Applications Of EDTA Chelation Therapy

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Abstract

Ethylenediamine tetraacetic acid, or EDTA, is a synthetic amino acid approved by the FDA for the removal of toxic metal ions such as lead. EDTA is used in isolation for heavy metal poisoning; however, the vast majority of practitioners who offer intravenous EDTA treatments utilize it as a part of a comprehensive therapy program for treating atherosclerosis and other chronic degenerative diseases. Treatment is aimed at removing accumulations in the body of harmful levels of aluminum, iron, copper, and toxic heavy metals, all of which enhance free radical damage. Treatment objectives also include the removal of metastatic calcium from soft tissues, enhancement of the levels of ionic magnesium intracellularly, and reduction of pathologically enhanced clotting mechanisms, especially platelet adhesiveness. Because of its mechanism of action, EDTA chelation therapy might be useful to prevent or treat rapid oxidation of LDL cholesterol, ischemia-reperfusion injuries, arrythmias, hypertension in the presence of low-level lead accumulation, and congestive cardiomyopathy due to iron overload. Reports also indicate autoimmune diseases such as rheumatoid arthritis, Wegener's granulomatosis, and scleroderma respond to EDTA chelation therapy.
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Chelating Actions of EDTA

Ethylenediamine tetraacetic acid, or EDTA, is a synthetic amino acid that is approved by the FDA for removal of toxic metal ions such as lead. EDTA chelation therapy for treating atherosclerosis and other chronic degenerative diseases is an off-label use, consisting of a series of intravenous infusions with EDTA, accompanied by vitamins, minerals, and other supplements.

"Chelation" derives from the Greek chele, which refers to the claws of a crab. It describes how certain molecules surround and bind metal ions. Many therapeutic agents act as chelators, including aspirin, ascorbic acid, tetracycline, and other antibiotics.[1] Naturally occuring examples of chelates include magnesium in chlorophyll, and iron in hemoglobin.

At physiologic pH, EDTA readily binds with calcium and promotes its excretion. It also binds and removes other metals in the body such as zinc, iron, copper, lead, arsenic, cadmium, and aluminum. The binding of these metals results in a variety of clinically relevant actions by EDTA.[2] The lowering of serum calcium during and immediately after a treatment stimulates the release of parathyroid hormone, resulting in the partial removal of metastatic calcium deposits, including those from atherosclerotic plaque. The removal of heavy metals and excessive iron and copper results in the reduction of free radical production and a decrease in lipid peroxidation.

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Improved calcium/magnesium balance leads to reduced platelet aggregation and improved blood flow characteristics.

History

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.[3] Clarke subsequently reported on the successful treatment of angina pectoris[4] and occlusive vascular disease[5] with EDTA. Meltzer, Kitchell and associates confirmed the work of Clarke.[6,7] 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" and was not a useful tool in the treatment of coronary artery disease.[8] Subsequent to 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 two articles showing improvement in blood flow to the brain[9] and increased cardiac output.[10] Casdorph and Farr described chelation as an alternative to amputation in peripheral vascular disease.[11] McDonagh, Rudolph and Cheraskin collaborated on numerous studies and showed various benefits from chelation.[12-16]

Olszewer and associaties published two reports suggesting a beneficial effect from chelation; a retrospective analysis of 2870 patients with vascular and other chronic degenerative diseases[17] and a single-blind, crossover study of a small group of patients with peripheral vascular disease.[18] In the former study, objective testing measures indicated marked or good improvement in 87 percent 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.[19]

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 percent ($p<0.001$). This study also demonstrated the smoothing over of ulcerated plaque. Since ulcerated plaque is associated with clot formation and subsequently in embolic strokes, this finding might be of particular clinical significance.[20]

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 percent of patients.[21] A second meta-analysis examining previously unpublished data reported virtually identical results.[22] The two meta-analyses covered 51 reports with

a total of 24,006 patients. In order 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[23,24] and New Zealand[25] 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.[26-31] Although it was not mentioned in the article,[25] 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.

The American College for Advancement in Medicine has spent a great deal of money and effort during the last 15 years to have unbiased academic researchers perform prospective, randomized studies utilizing chelation therapy for coronary artery disease and peripheral vascular disease. One major clinical trial was aborted before it was completed. Another was cancelled the day it was to be sent to government funding sources. Efforts to accomplish the research required to change the package insert to include an FDA-approved indication for vascular disease are continuing.

Recently, Messerli's standard cardiology textbook devoted an entire chapter written by Rubin to the appropriate use of EDTA chelation therapy in vascular disease.[32] 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 limited scientific studies suggest EDTA chelation therapy might be safer, more cost effective, and potentially more efficacious than these options.

Current Use of Chelation Therapy

EDTA is rarely used in isolation, except perhaps for heavy metal poisoning. The vast majority of practitioners who offer intravenous EDTA treatments utilize it as a part of a comprehensive therapy program. They reject the prevailing opinion that a systemic disease like atherosclerosis can be effectively treated with isolated surgical interventions. Likewise, these practitioners prefer to minimize the use of pharmaceutical agents that can both interfere with biochemical pathways and enzyme systems, and often result in unwanted side-effects. While EDTA is certainly a medication with potential side-effects, it is extremely safe if used according to accepted protocol.[33]

Large amounts of oral and intravenous antioxidants are given with chelation therapy, especially vitamins E and C. Treatment is aimed at removing accumulations in the body of harmful levels of aluminum, iron, copper, and toxic heavy metals, all of which enhance free radical damage. Treatment objectives also include the removal of metastatic calcium from soft tissues, enhancement of the levels of ionic magnesium intracellularly, and reduction of pathologically enhanced clotting mechanisms, especially platelet adhesiveness. These mechanisms of action were described in the extensive review article by Cranton and Frackelton.[34] Additional information about the complex mechanisms initiated by EDTA are listed in the book *Questions from the Heart* by Chappell.[35]

A treatment course usually consists of a series of 30-40 intravenous infusions of disodium magnesium EDTA in a mineral

solution that has been adjusted for appropriate osmolality and pH.[33] Infusions are administered weekly or semiweekly. The most common solution contains 3 grams (or 50 mg/kg) of EDTA in 500 cc, and is infused over 3-4 hours. Some practitioners choose to use 1.5 grams in 250 cc given in half the time. Patients who improve often elect to receive monthly maintenance treatments for an indefinite period of time following the basic course.

The FDA has long recognized the use of chelation therapy for heavy metal toxicity. However, the most common use of chelation therapy is for occlusive vascular disease of the coronary, peripheral and/or cerebral arteries. There have been a number of reports of improvement in critical limb ischemia with EDTA therapy.[11,36] Some patients with macular degeneration have had improvements documented by retinal vascular photographs.[37] EDTA treatment, for these conditions, merits immediate further study, especially since no other effective treatments exist. Chelation therapy might be particularly useful for patients who have prominent or diffuse vascular problems, are considered to be poor surgical candidates, or do not respond to other cardiovascular medications.

Excessive iron and copper accelerate oxidative reactions in the body and increase vascular complications. EDTA removes unhealthy accumulations of these metals. Therefore, EDTA chelation therapy might be effective in preventing or treating rapid oxidation of LDL cholesterol,[38] ischemia-reperfusion injuries,[39-41] arrythmias,[42,43] hypertension in the presence of low-level lead accumulation,[44] and congestive cardiomyopathy due to iron overload.[45] A report also indicates patients with thalassemia major can benefit from iron chelation.[46]

In addition to reports of improvement in carotid circulation and reduction in plaque ulceration, EDTA chelates aluminum, a metal which might have some relationship to Alzheimer's disease. Because of this, patients who have evidence of coexisting cerebrovascular disease and dementia should be considered for a chelation trial. However, if mercury is a concern, chelating agents such as DMPS or DMSA are more appropriate interventions than EDTA.

EDTA chelation has been used as an adjunct in treating Parkinson's disease and other neurologic disorders. There have been a few reports of improvement,[17] but no clinical trials have been performed. Autoimmune diseases such as rheumatoid arthritis,[47] Wegener's granulomatosis,[48] and scleroderma[49] have responded to treatment.

McDonagh and associates published reports of improvement in musculoskeletal problems,[50] mood disorders,[51] fatigue,[50,52] and diabetes mellitus.[53] Improvements were postulated to be a result of enhanced antioxidant capability, improved function of biochemical receptor sites, enhanced decalcification of soft tissues, and improved microcirculation. Bone density is reported to improve following the pulsatile administration of EDTA.[54] Patients with chronic obstructive pulmonary disease seem to benefit from treatment.[55] Blumer observed patients could be rapidly detoxified without suffering withdrawal effects, even if they were addicted to narcotic medications, with the use of chelation therapy.[56] Bjorksten suggested chelation therapy might be useful for life extension.[57] A report also documents a 90 percent reduction in the incidence of cancer over an 18-year follow-up for patients who had received chelation treatment to resolve low-level lead toxicity.[58]

Although the use of EDTA to modify genetic and other risk factors has not been studied, chelation appears to be an ideal agent for preventive medicine. This might be especially so for those with a positive family history and/or other strong risk factors for vascular disease. Because of potential regulatory agency actions against physicians,

it is probably prudent to treat the above-listed conditions with EDTA only if coexisting vascular disease is present.

Because chelation therapy removes toxic metals through the kidneys, its use could theoretically promote damage. Because of this, EDTA chelation therapy is contraindicated for individuals with advanced kidney disease.[59] Although the incidence is extremely rare, allergic reactions to EDTA have been reported. Physicians must be careful with patients who have significant congestive heart failure, due to the potential for fluid overload subsequent to frequent IV administration.

EDTA is a powerful drug that should be used only by knowledgeable physicians. Training programs are available through the American College for Advancement in Medicine (ACAM) and the Great Lakes College of Clinical Medicine. Certification of specialists in chelation therapy is provided by the American Board of Chelation Therapy (ABCT), following successful completion of oral and written examinations and a review of patient charts. Recertification is required every five years. ACAM and ABCT have also helped to establish certification organizations in several other countries.

Conclusion

EDTA chelation therapy is used by a small group of specially trained physicians in the treatment of a wide variety of chronic degenerative diseases associated with vascular problems. Chelation therapy protocol combines intravenous EDTA, nutrition therapies, and lifestyle changes. It is used as an adjunct to or as an alternative to bypass surgery and/or angioplasty. Frequently, cardiovascular and other medications can be reduced and quality of life improved by EDTA chelation therapy. Continued research is needed to fully assess its role in a comprehensive integrated approach to these difficult problems.

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