キレート療法はMI後患者において有望である (AHA 2012 LBCT-19786)

TACT:代替療法は動脈硬化治療に興味深い結果をもたらしたが疑問は残る

TACT: Alternative therapy produces intriguing results for treatment of atherosclerosis but questions remain

週1回のキレート点滴療法を受けた心筋梗塞既往患者は外観の同様なプラセボを投与された患者よりも心血管イベントが少なかったとのLate-Breaking Clinical Trialの結果が2012年American Heart Association学会で発表された。この多施設二重盲検有効性トライアルである、Trial to Assess Chelation Therapy（TACT）では、MI後患者1,708人（82%が男性、32%が糖尿病、68%が高血圧を有し、73%はスタチンを内服）が500mLのキレート液またはプラセボの点滴を40回施行される群に無作為に割り付けられ、次の無作為化では経口ビタミンおよびミネラル療法またはプラセボ内服に割り付けられた。キレート液には3グラムの合成アミノ酸エチレンジアミン四酢酸（EDTA）、7gのビタミンC、ビタミンB群、電解質、局所麻酔薬および抗凝固薬ヘパリンが含まれていた。キレート液を投与された患者はコントロール群よりも重篤な心血管イベント発現が少なかった（26%対30%）。心血管イベントは死亡、心臓発作、脳卒中、冠動脈血行再建術施行および狭心症による入院で定義された。糖尿病を有する者は特にこの点滴の有益性が高いようであったが、スタディチームは、サブグループ解析は信頼できない可能性があり再現する必要があると警告している。

Full Text

Myocardial infarction 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 myocardial infarcton. 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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