LLL Session - Nutritional support in renal disease

Chronic maintenance hemodialysis

N. Cano (FR)
Nutrition support in renal disease
Topic 15, Modules 15.3-15.4

Nutrition support in hemodialysis patients

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Human Nutrition Research Center
Clermont-Ferrand, France
Learning objectives

1. Prevalence and prognostic impact of protein energy wasting

2. Specific causes of PEW in MHD patients

3. Recommendations for nutritional follow-up and nutrient intakes

4. Data on the effects of nutritional support and Strategy for nutritional management

5. How to improve the efficacy of nutritional support?
# Protein-energy wasting

<table>
<thead>
<tr>
<th>Serum chemistry</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Albumin &lt; 38 g/L (Bromocresol ≈ 35 g/L by immunonephelometry)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Transthyretin (prealbumin) &lt; 300 mg/L</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Cholesterol &lt; 1 g/L</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Body mass</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>• BMI &lt; 23 kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unintentional BW loss &gt; 5% over 3 months or 10% over 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Total body fat percentage &lt; 10%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Muscle mass</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Muscle wasting &gt; 5% over 3 months or 10% over 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Reduced arm muscle mass area &gt; 10% in relation to 50th percentile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Creatinine appearance</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary intake</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unintentional DPI &lt; 0.80 g/kg/d for at least 2 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unintentional DEI &lt; 25 kcal/kg/d for at least 2 months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1. **Prevalence and prognostic impact of PEW**

- French multicenter study, 7,123 MHD patients

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 20 kg/m(^2)</td>
<td>24 %</td>
</tr>
<tr>
<td><strong>Muscle mass &lt; 90 % th.</strong></td>
<td>62 %</td>
</tr>
<tr>
<td>Serum Albumin &lt; 35 g/l</td>
<td>20 %</td>
</tr>
<tr>
<td>Serum transthyretin &lt; 300 mg/l</td>
<td>36 %</td>
</tr>
<tr>
<td>nPNA &lt; 1 g/kg/j</td>
<td>35 %</td>
</tr>
</tbody>
</table>

Aparicio M et al. Nephro Dial Transplant 1999
Protein-energy wasting & survival in MHD patients

- Reverse epidemiology

Kalantar-Zadeh K et al. Kidney Int 2003
Protein-energy wasting & survival in MHD patients

Reverse epidemiology during a 7-year follow-up?

- Standardized mortality rates were 10 times higher in HD vs controls.
- Hazard ratio for death, according to BMI:

<table>
<thead>
<tr>
<th>Ref HR: BMI=22.5-25</th>
<th>HD patients n=722 Hazard Ratio</th>
<th>Controls n = 2436 Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 18.5</td>
<td>2.0</td>
<td>2.3</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>1.2</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Longitudinal study (n = 60; n = 46 completed) body composition changes in incident PD and HD patients over 12 months
Total body protein by in vivo neutron activation (NI)

Nitrogen index changes by BMI in MHD patients

Figure 1. | Difference in nitrogen index by body mass index (BMI) groups.

Pellicano R et al. CJASN 2011
Body composition and survival in MHD patients

Incident patients

n = 70 028
Survival according to urinary creatinine before dialysis initiation and BMI

Prevalent patients

742 MHD patients,
• age of 54 ± 15 y
• men (n = 391)
• women (n = 351)
• LBM and FM measured by near-infrared interactance

Protein-energy wasting & survival in HD patients

2. Causes of PEW in dialysis

Causes of PEW in dialysis patients

**Anorexia**
- Dietary restrictions: Na, K, phosphorus, water
- Retention of low molecular weight product
- Abnormal plasma AA
- Socio-economic status
- Depression, multiples medications, hospitalizations
- Co-morbidities

**Metabolic and endocrine abnormalities**
- High prevalence of diabetes
- Acidosis
- Hyperparathyroidism
- Growth factor disturbances
- Nutrient losses due to hemodialysis
- Decreased protein anabolism and catabolic effect of dialysis
3. Recommendations for nutritional follow-up and nutrient intakes

ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure
Clin Nutr 2006

ESPEN Guidelines on Parenteral Nutrition: Adult Renal Failure
Clin Nutr 2009
## Nutritional follow-up in hemodialysis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Interval</th>
<th>Recommended levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary interview (3 d)</td>
<td>6 - 12 mo</td>
<td></td>
</tr>
<tr>
<td>BW</td>
<td>every HD</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>1 mo</td>
<td>&gt; 23 kg/m²</td>
</tr>
<tr>
<td>nPNA</td>
<td>1 mo</td>
<td>1 g/kg/d</td>
</tr>
<tr>
<td>Creatinine pre-HD</td>
<td>1 mo</td>
<td></td>
</tr>
<tr>
<td>Serum albumin</td>
<td>1-3 mo</td>
<td>40 ≥ g/L</td>
</tr>
<tr>
<td>Serum transthyretin</td>
<td>1-3 mo</td>
<td>300 mg/L</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>3 mo</td>
<td>&gt; minimal laboratory threshold value</td>
</tr>
</tbody>
</table>

Fouque D et al. EBPG. Nephrol Dial Transplant 2007
### Recommended macronutrient intakes in MHD

<table>
<thead>
<tr>
<th></th>
<th>ESPEN (1,2)</th>
<th>NKF (3)</th>
<th>EBPG (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein</strong></td>
<td>1.2 - 1.4</td>
<td>1.2</td>
<td>&gt;1.1</td>
</tr>
<tr>
<td><strong>g/kg/day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Energy</strong></td>
<td>35</td>
<td>&lt; 60 y: 35</td>
<td>30-40</td>
</tr>
<tr>
<td><strong>kcal/kg/day</strong></td>
<td></td>
<td>&gt; 60 y: 30</td>
<td></td>
</tr>
</tbody>
</table>

*1,2 g protein and 30-35 kcal/kg/day*

2 - National Kidney foundation. Am J Kidney Dis, 20003
3 - Fouque D et al. EBPG. Nephrol Dial Transplant 2007
4 - Cano N et al. Clin Nutr 2009
**Recommended intakes in MHD patients**

**Micronutrients**

<table>
<thead>
<tr>
<th>ESPEN 2000</th>
<th>Pyridoxin, mg</th>
<th>10-15</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vitamin C, mg</td>
<td>30-60</td>
</tr>
<tr>
<td></td>
<td>Folic Acid, mg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vitamin D</td>
<td>according to plasma Ca$^{++}$ &amp; PTH</td>
</tr>
<tr>
<td></td>
<td>Zinc, mg</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Selenium,µg</td>
<td>50-70</td>
</tr>
</tbody>
</table>

| EBPG 2007           | Thiamine, Riboflavin, cobalamine, Niacin, Biotine, pentothenic A & tocopherol should be supplemented (expert opinion) |

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Fouque D et al. EBPG. Nephrol Dial Transplant 2007
4. Nutritional support: hemodialysis

- Dietary counselling
- Oral supplements
- Intradialytic parenteral nutrition
- Enteral nutrition

- Grade of malnutrition
- Spontaneous alimentation
- Patient compliance
Dietary counselling in MHD patients

RCT in 83 hemodialysis patients. Six-month follow-up
Effect of dietician counselling on serum albumin changes

Independent from serum CRP

Leon JB et al. J Ren Nutr 2001
## Oral supplements vs. controls: studies in malnourished MHD patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Duration, days</th>
<th>Nutritional significant effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acchiardo et al. (1982)</td>
<td>15</td>
<td>105</td>
<td>↑ albumin, transferrin, bone density</td>
</tr>
<tr>
<td>Tietze et al. (1991)</td>
<td>19</td>
<td>120</td>
<td>↑ BW, arm muscle circumference</td>
</tr>
<tr>
<td>Eustace et al. (2000)</td>
<td>47</td>
<td>90</td>
<td>↑ albumin, grip strength, SF12 mental health</td>
</tr>
<tr>
<td>Hiroshige et al. (2001)</td>
<td>44</td>
<td>180</td>
<td>↑ DEI, DPI, fat mass, fat free mass, albumin</td>
</tr>
<tr>
<td>Sharma et al. (2002)</td>
<td>40</td>
<td>30</td>
<td>↑ albumin</td>
</tr>
<tr>
<td>Gonzalez et al. (2005)</td>
<td>28</td>
<td>180</td>
<td>↑ DEI, DPI, nPNA, albumin</td>
</tr>
<tr>
<td>Teixido et al. (2007)</td>
<td>65</td>
<td>180</td>
<td>↑ BW, AMC, LBM, prealbumine</td>
</tr>
<tr>
<td>Fouque et al. (2008)</td>
<td>86</td>
<td>90</td>
<td>↑ DEI, DPI, SGA, QOL</td>
</tr>
<tr>
<td>Moretti et al. (2009)</td>
<td>49</td>
<td>365</td>
<td>↑ nPNA, albumin</td>
</tr>
</tbody>
</table>
Practical rules to improve the efficiency of ONS

1) **ONS** should be given separately from regular meals, usually one to two hours after mains meals;

2) **ONS** should be given during dialysis sessions to prevent dialysis procedure-associated abnormalities of protein metabolism;

3) A late evening meal or **ONS** may be useful to reduce the length of nocturnal starvation and the associated increased use of endogenous protein and fat stores.

Intradialytic parenteral Nutrition

Overall population of Health care system IDPN, n=1679 Controls, n=22517

## IDPN: 4 controlled studies in malnourished hemodialysis patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Duration, days</th>
<th>Nutritional significant effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guarnieri et al. (1980) (3 groups: control, and 2 groups with different AAs)</td>
<td>18</td>
<td>60</td>
<td>↑ BW in treated patients</td>
</tr>
<tr>
<td>Cano et al. (1990) (2 groups: IDPN vs controls)</td>
<td>26</td>
<td>90</td>
<td>↑ DEI, BW, AMC, TSF, serum albumin, prealbumin, creatinine</td>
</tr>
<tr>
<td>Cano et al. (2006) (2 IDPN groups differing by fat emulsion olive vs soya)</td>
<td>35</td>
<td>35</td>
<td>In the two groups: ↑ nPCR, serum albumin, prealbumin, creatinine</td>
</tr>
<tr>
<td>Cano et al. (2007) (2 groups: IDPN+ONS vs ONS)</td>
<td>186</td>
<td>365</td>
<td>No advantage of IDPN addition to ONS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In the two groups: ↑ nPCR, BMI, serum albumin, prealbumin</td>
</tr>
</tbody>
</table>
Nutritional support

Oral Nutr. Suppl.

400-600 kcal/day
(standard formulas)
• 5 - 10 kcal/kg/d
• 0.4 - 0.6 g prot/kg/d

IDPN

800-1200 kcal/HD
• 5-8 kcal/kg/jour
  (glucose+fat emulsions)
• 0.2-0.4 g AA/kg/d

Both ONS and IDPN can only reach the nutritional objectives when spontaneous intakes are
≥ 20 kcal & 0.8 g protein/kg/d
Nutritional support
Oral supplements or IDPN?

- Both oral supplements and IDPN can improve nutritional status.
- Oral supplement are more simple and cheaper.

Is there any advantage to prescribe IDPN?
- on a nutritional point of view?
- in terms of morbidity and mortality?
French Intradialytic Nutrition Evaluation Study (Fines)

Control group (n=93): ONS during 12 mo.
IDPN group (n=93): ONS + IDPN during 12 mo.

Serum albumin, g/L

Transthyretin, mg/L

Figure 4. Independent predictors of mortality: Multivariate Cox regression analysis.
**Fines: Do inflammed patients respond to nutritional support?**

![Graph showing changes in serum albumin and prealbumin levels over time.](image)

- **Serum albumin (g/L):**
  - Baseline CRP < 10 mg/L, n=88
  - Baseline CRP ≥ 10 mg/L, n=86

- **Serum prealbumin (mg/L):**
  - Baseline CRP < 10 mg/L, n=88
  - Baseline CRP ≥ 10 mg/L, n=86

P<0.05

NS

Fines: Do diabetic patients respond to nutritional support?

Serum albumin, g/L

Months

Non diabetics, n=141
Diabetics, n=45

Outcomes Associated With Intradialytic Oral Nutritional Supplements in Patients Undergoing MHD: a Retrospective matched-cohort study

- Polymeric EN, administered via naso-gastric tube or gastrostomy

- Necessary during severe undernutrition, particularly when spontaneous intakes are < 20 kcal/kg/day (1):
  - ONS and IDPN cannot reach recommended supplies
  - Daily nutritional support is needed
  - Enteral nutrition should be preferred to parenteral nutrition

- Poorly investigated

Strategy for nutritional management in HD

5. How to improve the efficacy of nutritional support?

**Synthesis**

- Muscle growth
  - Amino acids
  - Exercise
  - Hormones

**Catabolism**

- Inadequate intakes
- Inactivity
- Hormone disturbances
- Inflammation
- Metabolic disturb., acidosis

Muscle mass

Muscle loss
Multimodal approach of malnutrition

INTEGRATED TREATMENT

- Healthy diet
- Nutritional support, n-3 FA, vitaminD
- Exercise
- Androgens, growth factors
- Anti-inflammatory agents
- Correction of acidosis
Beneficial effects of exercise

EBPG hemodialysis: androgens

• In case of severe malnutrition resistant to optimal nutritional intervention, a course of androgens should be proposed in MHD patients for three to six months (Evidence level II).

• Androgens should be administered weekly or bimonthly (Evidence level II).

• Patients should be monitored at regular intervals for side effects (hirsutism, voice change, priapism, alteration in plasma lipids, liver tests and prostatic markers) (Evidence level II)

• Patients with a known prostate cancer should not receive androgens (Evidence level II)

Fouque D et al. EBPG. Nephrol Dial Transplant 2007
EBPG hemodialysis: Daily dialysis

- A six to twelve month trial of daily dialysis (either short daily or long nocturnal) should be considered as a rescue therapy in unstable patients undergoing difficult haemodialysis sessions with symptoms of malnutrition or malnourished patients with poor appetite after a negative nutritional work-out (Opinion).

Fouque D et al. EBPG. Nephrol Dial Transplant 2007
Conclusion (1)

- In MHD patient with PEW, dietary counselling, oral supplements and IDPN can improve nutritional status, independent of serum CRP.

- The increase in serum transthyretin during nutritional support is associated with an increase in survival.

- IDPN is indicated in malnourished MHD patients not compliant to oral supplementation.
Exercise was shown to improve the efficacy or nutritional support.

In patients who do not respond to nutritional support, androgens and daily dialysis can be proposed.

A integrated therapy associating different approaches to improve muscle protein metabolism, such as nutritional supplements, exercise and androgens needs to be evaluated.