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Editorials

Calcium supplements in people with osteoporosis

Should not be given without concomitant treatment for osteoporosis

In the linked systematic review (doi:10.1136/bmj.c3691), Bolland and colleagues assessed whether calcium supplements increase the risk of cardiovascular events in people with, or at risk of, osteoporosis.[1] They found that calcium supplements increased the risk of myocardial infarction (hazard ratio 1.31, 95% confidence interval 1.02 to 1.67), but they found no significant difference in the risk of stroke, death, or the composite end point of myocardial infarction, stroke, or sudden death.

The effort spent on detecting and treating osteoporosis is only worthwhile if it translates into a health benefit for patients. The most common argument for detecting and treating osteoporosis is a reduction in bone fractures that are either subtle and progressive (for example, those that cause loss of vertebral height) or overt (for example, fractures of the hip and wrist). Bone mineral density, which is often used as a measure of treatment success, is a surrogate measure for real clinical benefit.

Surrogate measures may be useful in pilot studies but become problematic when they become the goal of treatment. [2 3] Bone fractures in older people are an important cause of disability, and more than 20% of patients will die within one year of a low trauma hip fracture.[4 5] Accordingly, a safe and effective treatment that can prevent fractures should reduce mortality if given to a large enough population at sufficient risk.

Calcium supplements, given alone, improve bone mineral density,[4] but they are ineffective in reducing the risk of fractures and might even increase risk,[4 5] they might increase the risk of cardiovascular events,[1] and they do not reduce mortality.[1] They seem to be unnecessary in adults with an adequate diet. Given the uncertain benefits of calcium supplements, any level of risk is unwarranted.

Why should calcium supplements increase cardiovascular risk? Calcium supplements may improve some conventional cardiovascular risk factors including blood pressure and lipids.[6] Accumulation of calcium in the arterial wall leading to reduced compliance would be expected to take years, but the increased risk of myocardial infarction reported by Bolland and colleagues occurred early after calcium supplementation (median follow-up of 3.6 years).

An alternative possibility is that the increased risk of myocardial infarction is not a true effect. If an intervention changes the rate of vascular events but is not associated with a commensurate change in mortality, the intervention may be changing the presentation rather than the incidence. Flecainide reduces the risk of non-fatal myocardial infarction by about 30% because infarctions are more likely to be fatal before patients reach hospital.[7] Similarly, long term treatment with aspirin seems to modify the presentation of vascular events with no effect on mortality and, possibly, with acceleration of the progression of vascular disease.[8] Although the risk of myocardial infarction seemed to increase substantially (by about 25%) with calcium supplementation this was not accompanied by an increase in mortality. Calcium supplements could simply be causing gastrointestinal symptoms that could be misdiagnosed as cardiac chest pain. However, even if calcium supplements really are safe, a neutral effect on mortality casts doubt on whether they are effective prophylaxis for fractures.

A combination of calcium and vitamin D is commonly used to treat osteoporosis. Vitamin D supplements might reduce the risk of falls, might have important clinical effects on cardiovascular function, do not increase mortality, and may mitigate the trend to excess mortality seen with calcium supplements alone.[9] However, no conclusive data are available to show that current doses of vitamin D supplements with or without calcium supplements reduce the rates of fracture, and meta-analyses found evidence of substantial reporting bias.[4 5 9]

Several agents that are, or might be, used to treat osteoporosis do reduce mortality, including bisphosphonates,[10 11] raloxifene,[10] and

thiazides.[12] However, biphosphonates and raloxifene were generally given in addition to calcium and vitamin D supplements. Other methods of reducing fractures should also be subject to scientific scrutiny. Reducing falls and bone trauma is, probably, the most effective method of reducing fractures, but if it leads to a sedentary lifestyle it might impair both quality of life and longevity. Exercise might be a good way to increase bone strength, although it also carries risk.[12]

Requiring companies to show before licensing that treatments for chronic diseases such as osteoporosis, diabetes, and hypertension reduce long term disability and death could lead to a cessation of research in these areas. The cost and commercial risk would be too high. However, we do need to know whether treatments are safe, effective, and value for money. Extending the patent life of drugs to that of the copyright on a song (50 years according to the Berne Convention) would have many benefits and few drawbacks if properly managed. Regulators could insist that drugs show benefits on symptoms, disability, and mortality rather than surrogate outcomes, which would give doctors and patients greater certainty about the benefits and risks. Regulators could also insist that more trials examine the added value of new compared with old drugs. Lower prices for innovative drugs could be negotiated. Companies could plan a more comprehensive research programme with the knowledge that their income streams were more reliable, although still vulnerable to price competition from other companies and to being superseded by more innovative drugs. There would be fewer impediments to the adoption of innovations on financial grounds and less reason to persist with low cost generic drugs if they are inferior.

In the meantime, on the basis of the limited evidence available, patients with osteoporosis should generally not be treated with calcium supplements, either alone or combined with vitamin D, unless they are also receiving an effective treatment for osteoporosis for a recognised indication. Research on whether such supplements are needed as an adjunct to effective agents is urgently required.

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