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Review Article

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CALCIUM AND VITAMIN D SUPPLEMENTS IN THE TREATMENT OF OSTEOPOROSIS

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Osteoporosis is widely distributed in our communities due to a lot of causes like aging of the population, lack of physical activities, limited outside life and avoidance of sun exposure.

Osteoporosis causes a lot of clinical disorders like backache, bone pain, and generalized fatiguability. In addition to that we face a lot of osteoporotic fractures with catastrophic sequalae on personal and community levels that cause increased morbidity and mortality rate which cost billions of dollars each year.

Prevention of this disorder is highly recommended to improve people's health and to decrease financial burden upon the society. Modifiable factors can be worked on to achieve the goal.

One of the best ways to prevent osteoporosis is optimization of people's dietary habits by inclusion of food rich in vitamin D and calcium which need special effort by medical personnel. So that, the primary care for osteoporosis needs to include good food habits.

The fracture risk assessment algorithm is a tool used by medical professionals to predict people at risk of fracture due to osteoporosis and to take steps to prevent that. The steps include antiresorptive drugs in addition to food supplements.

Treatment of osteoporosis by antiresorptive drugs like bisphosphonates and monoclonal antibody need special consideration regarding patients' general conditions and his serum calcium and vitamin D level.

This paper reviews the recent data regarding vitamin D and calcium supplements that utilized to prevent and treat osteoporosis.

Keywords: osteoporotic bone , calcium supplement , cholecalciferol, weak bone.

Reviews

Osteoporosis is a bone condition caused by low bone mass associated with abnormal bone structure that results in weak bone and predispose to bone failure.[1]

The diagnosis is by measuring bone density and comparing that to a healthy bone of the same race. When the bone density is less than 2.5 standard deviation of the normal, it is osteoporosis and if it is less than 1.5 standard deviation, so it is osteopenia according to the WHO.[1]

Prevention of osteoporosis is possible and better than treatment of osteoporosis. The authors point of view is that Prevention can be achieved through personal level and through community interventions.

The suggested Community environment modification include availability of walking and bicycle tracks in the city streets, provision of parks for sun exposure and sport spaces in each district of the city, tax legitimation to discourage unhealthy foods and habits, increase concern regarding the protocol for prescription of drugs like steroids, provision of antiosteoporosis drugs in the primary health centers or hospital. At personal level, encouragement of outside life, physical activities, healthy diet, avoid smoking, sports recreation.

There is controversy about the usage, efficacy and safety of vit D and calcium supplements alone or with other antiresorptive drugs in the treatment of osteoporosis. This paper will review the usage and significance of vitamin D and Calcium supplements for osteoporosis prevention and treatment.[2]

Calcium

Achieving the optimal dietary calcium intake is the best way to prevent osteoporosis. There are a lot of food rich in elemental calcium, especially dairy products and fresh vegetables. In addition to that, elemental calcium in dairy products has high absorbability and bioavailability compared to other sources of calcium with mostly cheaper

price. [2] To measure the daily consumption of calcium by diet we can estimate it by measuring the amount of food eaten. For example, one glass (200 ml) of milk provides the body with approximately 300 mg of elemental calcium.[2] The calcium intake from milk, eggs, fish, and fresh vegetables is proven to decrease risk of osteoporosis in contrary to calcium intake from cakes, biscuits, and bread.[3]

Another source which is available and simple way to provide the body with bioavailable calcium from mineral water enriched with calcium. Recent study proved that the absorbability of elemental calcium in mineral water is equal or even better than elemental calcium from the milk.[4]

When adequate dietary calcium could not be achieved, so we need to provide the body with another source of calcium which is in form of calcium salts drugs. Most widely used calcium salts in the markets are carbonate and citrate. Both salts have good absorbability and are the best source of calcium to the body. Calcium carbonate advised to be taken with food to enhance absorption and it is cheaper. Calcium citrate can be taken in empty stomach and with another antacid drugs. In the case of patients with kidney problems it is better to take calcium citrate which is safer.[5]

Recent studies support the benefit of ingestion of calcium carbonate supplements with food to enhance absorption. Optimum elemental calcium absorbability from calcium carbonate linked to the presence of acidic gastric secretions with foods, a recent trial proved that calcium carbonate taken in empty stomach in women without food resulted in decreased elemental calcium absorption.[6] Another case control study proves that not even calcium absorption decreases but also risk of hip fracture increased in patient chronically used proton pump inhibitors (omeprazole).[7] So, it is proved by evidence-based medicine to take calcium supplements with food to optimized calcium absorption.

The best calcium supplements regarding the amount of elemental calcium are the calcium carbonate supplements. It provides the body with about 40 % elemental calcium compared with about 21% of calcium citrate, 13 % calcium lactate salts and 9% calcium gluconate.[2] So, patients can take less amount of calcium carbonate supplements with better elemental calcium content than calcium citrate. To add, the price is cheaper.

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The best dosage interval for calcium supplements is 4-6 hours to ensure best absorption because the human digestive system is capable of absorbing 500-600 mg of calcium at the same time..[8]

Calcium salts adverse reactions have reported in many patients especially GIT symptoms, but in general it is not severe. According to a recent Women's Health Initiative (WHI) report, the rate of gastrointestinal adverse reactions, especially constipation is equal in both placebo group and group taken calcium supplements..[9] Patients that have risk of GIT problems should take the supplements gradually, start with very small dose and wide interval and then achieve the required dosage over 1-2 months.

Calcium interactions with other drugs.[10]

Calcium can decrease the oral absorption of some drugs:

- Iron.
- Tetracyclines.
- Fluoroquinolones.
- Bisphosphonates.
- Thyroid supplements.
- Phenytoin.
- Digoxin.

Drugs affect calcium supplements when taken together:

- Laxative and mineral oil both can inhibit calcium absorption.
- Aluminum and magnesium antacids increase urinary excretion of calcium.
- Thiazide and other diuretics increase risk of hypercalcemia and hypercalciuria.
- Digoxin with calcium supplements was found to highly increase the blood calcium level.[10,11]

Oral bisphosphonates it is recommended to be taken in an empty stomach before a meal with about 20-30 minutes interval from the meal. Bisphosphonates are highly adherent to calcium, so it is better to avoid calcium intake with bisphosphonates.

Accordingly, it is very important to know the drugs already taken by the patients before starting the calcium and vitamin D supplements to avoid possible drug interactions.

Food interactions

Dietary Calcium sometimes is inadequate, especially in lactose intolerant people, vegetarians and people with calorie restricted

diet. In such people calcium supplements are essential. .

To add, oxalate, protein, phytate, and caffeine were proven to affect body absorption of calcium, so it is advised to avoid food rich with these contents in order not to interfere with calcium absorption from other foods.[12]

Almonds, potatoes, raspberries and dates are highly nutritious food, but they advised to be moderated because they are high in oxalate which interferes with calcium absorption.

Wheat bran and beans, sesame seeds, sunflower seeds, and nuts, are high in phytate. So, to ensure adequate absorption of calcium, phytate containing food need to be taken separately to prevent calcium and other minerals bond to phytate.[11]

Cardiovascular diseases

According to a recent recommendation of National Osteoporosis Foundation and the American Society for Preventive Cardiology, dietary and supplemental calcium consider safe regarding cardiovascular diseases [2]

Renal calculi

Most common type of renal calculi are oxalate compound which is a crystallized form of calcium.

Most recent studies proved that there was no direct correlation between calcium supplements and formation of renal calculi. The main etiological factors for formation of renal calculi are consumption too much oxalate and inadequate water intake.[13] However, in contrast to several previous research that proved no harmful effect in renal calculi formation with calcium supplements a women health initiative (WHI) study shows an increment in renal calculi formation among patients used calcium supplement by about 17 % .[9] Recently, modest calcium supplementation dosage (1000-1200 mg/day) is recommended to avoid nephrolithiasis.[2]

Vitamin D

Bone health maintenance depends on vitamin D. The major role of cholecalciferol is the intestinal calcium absorption and secondarily enhancing bone resorption indirectly in case of prolonged hypercalcemia. So, vitamin D functions as the main factor in fine tuning of the serum calcium level.[14]

Sunlight exposure, diet, and dietary supplements are the main sources of vitamin D. Recent estimation reveals that dietary cholecalciferol is insufficient in 90 % of adult people.[15]

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The metabolism of cholecalciferol starts by UV ultraviolet interaction with the 7-dehydrocholecalciferol in the dermatome and converted to vitamin D3 precursor. vitamin D3 precursor is directly changed to vitamin D3 by interaction with body temperature. Vitamin D3 in the extracellular space transferred through venous blood to the liver by binding to albumin and lipoproteins that is called vitamin D binding proteins (DBP). DBP also has an immunomodulatory role and intervenes in bone development.[16] In the liver 25 hydroxylation occurs to vitamin D3 to form 25 hydroxy cholecalciferol. Then the 25 hydroxy cholecalciferol transferred in the kidney tubular cell in to 1,25 dihydroxy cholecalciferol by 1α-hydroxylase. The hydroxylation of vitamin D in the renal cells is adjusted by serum calcium together with phosphate level and PTH level.[16] 1,25 dihydroxy cholecalciferol which is the active vitamin d3 and it is major role in the calcium ion homeostasis in the blood.[16,17].

The oral source of vitamin D goes through the intestine and then via chylomicron in the lymphatic system enters the circulation. The vitamin binding protein transferred vitamin D to the liver. The same process of cholecalciferol hydroxylation occurred in hepatic cells and kidney.[18]

Cholecalciferol enhances calcium absorption in the intestines. Vit D deficiency causes low calcium level and in the case of hypocalcemia, osteoclast activation occurs which enhances calcium released through bone resorption.

Decrease dietary intake of calcium resulted in increased activation of cholecalciferol in the kidney. In turn cholecalciferol increases calcium released from bone resorption in favor of calcium resorption from intestine. If low serum calcium continues it results in increase release of PTH which in turn increase renal calcium reabsorption in the kidney together with osteoclast activation to freed calcium from osteoid matrix to the circulation. In case of continue low serum calcium level it will end with rickets in pediatric age group and osteomalcia and osteoporosis in adult.[19]

Sunlight exposure is the natural resources of cholecalciferol for the human body. Although there is increase in risk of skin cancer in direct exposure to Ultraviolet light. In addition to that people of dark skin or people use sunscreen cream usually has low vitamin D level.[20]

The practical recommendation to achieve normal vitamin D level in people of all skin types is to expose yourself to sun light in

summer, spring and winter season for 10 to 15 minutes from 10 o'clock morning time to 3 o'clock afternoon twice weekly minimum. The exposure should include the back, arm, hands and face. Sunscreen can be used after sun light exposure to limit skin burn.[20]

Dietary vitamin D is necessary in people with insufficient sun exposure. fish liver oil and fatty fish such as tuna, herring, and sword fish is rich with vitamin D and it can yield 300 to 600 units/3.5 ounces, cod liver oil can yield 400 units/teaspoonful, egg yolks can yield 20 units/yolk. Some cereals together with fortified drinks like milk, orange juice is rich source of vitamin D that can yield nearly 100 units per serving.[2]

In case of insufficient of vitamin D rich foods, vitamin D drugs are recommended to ensure sufficient vitamin D ingestion. Review of literature indicates that 800-1000 I.U. /day is an effective and safe method for both prevention and treatment of vitamin d deficiency. Vitamin D is a lipid soluble compound so the usage of vitamin D for long duration and continuous should be avoided.[21] However , recently it is advised to maintain optimal 25(OH)D levels by consumption of higher dose of vitamin D specially in elderly patients but not exceed 4000 I.U./ day to avoid vitamin D toxicosis. [22] So that the recommended vitamin D intake needs to be revised, especially in elderly people as higher intakes of vitamin D can enhance bone strength by reducing bone resorption. In general optimizing serum vitamin D level is crucial in treatment of osteoporosis. To add a recent report proved that normal serum level of vitamin D is associated with decrease rate of fall and low serum level of vitamin D below 10 ng/ml related with higher fall rate of about 78% in over 65 years old adult.[23]

The safe upper limit of vitamin D differs according to the state of the vitamin D in the body whether deficient, insufficient or normal. It also depends on the age and sex of the patient. However, we can control the amount of supplied vitamin D by regulation of the dose, the regime (continuous or interrupted) and the duration of the treatment. In addition, the regime of vitamin D provision depends on the outcomes of treatment like hypercalcemia, hypercalciuria and falls.(21). For example, in patient who receive Antiresorptive drugs, serum calcium level needs to be monitor as there is risk of hypocalcemia which corrected not only by calcium supplement but by the optimization of Vitamin D serum level.[2]

Dietary cholecalciferol supplements can be of either animal or plant origins. The vitamin

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D from plants source is called vitamin D2 or ergocalciferol and the vitamin d from animals' source called vitamin D3 or cholecalciferol. Although cholecalciferol is more available and abundant, both kinds of vitamin D were of the same potency and effectiveness for the optimization of the serum vitamin D level.[24]

Because of the long half-life of The Vit D 25(OH)D (two weeks); therefore, it is serum level mainly used to estimate vit D storage. Secondary hyperparathyroidism, osteomalacia and rickets are usually linked to low 25 hydroxycholecalciferol status .[24] The reference level of the serum 25 hydroxycholecalciferol is range from 25-80 ng/m.[25] The recommended adult level of 25 hydroxycholecalciferol in the blood should more than 30 ng/ml.[22]

Conclusions

1. Dairy products and fresh vegetables are rich in elemental calcium.
2. Calcium carbonate is taken with food to enhance absorption, and it is cheaper. Calcium citrate can be taken in an empty stomach, and it is safer for renal system.
3. No direct correlation between calcium supplements and formation of renal calculi.
4. Vitamin D is a main factor in fine tuning of the serum calcium level.
5. Vitamin D 800-1000 I.U. /day is an effective and safe method for both prevention and treatment of vitamin d deficiency.
6. The recommended vitamin D intake needs to be revised, especially in elderly people.

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References

1. Poduval M. and Vishwanathan K. Definition and Evolution of the Term Osteoporosis. Indian journal of orthopaedics. December 2023 (57)(1) 42-44. https://doi.org/10.1007/s43465-023-01013-2

2. Holly P. Kilim and Harold Rosen. Optimizing calcium and vitamin D intake through diet and supplements. Cleveland Clinic Journal of Medicine July 2018, 85 (7) 543-550. https://doi.org/10.3949/ccjm.85a.17106

3. Nasser M. Al-Daghri, Syed Danish Hussain, Abdullah M. Alnaami, et.al. Dietary Calcium Intake and Osteoporosis Risk in Arab Adults. Nutrients 2023, 15(13), 2829. https://doi.org/10.3390/nu15132829

4. Letizia Vannucci, Caterina Fossi, Sara Quattrini, et.al. Calcium Intake in Bone Health: A Focus on Calcium-Rich Mineral Waters Nutrients. 2018 Dec; 10(12): 1930. https://doi.org/10.3390/nu10121930

5. Heaney Robert P. Factors Influencing the Measurement of Bioavailability, Taking Calcium as a Model. The Journal of Nutrition 2001(131)(4),1344S-1348S. https://doi.org/10.1093/jn/131.4.1344S

6. da Maia T.F., de Camargo B.G., Pereira M.E., et al. Increased Risk of Fractures and Use of Proton Pump Inhibitors in Menopausal Women: Int J Environ Res Public Health. 2022 Oct; 19(20): 13501. https://doi.org/10.3390/ijerph192013501

7. Yu-Xiao Yang, James D. Lewis, Solomon Epstein, et al. Long-term Proton Pump Inhibitor Therapy and Risk of Hip Fracture. JAMA. 2006;296(24):2947-2953.https://doi.org/10.1001/jama.296.24.2947

8. John A Sunyecz. The use of calcium and vitamin D in the management of osteoporosis. Ther Clin Risk Manag. 2008 Aug; 4(4): 827-836. https://doi.org/10.2147/TCRM.S3552

9. Rebecca D Jackson, Andrea Z LaCroix, Margery Gass, et.al. Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med. 2006 Feb 16;354(7):669-83.

10. Aznar-Lou I., Carbonell-Duacastella C., Rodriguez A., et al. Prevalence of Medication-Dietary Supplement Combined Use and Associated Factors. Nutrients 2019, 11(10) 2466. https://doi.org/10.3390/nu11102466

11. Agnieszka Wiesner, Danuta Gajewska and Paweł Paśko. Levothyroxine Interactions with Food and Dietary Supplements-A Systematic Review. Pharmaceuticals 2021, 14(3), 206. https://doi.org/10.3390/ph14030206

12. Blerina Shkembi and Thom Huppertz. Calcium Absorption from Food Products: Food Matrix Effects. Nutrients 2022, 14(1), 180. https://doi.org/10.3390/nu14010180

13. Loris Borghi, Tania Schianchi, Tiziana Meschi, et.al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med. 2002 Jan 10;346(2):77-84. https://doi.org/10.1056/NEJMoa010369

14. Orwoll ES, Bliziotes M. Clinical aspects of the use of vitamin D and its metabolites. In Osteoporosis: Pathophysiology and Clinical Management. Totowa, NJ: Humana Press; 2003. pp. 293-307.

15. Moore C, Murphy MM, Keast DR, et al. Vitamin D intake in the United States. J Am Diet Assoc. 2004;104:9980-3. https://doi.org/10.1016/j.jada.2004.03.028

16. Prietl B., Treiber G., Pieber T.R., et.al. Vitamin D and immune function. Nutrients. 2013;5:2502-2521. https://doi.org/10.3390/nu5072502

17. Rosen Y., Daich J., Soliman I., et.al. Vitamin D and autoimmunity. Scand. J. Rheumato. 2016;45:439-447. https://doi.org/10.3109/03009742.2016.1151072

18. Bouillon R. Vitamin D: from photosynthesis, metabolism, and action to clinical applications. In. Endocrinology. Philadelphia, PA: WB Saunders; 2001. pp. 1009-28.
19. Holick MF. Vitamin D. In: Shrils M, et al. In Modern nutrition in health and disease. 10th edition. Baltimore, MA: Lippincott Williams and Wilkins; 2005a. pp. 329-45.
20. Young A.R., Narbutt J., Harrison G.I., et al. Optimal sunscreen use allows vitamin D synthesis. British Journal of Dermatology. 2019; 181(5): 124-124.https://doi.org/10.1111/bjd.18492
21. René Rizzoli. Vitamin D supplementation: upper limit for safety revisited? Aging Clin Exp Res. 2021; 33(1): 19-24. https://doi.org/10.1007/s40520-020-01678-x
22. Ian R Reid and Mark J Bolland. Calcium and/or Vitamin D Supplementation for the Prevention of Fragility Fractures: Who Needs It? Nutrients 2020, 12(4), 1011. https://doi.org/10.3390/nu12041011
23. Snijder MB, van Schoor NM, Pluijm SM, et al. Vitamin D status in relation to one-year risk of recurrent falling in older men and women. J Clin Endocrinol Metab. 2006;91:2980-5. https://doi.org/10.1210/jc.2006-0510
24. Van den Heuvel E.G., Lips P., Schoonmade L.J., et al. Comparison of the Effect of Daily Vitamin D2 and Vitamin D3 Supplementation on Serum 25-Hydroxyvitamin D Concentration (Total 25(OH)D, 25(OH)D2, and 25(OH)D3) and Importance of Body Mass Index: A Systematic Review and Meta-Analysis. Adv Nutr. 2024 Jan; 15(1): 100133. https://doi.org/10.1016/j.advnut.2023.09.016
25. Pagana KD, Pagana TJ, Pagana TN. Mosby's. Diagnostic & Laboratory Test Reference. 14th ed. St. Louis, Mo: Elsevier; 2019.

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