The Case for Intravenous EDTA Chelation Therapy, update 2000 -2014



Drs. Johanna Mendez and Martin Dayton discussing chelation therapy on site, 2006

Positive

Holliday, HJ **Prevention of Lower-Extremity Amputation with EDTA Chelation,** *Clinical Practice of Alternative Medicine 1(3):165-169, 2000*

The lower extremity amputation rates of 89 patients treated with traditional vascular surgical interventions for peripheral vascular insufficiency were compared with 22 patients with similar severity of vascular disease who received intravenous EDTA therapy. The overall amputation rate for the vascular surgery treated group was 9% compared to 0% for the chelation treated group. Rest pain disappeared in the 64 % of the surgical group 75% in the chelation group.

Chelation reduces need for amputation and may be used as an alternative or adjunct to vascular surgery.

Positive

Chappell, T. et al. **Brachial Artery Stiffness Testing as an Outcomes Measurement for Measurement for EDTA-Treated Patients with Vascular Disease** *Clinical Practice of Alternative Medicine 1(4):225-228, 2000*

Twelve of 18 patients with carotid and/or peripheral vascular disease were treated with 30 infusions of intravenous EDTA. Of the 13 who had abnormal arterial stiffness at the beginning of the study 12 had an average of 29% reduction in brachial artery stiffness index. All patients had improvement symptomatically and/or objectively in vascular symptoms and/or blood flow. Increased arterial stiffness correlates with increased atherosclerosis and endothelial dysfunction.

Block buster article

Betsy Bates **Angiograms Miss Most Atheromas,** *Family Practice News, July 15, 2001*

"Conventional Angiography fails to visualize 95%-99% of atherosclerotic plaque"
Dr. Steven Nissen, head of clinical cardiology at Cleveland Clinic.

Atheromas within arterial walls account for 2/3 myocardial infactions that occur at sites of "hemodynamically insignificant stenosis," that is, areas without significant blockage. An atheroma is a deposit or degenerative accumulation of lipid-containing plaques on the innermost layer of the wall of an artery. Atheromas primarily cause heart attacks by rupturing into the arterial lumen where blood flows initiating the formation of heart attack producing clots rather than as previously thought progressively increasing in size to block the blood flow in the arterial lumen or to produce emboli .

Thus, surgical interventions to reduce blockage would not be expected to reduce mortality from future heart attack. Statistically such interventions have not reduced rates of occurrence of or death from heart attack. Approaches affecting body chemistry, such as the use of aspirin (in men) and statin drugs, have been statistically proven and generally accepted as useful for this purpose. *Chelation is a chemical approach.*

In regard to preventing deaths due to heart attacks overall, have angiographers and radiologists been looking for and surgeons and interventional cardiologists been operating on the wrong plaque for the past 40 years, inappropriately promoting therapies which have never been subject to randomized double blind clinical study? Governmental and private insurance companies do not routinely pay for chelation therapy in part due to lack of a definitive randomized double blind clinical study. Are governmental and private insurance companies paying the wrong doctors?

Positive

Lin, J Et al**, Environmental Exposure and Progression of Chronic Renal Failure Diseases in Patients without Diabetes** *JAMA 2002; 287(4):481-486*

In this Taiwanese study 64 patients with chronic progressive renal (kidney) insufficiency and elevated lead body burden (lead toxicity) were randomized into two groups one receiving intravenous EDTA and the other placebo. The EDTA treated group demonstrated an almost three fold decrease in loss of kidney function versus placebo. The authors concluded that EDTA chelation may improve kidney function and slow progressing renal insufficiency. This study demonstrates what physicians using chelation have been maintaining: intravenous EDTA improves kidney function. Intravenous chelation critics had previously maintained that EDTA damaged kidneys

Negative

Knudtson, ML, Wyse DG, Et al., **Program to Assess Alternative Treatment Strategies to Achieve Cardiac Health (PATCH)-EDTA Study,** *N Engl J Med 2003;348(4):277-286.*

Canadian double blind, randomized, placebo controlled study involved patients with a history or myocardial infarction or evidence of coronary artery disease given 33 infusions intravenously with one group receiving EDTA and the other receiving placebo. 79 of 84 randomized patients completed the study. Exercise indices and quality of life increased in both groups without significant differences. The authors felt that there was insufficient evidence to support the benefit of chelation therapy for patients with stabile angina and positive stress test. The study findings and the conclusions of its authors were criticized by proponents of chelation therapy. Given the duration of the study was relatively short, the participants were relatively healthy and the number of participants relatively small, the authors agreed (along with their critics) that a larger study is needed.

Negative (sub-study)

Anderson TJ, Hubacek J, Wyse DG, et al **Effect of Chelation Therapy on Endothelial Function in Patients with Coronary Artery Disease: PATCH substudy.** ***J Am Coll Cardiol*****. 2003;41:420–425.**

A total of 47 patients with diseased coronary arteries enrolled in the Program to Assess Alternative Treatment Strategies to Achieve Cardiac Health (PATCH) study were measured before and after receiving 33 EDTA chelation infusions in combination with oral vitamins and minerals via high-resolution ultrasound testing for vasomotor related changes in brachial artery blood flow of the upper extremities at six months. Significant increments in brachial artery blood flow, one of the parameters involved with improved endothelial function, were not found.

Endothelial cells line the entire vascular system. Good endothelial function is required for:

- Regulating blood pressure, vascular smooth muscle tone, local blood flow, vascular growth and repair
- Balancing blood clotting and clot dissolution: maintaining a dynamic barrier between tissue and bloodstream
- Regulating immune function and inflammation, including inflammatory factors that underlie plaque formation and instability in occlusive (atherosclerotic) vascular disease
- Traffic through the vascular wall of immune cells, lipid particles and foreign bodies
- Tissue nourishment, ion transport and electrolyte balance

This study is limited in that it directly measures only vascular tone and blood flow, not all parameters of endothelial function inclusive of clotting, inflammation, etc. The patients were already under continuous optimal standard treatment, which affects endothelial function, as chelation was administered. Standard care may have left little room for improvement to be measured via ultrasound testing. The study does not measure the effect of chelation therapy when used without standard therapy. It does not evaluate the effect of adding optimized standard therapies to the care of patients already undergoing chelation.

Positive

Chappell L T, Shukla R, Yang J, Rene, B, Born T, Hancke C, et al **Subsequent cardiac and stroke events in patients with known vascular disease treated with EDTA chelation therapy – a retrospective study** *Evidence Based Integrative Med* 01/2005; 2(1):27-35.

In this three-year retrospective study involving 220 patients with known coronary disease EDTA was administered to all participants. The results were compared to that of what would be expected of a similar group treated conventionally without chelation therapy. In the treatment group no heart attacks or deaths were noted where 15 heart attacks and 6 deaths would ordinarily be anticipated. Two angioplasties and six bypass procedures were performed on patients receiving chelation therapy which is approximately 90% and 60% less than that which would be expected for like patients receiving only conventional treatment. Of the patients who had symptoms when treatment was initiated 69% had a complete resolution of symptoms.

Mixed, Large double blinded study:

Lamas G, Goertz C, Boineau R, Mark D, Rosema T, Nahin R, et al **Design of the trial to assess chelation therapy (TACT)** *Am Heart J, 2012 January;163 (1), 7 – 12 Jan*

Lamas, G. Goertz C, Boineau R, Mark D B, Rozema T, Nahin R L, et al **Effect of disodium EDTA chelation regimen on cardiovascular events in patients with previous myocardial Infarction: the TACT randomized trial** *Am Heart J.* 2012 Jan*;*163*(*1*):*7-12

Lamas G, Goertz C, Boineau R, Mark D B, Rozema T, Nahin R L, et al **Effect of disodium EDTA chelation regimen on cardiovascular events in patients with previous myocardial infarction: the TACT randomized trial.** *JAMA* 2013;309 (12):1241-1250

Lamas G, Boineau R, Goertz C, Mark D B, Rosenberg Y, Stylianou M, et al Oral **High-dose multivitamins and minerals after myocardial infarction: a randomized trial**. *Ann Intern Med*. 2013;159:797-80

Escobar E.; Lams G; Mark D; Boineau R; Goertz C; Rosenberg Y. et al **The effect of EDTA-based chelation regime on patients with diabetes mellitus and prior myocardial infarction in the Trial to Assess Chelation Therapy (TACT)** Cir. *Cardiovascular Qual Outcomes.* 2014 Jan; 7(1):15-24

Lewis E F, Lamas G; Mark D; Rosenberg Y; Boineau R; et al **Differential outcomes with chelation therapy among patients with anterior versus non-anterior myocardial infarction: a TACT substudy,** *J Am Coll Cardiol. 2014;63(12_S):*

Mark, D, Anstrom K, Clapp-Channing N, Knight J, Boineau R, Goertz C, et,al, **Quality-of-life outcomes with a disodium EDTA chelation regimen for coronary disease: results from the Trial to Assess Chelation Therapy Randomized Trial** *Circ Cardiovasc Qual Outcomes* 2014;7:508-516

Lamas *et al* published several papers on a placebo controlled double blind study National Institutes of Health (NIH) sponsored study, Trial to Assess Chelation Therapy (TACT). TACT involved 1708 randomized individuals, all with a history of at least one previous heart, attack followed for 5 years. In TACT the effects of intravenous chelation therapy administered according to the guidelines of an organization which promotes chelation, ACAM (American College for Advancement in Medicine,) versus placebo was studied. The primary end points of the study were the incidence of heart attack, stroke, need for invasive coronary vascularization, hospitalization for angina or death.

The study design had four arms: patients receiving IV(intravenous) chelation therapy and oral nutritional supplements, patients receiving IV chelation therapy and oral placebo supplements, patients receiving placebo IV therapy with oral nutritional supplements, and patients receiving placebo IVs and placebo oral supplements. Each arm received standard conventional care.

The chelation infusion was adjusted for weight and kidney function. The basic treatment infusion consisted of up to 3 grams disodium of EDTA, 2 grams magnesium chloride, 7 grams ascorbic acid, 2 milli-equivalents potassium chloride, 840 mg sodium bicarbonate, 100 mg procaine, 2500 units heparin, 250 mg pantothenic acid, 100mg thiamine, and 100mg pyridoxine in 500cc water.

The intravenous placebo was composed of saline and dextrose. For those who completed the study 40 infusions were administered weekly followed with 10 maintenance infusions administered at longer intervals. High dose oral nutritional supplements and placebo supplements containing vitamins were given in tablet form.

The outcome for the general population of patients receiving chelation was an 18 percent reduced risk of cardiovascular events as a composite of heart attack, stroke, hospitalization for angina, coronary revascularization or death from any cause.

Diabetic patients composing approximately 37% of the TACT patients demonstrated a 41% reduction in the composite of cardiac event related death, myocardial infarction, stroke, coronary vascularization, and hospitalization for angina; a 52 percent reduction in recurrent heart attacks; and a 43 percent reduction in death from all causes. No significant benefit of chelation treatment was found overall regarding these primary study end points for patients who were not diabetic. No significant benefit of chelation treatment was found overall regarding these primary study end points for patients who were not diabetic. Patients who had sustained a large anterior wall myocardial infarction prior to the study demonstrated a 40% reduction in risk in having further major cardiovascular events.

The primary end point was reached in 31.9% in the chelation + oral nutrients group, 33.7% in the chelation + oral placebo group, 36.6% in the placebo infusion + oral nutrients group, and 40.2% in the placebo infusions + oral placebo group. Comparing the oral nutritional supplements + chelation therapy group to the double placebo group a significant 8.3% reduction in cardiovascular events was found for the treated group. The group taking orally supplemented nutrients was compared to placebo group. The number of events was 37% at five years for placebo group versus 34% for the treated group, favoring oral supplementation by only 3%. Chelation therapy was found to not have a detectable effect on quality of life at 2 years follow-up. In regard to safety outcomes, adverse cardiovascular events occurred in 26% of the chelation treated group versus 30 % of the placebo group. Of those receiving chelation 16 percent stopped their infusions because of an adverse event versus 15 percent of those

receiving the placebo. Four events were serious; 2 in the chelation group with 1 death and 2 in the placebo group with 1 death. Heart failure was reported in 7 percent of chelation patients versus 8 percent of placebo patients. Over 55,000 infusions were given throughout the course of the study. Hypocalcemia, was reported in 6.2 percent of chelation patients and 3.5 percent placebo patients. Overall, the safety of IV chelation appeared to be similar to that of IV placebo

Discussion in light of what have we learned since 2000:

During the last several decades in which magnesium EDTA chelation therapy has been in clinical use many observations have been made. Outcomes using various study measurements, designs, patient populations, qualities of execution, time intervals, forms of statistical analysis, and perspectives through which conclusions are derived have been reported. Data and conclusions from different studies at times may appear complementary and at other times conflicting. The preponderance of evidence suggests that chelation therapy is beneficial at least under some circumstances and is generally safe when properly administered.

Explaining why diabetics did so much better than non-diabetics in the TACT study is challenging. Perhaps the marked cardiovascular benefits found for the diabetic patients versus non-diabetics may be in part be explained by EDTA chelation reducing hyperglycemia induced glycation or hyperglycemia enhanced transport of calcium into cells.

The chelation and removal of calcium excesses by magnesium EDTA (made by mixing magnesium chloride or magnesium sulfate with disodium ETDA) makes magnesium EDTA unique among the pharmaceutical chelators. Excess intracellular calcium is toxic to the cell. Metastatic calcium is associated in atheromatous plaque, arthritic joints, sclerosis and malignant tumors. Magnesium EDTA is only available intravenously.

Perhaps benefits would also have been revealed in the TACT study for the non-diabetics if additional observational parameters were used. Chappell, *et al* reported 87% objective improvement in a meta-analysis involving over 22,000 patients. Guldager, *et al* and Van Rij, *et al* reported chelation to not be beneficial in peripheral vascular disease while other studies by different investigators such as Olswer and Holliday reported the opposite, including dramatic reduction in frequency of lower limb amputations in advanced cases. The validity of various such studies in terms of design, execution and analysis have been questioned by both champions and opponents of intravenous chelation therapy.

According to the U.S. National Health Statistics Report of 2008 the estimated number of patients using chelation therapy to treat heart disease and other diseases in the United States was 111,000 patients per year in 2007, an increase of nearly 68 percent from 2002 to 2007. Of the seven most frequent causes death in the United States in 2011 positive impact of chelation therapy on six has been reflected in published clinical studies. In descending order the leading causes of death and corresponding prevalence in 2011 are as follows: (1) heart disease 596,577, (2) cancer 576,691, (3) chronic lower respiratory diseases 142,943, (4) stroke 128,932, (6) Alzheimer's disease 84,974, (7) diabetes 73,831. No medical literature is found on the direct impact of chelation on deaths due to (5) accidental injuries.

Based upon evidence presented thus far, being that coronary bypass surgery, stenting and angioplasty have been statistically discredited regarding their general ability to prevent myocardial

infarction and death in the chronic setting, would a diabetic patient with chronic angina be wise to consider opting for chelation? Would a patient with advanced peripheral vascular disease be wise to consider chelation before opting to undergo amputation? Is evidence in 2014 adequate enough to consider using intravenous EDTA to help prevent or ameliorate chronic degenerative diseases? Is it time for insurance to pay for evidence based EDTA chelation therapy?

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Reprinted on the LIFE LONG HEALTH data CD thanks to the gracious generosity of my long time friend, colleague, and professor, Dr. Martin Dayton.
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