Added Calcium Raises MI Risk in Older Women

BY DAMIAN McNAMARA
Miami Bureau

Calcium supplementation significantly increased the risk of a myocardial infarction among healthy postmenopausal women, compared with those taking placebo, in a secondary analysis of an osteoporosis study.

Physicians should consider this increased cardiovascular risk against other clinical benefits of calcium supplementation in older women until confirmatory studies can be completed, the authors suggested.

"It is an important finding because so many women are prescribed calcium supplements," Dr. Rita F. Redberg said in an interview. "I would not recommend calcium supplementation based on this finding. This raises enough concern. With any supplement, you have to show evidence of benefit without risk," said Dr. Redberg, who was not involved in the study.

The HDL to LDL cholesterol ratios improved among the 732 women who took daily calcium supplementation, compared with the 739 participants who took placebo. This suggests that a different mechanism spurred the increase in myocardial infarction.

"This is an interesting point. It shows that just improving cholesterol does not reduce the risk of a heart attack," said Dr. Redberg, a Robert Wood Johnson Foundation health policy fellow and director of women's cardiovascular services at the University of California, San Francisco. "It was the same finding with estrogen: It lowered LDL, increased HDL, but did not reduce the number of heart attacks in studies."

The current findings contrast with previous suggestions of cardiovascular benefit from calcium supplementation. One study found that calcium increases the HDL:LDL cholesterol ratio by almost 20% (Am. J. Med. 2002;112:343-7).

In addition, a one-third decrease in deaths from cardiovascular events was observed among women who had the greatest intake of calcium from either diet or supplements in the Iowa Women's Health Study (Am. J. Epidemiol. 1999;149:151-61).

Following completion of a 5-year osteoporosis study (Am. J. Med. 2006; 1119:777-85), Dr. Mark J. Bolland and his associates at the University of Auckland (New Zealand) reassessed their data to compare cardiovascular events. Women were randomized to 1 g/day of elemental calcium (Citracal) or placebo. All of the 1,471 participants were postmenopausal for at least 5 years and older than age 55 years at baseline, and 10% of those were older than age 80 at baseline.

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DR. REDBERG

Death, sudden death, myocardial infarction, angina, other chest pain, stroke, and transient ischemic attacks events were recorded every 6 months. In all, 336 women stopped taking the calcium and 296 stopped taking the placebo before the study end.

A total of 21 of the 732 women in the calcium group experienced 24 myocardial infarctions, a statistically significant difference vs. 10 of the 739 in the placebo group who had 10 such events. A composite end point of sudden death, myocardial infarction, angina, or chest pain was also higher in the calcium group (155 events among 87 women) vs. the placebo group (135 events among 93 women).

No significant differences were found in angina, chest pain, transient ischemic attack, stroke, or sudden death events between groups. There were 34 deaths in the calcium group and 29 in the placebo, a nonsignificant difference.

Dr. Redberg was not surprised by the elevated MI risk. She said research by Dr. Linda Demer, vice chair of medicine at the University of California, Los Angeles, has indicated increased cardiovascular risk associated with calcium.

"It's called the calcium paradox. Women lose calcium from their bones as they get older and it ends up in their arteries and the lining of their vessel walls, leading to accelerated atherosclerosis," Dr. Redberg said. "This study is a confirmation of that hypothesis, that calcium can end up in the walls of your arteries." Dr. Redberg is also a professor of medicine at the University of California, San Francisco.

The mean age was 74 years and participants were white, a possible limitation for generalizing results to other ages or racial groups, the authors said.

However, Dr. Redberg said that the inclusion of older women in the study is a strength because they are the most likely to be prescribed calcium supplements. It is very unusual for studies to include people older than age 80, she added. ■

Fewer Adverse Events With Cyclic OCs After Endometrioma Excision

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Continuous and cyclic administration of oral contraceptives appeared equally effective in preventing recurrent pain in women following laparoscopic endometrioma excision, but continuous administration was associated with significantly higher rates of side effects leading to treatment discontinuation in a prospective, randomized trial.

Evidence from the literature suggests that medical treatment following laparoscopic endometrioma excision can delay, though probably not prevent, recurrence of endometriosis. Although GnRH analogues can be given for 6 months, longer treatment is associated with high cost and significant side effects. Combination oral contraceptives represent a valid cost-effective alternative to GnRH analogues, but the question of whether they should be administered continuously or in a cyclic fashion has not been tested previously in a prospective randomized trial, said Dr. Ludovico Muzii, who presented data from such a trial at the annual meeting of the AAGL.

A total of 57 women who underwent laparoscopic excision of endometriomas by "stripping" were randomized to a 6-month cyclic regimen of monophasic combined ethinyl estradiol 0.020 mg and desogestrel 0.150 mg daily for 21 days followed by a 7-day interval (28 patients) or to a continuous regimen of the same monophasic oral contraceptive combination daily without the interval for 6 months (29), reported Dr. Muzii of Campus Bio-Medico University, Rome.

The two groups were comparable in age (30.3 years for cyclic, 30.6 for continuous), revised American Fertility Society (r-AFS) endometriosis classification (40.4 vs. 42.1), endometriotic cyst diameter (5.0 vs. 5.1 cm), and the proportion of patients with associated superficial implants (23 of 28 cyclic, 24 of 29 continuous). Twelve of the patients randomized to the continuous regimen did not complete the 6-month treatment because of moderate to severe side effects attributable to the OCs, compared with just four patients allocated to the cyclic treatment. The difference in discontinuation rates, 41% vs. 14%, was statistically significant, Dr. Muzzi said.

In a subsequent "intention to treat" analysis at a minimum of 12 months that included all 57 patients, endometriomas recurred in one cyclic (4%) vs. no continuous patients (0%), pain recurred in nine (32%) cyclic vs. five (17%) continuous; and mean time to recurrence was 12 months for cyclic compared with 16 months for continuous. Although none of these differences were statistically significant, they did represent trends that might have reached significance with a larger sample size, Dr. Muzii noted.

Both groups reported significant improvements in quality of life compared with baseline, despite the high dropout rate in the continuous group. This is probably due to a combination of factors: First, it is possible that patients who receive continuous treatment do experience less pain and recurrence—although not significantly—which might counterbalance the negative impact of the side effects, Dr. Muzzi explained in an interview. Also, most of the women who dropped the continuous regimen actually switched to the cyclic regimen, and therefore would still have been evaluated in the intent-to-treat analysis as having "continuous" treatment. ■

DMPA Users' Endometritis Tied To Inflammation, Not Infection

BY NANCY WALSH
New York Bureau

MINNEAPOLIS — *Chlamydia trachomatis* was not the cause of chronic endometritis in a new study of women using depot-medroxyprogesterone acetate, a finding that holds implications for treatment of endometritis, reported Dr. Andrea R. Thurman.

C. trachomatis is recognized as a cause of breakthrough bleeding—an occurrence often associated with chronic endometritis—among women using oral contraceptive pills.

About 70% of women using depot-medroxyprogesterone acetate (DMPA) also experience breakthrough bleeding during the first year, and a considerable number discontinue the contraceptive.

To determine if *C. trachomatis* is implicated in the breakthrough bleeding among DMPA users, a cross-sectional study compared endometrial biopsies from 20 women with bleeding and 20 women who were amenorrheic, Dr. Thurman wrote in a poster session at the annual meeting of the Association of Reproductive Health Professionals.

The most common histologic finding on the biopsies was chronic endometritis, which was defined as two plasma cells per endometrial sample, according to Dr. Thurman of the department of obstetrics and gynecology, University of Texas Health Sciences Center, San Antonio.

Chronic endometritis was the histologic diagnosis in 25% of the 40 participating women, and was seen in 35% of women experiencing breakthrough bleeding, compared with 15% of those without bleeding.

Polymerase chain reaction technology then was used to identify *C. trachomatis* in paraffin-embedded endometrial biopsy tissue sections. Only one patient in each group was infected, and neither of these two patients had chronic endometritis as their histologic diagnosis, Dr. Thurman said.

Despite the fact that the study population was predominantly African American, young, and medically indigent—all risk factors for *C. trachomatis* infection—there was no correlation between *C. trachomatis* infection and chronic endometritis in this group.

This finding suggests that chronic endometritis in DMPA users reflects an inflammatory state relating to endometrial atrophy, and supports the use of nonsteroidal anti-inflammatory drugs, rather than antimicrobials or hormonal medication, for treatment, she wrote. ■