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A Protocol for Systematic Review and Meta-analysis of Dietary Calcium and Fracture

Tong Yang

Food Science and Engineering, Wuhan Polytechnic University, Wuhan, HuBei,China, 430023

1056182501@qq.com

Abstract. Despite the fact that there are few and inconsistent randomized controlled studies investigating calcium obtained from food, calcium and vitamin D are frequently utilized as calcium supplements in people's daily lives, so the effectiveness of food-derived calcium and calcium or a combination of the two is in question. Through a review and qualitative research, this paper explores the connection between dietary calcium and fracture incidence. The link between dietary calcium, vitamin D, or combination dietary calcium and vitamin D supplements and fracture incidence in the elderly over 65 years of age was examined. Calcium intake was based on food sources.A comprehensive search of the PubMed database was conducted. Use the keywords dietary calcium, vitamin D, and fracture to search for relevant randomized controlled trials in English studies. Search the Cochrane Library and EMBASE databases to add additional randomized clinical trials. Data were extracted from papers independently by two reviewers and entered into data tables. By using Cochran's Q statistic and the I-2 statistic, it was possible to determine whether the rate estimates were heterogeneous. Hip fracture was the primary outcome and total fracture was the secondary outcome.

Key words: Dietary calcium, Fracture, Hip fracture, Meta analysis, Systematic review

1. Introduction

The gradual loss of calcium from people's bones as they age means that older people have a greater tendency to suffer fragility fractures when impacted by external forces or during their own movement. The cost of medical care for fragility fractures in the elderly population in the United States is estimated to be $20 billion per year[1].

In a study of osteoporosis in a Chinese population, it was concluded that changing lifestyle habits, increased sedentary time, and decreased physical activity would lead to an increased rate of osteoporosis in the population in general[2]. This leads to a higher risk of fracture.Hip fractures caused by osteoporosis are a significant and expensive social health issue [3]. For older adults, hip fractures pose a much greater risk than bone injuries. Ninety percent of annual hip fractures in the United States occur in patients older than 50 years of age[4]. Mortality from any other factor after hip fracture is increased 5 to 8 times[3].

In order to maintain healthy bones, calcium and vitamin D are necessary. Because the mineralization of tissue during fracture healing depends on proper calcium levels, calcium and vitamin deficiencies may lead to impaired fracture healing, common in patients with osteoporosis [5]. Zhu and Prince concluded that to lower their risk of future fractures, postmenopausal women (over 50 years of

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age) and men over 70 years of age should consume more calcium[6]. Therefore, it would appear that calcium and vitamin D are the most popular and generally advised ways to lower the risk of fractures. This has been validated in many previous studies. However, fewer previous reports have examined dietary calcium alone. Studies combining dietary calcium and vitamin D or dietary calcium and vitamin D alone are considerably less common. Dietary calcium is easier and more convenient to consume in the lives than pharmaceuticals. Therefore, investigating dietary calcium and fracture risk could help to explore more effective fracture prevention measures for the elderly and provide scientific guidance on the selection of calcium supplementation sources for the elderly, while at the same time, if the results of the study are valid, it could effectively reduce the annual investment in medical care for fractures in the elderly.

The purpose of this study was to look at the possible impact of dietary calcium, vitamin D, or dietary calcium plus vitamin D on the risk of fracture in older persons..

2. Literature review

Literature from PubMed, Cochrane Library, and EMBASE databases can be searched within the first five years from inception to ensure inclusion of the most recent studies. Restricted to English-language literature. The Medical Subject Headings (MeSH) used were: calcium, food-derived calcium, milk or other dairy products, fracture[7]. For example, study on calcium, vitamin D, and fracture risk in community-dwelling seniors, the literature search criteria were modified[8]. After identifying the literature, a manual search needs to be conducted and relevant reviews of this literature need to be read. In the systematic review or meta-analysis, the initial randomized clinical trials (RCTs) were completed.

The initial study needs to be included when the subjects were older than fifty years. The sources of food source calcium were milk, other dairy products, and hydroxyapatite. Hydroxyapatite was included because it is made from animal bone, and in addition to calcium, it contains substances, such as proteins, minerals[7]. It also needs the inclusion of randomized controlled trials with hip fracture, total fracture as the endpoint. The study should exclusion of studies without a placebo group or without a treatment group, exclusion of combined studies that included other diseases (such as coronary heart disease and type 2 diabetes), exclusion of fracture or osteoporosis at the time of the initial study, and exclusion of studies using vitamin D analogs (osteopontin) or hydroxylated vitamin D from trials[8].

3. Methods

3.1. Types of interventions

The experimental interventions included calcium, vitamin D and a combination of the two. The calcium is primarily of food origin, including milk, dairy products, and hydroxyapatite. Vitamin D effects are baseline (20 or 20 ng/mL) levels of blood 25-hydroxyvitamin D. The comparison intervention control intervention was placebo or no treatment.

The following studies will be conducted:

1. a controlled experiment with randomization that compares calcium supplementation to no therapy or placebo;
2. a study that compares vitamin D alone to placebo or no therapy in a random, controlled setting;
3. A placebo group or no treatment group in a randomized controlled study of calcium and vitamin D.

3.2. Types of outcome measures

The main result was the number of hip fractures among participants and the secondary outcome was the number of total fractures among participants. Total fractures was defined as severe whole-body multiple fractures and fractures without a detailed description of the fracture site, while fractures describing a single site were not considered to be total fractures.

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3.3. Data extraction and synthesis

For data extraction, two investigators will be required to work independently to navigate and collect the information, including

1. general characteristics (name of investigator, year of study, source of funding, country of study, year of publication);
2. details about the study population (age, sex, race, sample size, duration of fracture, type of fracture);
3. interventions (assessment methods, population distribution, drug measures, duration of follow-up);
4. outcomes (hip fracture and total fracture, time of measurement, methods of outcome assessment, adverse effects);
5. methods (type of statistical analysis);
6. results. Non-vertebral fractures were considered as total fractures in our study when the study did not consider non-vertebral fractures as total fractures.

It was noted that because hip fractures are the most severe fractures in the elderly, the number of hip fractures was considered as the primary study (primary outcome)[8].

3.4. Dealing with missing data

If the detailed data that cannot be identified due to the presence of data validation, we can try to contact the study authors to obtain verification and validation information. The following approach will be taken to assess missing information,

(1) Missing data for all participants will not be accepted.

(2) Missing data from the experimental group will not be accepted, but data from the experimental group with missing data from the control group will be accepted.

3.5. Assessment of reporting biases

When assessing the quality of a study, the assessment method that requires two independent researchers is universal. But often after ensuring that the most accurate studies are conducted, confusion and bias are still inevitable. The Newcastle-Ottawa Scale and the RoB 2 tool, both developed by the Cochrane Collaboration, will be applied to assess the probability of bias in retrospective cohort studies and RCTs, respectively. such as bias resulting from the randomization method, bias resulting from deviating from the targeted therapy, and bias resulting from the absence of study results[7],bias inside the results of measuring, and selection bias in reporting outcomes[9]. The Newcastle-Ottawa scale evaluates participant selection and study equivalence, identification of interesting results and exposures. Studies rated 9 stars or above are thought to have little chance of bias. Studies with 7- or 8-star rating indicates a moderate risk. And studies with 6-star or lower rating indicates a higher risk of bias[9]. For the guidelines for determining the chance of bias for each item, consult the Cochrane Handbook. The risk of bias assessment is important to help other researchers conducting reference to this article understand the extent to which each outcome is referable.

3.6. Evaluation of heterogeneity

Mantel-Haenszel χ 2 heterogeneity when testing for statistical heterogeneity test has considerable heterogeneity is defined by the Cochrane Handbook at I2 > 50% [10]. P values classify heterogeneity into four categories: minimal or no heterogeneity (P<40%); medium heterogeneity (30%<P<60%); significant heterogeneity (50%<P<90%); and substantial heterogeneity (75%<P<100%).

Also, if I 2 < 50% or P , we will use a fixed effects model > .10, otherwise,A random-effect model and an inferential statistical are options,[10]should always give 95% confidence intervals.

3.7. Check reporting bias

Publication bias is due to the inclusion of studies that are not sufficiently representative of the full range of studies published in the field. A funnel plot to assess publication bias is used in which

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asymmetry can be assessed visually. If the funnel is asymmetric, it may mean that additional included wen are needed.

3.8. Verify the reliability of the proof

You can grade the quality of the proof using the GRADE technique (Graded Assessment, Development, and Evaluation). The GRADE technique takes into account research design, reliability and straightforwardness of outcomes, and bias risk. Grades for the results range from extremely low to very high. Two reviewers separately completed the reviews, and in the event of a dispute, a third independent reviewer intervened and discussed.

3.9. Assessment of reporting biases

Publication bias was prevalent and we detected asymmetry by funnel plot using Egger's test.

4. Conclusion

Osteoporotic hip fractures and total fractures as well as are important influences on mortality in elderly populations of all races worldwide. This meta-analysis's thoroughness makes it strong. The minimal number of randomized controlled studies of calcium supplements and dietary supplies with fractures being an endpoint, despite the fact that the actual data were not processed, is one drawback that might be foreseen.

Only two modest randomized controlled studies of diet calcium sources, according to prior research, published fracture data[7]. A large proportion of studies of fracture have used bone mineral density as the final outcome, and this study did not include bone mineral density as an outcome, so inclusion of bone mineral density as the final outcome could be considered in the actual screening conducted afterwards.

Moreover, the study did not discuss the differences in risk among populations living in different regions, which may lead to large differences in fracture outcomes due to differences in dietary structure and lifestyle habits. For example, the proportion of dairy products in common foods is much higher in European countries than in Asian countries, and the final conclusions may not accurately guide the elderly population in different countries regarding fracture prevention.

Another limitation is that the timing of dosing was not clearly defined in this study, the use of diet calcium and vitamin D for the prevention and treatment of fracture are closely related to the timing of dosing, and it is possible that the effects of long-term small dosing may be very different from short-term large dosing, so the timing of dosing may be included as a variable in subsequent actual studies.

In addition, we need to note the high statistical heterogeneity among research with in meta-analysis (I 2 > 50%). This could be because we employed an arbitrary meta-analysis that accounts for heterogeneity, and the outcomes should be viewed as representing the situation results of the whole trial.

Owing to the dearth of research on dietary calcium, the final literature available in the literature base is limited, which could easily lead to final results that are not baked oil representative, and in subsequent studies we could also include articles that involve dietary calcium but are not the main subject of study and extract the information we need. This study only mentions the research method and does not have a detailed data analysis, which provides guidance for subsequent studies.

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