Original Article

Inverse Association of Serum Leptin with Serum C-reactive protein (CRP) in Regular Hemodialysis Patients.

Hamid Nasri, Azar Baradaran

From Hemodialysis section, Hajar Medical, Educational and Therapeutic Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

Correspondence: Dr Hamid Nasri, Email: hamidnasri@yahoo.com

Received:October 3, 2005   Accepted:December 20, 2005

ABSTRACT

Objective: To elucidate whether and how in patients with uremia on hemodialysis the level of CRP as the marker of inflammation correlate with serum leptin.

Patients and Methods: Serum leptin and CRP were determined on patients with ESRD on hemodialysis

Results: The total patients were 36 (f =15, m=21). The mean patient's age were 46 (±16) years. The median length of the time patients had received hemodialysis was 19 months. The mean serum CRP was 8.7±6.6 mg/L. The mean serum leptin was 9.4±14 ng/ml.

Conclusion: We found a significant inverse correlation of serum leptin with serum CRP (r= -0.57, p = 0.041). Our data supports the hypothesis that in patients on hemodialysis, the association of leptin with CRP levels was inverse which could show the positive effects of leptin on nutrition and support the theory of protective effects (reverse epidemiology) of leptin in hemodialysis patients.(Rawal Med J 2006;31:10-13)

Keywords: Hemodialysis, End-stage renal failure, Leptin, C-reactive protein(CRP)

INTRODUCTION

The adipose tissue cytokine leptin is a small peptide hormone that is mainly but not exclusively, produced in adipose tissue.\(^1\) Leptin exerts several important metabolic effects on peripheral tissue, including modification of insulin action, induction of
angiogenesis, and modulation of the immune system.\textsuperscript{1-3} Several recent studies have demonstrated that leptin is cleared principally by the kidney. Thus serum leptin concentrations are increased in patients with chronic renal failure and those undergoing maintenance dialysis,\textsuperscript{2} and it has been speculated that hyperleptinemia may contribute to uremic anorexia and malnutrition.\textsuperscript{4,5} In the general population, leptin is considered an “appetite inhibitor,” but in contrast to preliminary studies its role in chronic kidney disease (CKD) and hemodialysis (HD) patients is not completely understood. Although serum leptin is generally elevated in CKD and HD patients, some other studies have not been shown to be a cause of uremia-related anorexia.\textsuperscript{6-7}

More recent studies in maintenance dialysis patients suggest a paradoxically inverse association between higher serum leptin and improved markers of nutritional status,\textsuperscript{6-7} a finding that is consistent with the theory of reverse epidemiology.\textsuperscript{8} Indeed, leptin, similar to serum albumin, has been reported to be a negative acute phase reactant in end-stage renal failure patients.\textsuperscript{7} C-reactive protein (CRP) is an acute phase protein whose synthesis in the liver is regulated by different cytokines, particularly interleukin 6 (IL-6). Plasma levels of CRP in the absence of active disease are low, but can rise up to 1000-fold in patients with an inflammatory reaction. Besides being a marker of inflammation, CRP itself may have proinflammatory properties since it can activate the complement system.\textsuperscript{8,9} Thus, elevated plasma concentrations of CRP is a sensitive marker of underlying systemic inflammation.\textsuperscript{10-12} Serum CRP concentrations have also been found to be significantly elevated in hemodialysis patients\textsuperscript{13,14} and reflects chronic inflammation, and as an acute-phase reactant, is a sensitive and independent marker of malnutrition.\textsuperscript{15} The aim of the present study was to elucidate whether and how in patients with uremia on hemodialysis the level of CRP as the marker of inflammation correlate with serum leptin.

\section*{PATIENTS AND METHODS}
This cross-sectional study was conducted on patients with end-stage renal disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. The study was done in hemodialysis section of Hajar Medical, educational and Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord, Iran. It was carried out from July to August of 2005.
Patients with active or chronic infection and using NSAID drugs were excluded. Blood samples were collected after an overnight fast and complete blood count were measured using Sysmex-KX-21N cell counter. Levels of CRP, calcium (Ca), phosphorus (Phos), cholesterol (chol), magnesium (Mg), iron, albumin (alb) and ferritin were measured using standard kits. Intact serum PTH (iPTH) was measured by the radioimmunoassay (RIA) method using DSL-8000 kits of USA (normal 10-65 pg/ml). Serum Leptin (normal for males 3.84±1.79 and for females 7.36±3.73) ng/ml) was measured by enzyme-linked immunosorbent assay (ELISA) method using DRG kits of Germany. Plasma HCO₃⁻ was measured by arterial blood gas analysis. Duration and doses of hemodialysis treatment were calculated from the patients' records. The duration of each hemodialysis session was 4 hours. For the efficacy of hemodialysis the urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data. Body mass index (BMI) was calculated using the standard formula (postdialysis).

According to the severity, each patient was being treated with oral active vitamin D₃ (Rocaltrol), calcium carbonate, Rena-Gel capsules, IV iron therapy with iron sucrose (venofer) at various doses after each dialysis session, 6mg folic acid daily, 500mg L-carnitine daily, oral vitamin B-complex tablet daily and 2000U IV Eprex (recombinant human erythropoietin, rHuEPO) after each dialysis session routinely. Results are expressed as the mean ± SD and median values. Statistical correlations were assessed using partial correlation test. For leptin correlation, the logarithm of serum leptin values was used. All statistical analyses were performed using SPSS (version 12.00). Statistical significance was determined at a p-value <0.05.

RESULTS
There were 36 patients (f =15, m=21). The mean age was 46±16 years. The mean length of the time patients had received hemodialysis was 32±36 months (table 1). A significant inverse correlation of serum leptin with serum CRP (r = -0.57, p = 0.041) (adjusted for age, duration and doses of dialysis, gender, BMI, URR, DM, plasma HCO₃⁻, serum Mg, Ca, P , iPTH, serum iron, ferritin, BUN, Creat, Hb and chol) was seen (fig.1).
DISCUSSION
In this study we found a significant inverse correlation of serum leptin with serum CRP. The increased levels of leptin in hemodialysis patients are not only due to retention of the hormone, but probably from increased production. Anorexia of hemodialysis patients has been attributed to the increased leptin levels, even if this is largely a hypothesis.\textsuperscript{18} Although three previous longitudinal/observational studies in maintenance hemodialysis patients indicate that individuals with high serum leptin levels are more likely to lose weight.\textsuperscript{19} However, more recent studies in maintenance dialysis patients suggest a paradoxically inverse association between higher serum leptin and improved markers nutritional status,\textsuperscript{6-7} a finding that is consistent with the theory of reverse epidemiology.\textsuperscript{8} Indeed, leptin, similar to serum albumin, has been reported to be a negative acute phase reactant in ESRD patients.\textsuperscript{7}
Table 1: Demographic data of patients.

<table>
<thead>
<tr>
<th></th>
<th>Total patients= 36</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16</td>
<td>80</td>
<td>46±16</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>DH* (months)</td>
<td>2</td>
<td>156</td>
<td>32±36</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Dialysis dose (sessions)</td>
<td>36</td>
<td>1584</td>
<td>294±393</td>
<td>156</td>
<td></td>
</tr>
<tr>
<td>URR %</td>
<td>39</td>
<td>76</td>
<td>59±9</td>
<td>57.5</td>
<td></td>
</tr>
<tr>
<td>Creat mg/dl</td>
<td>3</td>
<td>18</td>
<td>9±3</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>BUN mg/dl</td>
<td>30</td>
<td>180</td>
<td>82±33</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Ca mg/dl</td>
<td>5</td>
<td>10</td>
<td>7.6±0.9</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Alb g/dL</td>
<td>2.4</td>
<td>4.8</td>
<td>3.8±0.5</td>
<td>3.95</td>
<td></td>
</tr>
<tr>
<td>CRP mg/L</td>
<td>3</td>
<td>40</td>
<td>8.7±6.6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Hgb g/dl</td>
<td>5</td>
<td>13</td>
<td>9±2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>HCT %</td>
<td>14</td>
<td>40</td>
<td>28±6</td>
<td>29.5</td>
<td></td>
</tr>
<tr>
<td>Leptin ng/ml</td>
<td>0.1</td>
<td>73</td>
<td>9.4±14</td>
<td>5.75</td>
<td></td>
</tr>
<tr>
<td>Mg mg/dl</td>
<td>1.6</td>
<td>73</td>
<td>9.4±14</td>
<td>5.75</td>
<td></td>
</tr>
<tr>
<td>iPTH pg/ml</td>
<td>16</td>
<td>1980</td>
<td>434±455</td>
<td>309</td>
<td></td>
</tr>
<tr>
<td>HCO3- mEq/L</td>
<td>14</td>
<td>25</td>
<td>20±2.5</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>16</td>
<td>34</td>
<td>22±4.4</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Iron micg/dl</td>
<td>1515</td>
<td>518±299</td>
<td>426</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferritin ng/dl</td>
<td>59</td>
<td>211</td>
<td>117±40</td>
<td>115</td>
<td></td>
</tr>
</tbody>
</table>

*Duration of hemodialysis treatment.

Although in the general population, leptin is considered an “appetite inhibitors,” its role in ESRD patients is somewhat unconventional. Serum leptin is generally elevated in ESRD patients, but this has not been shown to be related to anorexia, in contrast leptin has been shown to act synergistically with erythropoietin to stimulate the end-stage colony-forming-unit erythroid in humans.²⁰ Our data indirectly supports the some previous studies regarding the hypothesis that in patients on hemodialysis, leptin is a negative acute phase reactant and leptin might have a positive effects on nutrition and support the theory of protective effects of leptin in hemodialysis patients.

REFERENCES


17. http://www.halls.md/body-mass-index/av.htm

