Determination of hepcidin (25) level in hemodialysis Iraqi male patients and its relation with erythropoietin and some biochemical parameters

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Abstract

Background: Anemia is a common finding in patients with renal failure disease and it is, primarily, due to reduced production of iron and erythropoietin. Therefore, the aim of current study was to evaluate the relationship between serum level of hepcidin 25, on the one hand, and levels of serum iron, total iron-binding capacity, serum erythropoietin and transferrin saturation% in Iraqi male patients undrgoning haemodialysis. Methods: Serum from75 males in the end stage of hemodialysis, as group one, and 25 Iraqi healthy malecontrols, as group two, were recruited in this study. Results: Data from current study showed significant increase in hepcidin 25 and significant decrease in serum iron, total iron-binding capacity, transferrin saturation % and erythropoietin in group one as a compered with group two. In addition, current study showed non-significant positive and negative correlations between hipcidin 25 and serum iron, transferrin saturation%, total iron-binding capacity and erythropoietin. Conclusion: Patients with end-stage renal disease need to take iron supplements to correct iron-deficiency anaemia that probably results from elevated hepcidin 25 levels in those patients.

Keywords: End stage hemodialysis, hepcidin 25, serum iron, erythropoietin, total iron-binding capacity, transferrin saturation%.


Introduction

Anemia is a major factor that limits the quality of life in chronic renal failure patients and may affect their morbidity and mortality (1,2). It is primarily due to reduced production of erythropoietin by the kidney (a reflection to reduced renal mass) and secondary to shortened red cell survival (3,4). Hepcidin is a recently discovered low-molecular weight protein that plays an important role in iron homestasis (5). It is primarily produced by hepatocytes as an 84-amino acid pre prohepcidin and subsequent post translational processing results in the biologically active 25-amino acid to form hepcidin (25) which is secreted in the plasma and excreted in the urine (6,7). Hepcidin inhibits the release of iron from macrophages and absorption of dietary iron from intestine (8). Synthesis of hepcidin is increased by infection or inflammation (9). Also, both serum hepcidin 25 and total hepcidin levels have been found to be elevated in as series of patients with renal dysfunction (10). On the other hand, erythropoietin is a glycoprotein hormone that controls production of red blood cells precursors in the bone marrow (11). It is synthesized by renal peritubular cells in adults and has been shown that it increases iron absorption by suppressing hepcidin (25) hormone (12). Therefore, the aim of current study was to evaluate the relationship between serum levels of hepcidin 25, on the one hand, and levels of serum iron, total irin
binding capacity, serum erythropoietin and transferrin saturation% in Iraqi male patients undergoing haemodialysis.

Methods

Patient study

Serum samples were taken from (75) male patients suffering from end stage renal failure and undergoing hemodialysis with age range of (30-45) years. The study was conducted at the Iraqi dialysis center in Baghdad Teaching Hospital from January 2019 to March 2019. In addition, (25) Iraqi males were recruited as controls. All patients suffering from anemia (Hb \( \leq 11 \) mg/dl). Hepcidin 25 and erythropoietin levels were determined by sandwich enzyme immunoassay ELIZA and serum iron was determined by atomic absorption methods.

Statistical analysis

The data of present study were expressed as (mean ± SD). In addition, t-test was used for comparison study between patients and control groups. Also, a P value ≤0.05 was considered significant.

Results and Discussion

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients (N= 75)</th>
<th>controls (N= 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepcidin 25 (pg/ml)</td>
<td>26.748±1.42</td>
<td>15.972±1.3</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>S. iron (mg/dl)</td>
<td>56.984±3.74</td>
<td>87.726±4.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>TIBC (mg/dl)</td>
<td>174.612±1.550</td>
<td>181.9±2.3</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>TS%</td>
<td>32.364±2.081</td>
<td>48.516±3.4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Erythropoietin (u/ml)</td>
<td>6.67±1.5107</td>
<td>16.056±2.7</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Data in the table were expressed as mean ± SD.

The results in Table (1) showed significantly elevated levels of hepcidin 25 in Iraqi patients compared with their healthy controls. Also, results of current study showed significant decrease in levels of serum iron, TIBC, TS% and erythropoietin in hemodialysis patients compared with their healthy controls. Hepcidin 25, the bioactive form of hepcidin, is a key regulator of iron homeostasis as it induces internalization and degradation of ferroportin, a cellular exporter on enterocytes, macrophages and hepatocytes (13,14,15). It is well-known that iron is an essential element for all living organisms and its homeostasis is tightly regulated in mammals so it is regulated by hepcidin 25 (16). A higher levels of hepcidin 25 has been shown in patients with end stage renal disease (ESRD) on dialysis and it was observed that hepcidin is the intermediary between available iron stores, on the one hand, and Erythropoiesis, on the other hand (17, 18). Therefore, hepcidin might be useful to assess functional iron availability in patients with renal failure as high levels may indicate a blockade of iron release from its stores (19). Anemia is commonly seen in all stages of renal disease, but is much more common in end-stage renal disease (20,21). The main causes of anemia in these patients are decreased erythropoietin (EPO) production, chronic inflammation and iron deficiency (22). Hemodialysis (HD) is considered an inflammatory state and increased serum hepcidin 25 levels have been found in patients with ESRD on maintenance (HD) (23). These increased levels of hepcidin 25 maybe due to functional iron deficiency anemia and low grad inflammation (24).
Transferrin (TS) is a glycoprotein with two iron-binding domains that is synthesized in the liver \(^{(25)}\). It is most important for transporting iron into cells and in preventing iron to be toxic free radical. In addition, the sum level of all iron binding sites on plasma transferrin is known as Total Iron-Binding Capacity (TIBC) and Transferrin Saturation (TS) is the ratio of total number of occupied iron binding sites to TIBC \(^{(26)}\). So, the decrease in (TS) and (TIBC) may be due to decreasing iron levels. Therefore, the deficiency of iron, TS, TIBC, erythropoietin and hyperhepcidin 25 in patients with ESRD maybe due to anemia in that stage. So the patients in ESRD must take supplementation of erythropoietin to substitute the deficiency of iron which is the main cause of anemia. Results in Table (2) showed a non-significant negative correlation between hepcidin 25 and serum iron, TIBC and TS\% while there was non-significant positive correlation with serum erythropoietin level.

Table (2): Correlation between hepcidin 25 and serum iron, TIBC, TS\% and erythropoietin in Iraqi male patients with ESRD undergoing hemodialysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>S. iron µg/dl</th>
<th>TIBC (µg/dl)</th>
<th>%TS</th>
<th>Erythropoietin (u/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepcidin 25</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(pg/ml) r</td>
<td>-0.059</td>
<td>-0.236</td>
<td>-0.028</td>
<td>0.078</td>
</tr>
<tr>
<td>p</td>
<td>0.779</td>
<td>0.255</td>
<td>0.89</td>
<td>0.711</td>
</tr>
</tbody>
</table>

Conclusion

Patients with end-stage renal disease need to take iron supplements to correct iron-deficiency anaemia that probably results from elevated hepcidin levels in those patients.

Ethical Clearance: The research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of interest: The authors declare that they have no conflict of interest.

Funding: Self-funding.

References:


