Does Active Nutritional Interventions Affect Adipokine Secretion in Hip Fracture Operated Elderly Patients?

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Background

• Hip fractures are a significant health risk of the elderly population
• Approximately 50% of elderly hip fractured patients are malnourished on admission to the hospital and numerous others appear so after hospitalization
• Nutritional status and poor intake influence the prognosis of hip fracture patients
• Evidence has shown a positive effect of active nutritional interventions in acute settings including hip fractured patients
Randomized control trials

Tight Calorie Control in geriatric patients following hip fracture decreases complications: A randomized, controlled study☆

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Background: Adipokines

- Adipokines such as ghrelin, leptin, resistin and adiponectin are cytokines secreted by the adipose tissue.
- Adipokines play a role in the energy balance via dual effects on food intake and energy expenditure.
- Several adipokines seem to play a role in bone remodeling and respond to inflammatory states.
<table>
<thead>
<tr>
<th>Mediator</th>
<th>Effect</th>
</tr>
</thead>
</table>
| Adiponectin | Insulin-sensitizing properties  
Anti-inflammatory properties  
Hypoadiponectinemia associated with NASH  
Pro-inflammatory properties on innate and adaptive immunity  
Anorexigenic effects |
| Leptin | Antilipogenic effects in the liver  
Insulin resistance in obesity  
Susceptibility to autoimmune and infectious diseases |
| Ghrelin | Orexigenic action  
Anti-oxidant effect  
Anti-inflammatory effect  
Reduced levels in NAFLD |
| Resistin | Favours insulin resistance  
Interferes with oxidative stress  
Stimulates cytokine release  
Correlation with NAFLD severity and NASH development |
Aim

• To explore the impact of active nutritional interventions on adipokine (ghrelin, leptin, resistin and adiponectin) secretion in hip fractured operated elderly patients and their relationship to nutritional balance and clinical complications.
Methods

• Randomized controlled study.
• Days 1, 3, and 7 post op adipokine (ghrelin, leptin, resistin and adiponectin) levels in hip fractured geriatric patients.
• Patients receiving active nutritional support (tight calorie group) vs standard nutritional support
• The tight calorie group consumed calories with an energy goal determined by repeated REE measurements using indirect calorimetry
Methods

Inclusion
• > 65 years
• <48h after hip fracture
• Surgery was treatment of choice

Exclusion
• Steroids or immunosuppression therapy
• Active oncologic disease
• Multiple fractures, dementia.
• Patients in need of supplemental oxygen
### Results

#### Baseline characteristics of study participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study Group (n=22)</th>
<th>Control Group (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>82.27±6.06</td>
<td>83.75±6.43</td>
<td>0.876</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male n (%)</td>
<td>6 (27.3%)</td>
<td>11 (39.3%)</td>
<td>0.318</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>16 (72.7%)</td>
<td>17 (60.7%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.81±9.52</td>
<td>64.29±11.35</td>
<td>0.86</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.18±3.19</td>
<td>24.67±4.42</td>
<td>0.653</td>
</tr>
<tr>
<td>Mean serum albumin (mg/dl)</td>
<td>3.23±0.34</td>
<td>3.13±0.27</td>
<td>0.282</td>
</tr>
<tr>
<td>Mean blood glucose (mg/dl)</td>
<td>121.54±22.52</td>
<td>118.17±21.09</td>
<td>0.589</td>
</tr>
<tr>
<td>MNA</td>
<td>24.84±2.57</td>
<td>24.50±2.97</td>
<td>0.672</td>
</tr>
<tr>
<td>CCI</td>
<td>0.81±1.05</td>
<td>1.39±1.13</td>
<td>0.073</td>
</tr>
<tr>
<td>CIRS-G</td>
<td>7.45±3.59</td>
<td>7.39±2.60</td>
<td>0.944</td>
</tr>
<tr>
<td>FIM</td>
<td>80.00±17.62</td>
<td>79.1±17.17</td>
<td>0.863</td>
</tr>
<tr>
<td>MMSE</td>
<td>25.16±4.86</td>
<td>23.72±5.19</td>
<td>0.375</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation. Abbreviations: BMI, body mass index; MNA, mini-nutritional assessment; CCI, Charlson's comorbidity index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; FIM, Functional Independence Measure; MMSE, Mini-Mental State Examination.
## Results

### Table 1. Nutritional and Energetic Balance

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study group (n=22)</th>
<th>Control group (n=28)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean energy delivered/day (kcal/day)</td>
<td>1121.31±299.05</td>
<td>777.09±301.23</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean ONS delivered energy/day (kcal/day)</td>
<td>220.33±147.19</td>
<td>94.57±233.82^a</td>
<td>0.845</td>
</tr>
<tr>
<td>Mean protein delivered/day (g/day)</td>
<td>55.90±18.14</td>
<td>37.41±12.44</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean daily energy balance (kcal)</td>
<td>-176.90±273.16</td>
<td>-490.67±355.17</td>
<td>0.104</td>
</tr>
<tr>
<td>Cumulative energy balance (kcal)</td>
<td>-1229.93±1763</td>
<td>-4975.55±4368</td>
<td>0.001</td>
</tr>
</tbody>
</table>

^aIncluded 1 patient who required mechanical ventilation and received 1500 kcal/day via tube-feeding.

Data are expressed as mean ± standard deviation.

REE, resting energy expenditure; kcal, kilocalories; ONS, oral nutritional supplements
## Results

### Table 2. Adipokine Levels Pre Operation, 48h Post Operation and on the 7th Day

<table>
<thead>
<tr>
<th></th>
<th>Study Group</th>
<th>Control Group</th>
<th>P value between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Pre-Operation</td>
<td>48h Post Operation</td>
</tr>
<tr>
<td>Ghrelin (pg/ml)</td>
<td>21</td>
<td>925.3±373.5</td>
<td>1061.3±570.2</td>
</tr>
<tr>
<td>Leptin (pg/ml)</td>
<td>22</td>
<td>16601±9814</td>
<td>8291±4812b</td>
</tr>
<tr>
<td>Resistin (ng/ml)</td>
<td>21</td>
<td>19.3±7.8</td>
<td>19.0±7.87</td>
</tr>
<tr>
<td>Adiponectin (µg/ml)</td>
<td>21</td>
<td>9127±7481</td>
<td>4050±1993</td>
</tr>
</tbody>
</table>

¹Significant increase (p < 0.04) in serum Ghrelin levels from day 1 to day 7 in both study and control groups
²Significant change between the study and control group after 48h (p=0.038)
³Significant decrease (p < 0.001) in serum adiponectin levels from day 1 to day 7 in both study and control groups
N.S.- non significant
Discussion

• Overall, the adipokine kinetics levels did not significantly differ between the study groups.
• However, it seems that the adipokines ghrelin and leptin may be influenced from energetic balance.
Discussion - Ghrelin

• Ghrelin role in osteoblastic proliferation may explain the elevation in both study groups.

• Surprisingly Ghrelin levels were significantly lower in patients with complications during hospitalization
  ➢ lower response of the immune system to acute stress?
  ➢ mild complication?
  ➢ better osteoblastic proliferation?
Discussion - Leptin

• Several studies suggest a negative feedback control of leptin on bone remodeling.
• May explain the decline in both groups
• Lower acute inflammatory response in the intervention group or faster bone remodeling?
• Elevation in the intervention group may suggest leptin’s role in the body's energetic homeostasis
Discussion - Adiponectin

• The finding support adiponectin’s biphasic behavior theory, in response to acute stress.

• The short duration of the decline and the absence of change between the groups, suggests that adiponectin has no significant role in bone homeostasis or energetic balance in elderly patients post hip fracture.
Limitation

• Short duration and relatively small sample base.
• No post discharge FU.
• Relatively good nutritional status of the study participants.
Conclusion

• We found no correlation between improved energy balance in geriatric hip fractured patients and adipokine levels.
• Several changes in adipokine behaviors were observed.
• Differences may be the results of adipokine involvement in bone homeostasis and inflammatory states.
• A larger scale research study is needed to expand our knowledge of these fascinating cytokines and their interactions with nutritional support.
I am ready for Questions 😊