Effect of EDTA Chelation on Serum Iron

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ABSTRACT: One hundred and twenty-two patients suffering from various chronic degenerative disorders were evaluated objectively for fasting serum iron values before and after EDTA (ethylenediamine tetracetic acid) chelation plus multivitamin mineral (excluding iron) supplementation. After 30 intravenous 3 gram treatments of EDTA, average serum iron levels dropped 17.5% (t = 4.230, p < 0.001). Abnormally high initial iron decreased 43.1% (t = 7.602, p < 0.001), while low initial iron increased 41% (t = 3.30, p < 0.010).

Introduction

This continues a series of papers analyzing effects of EDTA chelation therapy (1-13). For years EDTA has been used to remove toxic heavy metals in the human body (14-16). This research in particular is studying fasting serum iron values before and after EDTA infusions.

Patients and Methods

Over a period of 17 months, one hundred and twenty-two patients suffering from degenerative disorders participated in this experiment in a private practice environment. Included were 73 males ranging in age from 32-84 years old (with a mean and a standard deviation of 61.5 ± 10.10) and 49 females ranging in age from 39-84 years old (with a mean and a standard deviation of 64.0 ± 10.30).

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At the initial examination 13.0 ml of fasting blood was collected in a sterile iron-free collection tube by vacutainer using a 21 gauge stainless steel needle. The collection tube contained inert Barrier material, a clot activator on interior walls, and had a silicone lubricated stopper (Barrier tube SST #6512). Blood was set aside for 15 minutes, then centrifuged for 10 minutes, avoiding hemolysis.

Serum iron was measured in a Technicon SMA-II autoanalyzer using method #S4F-0025FDO (17). The following reagents (a,b,& c) were placed in the Technicon PN 157-A021-01 analytical cartridge, then transferred to the SMA II at the given flow rates. The absorbance (A) of the analytical stream was measured at 1.5nM. The linearity range was −0 mcg/dl to 500 mcg/dl and the sensitivity coefficient was −0.0035 (A) per unity of concentration (17).

Reagents

a. Acid diluent flow rate (0.42ml/min.) ascorbic acid 1.0g (Technicon Product #T21-0153)
   2 vials
   iron acid reagent (Technicon Product #T21-0654)
   QS 200ml
   One liter contained:
   Water
   Hydrochloric acid 10.7gm
   Sodium chloride 35.1gm
   Neocuprone hydrochloride 1.0gm
   Surfactant

Preparation Instructions of Acid Diluent

Place approximately 100ml of iron acid reagent in a 200 ml iron free volumetric flask. Add 2 vials of ascorbic acid and stir the contents of the flask until completely dissolved. Dilute to volume with iron acid reagent, and mix.

b. Sodium acetate 1.0 N (Technicon Product #T01-0655)
   Flow rate (0.23 ml/min.)

c. Iron color reagent (Technicon Product #T01-0656)
   Flow rate (0.80 ml/min.)
   One liter contained:
   water
   3-(2-pyridyl)-5,6-bis (4-phenyl-sulfonic acid)-1,2,4-triazine,
   disodium salt 350mg
   Surfactant
Summary of SMA-II Procedure for Serum Iron

3-ml of the serum sample was added to an air-segmented stream of the acid diluent which freed the iron from the transferrin and reduced it to the ferrous state. The acid diluent contained sodium chloride to prevent Donnan equilibrium effects (18,19) and neocuproine hydrochloride to reduce copper interferences (17). Free ferrous ions were removed from serum interferences by an air-segmented stream of the iron color reagent. A constant pH was maintained by addition of sodium acetate (19). The red ferrozine complex formed in direct proportion to the amount of ferrous ions present (17).

After 30 intravenous EDTA infusions serum iron levels were tested using methods identical to those at the initial examination.

Results

The data were analyzed from three different perspectives; first, serum iron concentrations of the entire group before and after treatment, then those with initially elevated serum iron, and finally, those with initially low serum iron levels.

After the series of EDTA infusions, the decreases in serum iron concentrations were statistically significant for both males and females within the whole group. Table 1 reveals that serum iron decreased overall by 17.15% (t=4.230, p .001). For the men the decrease was 14.14% (t=2.832, p .01) and 21.69% for the women (t=3.268, p .001).

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
</table>

Serum Iron Values in mcg/dl before and after EDTA Chelation Therapy

<table>
<thead>
<tr>
<th>Total Group</th>
<th>Initial</th>
<th>Final</th>
<th>Decrease (%)</th>
<th>t-Score</th>
<th>p-Value</th>
<th>Age (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=122</td>
<td>92.55</td>
<td>76.68</td>
<td>15.87±3.45</td>
<td>4.2300</td>
<td>0.001*</td>
<td>62.5±3.45</td>
</tr>
<tr>
<td>Men</td>
<td>n=73</td>
<td>93.03</td>
<td>78.88</td>
<td>14.15±4.54</td>
<td>2.8370</td>
<td>0.010*</td>
</tr>
<tr>
<td>Women</td>
<td>n=49</td>
<td>91.84</td>
<td>71.92</td>
<td>19.92±5.29</td>
<td>3.2684</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*Statistically significant difference of the means
### TABLE 2

**Serum Iron Values in mcg/dl before and after EDTA Chelation Therapy Comparing Individuals with Initial Levels Higher than 30.0% Above Mean**

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Final</th>
<th>Decrease (mcg/dl)</th>
<th>Decrease (%)</th>
<th>t-Score</th>
<th>p-Value</th>
<th>Age (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group</td>
<td>149.83</td>
<td>84.44</td>
<td>65.39 ± 8.6</td>
<td>(-43.6%)</td>
<td>7.602</td>
<td>&lt;0.001*</td>
<td>62.44 ± 6.83</td>
</tr>
<tr>
<td>Men</td>
<td>149.10</td>
<td>88.00</td>
<td>61.10 ± 11.8</td>
<td>(-41.0%)</td>
<td>5.465</td>
<td>&lt;0.001*</td>
<td>60.30 ± 6.4</td>
</tr>
<tr>
<td>Women</td>
<td>150.75</td>
<td>80.00</td>
<td>70.75 ± 14.07</td>
<td>(-47.04%)</td>
<td>5.026</td>
<td>&lt;0.001*</td>
<td>65.10 ± 3.6</td>
</tr>
</tbody>
</table>

*Statistically significant difference of the means.

### TABLE 3

**Serum Iron Values in mcg/dl before and after EDTA Chelation Therapy Comparing Individuals with Initial Levels Lower than 30.0% Below Mean**

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Final</th>
<th>Increase (mcg/dl)</th>
<th>Increase (%)</th>
<th>t-Score</th>
<th>p-Value</th>
<th>Age (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group</td>
<td>40.81</td>
<td>68.95</td>
<td>28.14 ± 5.96</td>
<td>(+41.00)</td>
<td>3.300</td>
<td>&lt;0.001*</td>
<td>63.53 ± 5.18</td>
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<tr>
<td>Men</td>
<td>52.88</td>
<td>77.31</td>
<td>24.43 ± 7.47</td>
<td>(+31.61%)</td>
<td>3.340</td>
<td>&lt;0.010*</td>
<td>60.77 ± 3.02</td>
</tr>
<tr>
<td>Women</td>
<td>44.13</td>
<td>55.38</td>
<td>11.25 ± 9.80</td>
<td>(+10.40%)</td>
<td>1.159</td>
<td>&gt;0.500</td>
<td>68.00 ± 8.70</td>
</tr>
</tbody>
</table>

*Statistically significant difference of the means.
Serum iron concentrations were considered to be abnormally high or low when plus or minus 30.0% of the mean, calculated from the normal range. Table 2 reveals a 43.6% decrease in serum iron concentrations in 18 subjects whose initial values were abnormally high (p .001).

There were 21 subjects with serum iron concentrations that were abnormally low at the outset of the study. As a group, there was a slight increase which did not reach statistical significance. However, in the 13 men there was a mean increase of 31.6% (t=3.34, p .01), whereas those of the women only increased by 10.4% (t=1.159, p 0.05) (Table 3).

Discussion

Iron has been clearly established as a necessary catalyst for many forms of free radical reactions (14,20-22). Disorders such as chronic liver disease, congestive cardiomyopathy, and neoplastic disease of the bone marrow have been associated with high serum iron levels (23-25). Iron chelators, notably EDTA, have been mentioned as possible therapeutic alternatives to prevent reperfusion injury following a pathological process that results in acute tissue anoxia followed by a rapid re-introduction of oxygen (26). This mechanism involves the generation of superoxide radicals by free tissue iron.

\[
\text{Fe}^{++} + \text{O}_2 \rightleftharpoons \text{Fe}^{++} + \text{O}_2^-
\]

Iron then becomes doubly pathogenic because it can further catalyze the breakdown of superoxide radicals into hydroxyl free radicals (\text{OH}\cdot) which are even more devastating to the tissue than are superoxide radicals (27).

\[
2\text{O}_2 + 2\text{H}^+ \rightleftharpoons \text{H}_2\text{O}_2 + \text{O}_2
\]
\[
\text{H}_2\text{O}_2 + \text{Fe}^{++} \rightleftharpoons \text{Fe}^{++} + \text{OH}^- + \text{OH}^-
\]

Reducing tissue iron concentrations, therefore, is of paramount importance to reduce free radical injury and cell destruction. The results of this study reinforce previous findings that EDTA will aid in control of excess iron (14,20-22). Reduction may serve to retard lipid peroxidation and therefore diminish chain reactions of unwanted free radical reactions. The data presented here suggest that EDTA infusions
will remove free iron. An additional goal of the research was to show that this therapy did no harm. It might not be clinically desirable to lower serum iron in patients with established low concentrations. However, when these subjects with low serum iron levels were examined, it was noted (Table 3) that there was a tendency for them to increase or remain the same. Hence EDTA may have a paradoxical homeostatic effect on the serum iron similar to that on creatinine (1) and bone calcium (3). It is suggested that direction for future research should expand on this study by analysis of ferritin levels before and after EDTA chelation therapy.

References
