ORIGINAL ARTICLE

EFFECT OF INTRAMUSCULAR 600000 IU OF VITAMIN D3, ON BLOOD LEVEL OF VITAMIN D3.

Jah Mirza Mohsin Ali

ABSTRACT

OBJECTIVE: To assess the effects of intramuscular 600,000IU of Vitamin D3 on blood level of Vitamin D3.

STUDY DESIGN: Cross-sectional, prospective, observational and analytical study.
PLACE AND DURATION OF STUDY: Fatima hospital, Baqai medical university, from Jan 2010 to July 2010.

METHODOLOGY: We included 40 patients with proven vitamin D3 deficiency in this study. All of these patients were having unexplained aches and pains. Patients having diagnosed reasons for aches and pains were excluded from this study. Patients were divided in four groups. Control, group A, B and C. Control received no external Vitamin D3, A weekly, B fortnightly and C monthly injection of 600000 IU .All four groups were followed for three months and monthly blood level of Vitamin D3 was carried out. Patients whose blood level reached normal levels were not given any further dose of vitamin.

RESULTS: Out of 40 patients, 30 (75%) were females and 10 (25%) were males. Group A 9(90%) reached normal levels in one month and 1(10%) showed toxic level but no clinical sigh of toxicity. In group B 2(20%) reached normal levels in one month and 2(20%) at two months, further 3(30%) at three months and 3(30%) remained deficient at the end of three month. In group C 1(10%) reached normal in one month, 2(20%) at two months, 2(20%) at three months and 5 (50%) showed improvement but not reached normal levels. All those patients in group A and B who reached normal level and were stopped getting injection showed gross fall in blood level at the end of three months.

CONCLUSION: The intramuscular injectable Vitamin D3 has remarkable effect on improving blood levels of Vitamin but need a maintenance dose and monitoring. This study has limitations because of sampling size is quite small so it cannot be recommended to adopt its results. There is a strong need for multicenter study including substantial number of patients to recommend a dose regimen.

KEY WORDS: Vitamin D3. Deficiency, intramuscular injection, 600000 IU Doses.

INTRODUCTION

There may be a strong relationship between lower rates of vitamin D3 in blood and a variety of chronic diseases [1]. In our population there is very high incidence of Vitamin D deficiency[2, 3].
An objective review is still necessary for the clinician to separate fact from fiction regarding this specific vitamin [4, 5]. Vitamin D deficiency has negative effects across the lifespan [6]. There is strong need for vitamin D education, supplementation, and follow-up in all ages and treatment settings.
Metabolism of vitamin D3 is well understood [7, 8]. It has been recently determined that there are vitamin D receptors in a variety of cells and therefore, vitamin D has a biological effect on more than mineral metabolism.
Various factors that can cause vitamin D deficiency are shown in Table I [9, 10, 11].
Recent studies suggest that the regular intake of vitamin D may increase blood levels greater than weekly or monthly oral intakes of equivalent doses [9].
The daily doses of Vitamin D3, recommended in literature is 400 to 1000 IU , has no or very little effect on blood level of Vitamin D3.[4] There is a strong need to readdress the required doses of this vitamin.
In this paper we are limiting our attention to changes on Blood level of vitamin D3 only, following injections of Vitamin D3. Other variables included in the study are not touched (to be presented as separate paper).

Crosspondance to:
Dr. Jah Mirza Mohsin Ali
Fatima Hospital, Baqai Medical University,
Karachi, Pakistan
Email: malijah@yahoo.com
mirzamohsinalijah@hotmail.com

METHODOLOGY

This cross-sectional, Prospective and analytical study was carried out at the department of surgery, orthopedics unit. Fatima hospital , Baqai medical

university. Karachi Pakistan from Jan 2010 to July 2010. In this study 40 adult subjects who presented at orthopedic OPD with deficiency of vitamin D3 blood levels were included (table II). Only adult female patients clinically healthy with regular menstrual periods but having chronic musculoskeletal aches and pains of more than six months duration were included in this study. Male patients were also clinically healthy and below 60 years of age were included in this study. Subjects who had known reasons for pain were excluded from this study. All subjects were formally explained in detail about the test and consent was taken. Once enrolled for the study, a complete history and detail clinical examination was performed in all patients and other relevant investigation were done. Investigations carried out in these patients included Blood complete picture, ESR , Random blood sugar , Urea , creatinine , uric acid , serum calcium , serum phosphates, LFT, Vitamin D 2 and D3,lipid profile and serum parathyroid level .Other variables included age , sex , occupation, body weight, pulse , blood pressure, frequency of passing routine daily urine and stool habits and urine analysis.

We divided our patients in four groups randomly, each group of 10 patients. They were labeled as control, group A ,group B and C. Control received no external source of Vitamin D3.Group A was given intramuscular 600,000IU of 1,25-dihydroxycholecalciferol(vitamin D 3) weekly, group B 600,000IU fortnightly and C monthly. All of the patients were given intramuscular injection in non dominant arm. All patients had their blood level of D3 checked at monthly interval and followed in outpatient at weekly interval. At each visit detailed examination with respect to vitamin D3 toxicity was carried out. Symptoms and signs we looked for vitamin D intoxication were related to hypercalcemia include. Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia, abdominal pain or stomach ache, polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, hypercalcemia hyperphosphatemia, albuminuria, hypercholesterolemia, elevated SGOT (AST) and SGPT (ALT), hypercalciuria, , nephrocalcinosis, hypertension, cardiac arrhythmias, dystrophy, sensory disturbances, dehydration, apathy, urinary tract infections, and overt psychosis.

Any new lump in body for ectopic calcification (soft-tissue calcification) with radiographic confirmation. Hypersensitivity reactions (pruritus, rash, hives, urticaria, and very rarely severe erythematous skin disorders, difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue) may occur in susceptible individuals.

Patient once reached normal level were not given further injection .These patients received oral paracetamol 500 mg three times per day for pain and no calcium supplements.

RESULTS

In this study 40 patients were investigated in a period of 3 months(table III). Out of these 30(75%) were females and 10(25%) were males. All the four groups had their blood level of vitaminD3 checked at monthly interval. Group A 9(90%) reached normal levels (20 to 60 ng/ml) in one month and 1(10%) showed toxic level but no clinical sign of toxicity. In group B 2(20%) reached normal levels in one month and 2(20%) at two months, further 3(30%) at three months and 3(30%) remained deficient at three months. In group C 1(10%) reached normal in one month, 2(20%) at two months, 2(20%) at three months and 5 (50%) showed improvement but not reached normal levels. All those who reached normal levels during this period were stopped getting further injection showed gradual decline in their levels. At the end of first month 12 patients showed normal blood level but showed gradual fall in blood levels . One patient with toxic level at first month ,only in blood with no clinical feature of toxicity, also showed drop in next month and deficient level at the end of third month. In this study 3(30%) of group B and 5(50%) of group C showed no improvement In our study no patient showed local sign of inflammation at the site of injection.

TABLE I[9,10,11]**:** The primary factors that can potentially determine an individual's vitamin D blood level.

FACTORS
AGING
BELLY FAT (OBESITY OR GREATER AMOUNT OF VISCERAL FAT)
CHOLESTEROL-LOWERING MEDICATIONS(STATINS)
DIETARY VITAMIN D INTAKE (NATURAL OR NON FORTIFIED SOURCES).
DIETARY VITAMIN D INTAKE (FORTIFIED VITAMIN D SOURCES)
FREQUENCY OF VITAMIN D INTAKE(DAILY VERSES WEEKLY VERSES MONTHLY)
SKIN PIGMENTATION
SUNLIGHT EXPOSURE DUE TO OUTSIDE ACTIVITIES
SUNSCREEN / SUN PROTECTIVE CLOTHING AND OTHER MEASURES
SUPPLEMENTAL VITAMIN D
ULTRA B (UV-B) LIGHT RADIATION(WAVE LENGTH = 290 TO 315 nm; EXPOSURE BASED ON WHERE ONE LIVES)
MEDICATIONS THAT CAN REDUCE VITAMIN D LEVEL: ANTICONVULSANTS (PHENYTOIN, CARBAMAZEPINE, PHENOBARBITAL), THIAZIDE DIURETICS, CIMETIDINE, CORTICOSTEROIDS, HEPARIN, NICOTINE. CHOLESTEROL-LOWERING MEDICATIONS: (CHOLESTYRAMINE, COLESTIPOL, EZETIMIBE). DIET AGENTS (XENICAL, ALLI)

TABLE II: Vitamin D Sufficiency Level
Although there is no consensus document on serum 25-hydroxy-vitamin D level, most experts[6]

DEFICIENT LEVEL	BELOW 20 ng/ml	50 nmol/L
INSUFFICIENT LEVEL	BETWEEN 20 AND 30 ng/ml	50 TO 75 nmol/L
SUFFICIENCY	ABOVE 30 ng/ to 100ng/ml	75 nmol/l to 250 nmol/L
TOXICITY	ABOVE 100 ng/ml.	ABOVE 250 nmol/L

TABLE III: RESULTS.

	0 month				after First month				after Second month				Third month			
No. of pts reached normal / SUFFICIENCY level					12 normal				4 normal				5 normal			
	Control	A	B	C	Control	A weekly inj	B fortnightly	C monthly	Control	A **No** Inj=10	B Fortnightly Inj = 8 **No** inj=2	C Monthly=9 No =1	Control	A **No** injection No inj =10	B Fortnightly =8 **No** inj =4	C Monthly = 8 **No** = 3
Female to male ratio n=40 30:10	7:1	7:1	7:1	9:1												
DEFICIENT LEVEL < 20 ng/mL	10	10	10	10	10	0	0	0	10	5	1	8	10	5	4	3
INSUFFICIENT LEVEL b/w 20- 30 ng/ml	0	0	0	0	0	0	8	9	0	3	7	0	0	5	3	5
SUFFICIENCY b/w 30 – 100 ng/ml	0	0	0	0	0	9	2	1	0	2	2	2	0	0	3	2
Toxic level-more than 100ng/ml	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

DISCUSSION

Vitamin D3 deficiency disrupts phosphorus and calcium homeostasis, causing disruption in neuromuscular function, muscle strength, cancer, diabetes, bone mineralization and inflammatory illnesses [13]. It may have some involvement in the pathogenesis of autoimmune diseases and cancer[14, 15,16].

Deficiency occurs in most, when people do not have adequate exposure to UVB rays or adequate dietary intake. The blood test for vitamin D reflects the total amount of vitamin D in the body that was coming from all sources (diet, dietary supplements, and the sun), which makes this test extremely important in the field of nutrition.

There has been no consensus on the optimal level of vitamin D intake, and this is why many laboratories report the normal range of vitamin D to be so wide (20 to 100 ng/ml). Best blood level of vitamin D and at what level of vitamin D could maintain muscle strength, prevent falls, improve dental health, prevent different diseases is not clear yet. However, according to recent research and recommendations from vitamin D experts, ideal serum levels are between 30 and 60 ng/ml[3,6,17].

In general, 100 IU (2.5 mcg) of vitamin D per day can raise the vitamin D blood test only 1 ng/ml or just 2.5 nmol/L after 2 to 3 months[6]. This amount can be obtained through diet, supplements, and sun

exposure. The Oral forms of Vitamin D3, Tablet form, are easily available and prescribed indiscriminately. The effect of oral (Tablet) Vitamin D3 , which is usually taken as 400 to 1000 i/u per day, is not clear and there is not a single study found in literature to establish the appropriate dose and it effect on blood levels. These tablets are expensive as compared to injections. Likewise Injectable form of vitamin D also available in different strength with no uniformity in recommendation .This study shows the changes brought by injectable Vitamin D3 on blood level of same but has limitation due to small sample size.

Injectable Vitamin D3 is a good source of this Vitamin. These are far cheaper than tablets and appears to be safe as well. Class of patients attending our Outpatient are very poor .Low cost of injection is the only option which improves their compliance for treatment. But with a drawback of getting their regular expensive blood test.

CONCLUSION

Optimal level of vitamin D intake to get, ideal serum levels (between 30 and 60 ng/ml) is not yet uniform in literature. The daily recommended doses are found to be very low or inadequate to achieve ideal level. The dose of injectable D3 is also not uniform in literature. In our opinion the dose of vitamin D3 should be individualized on the basis of blood level. There is a strong need for a maintenance dose otherwise keeping D3 level to normal appears to be not possible. There is a possibility for having toxic level of Vitamin D3 with injectable doses. This observation gives a rational advice to have blood levels done regularly , at monthly interval and regular clinical checkup for any symptoms or signs of toxicity when on this injections. The injection of Vitamin D3 600000 I/U when given on weekly basis , raises the blood level. But when discontinued the level drops back to deficiency level.

Our study has its limitation because of small size. There is a strong need to have a study of substantial number of patients to give scientific guideline for loading and maintenance doses.

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