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Editorial

The calcium and vitamin D dilemma: To D or not to D?

Vitamin D (Vit D), the sunshine vitamin and calcium, its partner in metabolism are under intense scrutiny after having been raised to a pedestal as panacea for all ills. After the marine creatures living in calcium-rich ocean evolved into vertebrates with skeletons and ventured into land where availability of calcium was at a premium, the maintenance of skeletal homeostasis became a major physiological challenge. Vit D ensured that intestinal calcium absorption from dietary sources was efficient and thus helped in the development and maintenance of a mammalian skeleton. This makes obtaining Vit D from either diet or sunlight crucial for the skeletal health. Lighter skin color seen as part of evolution as humans migrated away from the tropics ensured adequate UV-B penetration to produce greater levels of Vit D. Similar adaptive changes with lighter skin color are seen in female gender which could explain their higher needs of Vit D during pregnancy and lactation. With time, the role of Vit D in various extra-skeletal functions has been discovered in regulating up to estimated 2000 genes that places this hormone vitamin at a prime place of metabolic significance way beyond its role in skeletal physiology.^{1,2}

Vit D deficiency is widespread amongst children, adults, and pregnant women in India.³ This is despite the availability of adequate sunshine all year round due to various reasons like skin pigmentation, clothing, inadequate exposure to mid-day sun, and non-availability of Vit D fortified foods. Calcium deficiency is also rampant due to poor consumption of calcium-rich foods, excess dietary phytates, and co-existent Vit D deficiency.^{4,5} While levels of >30 ng/ml of 25-OH Vit D are considered sufficient for skeletal metabolism, optimum extra-skeletal benefits require levels of 40–60 ng/ml or even higher. These levels cannot be achieved by the existing recommended dietary allowance (RDA) and require a daily intake of 800–1000 IU of Vit D. The existing recommendations on dietary calcium and Vit D requirements are being proposed to be further enhanced. This has also led to rising demand for fortification of commonly used food products with Vit D which is being proposed to be implemented at the national level. During the period of active skeletal buildup to a peak bone mass in the third decade of life, and during bone loss which starts around the menopausal age in women and in the seventh decade in men, the requirement of increasing intake of calcium and Vit D has been well appreciated. Similar

requirements are noted during pregnancy and lactation. In those with low bone mass (osteoporosis or osteopenia) or osteoporotic fractures, calcium and Vit D supplementation is imperative to optimize therapy and accrue the benefit of the anti resorptive or anabolic therapy being administered.

The role of calcium and Vit D supplementation alone in preventing post-menopausal bone loss also has been shown in some studies.^{6,7} This is especially so in areas which have lower dietary intake of calcium and Vit D deficiency. However, there is no benefit in terms of fracture risk reduction with this modality of treatment.⁸ Causal role of Vit D deficiency in its extra-skeletal role like cardiovascular diseases, metabolic syndrome, Type 2 Diabetes, allergic disorders, certain cancers, and chronic infections is not yet conclusively proven by strong statistical evidence. Circumstantial evidence and data collected by observational studies and meta-analyses can only generate a hypothesis. Proving this hypothesis will require well-designed trials with pre-defined end points. Use of Vit D or calcium supplementation for these indications is hence not recommended. Studies targeted to gather evidence in this regard are the need of the hour.

This fairy tale fantasy of search for this panacea is not without its share of a villain. There is a rising voice that points toward the role of Vit D and calcium combination in its alleged contribution toward increased prevalence of cardiovascular morbidity and mortality and renal stones. The devil's advocates quote large observational studies, meta analyses, and certain Randomized Control Trials (RCTs) where these were not the intended end points but an observation in post-hoc analysis that calcium and Vit D supplementation contributed to increased myocardial infarctions.^{9,10} These studies were conducted in countries where daily calcium intake is to the tune of 800–1200 mg. Countries where calcium intake is lower than 300–500 mg daily have excess CV mortality by itself likely due to this reason.¹¹ Use of calcium and Vit D supplementation in such a population may in fact benefit them. Calcium supplementation might be beneficial in terms of fracture prevention and reduction of all-cause mortality particularly for those who live in regions with low dietary calcium intake. So to extrapolate the findings of such a study done in a calcium sufficient region and to apply it to those with low calcium intake is likely to yield incorrect conclusions and unfairly malign calcium supplements.

This has raised a debate in the scientific community regarding the role of such supplementation and the need for stringent guidelines as to its implementation in clinical practice. This has also created a dilemma in the minds of patients and general public at large regarding the use of calcium and Vit D supplements. Role of commercial interests of the pharmaceutical industry in promoting such prescription practices which in itself is a multi-million dollar industry is always a matter of concern. This makes it imperative for the medical fraternity to take a relook at its practice on the use of calcium and Vit D supplementation on a widespread basis. There is a need to stratify various clinical situations on the basis of essentiality of requirement for these supplements and issue necessary practice guidelines in this regard. Generation of region-specific data regarding prevalence of deficiency, dietary intakes, food types and their content, and toxins that may hamper absorption is important.

India is a country of widespread calcium and Vit D deficiency. Enhancing dietary intake of calcium-rich foods and Vit D supplementation is essential to optimize the skeletal benefits especially during the crunch periods of infancy, adolescence, peak bone mass accrual, pregnancy, lactation, and old age. Use of calcium-rich foods to increase calcium intake should be promoted over and above the use of supplements.

Vit D supplementation is indicated in the subset of patients where optimum levels are essential to be maintained as in patients of osteopenia/osteoporosis on therapy, pregnancy, perimenopausal age, and in the elderly. Large prospective interventional studies are required to prove the extra-skeletal benefits of calcium and Vit D supplementation. Till that happens, these benefits may only be restricted to the realms of fantasy and cannot be used as an evidence to promote widespread supplementation.

The scare generated regarding adverse impact of this supplementation is mainly from studies with weak evidence and generated from populations which are largely calcium and Vit D sufficient. However, scientific wisdom guides that such red signals should not be ignored and a close watch must be kept for these adverse events through stringent analysis of data from prospective studies which are pre-designed to adjudicate such an end point. Only then this hanging sword over the role of calcium and Vit D can be totally removed and the status of a true panacea be bestowed upon this combination.

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