NUHS Journal Club
Topic: Chelation Therapy

Date: 9-20-2006

Group Members:

Christopher Wolcott DC
Jerrilyn Cambron DC, PhD
Barbara Sullivan PhD
**Patient**: A 59 yoWM with angina pectoris and confirmed coronary artery disease wants to know if chelation therapy is effective in treating atherosclerosis. His GP has recommended angioplasty and the patient is considering alternative options.

<table>
<thead>
<tr>
<th><strong>Patient, Population, Disease</strong></th>
<th>59 year old white male with angina and confirmed coronary artery disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention, Comparison (optional)</strong></td>
<td>Chelation therapy, Angioplasty</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Clinical improvement</td>
</tr>
</tbody>
</table>

**Question**: Is chelation therapy as effective as angioplasty in improving clinical outcomes in adults with coronary artery disease? OR Is chelation therapy effective in improving clinical outcomes in adults with coronary artery disease?
Search Strategy

• Search Program(s):
  – EbscoHost, Scirus.com and PubMed

• Databases searched:
  – Medline, CINAHL, AMED, Academic Search Premier, and Cochrane Database of Systematic Reviews

• Key Search Terms:
  – Coronary artery disease, chelation, atherosclerosis

• Operators used:
  – Chelation AND "coronary artery disease" NOT (heavy OR thalassemia)

• Limits Used:
  – In EBSCO: Scholarly (Peer Reviewed) Journals
  – In PubMed: Ages: Adult, Language: English, Published within the last: 10 years
  – With Scirus: only Journal Sources

• Additional Strategies used:
  – With PubMed and Ebsco: checked “related articles”
  – We checked the Reference and Introduction section of all papers

• Where the paper was located:
  – We found this paper in Medline by searching both PubMed and Scirus.com

• Full text access:
  – Full text was obtained from JAMA online using the NUHS LRC password
Search Strategy Resources


**EbscoHost on campus link:**
(NUHS home > Student Services > LRC > databases > Via EbscoHost login


**EbscoHost off campus:**
Passords document > ..\..\LRC Passwords 2006.07.31.doc

- **Service:** EbscoHost [http://search.epnet.com/](http://search.epnet.com/)
- **Login Info:** User ID: s9817535 **Password:** password

**A-to-Z:** Provides users with a single, comprehensive online list of almost 10,000 electronic journals we have access to. Users can search for journals by keyword or browse an alphabetical list by title or subject

http://atoz.ebsco.com/home.asp?Id=NATIEB8F
then, probably use the [LRC password list](#) IDs and passwords
Search Strategy Resources

PubMed Tutorials

**Pub Med Search Tutorial -- Basics**
This link brings you to the Pub Med web page that links you to several different, short tutorials regarding how to search PubMed using simple subject, author, journal titles and dates. View the general Pub Med Quick Start and Searching Pub Med tutorials (on the left hand side). Click on the "Quick Tour“ icons for an automated video tour.

**Pub Med Tutorials - Refining and Saving**
These short tutorials, again on the National Library of Medicine's PubMed Tutorial page provide more detailed information about refining your searches to find more relevant citations, using MeSh terms and limits, as well as saving your search queries and results.

EbscoHost Tutorials

**EBSCO host tutorial: search basics**
This links you to the EBSCO host database search tutorials. The tutorials are very short and will help you form effective searches to access NUHS subscribed journals.
Search Strategy

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Chelation Therapy for Ischemic Heart Disease
A Randomized Control Trial
Knudtsen M., Wyse D., Galbraith P., Brant R., Hidebrand K., Peterson D., Richardson D., Burkart C., Burgess E.

Journal of the American Medical Association (JAMA)
January 23/30 2002
Volume 287, Number 4
Pages 481-486

Type of study: Therapy
Study Design: Randomized Controlled Trial
Introduction

• Ischemic heart disease is the leading cause of death in the United States
• Chelation therapy is a widely used alternative therapy for ischemic artery diseases that involves administration of the chelating agent EDTA
• The authors estimate that in the United States, 100,000 people have tried chelation therapy for ischemic heart disease
• Significant anecdotal evidence exists in support of chelation therapy
• There is a lack of scientific evidence to support the use
Methods

3140 Patients Screened

2969 Excluded
- 690 Refused Consent
- 576 Were Unable to Perform Treadmill/ECG
- 470 Had Nonsignificant Disease
- 412 Had Planned Revascularization
- 296 Had Comorbidity Factors
- 137 Were Unavailable for Follow-up
- 31 Had Previous EDTA Therapy
- 21 Died
- 336 Other

171 Eligible for Treadmill Test

87 Did Not Meet Treadmill Test Criteria

84 Randomized

43 Assigned to Receive Placebo Therapy
- 4 Unable to Complete Protocol
  - 1 Cancer
  - 1 Pneumothorax
  - 1 Unstable Angina and Angioplasty
  - 1 Coronary Artery Bypass Graft Surgery
- 39 Completed Trial and Treadmill Test at 27 Weeks
- 43 Included in Analysis

41 Assigned to Receive EDTA Therapy
- 2 Unable to Complete Protocol
  - 1 Creatinine Elevated Above Study Limit
  - 1 Hospitalization for Unstable Angina and Withdrawal of Consent
- 39 Completed Trial and Treadmill Test at 27 Weeks
- 41 Included in Analysis
<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 43)</th>
<th>Chelation (n = 41)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean (SD), y</strong></td>
<td>55 (8.5)</td>
<td>56 (9.1)</td>
<td>.86</td>
</tr>
<tr>
<td><strong>Male sex, No. (%)</strong></td>
<td>32 (83.7)</td>
<td>33 (85.4)</td>
<td>.93</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction, mean (SD), %</strong></td>
<td>58 (13.1)</td>
<td>62 (11.2)</td>
<td>.11</td>
</tr>
<tr>
<td><strong>Extent of CAD, No. (%)</strong></td>
<td>17 (39.5)</td>
<td>21 (51.2)</td>
<td>.39</td>
</tr>
<tr>
<td>Single vessel</td>
<td>26 (60.5)</td>
<td>20 (48.8)</td>
<td></td>
</tr>
<tr>
<td>Multivessel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CCS angina class, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>14 (32.6)</td>
<td>12 (29.3)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>17 (39.5)</td>
<td>22 (53.7)</td>
<td>.53</td>
</tr>
<tr>
<td>II</td>
<td>9 (20.9)</td>
<td>5 (12.2)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>2 (4.7)</td>
<td>2 (4.9)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1 (2.3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Previous cardiac events, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>12 (27.9)</td>
<td>20 (48.8)</td>
<td>.08</td>
</tr>
<tr>
<td>Percutaneous coronary intervention</td>
<td>19 (44.2)</td>
<td>19 (46.3)</td>
<td>.98</td>
</tr>
<tr>
<td>Coronary artery bypass graft surgery</td>
<td>12 (27.9)</td>
<td>10 (24.4)</td>
<td>.91</td>
</tr>
<tr>
<td><strong>Comorbid conditions, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (14.0)</td>
<td>7 (17.1)</td>
<td>.93</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (65.1)</td>
<td>23 (56.1)</td>
<td>.53</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>34 (79.1)</td>
<td>34 (82.9)</td>
<td>.86</td>
</tr>
<tr>
<td><strong>Laboratory values, mean (SD), mg/dL†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>185 (34.7)</td>
<td>185 (30.9)</td>
<td>.77</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>43 (8.9)</td>
<td>45 (13.1)</td>
<td>.54</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>106 (27.0)</td>
<td>107 (22.4)</td>
<td>.97</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>177 (132.7)</td>
<td>177 (79.6)</td>
<td>.97</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.0 (0.20)</td>
<td>1.0 (0.23)</td>
<td>.19</td>
</tr>
<tr>
<td><strong>Medication use, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>32 (74.4)</td>
<td>30 (73.2)</td>
<td>.90</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>23 (53.5)</td>
<td>19 (46.3)</td>
<td>.51</td>
</tr>
<tr>
<td>Nitrates</td>
<td>19 (44.2)</td>
<td>10 (24.4)</td>
<td>.06</td>
</tr>
<tr>
<td>Triple therapy‡</td>
<td>11 (25.6)</td>
<td>5 (12.2)</td>
<td>.12</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>13 (30.2)</td>
<td>11 (26.8)</td>
<td>.73</td>
</tr>
<tr>
<td>Aspirin</td>
<td>41 (95.3)</td>
<td>38 (92.7)</td>
<td>.61</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
<td>37 (86.0)</td>
<td>28 (68.3)</td>
<td>.05</td>
</tr>
</tbody>
</table>

*CAD indicates coronary artery disease; CCS, Canadian Cardiovascular Society; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and ACE, angiotensin-converting enzyme. The CCS scale is measured from I to IV, with a higher score indicating greater severity.
†To convert cholesterol values to mmol/L, multiply values by 0.0259. To convert triglycerides to mmol/L, multiply values by 0.0113. To convert creatinine to µmol/L, multiply values by 88.4.
‡Triple therapy includes β-blockers, calcium channel blockers, and nitrates.
Methods cont.

• The primary end point was the change in time to reach at least 1 mm of ST-segment depression at the 27-week evaluation.

• All patients were followed for 1 year from randomization.
  – All clinical events were tabulated, including death, myocardial infarction, coronary artery bypass graft surgery, and percutaneous coronary intervention.

• Quality of life surveys and VO2 max were also evaluated.
Results

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Placebo Group</th>
<th>Chelation Group</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline, Mean (SD)</td>
<td>27 Weeks, Mean (SD)</td>
<td>Change, Mean (95% CI)</td>
</tr>
<tr>
<td>Time to ischemia, s</td>
<td>572 (172)</td>
<td>626 (186)</td>
<td>54 (23 to 84)</td>
</tr>
<tr>
<td>Time to anaerobic threshold, s</td>
<td>555 (151)</td>
<td>571 (195)</td>
<td>16 (−27 to 59)</td>
</tr>
<tr>
<td>( \dot{V}o_{2} \text{max}, \text{mL/min} )</td>
<td>1606 (484)</td>
<td>1646 (419)</td>
<td>40 (−53 to 134)</td>
</tr>
<tr>
<td>DASI</td>
<td>37.4 (13.4)</td>
<td>39.3 (14.5)</td>
<td>1.9 (−0.6 to 4.5)</td>
</tr>
<tr>
<td>SAQ exertion</td>
<td>64.8 (20.3)</td>
<td>73.2 (17.8)</td>
<td>8.3 (3.9 to 12.8)</td>
</tr>
<tr>
<td>SF-36 mental component summary</td>
<td>48.3 (10.4)</td>
<td>50.4 (9.2)</td>
<td>2.1 (−0.4 to 4.5)</td>
</tr>
<tr>
<td>SF-36 physical component summary</td>
<td>39.9 (11.0)</td>
<td>44.9 (10.7)</td>
<td>5.0 (2.7 to 7.3)</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval. Maximum score on the Duke Activity Status Index (DASI) is 58.2, with a higher score indicating better physiologic reserve. Scores on the Seattle Angina Questionnaire (SAQ) range from 1-100, with a higher score indicating better levels of functioning. Scores on the Short-Form 36 (SF-36) range from 0-100, with a higher score indicating better health-related quality of life. Mean change values were rounded.
Conclusion - The Author’s

• The authors conclude: chelation therapy had no beneficial effect on exercise time to ischemia, functional reserve for exercise, and quality of life in patients with proven ischemic heart disease, stable angina, and evidence of ischemia on treadmill examination.

• Possible explanations for the increase in time to ST depression in both groups include:
  – Multivitamin supplementation may have contributed
  – Training effects
  – Both groups were treated with optimal risk reduction therapy
**Discussion—Your Views**

<table>
<thead>
<tr>
<th>Potential bias or problems with the study</th>
<th>No apparent bias. The sample size was small. The chelation group did show improvement in both time to ST depression and VO2 max. However, so did the control.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Is this study Valid?</strong></td>
<td>Yes. Blinding was used. The study was randomized and all participants were accounted for. Follow-up was complete.</td>
</tr>
<tr>
<td><strong>What are the results?</strong></td>
<td>The results of this study suggest that little evidence exists to support the use of chelation therapy in the treatment of ischemic heart disease however the authors conclusions are questionable based on the results.</td>
</tr>
<tr>
<td><strong>Impact Statement</strong></td>
<td>In patients exploring alternative therapy for atherosclerosis, caution should be utilized regarding chelation therapy. While the therapy is relatively safe, controversy exists as to its efficacy. This issue needs further exploration</td>
</tr>
<tr>
<td><strong>Are these results applicable to Chiropractic Practice?</strong></td>
<td></td>
</tr>
</tbody>
</table>
Discussion - Your Views

• Significant anecdotal evidence exists to support the use of chelation therapy.
  – Some peer-reviewed literature also supports the use, but the studies are deficient for various reasons including small sample size, lack of blinding, and lack of randomization.

• The National Institutes of Health (NIH) have recognized the potential importance of chelation therapy and the lack of evidence to support or disprove the use. They have initiated a $30 million multi-state project to investigate the topic further.

• We found additional literature on the topic. One paper was a systematic review of the literature and is posted on CygNET. The conclusions were similar (and based upon) this paper. We chose to present this paper instead to observe the methods section of the paper in relation to chelation therapy.
Discussion cont.
Discussion Questions

• Did you see any flaws or bias with this study?
• Do you agree with the impact statement?
  – Why or Why Not?
• How would you treat the patient?
• Do you feel this topic is applicable and important to the chiropractic profession?
Discussion cont.

• With our patient with confirmed coronary artery disease, we informed him that the evidence was not very strong. He wanted to try the chelation therapy anyway before he committed to angioplasty. We suggested he discuss it with his GP. His GP expressed doubt, but thought that his condition was stable enough to try the therapy. We began a trial of suppository chelation therapy (750 mg ca-EDTA). We followed the company’s recommendation of 1 suppository/day for 60 days followed by a single weekly dose. Currently he has completed the two month treatment. He reports less fatigue, feels “more awake”, and is able to exercise longer (swimming) before symptoms arise. Interestingly his serum cholesterol levels (total) have dropped from 248 to 180. He takes Lipitor but his dose has remained the same for 3 years. He has begun an exercise routine (swimming) which may explain many or all of the above changes. Nonetheless, he is happy and his GP has recommended “keep doing whatever it is you are doing.”
TO DO:

• Post your PICO question if you have not already done so
• Finish searching for one or two papers related to your topic that you would like to present and e-mail them to me so I can post the papers on CygNET cwolcott@nuhs.edu by next week
• Read the paper to be presented prior to the next meeting
• See you in week 5
THANK YOU!