per liter of IDPN
IDPN Monitoring

- **IV Lipids**
  
  Serum Triglyceride (TG) level before first dose and second treatment using IV lipids

  Discontinue IV lipids if:
  - 50% rise in pre HD TG level
  - Allergic to IV lipids
E Doberer et al conducted open label, cross over study in 13 chronic, malnourished non-diabetic HD patients; > 3 months on HD

- One session with IDPN (50 gm of amino acids, 60 gm of glucose, and 20 gm of lipids)
- One session of IDPN with insulin (50 gm of amino acids, 60 gm of glucose, 20 gm of lipids, and 4-6 units insulin)

- Monitoring: Metabolic profile, plasma and dialysate amino acids concentration were measured by HPLC
Insulin in IDPN

Outcomes

- No metabolic derangements were recorded during IDPN
- Mean plasma amino acid concentrations were increased with IDPN containing insulin
- The net-loss of amino acids into dialysate was $6.7 \pm 1.8 \text{ gm}$ during HD without IDPN, increased to $9.7 \pm 3.7 \text{ gm}$ with IDPN and was significantly reduced by 22% to $7.6 \pm 3.3 \text{ gm}$ by adding insulin to IDPN ($p<0.05$)
IDPN Discontinuation

Discontinue if patient meets any three of the following criteria:

• 3-months average serum albumin concentration > 34 gm/L
• Increasing dry body weight
• Improved SGA score: A or B
• Increased protein intake > 1 g/kg/day and calories to 25-30 kcal/kg/day

OR

• Shows no improvement after 6 months or develops complications or intolerance to IDPN

*Am J of Health Syst Pharm (2002)59;18*
The Outcomes of IDPN

• Nutritional status

• Quality of life

• Hospitalization rate

• Patient survival
The Effect of IDPN on Nutrition Status

- Cherry et al performed nonrandomized uncontrolled prospective study about IDPN in 24 malnourished patients
- A total of 26 courses of IDPN (mean duration of treatment = 4.3 months)
- 750 mL containing 250 mL 10% AA/250 mL 50% Dextrose/ 250 mL 20% Fat emulsion or
- 1000 mL containing 500 mL 10% AA/250 mL 50% Dextrose/ 250 mL 20% Fat emulsion
The Effect of IDPN on Nutrition Status

- Patient data was collected up to 6 months before IDPN began allowing patients to act as their own controls
- Follow-up at 3, 6, 9, and 12 months after therapy began
- Outcomes: Patients who received IDPN for 3-6 months showed increased dry body weight at 6, 9, and 12 months (p < 0.05 and p < 0.003, respectively) and significantly increase in albumin at 3 and 9 months

The effect of IDPN on Long-Term

- Pupim LB et al did randomized cross-over study (7 HD patients during 2 HD sessions) with 4 week period between sessions

- Results indicate that IDPN significantly improves Fractional synthetic rate (FSR) of albumin (84% increase in IDPN session vs 54% increase in control session)

- IDPN also increased whole body protein synthesis by 83% vs 17% increase in control session
The effect of IDPN on Long-Term Outcomes:

- The study demonstrated that IDPN has a short term effect on non-malnourished patients

- IDPN has a positive effect on protein and calories in stable chronic HD patients

The effect of IDPN on Mortality Rate

Cano N et al performed a multicenter, prospective, randomized trial (n=186), malnourished hemodialysis patients received oral nutritional supplements with (n-93) or without (93) 1 year of IDPN.

- Oral supplements consisting of 500 kcal/d and 25 gm/d protein, IDPN was not standardized among the patients.
The effect of IDPN on Mortality Rate

Outcomes

• IDPN did not improve 2-year mortality (primary end point), between the 2 groups (38.7% control vs 43% IDPN)
• Both groups demonstrated improvement in BMI (P < 0.05)
• Increase in serum albumin at 3, 6, 12, 18 months (p < 0.01), prealbumin at 3 to 24 months (p < 0.02) in both groups

The effect of IDPN on Patient Survival

• A review of the current literature regarding oral nutritional supplements (ONS) and IDPN in the treatment of malnutrition in HD pts

• Bossola et al 34 studies (3223 patients) were identified and included randomized clinical trials, comparative nonrandomized clinical trials

• 17 studies were on ONS (778 patients) and 17 were on IDPN (2475 patients)
The effect of IDPN on Patient Survival

• ONS may improve serum albumin and/or other nutritional parameters, whereas there are insufficient data on clinical outcome
• IDPN improves serum albumin and body weight
• Concluded data on survival are conflicting
• The only study with adequate sample size shows that IDPN does not influence survival
• A randomized, controlled studies to clarify the role of ONS and IDPN in the treatment of malnutrition in HD is needed

Decisional Algorithm for the Management of PEW in HD patients

Dietary intakes and nutritional status evaluation

Moderate undernutrition
Spontaneous intakes
- ≤ 30 kcal/kg/day
- ≤ 1.1 g protein/kg/day

Severe undernutrition
BMI < 20
Body weight loss > 10% within 6 mo
Albumin < 35 g/l
Transthyretin < 300 mg/l

Spontaneous intakes
- > 20 kcal/kg/d

Lack of compliance

Dietary counselling

Oral supplements

IDPN

No Improvement

Enteral Nutrition if EN is not possible: Central venous PN

Clinical Nutrition 2009
Non-acutely ill malnourished HD patients with mild PEW as defined by insufficient spontaneous intake, dietary counseling, and, if necessary, ONS should be prescribed

Clinical Nutrition 2009
ESPEN Recommendations

- Patients with severe PEW, with spontaneous intakes > 20 kcal/kg/day: dietary counseling and ONS should be prescribed; IDPN is indicated in patients unable to comply with ONS; EN can be necessary when ONS or IDPN fail to improve nutritional status.

- Patients with severe PEW, with spontaneous intakes < 20 kcal/kg/day, or in stress conditions: both ONS and IDPN are not recommended; daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient.
Conclusion

• Protein energy wasting is very common in patients receiving dialysis

• IDPN should be considered for hemodialysis patients who are not able to receive adequate oral/enteral feedings to meet energy and protein requirements

• In the most studies done on IDPN, appear to show that IDPN for malnourished patients on hemodialysis may decrease morbidity and mortality but large randomized controlled studies are needed