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EDTA Chelation Therapy

Chelation is the binding of metals (like lead and cadmium), or minerals (like calcium) to a protein “chelator”, forming a ring-like structure. The Greek word “chele” means claw. Initially, the medical use of chelating agents was to treat heavy metal poisonings, for example, British Anti-Lewisite (2,3-dimercaptopropanol), a medication used to treat acute poisoning by arsenic, mercury, gold, and lead. Another chelating agent, ethylene diamine tetraacetic acid (EDTA), a synthetic amino acid, was first introduced into medicine in the U.S. in 1948 as a treatment for the lead poisoning of workers in a battery factory. Shortly thereafter, the U.S. Navy advocated EDTA chelation for sailors who had absorbed lead while painting government ships and facilities. The U.S. Food and Drug Administration (FDA) later approved EDTA chelation therapy as a treatment for lead and heavy metal poisoning. EDTA is also used to treat poisonings by radioactive materials such as plutonium, thorium, uranium, and strontium; for removing copper in patients with Wilson's disease. It is also used as an emergency treatment for hypercalcemia (excessive calcium levels) and the control of ventricular arrhythmias (abnormal heart rhythms) associated with digitalis toxicity.

EDTA traps lead and other metals, forming a compound that the body can eliminate in the urine. Some other metal poisonings treated with chelation include iron, arsenic, cadmium, aluminum, nickel, and thallium. Lead induces oxidative stress, inflammation, and a reduction in bioavailable nitric oxide needed for circulation regulation.[1] Excessive iron and copper accelerate oxidative reactions in the body and increase vascular complications. The removal of heavy metals and excessive iron and copper results in the reduction of free radical production and a decrease in lipid peroxidation.

Lead-induced hypertension was reversible after treatment with an intravenous chelating agent or anti-oxidant therapy in animal models. Lead can induce epigenetic modifications, including hypomethylation in a collagen type I alpha 2 gene promoter[2], a genetic sequence that plays a role in the production of connective tissue. Cadmium, at levels that are well below those associated with clinical signs and symptoms of cadmium intoxication, is associated with hypertension, stroke, MI, peripheral artery disease, and death in population-based studies such as the Strong Heart Study and National Health and Nutrition Examination Survey.[3] Cadmium may also contribute to the progression of atherosclerosis by causing damage to DNA or through oxidative mechanisms.[4]

Cadmium may be connected to an increased risk of premature atherosclerosis, and it may function in the induction of occlusive atherosclerotic disease. Experimental studies have demonstrated that cadmium exposure can result in endothelial damage and induce cell death. Cadmium exposure has been associated with altered methylation

patterns in genes encoding proteins that play roles in longevity, cardiovascular disease, and vascular calcification.[5]

Heavy metal toxicity in humans has been associated with many health conditions, including heart disease, attention deficit/hyperactivity disorder (ADHD), immune system disorders, gastrointestinal disorders (including irritable bowel syndrome, or IBS), and autism. Although there is less published research in these areas, EDTA chelation therapy is also being used to treat macular degeneration, osteoporosis, mild to moderate Alzheimer's disease associated with heavy metal toxicity and certain autoimmune diseases, especially scleroderma.

At physiologic pH, EDTA readily binds with calcium and promotes its excretion. The lowering of serum calcium during and immediately after a treatment stimulates the release of parathyroid hormone, resulting in the partial removal of abnormal calcium deposits, including those from atherosclerotic plaque.

Numerous studies since the late 1960s have also shown EDTA chelation to be effective in the treatment of atherosclerotic cardiovascular disease, especially heart disease and peripheral artery disease. However, many medical organizations, including the National Institutes of Health, the American Medical Association, the American Heart Association, and the American College of Cardiology, have publicly criticized and denounced the practice of EDTA chelation therapy for heart disease, claiming that the evidence is mixed. Most doctors who offer intravenous EDTA chelation utilize it as a part of a comprehensive therapy program for treating atherosclerosis and other chronic degenerative diseases. Hence, EDTA chelation therapy for treating atherosclerosis and other chronic degenerative diseases is an off-label use, usually consisting of a series of intravenous infusions with EDTA, accompanied by vitamins, minerals, and other supplements.

Evidence for effectiveness of EDTA chelation therapy is cumulative over many years. The following is a historical account of EDTA chelation therapy research in the treatment of cardiovascular disease.

In 1955, Norman Clarke observed that patients treated for lead toxicity, who had coexisting atherosclerosis, not only excreted lead effectively, but also experienced major improvements in their arterial disease.[6] Clarke subsequently reported on the successful treatment of angina pectoris[7], and occlusive vascular disease[8] with EDTA. Meltzer, Kitchell and associates confirmed the work of Clarke.[9, 10]

Favorable articles appeared in mainstream medical journals with EDTA chelation featured in the American Medical Association's Medical World News. A brief but intensive interest in EDTA by researchers in such fields as rheumatology, cardiology and endocrinology followed. However, although Meltzer, Kitchell and associates' final article on the subject in 1963 reported rather impressive improvements in a group of patients with severe coronary artery disease, the authors concluded the therapy "did not benefit patients more than commonly used therapeutic methods."[11]

After this publication, interest in EDTA moved into the realm of alternative medicine and faded from mainstream academia. A re-emergence of interest in EDTA occurred in the 1980's, with a number of reports in the medical literature documenting improvement of vascular disease with objective testing measurements following treatment with chelation therapy. Casdorph published articles showing improvement in blood flow to the brain[12] and increased cardiac output.[13]

Casdorph and Farr described chelation as an alternative to amputation in peripheral vascular disease.[14] McDonagh, Rudolph and Cheraskin collaborated on numerous studies and showed various benefits from chelation.[15, 16, 17, 18, 19]

Olszewer and associates published reports suggesting a beneficial effect from EDTA chelation; a retrospective analysis of 2870 patients with vascular and other chronic degenerative diseases[20], and a single blind, crossover study of a small group of patients with peripheral vascular disease.[21] In the former study, objective testing measures indicated marked or good improvement in 87% of patients. The results for vascular disease patients were even more impressive. All ten subjects receiving chelation therapy improved. Half of these individuals showed no change while they were receiving placebo.

In the 1990s, Hancke and Flytlie published an outcome study with an interesting subset of patients who were on the waiting list in Denmark for surgery. After electing to receive EDTA chelation therapy, 58 of 65 patients awaiting cardiac bypass surgery no longer required this procedure. Twenty-four of 27 patients being prepared for amputation because of critical limb ischemia were also treated successfully and did not require amputation.[22]

Rudolph, McDonagh and Barber reported good results in 30 patients treated with EDTA for carotid artery stenosis. Doppler ultrasound showed improvement in all patients with an average reduction in intra-arterial obstruction of 20.9%.[23]

Chappell and Stahl conducted a meta-analysis to determine if a correlation between improvement in vascular disease and treatment with EDTA exists. They found a correlation coefficient of 0.88 and a measurable improvement in 87% of patients.[24]

A second meta-analysis examining previously unpublished data reported virtually identical results.[25] The two meta-analyses covered 51 reports with a total of 24,006 patients. To ensure the few large studies did not skew the results, a comparison was made between the large and small studies. Once again, the results were almost identical.

Two prospective trials conducted by groups of vascular surgeons in Denmark[26, 27] and New Zealand[28] reached negative conclusions regarding the use of EDTA in peripheral vascular disease. Both studies consisted primarily of subjects who continued to smoke throughout the trial. These studies have also been severely criticized for protocol discrepancies.[29, 30, 31, 32, 33, 34]

Although it was not mentioned in the article, the latter study contained an outlier in the control group who had improved far more than any other subject in the study. The study group was so small (15 treated patients) the outlier severely distorted the results. If the outlier were excluded, the study would have shown an improvement in the group treated with EDTA.[35]

In 1993, a retrospective study reported the results of EDTA chelation in 470 patients, using a number of parameters, most of them objective. Although the patients acted as their own control, they observed improvement of 80 to 91%, depending upon the measurement used. Of 92 patients referred for surgical intervention, only 10 required ultimate surgery after or during their chelation therapy, thus saving an estimated 3 million dollars of insurance money, The researchers concluded that EDTA chelation therapy is safe, effective and cost-saving.[36]

More recently conducted was the Trial to Assess Chelation Therapy, or TACT, a large, study published in Journal of the American Medical Association that randomized patients to a series of IV chelation using EDTA or placebo. This study found a 40% reduction in total mortality, 40% reduction in recurrent heart attacks, and about a 50% reduction in overall mortality in patients with diabetes who had previously suffered from a heart attack. These results led to the revision of the ACC/AHA guideline recommendations for chelation therapy, changing its classification from class III to class IIb. The researchers concluded “In stable patients with a history of MI, the use of an intravenous chelation regimen with disodium EDTA, compared with placebo, modestly reduced the risk of a composite of adverse cardiovascular outcomes.”[37, 38]

EDTA chelation therapy is not taught in conventional medical school, but rather through various professional medical organizations. The most recognized leader in educating and certifying healthcare professionals, including MDs, DOs, and NDs, in chelation therapy is the American College for the Advancement of Medicine (ACAM).[39] ACAM’s chelation therapy training teaches doctors how to diagnose and treat patients with heavy metal toxicity as well as how to use diet and nutrients to optimize toxic metal chelation strategies and protocols. ACAM has spent a great deal of money and effort during the last several decades to have unbiased academic researchers perform prospective, randomized studies utilizing chelation therapy for coronary artery disease and peripheral vascular disease. Efforts to accomplish the research required to change the package insert to include an FDA-approved indication for vascular disease are continuing.

Proponents of EDTA chelation for the treatment of cardiovascular disease believe that EDTA should be treated like many other cardiovascular drugs which are utilized for off-label indications, but have not yet been subjected to rigorous, large-scale, double-blind, clinical trials for those purposes. Surgical therapies such as bypass, angioplasty and stents have been broadly accepted and widely utilized without such trials to prove their efficacy. Clinical experience and the above limited scientific studies suggest EDTA chelation therapy might be safer, more cost effective, and potentially more efficacious than these options.

The American College for the Advancement of Medicine recommends the follow sources of information on EDTA chelation protocols:

Calcium Disodium Versenate (edentate calcium disodium injection), Thomson PDR, 60th Edition, 2006; 1819-20.
http://www.pdr.net/drug-summary/Calcium-Disodium-Versenate-edetate-calcium-disodium-2852

Tim S. Nawrot, PhD; Jan A. Staessen, MD, PhD. Low-Level Environmental Exposure to Lead Unmasked as Silent Killer, Circulation, Sept 26, 2006;114(13):1347-49.
http://circ.ahajournals.org/content/circulationaha/114/13/1347.full.pdf

Menke A, Muntner P, Batuman V, Silbergeld EK, Guallar E.. Blood Lead Below 0.48 μmol/L (10 μg/dL) and Mortality Among US Adults, Circulation, Sept 26, 2006;114:1388-94
https://www.ncbi.nlm.nih.gov/pubmed/16982939

The Protocol for the Safe and Effective Administration of EDTA and Other Chelating Agents for Vascular Disease, Degenerative Disease, and Metal Toxicity,Journal of Advancement in Medicine, Spring 1997;10(1):5-100.
https://link.springer.com/article/10.1023/B%3AJAME.0000008701.26923.ab

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