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IADSA SCIENTIFIC RESPONSE IADSA SCIENTIFIC ALERT SERVICE

Issue: Calcium supplements and risk of CVD

Publication: Heart 2012; 98: 920-925

Title: Associations of dietary calcium intake and calcium supplementation with myocardial infarction and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg)

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SUMMARY OF THE PUBLICATION

Objective:

- To evaluate any associations between dietary calcium intake, including from supplements, with risk of heart attack (MI) and stroke, and with overall death rates from cardiovascular disease (CVD).

Design:

- Prospective epidemiological study.
- Data were taken from a German cohort of the EPIC (European Prospective Investigation into Cancer and Nutrition study).
- This included 23980 participants aged 35-64 years at recruitment.
- Average follow-up time was 11 years.
- Food intake was assessed at baseline by means of a self-administered food frequency questionnaire (FFQ). Supplement intake was ascertained by baseline interview.

Main Outcome Measures:

- Incident cardiovascular events (MI, stroke and overall CVD mortality) during follow-up were self-reported by participants or their next of kin in follow-up surveys, and were verified by tracking medical records or death certificates.
- CVD events were not the primary outcome measure of the trial.

Results:

- For total calcium intake, after adjustment for confounders, there was a statistically significant inverse association between total dietary calcium intake and MI risk for the third quartile compared with the lowest quartile (HR=0.69; 95% CI 0.50 to 0.94).

- Compared with the lowest quartile, the second quartile of total calcium intake had a statistically significantly increased stroke risk (HR=1.50; 95% CI 1.06 to 2.11), which became non-significant after exclusion of the first 2 years of follow-up.
- Users of calcium supplements had a statistically significantly increased MI risk compared with non-users of any supplements (HR=1.86; 95% CI 1.17 to 2.96).
- This association was more pronounced for calcium supplement only users (HR=2.39; 95% CI 1.12 to 5.12) and persisted after MI cases that occurred in the first 2 years of follow-up were excluded (HR=2.70; 95% CI 1.26 to 5.79).
- The most recent but not the cumulative calcium only supplementation was significantly positively associated with MI risk (HR=2.17; 95% CI 1.06 to 4.42).
- No statistically significant association was found between calcium supplementation and either stroke risk or overall CVD mortality.

Authors identified limitations of the study:

- One, baseline measurement of dietary intake by FFQ does not capture long-term variation, particularly if individuals modify their diet after the onset of disease.
- Participants did not report the names of the supplements taken, and hence only a limited number of calcium supplement users were identified, accounting for 3.6% of all cohort participants. Unreported calcium supplementation could affect the accuracy of the results if these users had a different cardiovascular risk profile compared with reported calcium supplement users
- While the study excluded pre-existing MI, stroke and transient ischaemic attack, individuals with other pre-existing CVD subtypes were not excluded.

Authors conclusions:

- The study findings suggests that increasing dietary calcium intake from diet might not confer significant cardiovascular benefits, while calcium supplements, which might raise MI risk, should be taken with caution.

IADSA COMMENTS - EXPERT RESPONSE

1. Calcium supplements have a long history of safe use, backed by a strong evidence base of observational and clinical studies.
2. Calcium is an essential nutrient that along with vitamin D is vital for good bone health. In Europe, The European Food Safety Authority (EFSA) has endorsed the role of calcium and vitamin D in reducing the rate of bone loss in post-menopausal women. Additionally, a significant protective effect is also seen in men and younger women.
3. Since dietary survey data indicate that intakes of calcium and vitamin D are lower than desirable in some adults, including older adults, taking a supplement can help to ensure adequate intakes.

4. Overall, the scientific literature suggests that calcium in food, with or without supplements, has an overall neutral effect on the cardiovascular system.
5. The findings in this study that users of calcium supplements had an increased risk of heart attack are based on weak data. While the effect was supposedly more pronounced in calcium only supplement users, this finding only held for the most recent calcium intake and not for cumulative calcium intake.
6. There was no statistically significant association between calcium supplementation and either stroke risk or overall CVD mortality. In addition, participants with moderately high total calcium intakes (third quartile of intake) had a significantly reduced risk of MI compared with those with the lowest intakes.
7. This study has a number of limitations:
 - The study design does not allow prediction of cause and effect – it is an observational study and can thus only identify associations.
 - The study was not designed to measure CVD events as the primary outcome.
 - The study did not exclude people with risk factors for CVD such as high blood cholesterol and high blood pressure.
 - Calcium intake was measured only once, at the start of the study, and did not account for any dietary changes made by participants within the follow-up period.
 - Determination of calcium supplement intake was highly inaccurate since nearly 50% of users did not report the names of the supplements, and no information was collected about the dose taken. Calcium supplement users accounted for just 3.6% of the cohort (n=256) of nearly 24,000 participants.
 - The authors identified that calcium supplement users were more likely to be female, to be older, had a greater incidence of high cholesterol at baseline, were more likely to take lipid-lowering drugs, had an overall lower educational level and a longer duration of smoking, which could have influenced the findings as such factors increase the risk for heart disease.

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