CHELATION THERAPY

Council on Coronary Artery Disease and Atherosclerosis
Isabelo V. Ongtengco Jr., MD, (Chairman), Jose Santos G. Abad, MD, Edna G. Monzon, MD
Roland De los Reyes, MD, Vivian L. Serrano, MD, Antonio L. Dans, MD
Bernadette A. Tumanan, MD, Mariano B. Lopez, MD

INTRODUCTION

The Philippine Medical Association has requested the Philippine Heart Association to draft a position paper on Chelation Therapy, its rationale, safety and effectiveness and whether it is a replacement as a non-surgical declogging of arteries in arteriosclerotic heart and peripheral vascular diseases. The Council on Coronary Artery Disease was tasked to draft the PHA recommendation.

Chelation therapy consists of a series of intravenous infusions containing ethylene diamine tetra acetic acid (EDTA) in combination with other substances. EDTA is water soluble and chelates metallic ions from the blood. At normal pH the strength with which EDTA binds dissolved metals, in decreasing order, is iron, mercury, copper, aluminum, nickel, lead, cobalt, zinc, cadmium, manganese, magnesium and calcium. Proponents believe that it is effective against atherosclerosis as removing calcium will lead to softening of hardened arteries.

METHODS

A computerized literature search was done using Medline and Cochrane Database. All the studies acquired through this search was analyzed by the Cardiovascular Research Group. The two leading practitioners of chelation therapy in the Philippines were requested to provide the Council with additional documents.

RESULTS

Based on extensive reviews of available literature, the Council on CAD found no scientific evidence that chelation therapy is beneficial in treating patients with atherosclerosis, coronary artery disease and peripheral vascular disease. There are no adequate controlled studies using currently approved methodology to support the therapy. We found only seven randomized controlled trials of EDTA on peripheral vascular disease and the results revealed that EDTA chelation is no more effective than placebo in treating men and women with peripheral vascular disease. No published randomized controlled trials have evaluated their use in patients with coronary or cerebrovascular disease.

The proponents claimed that more than five hundred thousand patients have safely benefited from chelation therapy. However, their evidence consists of anecdotes, testimonials and poorly designed experiments.

Chelation therapy is not risk free. Cases of fatal renal and depletion of mineral contents has been reported.

SUMMARY AND CONCLUSION

There is no scientific evidence to demonstrate that chelation therapy is beneficial in treating arteriosclerotic heart disease and peripheral vascular disease.

Furthermore, using this form of unproven treatment may deprive patients of receiving the well established treatment modalities of proven efficacy. There is no scientific evidence to demonstrate that chelation therapy is beneficial in treating arteriosclerotic heart disease and peripheral vascular disease.

Chelation therapy is expensive and is not devoid of side effects.
INTRODUCTION

Chelation therapy consist of a series of intravenous infusions containing disodium ethylene diamine tetraacetic acid (EDTA) in combination with other substances. EDTA, a water-soluble compound, has been found to be effective in chelating and removing toxic metals from the blood [1]. It is capable of combining with polyvalent cations, such as calcium ion, to form a soluble non-ionic complex that can be excreted [2]. Proponents believe that it is this mechanism that may lead to the softening of hardened arteries as calcium is removed from its walls [1, 3]. Case reports have even shown that EDTA chelation therapy in patients with angina pectoris leads to alleviation of symptoms [4].

At present, the benefit of chelation therapy in patients with atherosclerosis remains controversial. Filipinos are clamoring for information on this novel form of treatment that allegedly improves cardiovascular function. The primary aim of this paper is to determine the effectiveness of chelation therapy in improving clinical outcomes among patients with atherosclerotic cardiovascular disease.

METHODS

A computerized literature search was done using Medline (National Library Medicine, 1966-1998) and the Cochrane Database of Clinical Trials. The following search terms were used: "chelation" or EDTA (MeSh Major Topic)" and "Cardiovascular Disease (MeSh Major Topic)" with additional terms such as "Vascular Disease (MeSh Major Topic)" and "Randomized in PT". Studies were also requested from known "experts" in the procedure.

Trials were included if they satisfied the following criteria:

1. They must recruit patients with atherosclerotic cardiovascular disease (cerebrovascular disease, coronary artery disease and peripheral vascular disease);
2. They must be designed to evaluate the use of Disodium EDTA compared with an appropriate control group; and
3. They must be randomized controlled trials.

Our search strategy yielded 203 citations, only 7 of which were randomized controlled trials fulfilling our inclusion criteria. Full text articles were available for 6 of these 7 trials [5,6,7,8,9,10]. No detailed abstract accompanied the only trial not retrieved. This study was published in Danish [11]. All articles obtained were reviewed independently by two reviewers.

The randomized controlled trials identified, their respective patient characteristics, intervention and outcomes of interest are summarized in Table I.

RESULTS

All studies recruited patients with peripheral vascular disease and evaluated the use of disodium EDTA. No randomized trials were found on patients with cerebrovascular disease or coronary artery disease.

The study by Sloth-Neilson [5], analyzed a group of 30 patients. The outcome reported focused on digital subtraction angiograms. The result showed no significant difference between EDTA chelation and placebo.

Van Roy [6] included 92 patients in their study. Fifteen patients were randomized to chelation and 17 to the control group. The major endpoints monitored were walking distance based on onset of pain or disabling claudication, subjective walking distance, or ankle/brachial indices while resting and no exertion. There was no significant difference between the control and treatment groups on major endpoints. Other endpoints included lifestyle measures (i.e. quality of life and physical well-being). Again, results showed no significant difference.

There were 3 studies authored by Guldager, et. al. [7,8,9] that recruited patient with intermittent claudication. However, 2 of these were only sub-studies. The outcomes measured on one sub-study [7] focused on urinary metal excretion and magnesium retention. The conclusion showed that repeated intravenous infusions of EDTA leads to loss of essential minerals and possible redistribution of lead in the body. The sub-study on the effect of EDTA on blood lipids [8] measured plasma concentration of cholesterol, LDL, HDL or triglycerides. Again, treatment with EDTA did not alter blood lipid levels, Guldager’s main trial of 153 patients [9] monitored pain free and maximal walking distance measured on a treadmill, as well as ankle/brachial blood pressure index. The results failed to demonstrate any significant effect.

Only 1 article reported improvement in the application of chelation therapy [10]. This study by Olswesser, et. al. started with a randomized double-blind method, but was eventually completed as a
### Table I. Randomized Controlled Trials on EDTA Chelation Therapy

<table>
<thead>
<tr>
<th>Trials/Study Design</th>
<th>Participants</th>
<th>Interventions compared</th>
<th>Outcomes measured (Duration of observation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sloth-Nielsen J, et al [5] RCT double-blind</td>
<td>30 patients, &gt; 40 years of age (+) stable intermittent claudication walking range of 50 to 200 m ankle/brachial index below 0.8</td>
<td>1. Disodium EDTA 3 g NaCl 8.4 g in sterile water 1 L isotonic solution 2. 1L isotonic solution</td>
<td>Digital subtraction angiography (6-10 weeks)</td>
</tr>
<tr>
<td>Van Rijn A, et al [6] RCT double-blind</td>
<td>32 patients, &gt; 45 years (+) intermittent claudication less than 20% in measured walking distance</td>
<td>1. Disodium EDTA 3 g MgCl 0.76 g NaHCO3 0.84 g 500 ml Normal saline 2. 500 ml Normal saline</td>
<td>1. Measured walking distance as total distance the patient was able to walk at 4 km/hr on a treadmill at 10% gradient to onset of pain or before stopping because of claudication. 2. Subjective walking distance as distance the patient considered they were able to walk before stopping because of claudication. 3. Ankle/brachial indices at rest and immediately after TET. (12 weeks)</td>
</tr>
<tr>
<td>Guldager B, et al [7] RCT double-blind</td>
<td>60 patients, 40-80 years old; renal function normal (+) intermittent claudication</td>
<td>1. Disodium EDTA 3 g NaCl 8.4 g in sterile water 1L isotonic solution 2. 1L isotonic solution</td>
<td>1. 24-h urinary excretion of lead copper, calcium, zinc, magnesium &amp; creatinine. 2. Serum calcium, magnesium, copper, mercury, zinc &amp; creatinine; and lead in whole blood (5-9 weeks)</td>
</tr>
<tr>
<td>Guldager B, et al [8] RCT double-blind</td>
<td>29 patients, diabetes (+) intermittent claudication for 1 year; systolic ankle-brachial blood pressure index &lt; 0.8; pain free walking distance 50-200 m</td>
<td>1. EDTA 3 g; 1L isotonic solution 2. 1L isotonic solution</td>
<td>Plasma concentration, cholesterol, LDL, HLD and triglycerides (5-9 weeks)</td>
</tr>
<tr>
<td>Guldager B, et al. [9] RCT double-blind</td>
<td>159 patients, &gt; 40 years (+) stable intermittent claudication for at least 12 mos. Pain free walking distance range of 50-200 meters measured on treadmill at a speed of 3.6 km/hr with 10° inclination Ankle/brachial blood pressure index of worse leg &lt; 0.8</td>
<td>1. EDTA 3g NaCl 8.4 g 1L normal saline sol. 2. 1L normal saline sol.</td>
<td>1. Subjective evaluation 2. Pain-free and maximal walking distances measured on treadmill 3. Ankle/brachial blood pressure index (6 months)</td>
</tr>
<tr>
<td>Olsvøen E, et al [10] RCT initially double-blind, then completed as a single-blind fashion</td>
<td>10 patients, all male, 41-53 years old (+) peripheral vascular disease type 2 (in Fontaine) (+) intermittent claudication but no pain at rest or at night and no gangrene Walking Test, claudication between 100-300 m Master Exercise Test, claudication with less than 40 steps Bicycle Stress Test, claudication before 3 minutes at 50 km/hr</td>
<td>1. Disodium EDTA 10 ml (1.5g) 2. Distilled water 10 ml</td>
<td>1. Walking distance measured by Walking Test 2. Number of steps measured by Master Exercise Test 3. Cycling time at 25 km/hr by Bicycle Test (observation done after 10 infusions and after 20 infusions)</td>
</tr>
</tbody>
</table>

Single-blind study with no control group. Ten patients were recruited and initially received either disodium EDTA or placebo. The study was arbitrarily stopped, when, according to the authors, "after 10 treatments it was apparent that some patients were improving substantially but others were not. We therefore, decided to break the code. The investigators then decided to finish the study in a single-blind basis with no control group, convinced with improvements obtained from EDTA treatment.

**SUMMARY AND CONCLUSION**

In summary, the studies published to date have failed to demonstrate significant benefit with the use of disodium EDTA chelation therapy in patients with peripheral vascular disease. A single
study showed benefit, but conclusions were weak because of serious methodologic flaws seen upon review. No published randomized controlled trials have evaluated the use of disodium EDTA in patients with coronary or cerebrovascular disease.

REFERENCES