PHARMA & HEALTHCARE

NIH Trial Gives Surprising Boost To Chelation Therapy

With a result that is likely to surprise and baffle much of the mainstream medical community, a large NIH-sponsored trial has turned up the first substantial evidence in support of chelation therapy for patients with coronary disease. Known as TACT (Trial to Assess Chelation Therapy), the highly controversial trial was presented today at the AHA by Gervasio Lamas. The trial was sponsored by two NIH institutes, the National Center for Complementary and Alternative Medicine and the National Heart Lung and Blood Institute.

Chelation therapy with EDTA to remove heavy metals from the blood in order to treat coronary disease has been around—and provoked criticism—since the 1950s. Despite a lack of evidence and the skepticism of the medical community, passionate supporters have kept the therapy alive in alternative medicine circles.

TACT was funded by the NIH more than a decade ago as part of a much-publicized initiative to study the claims of alternative medicine. In 2008 enrollment in TACT was temporarily suspended in response to claims that the trial was unethical. The trial was additionally hampered by slow enrollment.

Now the results of TACT will likely provide ammunition to chelation defenders, but the trial investigators and other experts have expressed considerable caution about the proper interpretation of the results.

TACT was a double blind study testing active or placebo infusions of chelation in stable patients with a history of MI. Due to slow enrollment the trial was downsized, ultimately enrolling 1,708 patients instead of the planned 2,372 patients. To maintain the trial’s power to achieve a meaningful result the follow-up time was increased. Because of the this change, and because the data and safety monitoring board reviewed the data multiple times over the course of the study, the threshold for statistical significance was lowered to 0.036.

The primary endpoint of the trial—the composite of death, MI, stroke, coronary revascularization, or hospitalization for angina—was significantly lowered in the chelation group:

- 26.5% in the chelation group versus 30% in the placebo group (HR 0.82, 0.69-0.99, p=0.035)
There were no significant differences in any of the individual components of the primary endpoint. Most of the difference between the groups was due to a lower rate of coronary revascularization in the chelation group:

- 15.5% versus 18.1% (HR 0.81, CI 0.64-1.02, p=0.076)

Nearly all the benefit in the trial was found to occur among the one-third of patients in the trial who had diabetes:

- 102 events versus 67 events (HR 0.61, CI 0.45-0.83, p=0.002)

The investigators were cautious in their interpretation, noting that the trial barely achieved statistical significance, most of the difference was found in the softer endpoint of revascularization, and the finding is less reliable since there was a high withdrawal rate (17%) of patients in the trial.

The authors said their findings were “unexpected and additional research will be needed to confirm or refute our results and explore possible mechanisms of therapy.” TACT, they concluded, “does not constitute evidence to recommend the clinical application of chelation therapy.”

At an AHA press conference, Paul Armstrong said that TACT was a response to an unusual situation. On the one hand, most physicians and scientists have dismissed chelation therapy as lacking any evidence or rationale. On the other hand, chelation therapy is strongly supported by the alternative medicine community and more than 100,000 people receive chelation therapy each year. Armstrong said the results of the trial were “hypothesis generating, not practice changing.”

Here is the AHA press release:

Alternative therapy produces intriguing results in some heart patients but many questions remain

Study Highlights:

- Patients with prior heart attacks enrolled in a clinical trial of a weekly chelation infusion regiment that included disodium EDTA and vitamin C had fewer cardiovascular disease complications than those who received placebo infusions.

- Chelation therapy removes heavy metals like lead and iron from the body. Disodium EDTA, the agent used in the study, does not have an FDA indication.

- Investigators caution that the results need to be reproduced and understood before consideration of clinical application.

LOS ANGELES, Nov. 4, 2012 — Heart attack patients given weekly infusions of chemicals used for chelation therapy had fewer cardiovascular events than those who received identical appearing placebo infusions, according to late-breaking clinical trial results presented at the American Heart Association’s Scientific Sessions 2012.

In the multicenter, double-blind efficacy trial, Trial to Assess Chelation Therapy (TACT), 1,708 heart attack patients were randomized to receive 40 infusions of a 500 mL chelation solution or a placebo infusion, with a
second randomization to an oral vitamin and mineral regimen or an oral placebo. The chelation solution contained three grams of the synthetic amino acid ethylene diamine tetra-acetic (EDTA), seven grams of vitamin C, B-vitamins, electrolytes, a local anesthetic and heparin, an anti-clotting drug. The placebo infusion was salt water and a small amount of sugar.

Researchers found that patients receiving the chelation solution had fewer serious cardiovascular events than the control group (26 percent vs. 30 percent). Cardiovascular events were defined as death, heart attack, stroke, coronary revascularization and hospitalization for angina.

Although participants with diabetes appeared to have a particular benefit from the infusions, the study team cautioned that subgroup analyses can be unreliable and need to be reproduced.

Chelation therapy is used to remove metals from the bloodstream. The more common calcium EDTA is approved to treat lead poisoning and other chelation drugs are used to manage iron overload following repeated blood transfusions. The study used the less common disodium EDTA and the infusion regimen contained other components including vitamin C.

There has been decades-long debate about whether chelation therapy could be effective as a treatment for patients with atherosclerosis, or fatty deposits in arteries that can cause heart attacks. Until now, there have been no large, long-term clinical trials to determine if these intravenous infusions might work for patients with coronary artery disease.

“We have to look carefully at these unexpected results,” said Gervasio A. (Tony) Lamas, M.D., lead author of the study and chief of Columbia University Division of Cardiology at Mount Sinai Medical Center in Miami Beach, Fla. “Although not approved by the Food and Drug Administration for treating heart disease, chelation therapy has been used for over 50 years and has generally been believed by conventional medical practitioners and cardiologists to be without value. A definitive answer on chelation therapy will take much additional research. The most exciting part of this study is that there may be an unexpected signal of benefit. We need to understand whether the signal is true, or whether it occurred by chance.”

The patients in the trial were 82 percent male, 94 percent Caucasian and about half were obese. All had experienced a previous heart attack, 83 percent had already had bypass surgery, stent implantation or balloon angioplasty. Thirty-two percent had diabetes, 68 percent had high blood pressure and 73 percent had been prescribed cholesterol-lowering statins. Patients were followed for an average of 55 months.

The trial was conducted in 134 sites in the United States and Canada from 2002-2011.

“The chelation therapy was an arduous regimen,” Lamas said.

Each patient received 40 infusions, each lasting at least three hours. The first 30 infusions were one week apart. The last 10 were two weeks to two months apart depending on the patient’s schedule. All told, researchers delivered 55,222 infusions.

Lamas said there is still much work to do before the treatment would be considered standard.

“This is a one-of-a-kind study, so we do not know if the effect will be reproducible,” he said. “The level of statistical difference between groups was small.”
A stringent safety infrastructure made sure patients experienced no undue risk. In addition, the research team worked with a central pharmacy to ensure the safety and purity of the infused products and had in place a computerized system that calculated doses based on the patient’s kidney function and the system sent an alert if an infusion was completed faster than usual.

“Unless we can show a consistent effect across studies, understand why this treatment might work and establish a similar mechanism to deliver the treatment safely, it will be difficult for chelation to enter the mainstream of other cardiovascular therapies,” Lamas said.

“The American Heart Association applauds the National Heart, Lung, and Blood Institute and the National Center for Complementary and Alternative Medicine for sponsoring this study and the investigators for performing a trial that was difficult to conduct,” said Elliott Antman, M.D., chair of the AHA Scientific Sessions Program Committee, cardiologist at Brigham and Women’s Hospital and Professor of Medicine at Harvard Medical School in Boston, Mass. “Intriguing as the results are, they are unexpected and should not be interpreted as an indication to adopt chelation therapy into clinical practice.”

“More information is needed about which elements of the complex infusion mixture might provide benefit, the marked differences between the observed treatment effect in diabetics versus non-diabetics needs to be understood and we need to be sure that the findings can be replicated. Like many trials, TACT raises more questions that must be answered before we’re ready to act on the observations reported today,” he said.

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The National Center for Complementary and Alternative Medicine and the National Heart, Lung, and Blood Institute funded the study.

Disclosures are here http://newsroom.heart.org/pr/aha/document/DISCLOSURES.pdf

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