



Review Article

Expulsion by Ionic Complexation: Benchmark Therapy for Atherosclerosis A Review

Mali Sachin S^{1*}, Hajare Ashok A¹, Karade Raviraj S¹, Salunkhe Sachin S², Nadaf Sameer J¹, Honmane Sandip M¹, Bhatia Neela M²

¹ Department of Pharmaceutical Technology, Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, Kolhapur, 416 013, Maharashtra, India.

² Department of Quality Assurance Technique, Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, Kolhapur, 416 013, Maharashtra, India.

ARTICLE INFO:

Article history:

Received: 11 February 2014

Received in revised form:

21 February 2014

Accepted: 25 February 2014

Available online 7 March 2014

Keywords:

EDTA,

Chelation therapy,

Cholesterol,

Cardiovascular diseases,

Atherosclerosis.

ABSTRACT

Ethylenediamine tetraacetic acid (EDTA) chelation therapy has been practiced since longtime for the treatment of cardiovascular diseases, alone or in combination with other treatments. It has been recommended as a harmless, relatively inexpensive and non-surgical method of restoring blood flow in atherosclerotic vessels. Ability of EDTA to form complex with heavy metals like calcium, lead, copper is used to remove calcium from atherosclerosis plaques which ultimately improves the condition. It can be concluded that chelation therapy is emerging form of complementary or alternative medicine to surgery and can be used in safe manner. Still there is insufficient evidence to decide on the effectiveness or ineffectiveness of chelation therapy in improving clinical outcomes of patients with atherosclerotic cardiovascular disease.

1. Introduction

1.1 Atherosclerosis

Atherosclerosis is a disease, characterized by thickening of artery wall as a result of the accumulation of calcium and fatty materials such as cholesterol and triglyceride. It occurs largely due to accumulation of macrophages and white blood cells and promoted primarily by LDL (low-density lipoproteins).[1,2] atherosclerosis are directly related to the oxidation of lipids in LDLs that become trapped in the extracellular matrix of the subendothelial space.[3] The cells of the artery wall secrete oxidative products from multiple pathways that can seed the LDL trapped in the subendothelial space and initiate lipid oxidation.[4,5,6] These

oxidized lipids activate an NFκB-like transcription factor and induce the expression of genes containing NFκB binding sites. The protein products of these genes initiate an inflammatory response that initially leads to the development of the fatty streak.[7] Middle-aged and older people are more likely to suffer the atherosclerosis, because this fatty buildup usually starts early in life and gradually gets worse over many years.[8] Continuation in plaque builds up, leads to constriction and hardening of the arteries. They become narrower due to loss of their ability to expand and contract as blood flows through them.[9]

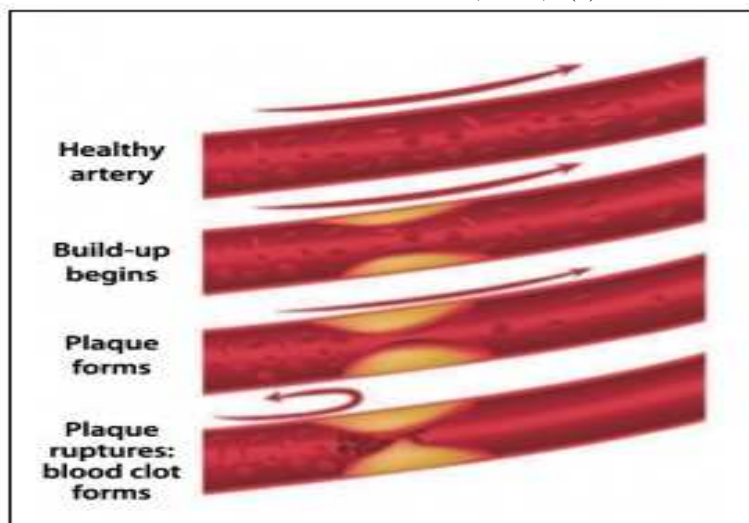


Figure 1: Steps showing plaque formation in Atherosclerosis

1.2 Cholesterol

Cholesterol is a fatty substance that circulates in our blood, required to build and maintain membranes i.e. modulates membrane fluidity.[10,11] Although cholesterol is cooperative for body function, when it crosses its level, it raises our risk of cardiovascular disease, heart attack, stroke and mainly leads to Atherosclerosis.[12,13] So the better way to reduce risk of atherosclerosis is to reduce cholesterol i.e. LDL (Low density lipoprotein) from blood. Generally conventional cardiologists prefer the use of bypass surgery to deal with atherosclerosis. In contrast, the American Heart Association admits that a huge number of these surgeries are, indeed, worthless.[14]

So, Chelation therapy is viewed, promoted, and accomplished as a form of complementary/alternative approach to deal with by-pass surgery in atherosclerotic cardiovascular disease.[15] Chelation therapy is the process of removing from the body the undesirable ionic material by the infusion, or taking orally, of an organic compound which has suitable chelating properties.[16] The word chelation is derived from the Greek word *chele* that means claw (like that of a scorpion or crab).[17] The perception of chelation is

based on the surveillance that when a certain amino acid complex called EDTA (ethylene-diamine-tetra-acetic acid) make contact with certain positively charged metals and other substances such as lead, iron, copper, calcium, magnesium, zinc, plutonium and manganese, it get complexes with them, and sweeps them. In EDTA, a metal ion, two oxygen atoms and two Nitrogen atoms comprise squares (Figure 3).[18] EDTA is thought to attach itself to life threatening plaque and cholesterol deposits on artery walls and then remove these deposits gently, allowing them to be ultimately filtered out of the blood by the kidneys.[19,20] EDTA binds and chelates calcium, one of the components of atherosclerotic plaque, it removes calcium from plaque, which leads to the loosening and breaking of plaques. This is the rationale behind chelation therapy for high cholesterol. So in short Chelation therapy involves, repeated intravenous administration of EDTA [21,22] and EDTA therapy as prescribed is not considered a highly invasive or harmful therapy. [23] Olszewer and Carter during their study on 2870 patients, demonstrated the marked effect in peripheral vascular disease using EDTA chelation.[24]

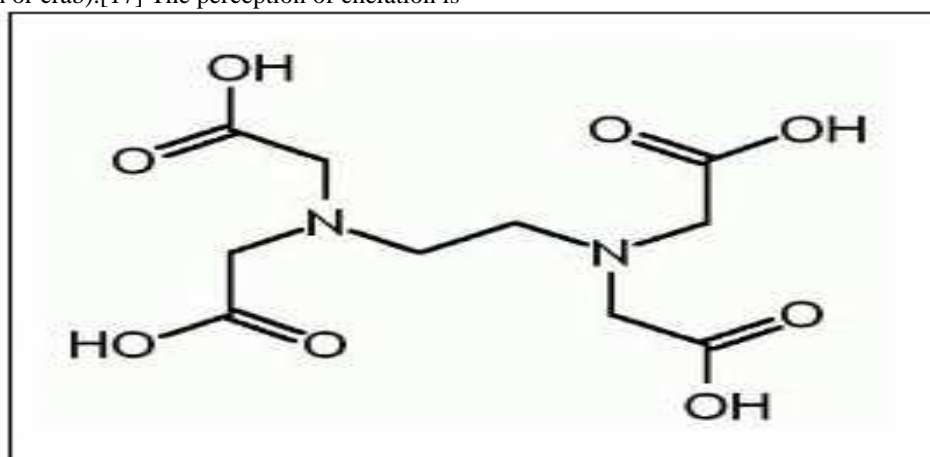


Figure 2: Structure of EDTA

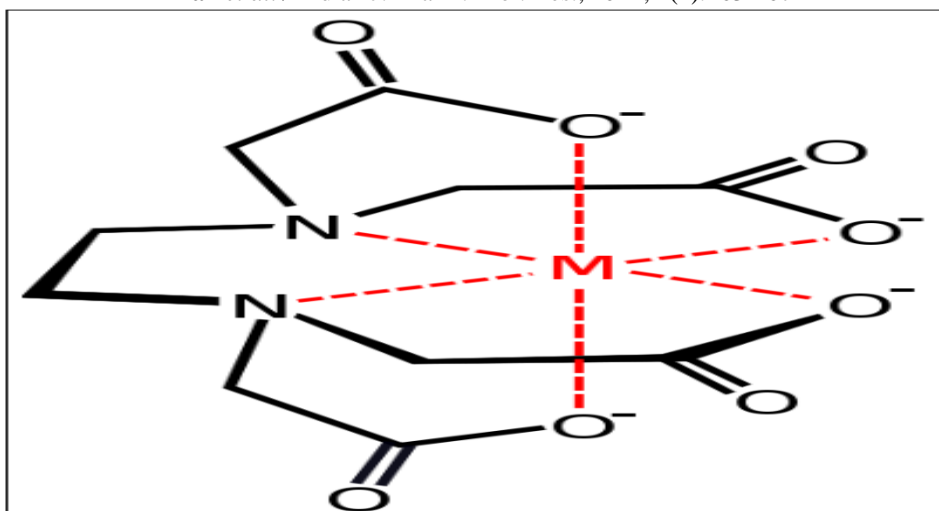


Figure 3: Chelation Mechanism of EDTA with metal (M)

Some people may assume that EDTA depletes, needed level of calcium in the body. However, EDTA not only lowers blood calcium but also stimulates the parathyroid gland to produce a hormone called parathormone. These further accounts for removing calcium from places such as the inside of arteries and deposits it in the right places, such as bone. So, IV chelation makes us physiologically younger because it moves calcium from our arteries and makes our bones more stronger.[25] Dr. Gordon, the pioneer of chelation therapy comments, "The more chelation we give people, the less osteoporosis they have and the less calcium accumulation there is in their blood vessels." [26]

2. Methods

Once it has been established that there is a problem which could benefit from EDTA infusion, a series of treatments are scheduled, about two or three times per week. Most chelation centers treat patients in a group setting.

2.1 Intravenous EDTA chelation

Intravenous EDTA is preferred as it has a direct and powerful effect on the body almost immediately. This treatment last for 3 to 4 hours, in which about 1,500 mg to 3,000 mg of EDTA is administered along with vitamin C and other nutrients. The infusion will usually be administered in a large room with appropriate seating. [27, 28]

2.2 Oral EDTA

Generally oral EDTA is Appropriate for people whose condition is less severe and does not demand attention without delay. About 5%-10% of an oral dose of EDTA is absorbed into the bloodstream, compared with 100% of an IV dose. Over the course of 5 or 6 weeks, regular use of oral EDTA can be as beneficial as a single IV EDTA session. [27, 28]

2.3 Administration of chelation therapy

Medical Examination [29, 30]

Prior to administering EDTA infusion, it is necessary to check whether the patient has a condition that will benefit or not from the therapy. After primary test, comprehensive personal and family history is taken with special emphasis on all aspects of

previous health problems and current status. All details related with Patients diet, habits, emotional status, exercise, stress levels and a detailed listing of symptoms is also taken. A full physical examination will also be performed with special emphasis on the circulatory and respiratory systems.

After that, a series of medical tests such as electrocardiogram, chest X-Ray, blood tests, urine tests, diet and other tests and hair analysis is also carried out. To determine how the heart, lungs and circulation respond to activity, an exercise tolerance tests are used. A Doppler (sound wave) examination will be carried out to establish a 'before' picture of circulatory system.

2.4 Four phases of cleansing in chelation therapy [31]

i. Phase I

Phase I involves few sessions (usually 3 to 5) which are most difficult one. During this patient may go through various cleansing reactions, the intensity of which varies in every individual depending on their health status, dietary habits and life style. The patient may suffer from most common reactions like tiredness, headache, gastric upset, sometimes loose stools, dizziness etc, but it may not last more than 24 hrs after the Chelation session.

ii. Phase II

After first few extreme sessions, intensity of symptoms subsides completely or decreases in some extent. Chelation sessions leave one slightly exhausted and indolent for the rest of the day.

iii. Phase III

After about 10 to 15 days of the first session, first signs of improvement may begin to show up in the form of increased vitality, and clarity of sensory perceptions. These signs are usually clearer in patients who are pretty toxic and weak at the beginning of the treatment.

iv. Phase IV

This phase comes about 6 to 10 weeks after the course of Chelation therapy. Here beneficial detoxification effects start to show in more pronounced manner. This health benefits may vary from person to person. This effects may include; improvement in overall health status, improvement in skin texture, increased joint flexibility and decrease or complete healing of joint pains (e.g. knee pain, back pain), weight reduction in overweight individuals, improved fertility and sexual potency etc.

2.5 Applications of chelation [32-37]

- Reduction of blockages in the heart and brain.
- Ease chest pain.
- Lower high cholesterol and high blood pressure to normal levels.
- Helps to rejuvenate your cardiovascular system.
- Reduces toxic lead and metal deposits and abnormal calcium deposits
- Prevents abnormal blood clotting.
- Helps increase in life expectancy
- Soothe painful, stiff and inflamed joints.
- Restore blood sugar balance.
- conquer male erectile problems
- Rebirth of blood flow
- Helps to improve conduction in all degrees of A-V heart block
- Helps to abolish extra heart beats, skipped beats and rapid heart beats.

2.6 Cost of treatment [38]

Depending upon geographical area and what materials are placed into the infusion, chelation costs approximately in the range of \$60 to \$150 per infusion. Different nutritional supplements like Vitamins, worth of \$20 to \$200 per month is also prescribed during the course of therapy.

Conflict of interest statement

The authors report no conflict of interest. The authors, alone are responsible for the content and writing of the paper.

References

1. Gerald H. Tomkin and Daphne Owens., LDL as a Cause of Atherosclerosis, *The Open Atherosclerosis & Thrombosis Journal* 2012;5:13-21.
2. <http://www.webmd.com/heart-disease/what-is-atherosclerosis>
3. Witztum JL, Steinberg D. Role of oxidized low density lipoprotein in atherogenesis. *J Clin Invest.* 1991;88:1785-1792.
4. Parthasarathy S. *Modified Lipoproteins in the Pathogenesis of Atherosclerosis.* Austin, Tex: RG Landes Co; 1994:91-119.
5. Parthasarathy S. Mechanism(s) of cell-mediated oxidation of low density lipoprotein. In: Nohl H, Esterbauer H, Rice Evans C, eds. *Free Radicals in the Environment, Medicine and Toxicology.* London, England: Richelieu Press; 1994:163-179.
6. Witztum JL. The oxidation hypothesis of atherosclerosis. *Lancet.* 1994;344:793-795.
7. Judith A. Berliner, Mohamad Navab, Alan M. Fogelman, Joy S. Frank, Linda L. Demer, Peter A. Edwards, Andrew D. Watson, Aldons J. Lusis, *Atherosclerosis: Basic Mechanisms Oxidation, Inflammation, and Genetics* *Circulation.* 1995; 91: 2488-2496.
8. Elspeth. B. Smith. The influence of age and atherosclerosis on the chemistry of aortic intima: Part 1. The lipids. *Journal of Atherosclerosis Research.* 1965;5(2):224-240.
9. W A Riley, R W Barnes, G W Evans and G L Burke. Ultrasonic measurement of the elastic modulus of the

2.7 Side effects [39-41]

The most serious potential adverse effect of EDTA chelation is nephrotoxicity (kidney damage). This is dependent on the dose, the rate of infusion, the patient's kidney function, and the patient's body burden of toxic heavy metals. But this is rare now days because the frequency, dose and rate of EDTA administration is carefully adjusted and monitored, with respect to age, weight, and blood tests.

In certain cases it rarely causes hypocalcemia (excessively low blood levels of calcium), hypoglycemia (low blood sugar, causing dizziness, sweating or rapid heart rate); and phlebitis (inflammation of the vein) usually due to improperly prepared solutions. Rarely reported side effects include chills and fever.

3. Conclusion and future perceptives

Atherosclerosis requires lifelong care. Patients who have less severe atherosclerosis may achieve adequate control through lifestyle changes and drug therapy. Chelation therapy is an approved treatment for poisonings caused by such heavy metals as iron, mercury, arsenic, and lead. Chelation therapy is effective, safe for treatment of atherosclerosis. EDTA makes stronger bones and reduces cholesterol by improving calcium and cholesterol metabolism. EDTA chelation therapy can successfully remove plaque from arteries, veins, and capillaries and restore blood flow to normal or near-normal functioning - often even in severe cases. Chelation therapy bypasses the bypass surgery. Still Acceptable evidence supporting chelation therapy for atherosclerotic vascular disease is lacking.

- common carotid artery. The Atherosclerosis Risk in Communities (ARIC) Study. *Stroke*. 1992; 23: 952-956.
10. Ohvo-Rekilä H, Ramstedt B, Leppimäki P, Slotte JP. Cholesterol interactions with phospholipids in membranes. *Prog. Lipid Res*. 2002; 41 (1): 66-97.
 11. <http://www.buffalohearthealth.com>
 12. <http://www.livestrong.com>
 13. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, Witztum JL. Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care* 2008;31(4): 811-22.
 14. Winslow CM, Kosecoff JB, Chassin M, et al. The appropriateness of performing coronary artery bypass surgery. *JAMA* 1988;260:505-509.
 15. E. Ernst. Chelation Therapy for Peripheral Arterial Occlusive Disease . A Systematic Review. *Circulation*. 1997; 96: 1031-1033
 16. Henryk Kozlowski, David Ronald Brown, Gianni Valensin. Metallochemistry of Neurodegeneration: Biological, Chemical, and Genetic Aspects. In: Chelating agents in metal neurotoxicity. 2006 p.-223.
 17. Rashmi Sanghi. What's up with chelates. *Current science*, 2000;78(11):1286-1290.
 18. B Sun, F.J Zhao, E Lombi, S.P McGrath. Leaching of heavy metals from contaminated soils using EDTA. *Environmental Pollution* 2001;113(2):111-120.
 19. Diagnostic and therapeutic technology assessment: chelation therapy. *JAMA*. 1983;250:672.
 20. Perry W. Chelation therapy. *Compl Ther Med*. 1994;2:17-18.
 21. Olszewer E, Carter JC. EDTA chelation therapy in chronic degenerative disease. *Med Hypotheses*. 1988;27:41-49.
 22. Rathmann KL, Golightly LK. Chelation therapy of atherosclerosis. *Drug Intell Clin Pharm*.1984;18(12):1000-3.
 23. D. M. Seely, P. Wu and E. J. Mills. EDTA Chelation Therapy for Cardiovascular Disease: A Systematic Review. *BMC Cardiovascular Disorders*, 2005;5:32.
 24. Olszewer E, Carter JP. EDTA chelation therapy: a retrospective study of 2,870 patients. *J Adv Med*. 1989;2:197-211.
 25. Heynen G, Franchimont P. Normal and pathologic secretion of parathormone and calcitonin. *Bull Mem Acad Roy Med Belg* 1975;130(4-5-6):234-57.
 26. Questions most commonly asked about EDTA. 2002. Available from: <http://wellnessadvantage.com>
 27. <http://www.life-enhancement.com>
 28. <http://www.healingdaily.com>
 29. <http://holisticonline.com/chelation>
 30. Saul Green Chelation Therapy: Unproven Claims and Unsound Theories. Available from: <http://www.quackwatch.com>
 31. <http://healthyhealingcentergoa.blogspot.in>
 32. Kindness G, Frackelton JP. Effect of ethylene diamine tetraacetic acid (EDTA) on platelet aggregation in human blood. *J Adv Med*. 1989;2:519-530.
 33. Zucker MB, Grant RA. Nonreversible loss of platelet aggregability induced by calcium deprivation. *Blood*. 1978;52:505-513.
 34. Michael Cutler Chelation: Natural Miracle For Protecting Your Heart and Enhancing Your Health 2011. Published by *Easy Health Options* Cullman, AL p. 1-87.
 35. Swaran J.S. Flora and Vidhu Pachauri. Chelation in Metal Intoxication *Int J Environ Res Public Health*. 2010; 7(7): 2745-2788.
 36. S. Dipu, Anju A. Kumar, Salom Gnana Thanga Effect of chelating agents in phytoremediation of heavy metals, *Remediation Journal* 2012;22:2:133-146.
 37. S.J.S. Flora, Megha Mittal & Ashish Mehta. Heavy metal induced oxidative stress & its possible reversal by chelation therapy. *Indian J Med Res* 2008; 128:501-523.
 38. <http://www.doczine.com>
 39. Lin JL, Lin-Tan DT, Hsu KH, Yu CC. Environmental lead exposure and progression of chronic renal diseases in patients without diabetes. *N Engl J Med*. 2003; 348:277-286.
 40. Brown MJ, Willis T, Omalu B, Leiker R. Deaths resulting from hypocalcemia after administration of edetate disodium: 2003-2005. *Pediatrics* 2006;118 (2): e534-6.
 41. Arla J. Baxter and Edward P. Krenzelok. Case report Pediatric fatality secondary to EDTA chelation *Clinical Toxicology* 2008; 46:1083-1084.

Cite this article as: Mali Sachin S, Hajare Ashok A, Karade Raviraj S, Salunkhe Sachin S, Nadaf Sameer J, Honmane Sandip M, Bhatia Neela M. Expulsion by Ionic Complexation: Benchmark Therapy for Atherosclerosis A Review. *Indian J. Pharm. Biol. Res.* 2014; 2(1):103-107.