Nutritional support in patients on chronic dialysis

Noël CANO
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Protein-energy wasting

A proposed nomenclature and diagnostic criteria for protein-energy wasting in kidney disease

• low serum levels of albumin, transthyretin, or cholesterol

• reduced body mass (low or reduced body or fat mass or weight loss) with reduced intake of protein and energy,

• reduced muscle mass (muscle wasting or sarcopenia, reduced mid-arm muscle circumference).

# Protein-energy wasting

- **French multicenter study, n=7,123**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI $&lt; 20$ kg/m$^2$</td>
<td>24 %</td>
</tr>
<tr>
<td>Muscle mass $&lt; 90%$ th.</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
Muscle structure in organ failure:
Fiber type shift from type I (oxidative) to type II (glycolytic)

Figure 1. ATPase staining (pH 4.30) of cryosections of muscle biopsies from the vastus lateralis muscle of a patient on HD and an untrained healthy subject. Dark fibres = type 1 fibres; white fibres = type 2 fibres (2a, 2ax and 2x); grey fibres = type 1/2a fibres. Notice that there are significantly fewer type 1 fibres in the skeletal muscle of the patient on haemodialysis compared with the healthy subject.
Body composition and survival

70,028 patients
Survival according to urinary creatinine before dialysis initiation and BMI

Protein-energy wasting & survival


Serum albumin
- Quartiles
  - < 36.4 g/L
  - 36.4 - 40 g/L
  - 40.0 - 43 g/L
  - > 43 g/L

n=1,620

p< 0.00001
RR / g/L = 0.95
95% CI 0.93 - 0.97

Transthyretin
- Quartiles
  - < 0.27 mg/L
  - 0.27 - 0.33 mg/L
  - 0.33 - 0.39 mg/L
  - > 0.39 mg/L

p< 0.00001
RR / 0.1 g/L = 0.83
95% CI 0.73 - 0.96
# Recommandation for nutritional follow-up

<table>
<thead>
<tr>
<th>Routine follow-up</th>
<th>K/DOQUI, NKF (1)</th>
<th>EBPG, EDTA (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Serum albumin:</td>
<td>monthly (≥ 40 g/l)</td>
<td>• Dietary interviews: every 6–12 mo. or every 3 mo in patients &gt; 50 y. or hemodialysis &gt; 5 y.</td>
</tr>
<tr>
<td>• % of usual postdialysis BW</td>
<td>• % of standard (NHANES II) BW, every 4 months</td>
<td>• Average postdialysis BW/mo. and % change</td>
</tr>
<tr>
<td>• SGA every 6 months</td>
<td>• Dietary interview and/or diary nPNA, every 6 months</td>
<td>• BMI &gt; 23.0</td>
</tr>
<tr>
<td>• Serum albumin:</td>
<td></td>
<td>• nPNA &gt; 1.0 g/kg ideal BW/day</td>
</tr>
<tr>
<td>• Dietary interview and/or diary nPNA, every 6 months</td>
<td></td>
<td>• Serum albumin: 1 mo. after beginning of hemodialysis and three monthly thereafter: &gt; 40 g/l</td>
</tr>
<tr>
<td>• Serum transthyretin:</td>
<td></td>
<td>• Serum transthyretin: &gt; 300 mg/l</td>
</tr>
<tr>
<td>• Serum cholesterol:</td>
<td></td>
<td>• Serum cholesterol: &gt; minimal laboratory threshold value</td>
</tr>
</tbody>
</table>

## Recommended intakes: Macronutrients

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

3 - Fouque D et al. EBPG. Nephrol Dial Transplant 2007
### Recommended intakes: Micronutrients

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

<table>
<thead>
<tr>
<th>EBPG 2007</th>
<th>Thiamine, Riboflavin, cobalamine, Niacin, Biotine, pentothenic A &amp; tocopherol should be supplemented (expert opinion)</th>
</tr>
</thead>
</table>

Fouque D et al. EBPG. Nephrol Dial Transplant 2007
Nutritional objectives in hemodialysis

Nutritional objectives: 1.2 g protein & 30-35 kcal/kg/d

Mean nutritional intakes in malnourished HD patients:
20-25 kcal/kg/d
0.8-1 g protein/kg/d

Required nutritional supplementation:
5-10 kcal et 0.2-0.4 g de protein/kg/d
Nutritional support

Dietary counselling
Oral supplements
Intradialytic parenteral nutrition
Enteral nutrition

Grade of malnutrition
Spontaneous alimentation
Patient compliance
## Oral supplements: six RCTs in malnourished hemodialysis patients

<table>
<thead>
<tr>
<th>Study design</th>
<th>Energy supply</th>
<th>Protein supply, g</th>
<th>Suppl. length</th>
<th>Improved Nutritional Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acchiardo 1982</td>
<td>AA+ E., n = 7, E., n = 8</td>
<td>660 kcal/d</td>
<td>EAA + His 6.6</td>
<td>105</td>
</tr>
<tr>
<td>Allman 1990</td>
<td>Suppl, n = 9, Cont., n=12</td>
<td>400-600 kcal/d</td>
<td>-</td>
<td>180</td>
</tr>
<tr>
<td>Tietze 1991</td>
<td>Cross-over n = 19</td>
<td>-</td>
<td>Fish protein, 8</td>
<td>120</td>
</tr>
<tr>
<td>Eustace 2000</td>
<td>Suppl, n = 23, Cont., n=24</td>
<td>-</td>
<td>EAA+His+Tyr, 10.8</td>
<td>90</td>
</tr>
<tr>
<td>Hiroshige 2001</td>
<td>Cross-over n=14</td>
<td>-</td>
<td>BCAA, 12</td>
<td>180</td>
</tr>
<tr>
<td>Sharma 2002</td>
<td>Suppl, n = 23, Cont., n=24</td>
<td>500 kcal/HD</td>
<td>15 g /HD</td>
<td>30</td>
</tr>
</tbody>
</table>
Oral supplements: effects of BCAAs

N=44, cross-over study, BCAA 12 g/d during 6 months vs. placebo

Hiroshige K et al. Nephrol Dial Transplant
# Nutritional effect of IDPN: RCTs

<table>
<thead>
<tr>
<th>Study design</th>
<th>Energy (kcal/HD)</th>
<th>Protein (g/HD)</th>
<th>Length (days)</th>
<th>Improved NP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guarnieri</strong> Am J Clin Nutr, 1980</td>
<td>G1: 6, G2: 6, G3: 6</td>
<td>G1: 0, G2: 0, G3: G5%</td>
<td>G1:EAA+his, 14g, G2 :sd AA, 14g, G3 : 0</td>
<td>60</td>
</tr>
<tr>
<td><strong>Cano</strong> Am J Clin Nutr, 1990</td>
<td>G1: 12, G2: 14</td>
<td>G1: 1000, G2: 0</td>
<td>G1: sdAA+tyr,30 g, G2: 0</td>
<td>90</td>
</tr>
<tr>
<td><strong>Navarro</strong> Am J Clin Nutr, 2001</td>
<td>G1: 10, G2: 7</td>
<td>G1: 0, G2: 0</td>
<td>G1: sdAA+tyr,26 g, G2: 0</td>
<td>90</td>
</tr>
<tr>
<td><strong>Cano</strong> Br J Nutr, 2006</td>
<td>G1: 17, G2: 18</td>
<td>G1: 0, G2: 0</td>
<td>G1: AA+G+soja oil, G2: AA+G+olive oil</td>
<td>35</td>
</tr>
</tbody>
</table>
Intradialytic Parenteral Nutrition

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

IDPN initiation

Both ONS and IDPN can only reach the nutritional objectives when spontaneous intakes are \( \geq 20 \text{ kcal} \) & \( 0.8 \text{ g protein/kg/d} \).
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)

- Main objective: to evaluate, in a intention-to-treat study, the effects of a one-year IDPN on nutritional status, morbidity and mortality in malnourished MHD patients.
- Secondary objective: to define the parameters predicting the response to nutritional therapy.
French Intradialytic Nutrition Evaluation Study (Fines)

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

Body weight & albumin changes before, during and after refeeding

<table>
<thead>
<tr>
<th>Body weight, kg</th>
<th>Serum albumin, g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td>31</td>
</tr>
<tr>
<td>57</td>
<td>32</td>
</tr>
<tr>
<td>58</td>
<td>33</td>
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<tr>
<td>59</td>
<td>34</td>
</tr>
<tr>
<td>60</td>
<td>35</td>
</tr>
<tr>
<td>61</td>
<td>36</td>
</tr>
</tbody>
</table>

French Intradialytic Nutrition Evaluation Study (*Fines*)

**Figure 4.** Independent predictors of mortality: Multivariate Cox regression analysis.

**Fines: Do inflamed patients respond to nutritional support?**

Serum albumin, g/L

- **Baseline CRP < 10 mg/L, n=88**
- **Baseline CRP ≥ 10 mg/L, n=86**

Prealbumin, mg/L

- **Baseline CRP < 10 mg/L, n=88**
- **Baseline CRP ≥ 10 mg/L, n=86**

**Fines: Do diabetic patients respond to nutritional support?**

<table>
<thead>
<tr>
<th>Serum albumin, g/L</th>
<th>Prealbumin, mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non diabetics, n=141</td>
<td>Diabetics, n=45</td>
</tr>
</tbody>
</table>

**Tube feeding**

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

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

- Poorly investigated

Decisional algorithm for the management of undernutrition in HD patients

1. Dietary intakes and nutritional status evaluation
2. Moderate undernutrition
   - Spontaneous intakes ≤ 30 kcal/kg/day
   - Spontaneous intakes ≤ 1.1 g protein/kg/day
   - Dietary counselling
   - Oral supplements
   - Lack of compliance
   - No improvement
3. 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
   - Stress conditions
   - Enteral Nutrition if EN is not possible: Central venous PN
   - IDPN
   - No improvement

Use of a renal-specific oral supplement by haemodialysis patients with low protein intake does not increase the need for phosphate binders and may prevent a decline in nutritional status and quality of life.

Denis Fouque¹, Jane McKenzie²,*, Renée de Mutsert³,*, Raymond Azar⁴, Daniel Teta⁵, Mathias Plauth⁶, Noel Cano⁷ and the Renilon Multicentre Trial Study Group.

Energy intake

Protein intake

Nephrol Dial Transplant 2008
How to improve the efficacy of nutritional support?

Muscle growth

Muscle mass

Inadequate intakes
Sedentarity
Hormone dysfunction
Inflammation
Insulin resistance
Metabolic disturbances

Amino acids
Exercise
Hormones

Muscle loss
Multimodal approach of malnutrition

INTEGRATED TREATMENT

- Orexigens
- Healthy diet
- Nutritional support
- Exercise
- Androgens
- Other agents:
  - n-3 FA
  - N-acetylcysteine
  - anti-TNF ..
EFFECTS OF EXERCISE TRAINING ON MYOCYTES

Activation of PPARs

- Modulation of inflammation through NF-kB pathway

Activation of AMPKInase

- Oxidative capacity, GLUT4
- Myofiber type Composition
- Insulin Sensitivity
- Increased endurance
- Cell energy control

Activation of IGF I and II

- Increased protein synthesis
- Decreased protein breakdown

Authors:
- Luquet S et al. Faseb J 2003
- Sandri M et al. PNAS 2006
Daily dialysis

Protein (g/kg/day)

Energy (kcal/kg/day)

- Standard HD
- Daily HD (6 mo)
- Daily HD (12 mo)

Galland et al. Kidney Int 2001
In HD patient, protein-energy wasting is associated with increased morbidity and mortality

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

A multimodal approach of malnutrition, integrating exercise and, in selected patients androgen and daily dialysis may increase the response rate to the treatment of malnutrition

Conclusions
Thank You !!