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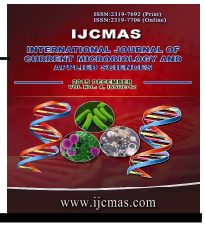

Review Article

Calcium and Vit D Supplementation in Patient of Type 2 DM

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K e y w o r d s

Calcium,
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Type 2 DM,
glucose
toxicity,
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resistance

A B S T R A C T

This review paper focuses on the use of the oral calcium and oral vit D supplementations in the persons already suffering from type 2 DM. As already known the diabetes is a disease with multi system involvement mainly it involves nerves ,eyes &kidneys but in long term disease and poorly controlled blood sugar levels leads to hyperglycemia and due to inappropriate treatment associated history of recurrent falls leading to multiple minor and major fractures leading to disruption of the microarchitecture of the bone .Various studies conducted during last two decades provided the information that neither the bone quality nor the strength is upto the level in comparison to normal subject. This review article focuses mainly on the need of calcium and vit D supplementation in patient of type 2 DM for improvement of bone quality and decrement of morbidity due to skeletal insufficiency in same.

Introduction

Diabetes and osteoporosis are common and complex disorders with a significant health burden. These disorders can be often associated in middle-age and elderly individuals. In fact, a consistent increase in fracture risk has been specifically described in subjects with both type 1 (DM1) or type 2 (DM2) diabetes[1]

Although common age-related conditions (i.e. a decrease in sex hormone or vitamin D levels) or risk factors (i.e. reduced physical activity) may explain at least in part the association between diabetes and osteoporosis, detrimental skeletal effects of glucose toxicity and insulin resistance or deficiency, adipose derived hormones, diabetic complications and pharmacological treatment have been also postulated [2,3].

However, the pathogenetic mechanisms of impaired skeletal strength in DM1 and DM2 remain to be clarified in detail and are only in part reflected by variation in BMD [4].

To date, however, the exact mechanism behind the bone fragility and fracture in diabetes mellitus is not yet known. Previous experimental and histomorphometry observations often evidenced a condition of low bone turnover and decreased osteoblast activity in both DM1 and DM2 [5].

Role of Vit D and Calcium on Bone Metabolism

Apart from local regulatory system present in bones harmones also play a vital role in bone homeostasis. Osteocytes and other osteoblastic cells express membrane receptors for hormones including the parathyroid hormone (PTH), carboxy terminal PTH, estrogen, VIT D3 and corticosteroids, Insulin and thyroid harmone which all contribute to the regulation of the production and apoptosis of osteoblasts and osteocytes and thus bone homeostasis[6].

Vitamin D is acquired from dietary sources, or through UV light induced synthesis in the skin from 7-dehydrocholesterol, and hepatic 25 hydroxylation and subsequent renal 1α hydroxylation results in the active form 1α, 25dihydroxy vitaminD3.

A potent hormone responsible for the biological actions on the regulation of calcium/phosphate homeostasis via binding to vitamin D receptor (VDR). 1α25(OH)2D3 can stimulate bone resorption and formation, regulating bone remodeling by acting on both osteoclastic and osteoblastic cell lineages, respectively [7]. The various antiresorptive and anabolic agents available would not be able to inhibit bone loss without the balance of nitrogen and minerals.

Daily intakes of 1000 mg/day by men and women under the age of 50 and 1200 mg/day for those over 50 are recommended by National Osteoporosis Foundation (2003).Vitamin D is also essential for the maintenance of healthy bone in addition to the promotion of calcium absorption.

Various treatment modalities are present to treat the decreased bone mineral density such as **A preventive approach**:- That tends to reduce or at least slow the onset of osteoporosis and pharmacological one for osteoporotic patients who have an increased risk of bone fractures.

Recommended doses of calcium supplements should be proportionate to the degree of deficiency (typically 500-1000 mg/day). The only calcium supplementation has been shown to be capable of producing modest density increases in subjects with deficient intake or menopause by at least 5 years.

The calcium addition, administered with vitamin D, also reduces the risk of falling apart to fractures[8].

Vit D

Vitamin D may be administered in a bolus from 100,000 to 1,200,000 IU in order to restore deposits, followed by a maintenance dose from 800 IU/day in daily doses or firewalls; actually it was seen that these are the minimum dose and that it would be necessary to arrive at 1200 IU/day to ensure the daily requirement.

Drugs used in Treatment of Osteoporosis

Currently approved drugs for the treatment of osteoporosis include bisphosphonates, parathyroid hormone (PTH), strontium ranelate,hormone replacement therapy and selective receptor modulators of estradiol (SERM).

Bisphosphonates

Are synthetic compounds can block osteoclastic activity by binding selectively to the bone surface undergoes remodeling; they are called so because they are characterized by a bisphosphonate link. This class of drugs reduces bone turnover in a dose-dependent and is absorbed only for 0.5-1% from the gastrointestinal tract.

Etidronate and clodronate are drugs of second choice who are today less used especially for the low antifracturative effect, emerged during clinical studies. Alendronate and risedronate are aminophosphonates and they can increase bone density and have an extensive documentation of effectiveness for the prevention of vertebral or non-vertebral fractures.

Zoledronate, an aminobisphosphonate, usable due to proved able to reduce the risk of new fractures clinics administered annually at a dosage of 5 mg; published studies have also shown that this drug can reduce the mortalities in osteoporotic patients.

Side effects are most important for this class of drugs include:-esophegeal erosion, osteonecrosis of jaw, subtrochantric fractures.

The parathyroid hormone (1-84) and the fragment 1-34 (Teriparatide), administered subcutaneously, stimulates osteoblastic activity with an anabolic effect on bone. BMD gains are much higher compared to the results obtained with bisphosphonates, but only at the level of trabecular bone. A very costly therapy reserved for the patients not responding to regular treatment.

Strontium ranelate is a labile adsorb to the bone hydroxyapatite crystals and appears able to stimulate the subperiosteal new bone while reducing the reabsorption of bone tissue and is ranked among the medications for joint action. But increased risk of thromboembolism is present. In a recent publication of the WHO reported numerous tables was related the risk of fracture (for multiple sites or for the femur) to 10 years with age, BMI (weight in Kg/height in m2), the T-score to the femoral neck and other clinical risk factors.

Processing these data is been developed an algorithm called free-use predictive FRAX. (38) The availability of these algorithms has allowed the development of a new instrument of risk estimation of fracture as "DerivedFracture Risk Assessment" or DeFRA. Using the latter guarantees a rational and uniform diagnostic and therapeutic approach of osteoporosis. (9).

Correlation with Diabetes

In the years ' 50, Albright and Regina were able to prove that diabetes was associated with a loss of bone mass due to osteoporosis[10].

In recent years, in particular, many studies were carried out to try to better understand the effects of diabetic pathology on bone it is known that the States of acute hyperglycemia that chronic, suppress the expression of genes associated with maturation in mouse osteoblastic diabetic models, while increasing the expression of genes such as PPAR which stimulates the differentiation of mesenchymal stem cells in adipocytes. [11]. Indeed, the results of recent experimental investigations have shown that, similarly to what happens in other tissues, a State of chronic Hyperglycemia is able to induce non-enzymatic glycosylation and transformation of various proteins in AGE, especially at the level of collagen type 1 (12). The hyperglycemia and its high oxidative stress, frequently observed in diabetes, would lead to creations of cross-glycosylated links to collagenic chains that constitute the bone matrix, leading to a deterioration of the mineralization of biomechanical properties of the skeleton. The AGEs can also affect bone metabolism by inducing the expression of proinflammatory cytokines that promote resorption, i.e."TNF", or inhibiting osteoblastic activity and maturation. (13).

Several studies have shown that insulin exerts an anabolic effect of the skeleton, so that changes in insulin secretion results in a State of low bone turnover with a considerable reduction of the number of osteoblasts and of their activity(14).

The anabolic action of insulin on bone tissue are at least partly mediated by IGF-1, therefore, a deterioration of the axis GH/IGF-1 has acquired more importance which further inadequate bone formation mechanism in insulin deficiency conditions. (15).

In addition, higher levels of blood glucose and principally the duration of the disease were associated with increased bone resorption parameters, while low levels of IGF-1 could be regarded as the greatest predictors of bone strength. It is important to emphasize that these same bone abnormalities have been described in young diabetic patients and with a fairly good glycemic control (HbA1C 8.1%); this media reinforces the concept that the skeleton is a major target organ that reacts quickly to relatively little control metabolic(16).

It is important to emphasize that recent evidence has shown that the skeleton can in turn affect carbohydrate metabolism; in particular, it seems that bone proteins such as Osteocalcin (the main protein secreted by osteoblasts) can mediate the secretion of insulin in the pancreas and the expression of adiponectin in adipose tissue cells, suggesting that factors of skeletal derivation might influence the secretion of insulin and glucose tolerance in vivo. (17).

Previous experimental and histo-morphometry observations often evidenced a condition of low bone turnover and decreased osteoblast activity in both DM1 and DM2 .

As discussed earlier there is a decrement in the bone mineral density in both type 1 and type 2 DM patients various studies were done regarding supplementation of vit D and calcium from outside to the patients.

A study conducted by Anastassios G. Pittas et al published in 2007 (18) was a meta analysis its results were favouring the supplementation of calcium and vit D in patient of type 2 DM. vitamin D and calcium insufficiency may negatively influence glycemia while combined supplementation with both nutrients may be beneficial in optimizing glucose metabolism. evidence to date suggests that vitamin D and calcium deficiency influences post-prandial glycemia and insulin response while supplementation may be beneficial in optimizing these processes, our understanding of the exact mechanisms by which vitamin D and calcium may promote beta cell function, or ameliorate insulin resistance and systemic inflammation is incomplete.

A report from Martins and colleagues on data from over 15,000 adults in the Third National Health and Nutrition Examination Survey is perhaps the best recent evidence on vitamin D and the general population. The 25(OH)-vitamin D levels were lower in diabetics, women, the elderly, and racial minorities, groups that are at increased risk of having chronic kidney disease (CKD) Scragg and colleagues reported in 1995 the association of low 25(OH)-vitamin D levels with the presence of DM or glucose intolerance.] Consistent with these findings, low vitamin D levels are associated with obesity, as assessed by body mass index or waist circumference, and weakly with elevated glycated hemoglobin (A1C) levels(19).

One study titled as Effect of vitamin D supplementation on glycemic control in patients with type 2 diabetes by Nisha Nigil Haroon et al Results of the various short-term studies (follow up≤3 months) suggested that vitamin D supplementation had a positive impact on glycemic control and metabolic parameters such as insulin resistance and beta cell dysfunction. However, the evidence was weak due to the low methodological quality of the studies. There was no significant effect on HbA1c, beta cell function and insulin resistance in the long-term studies (follow up > 3 months) (20).

Serum Vitamin D Levels in Newly Detected Type 2 Diabetes Mellitus Dr. G. B. Doddamani1 et al in 2013 research signifies the role of hypovitaminosis D in patient newly detected of type 2 DM (21)

Various studies conclude that the supplementation of calcium & VIT D in a patient of type 2 DM in recommended doses not only improves the bone microarchitecture but also delays the development of atherosclerosis and insulin resistance in subjects. However long and detailed clinical trials should be conducted in future to prove its beneficial effect for the same.

Until now it can be said that it is beneficial and recommended to give calcium and vit D in patients suffering from type 2 DM even in impaired fasting glucose subjects.

Reference

1. Vestergaard P 2007 Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes--a metaanalysis Osteoporosis Int 18:427-444
2. Maurer MS, Burcham J, Cheng H 2005 Diabetes mellitus is associated with an increased risk of falls in elderly residents of a long-term care facility. J Gerontol A Biol Sci Med Sci 60:1157–1162; 3
3. Hofbauer LC, Brueck CC, Singh SK, Dobnig H 2007 Osteoporosis in Patients With Diabetes Mellitus J Bone Miner Res 22:1317–1328
4. Merlotti D, Gennari L, Dotta F, Lauro D, Nuti R 2010 Mechanisms of impaired bone strength in type 1 and 2 diabetes. Nutritional Metabolic Cardiovascular Dis 20:683-690
5. McCabe LR 2007 Understanding the pathology and mechanisms of type I diabetic bone loss. J Cell Biochem102:1343-1357
6. Ardawi MS, Rouzi AA, Al-Sibiani SA, Al-Senani NS, Qari MH, Mousa SA. High serum sclerostin predicts the occurrence of osteoporotic fractures in postmenopausal women: the Center of Excellence for Osteoporosis Research study. *J Bone Miner Res*. 2012;27: 2592–2602.
7. Chapuy MC, Alrot ME et al (1992) Vitamin D and calcium to prevent hip fracture in elderly women. N Engl J Med; 327: 1637-42
8. Kato M, Patel MS, Levasseur R et al (2002) Cbfa1-independent decrease in osteoblast proliferation, osteopenia, and persistent embryonic eye vascularization in mice deficient in Lrp5, a Wnt coreceptor. J Cell Biol; 157: 303-14
9. Isaiah G, R, Rini GB Giorgino, Bevilacqua M et al (2003) Prevalence of hypovitaminosis D in elderly women: clinical consequence and risk factors. Osteoporos Int; 14: 577-82
10. McCabe LR (2007) Understanding the pathology and mechanisms of type 1 diabetic bone loss. J Cell Biochem; 102: 57-1343

11. Botolin S, LR (2006) McCabe's Chronic hyperglycemia osteoblast modulates gene expression through osmotic and non-osmotic pathways. J Cell Biochem; 99: 411-24
12. Saito M, Marumo k. (2010) Collagen cross links as a determinanten of bone quality: a possible explanation for bone fragility in again, osteoporosis, and diabetes mellitus. Osteoporos Int; 21: 195-214
14. Katayama Y, Akatsu T, Yamamoto M (1996) Role of nonenzymatic glycosylation of type 1 collagen in diabetic osteopenia. J Bone Miner Res; 11: 931-7
15. Goodman WG, Hori MT (1984) Dimished bone formation in experimental diabetes. Relationship to osteoid maturation and mineralization. Diabetes; 33: 825-33
16. Bereket to et al. (1999). Alterations in the growth hormone-insulinlike growth axis in insulin dependent diabetes mellitus. Horm Metab Res; 31: 172-81
17. De Schepper, Smiths J, Rosseneu S, Bollen P, Luis o. Lumbar spine bone mineral density in children with recent onset diabetes. Horm Res 1998; 50: 193-6)
18. The Role of Vitamin D and Calcium in type 2 diabetes. A systematic Review and Meta-Analysis by Anastassios G pittas, Joseph lau ,Frank Hu J Clin Endocrinol Metab. PMC 2007 Nov 21.
19. Scragg R, Holdaway I, Singh V, Metcalf P, Baker J, Dryson E. Serum 25-hydroxyvitamin D3 levels decreased in impaired glucose tolerance and diabetes mellitus. Diabetes Res Clin Pract. 1995;27:181-188
20. Nigil Haroon et al. Journal of Diabetes & Metabolic Disorders (2015) 14:3 DOI 10.1186/s40200-015-0130-9
21. Scholars Journal of Applied Medical Sciences (SJAMS) Serum Vitamin D Levels in Newly Detected Type 2 Diabetes Mellitus Dr. G. B. Doddamani1, Dr. Umakant Boke, Dr. Shreeram Kora, Dr. Renuprasad Chickmath Sch. J. App. Med. Sci., 2013; 1(6):786-788.