Hypervitaminosis D in Kashmiri Population: A Case Series of 11 Patients

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Abstract

Vitamin D,although safe in usual doses can be toxic in higher doses and can affect different body organs due to hypercalcemia.As vitamin D deficiency is quiet common in Kashmir,so people either by self medication or as prescribed by clinicians take vitamin D empirically leading to hypervitaminosis D.We undertook a similar study of 11 cases of hypervitaminosis D who developed symptoms of hypercalcemia due to excess intake vitamin D supplements for back pains, osteoarthritis, osteoporosis, diabetes, etc. From this study we finally concluded that before prescribing vitamin D supplements, we should properly look into the background history of the patient along with biochemical parameters to know the status of vitamin D so that toxicity is prevented.

Keywords: *Vitamin D,Hyervitaminosis D,25-hydroxy vitamin D,Hypercalcemia, Postmenopausal females, Biochemical parameters.*

I. INTRODUCTION

Vitamin D which plays an important role in maintaining calcium homeostasis, not only controls calcium absorption from intestine but also has effects on bone and parathyroid hormone levels.[1,2]As vitamin D keeps in check extracellular calcium levels, thus is vital for many neuromuscular and metabolic functions.[1,2] Most of the vitamin D is formed in the body as a result of sunlight on skin(80-90%),rest of it is achieved from dietary means(10-20%).[3] After vitamin D_2 or D_3 is acquired in the body, it undergoes hydroxylation in liver and kidney by their respective enzymes leading to final formation of active vitamin D,calcitriol or 1,25$(OH)_2$D which carries the requisite functions of vitamin D.Vitamin D deficiency results in defective bone mineralization, secondary hyperparathyroidism, cortical bone loss which results in osteoporosis and hip fractures[4,5] ,also it has been found to be linked to psoriasis[6],cancers[7,8],multiple sclerosis[9],diabetes[10],blood pressure[11],muscle power[12,13] ,depression[14],asthma[15] ,etc.

Although the usual intake of vitamin D rarely causes toxicity or hypercalcemia[16](as approved by food and nutrition board,daily intake upto 2000 IU can be consumed without any risk of toxicity[17]) but large doses of vitamin D can be toxic[18].Patients on anticonvulsants or with intestinal malabsorption usually require oral(50000 IU/week for 6-8 weeks[14]) or intramuscular administration(250000 IU biannually) of vitamin D but even in these patients regular 24 hour urine calcium excretion monitoring should be done to check toxicity which should be less than 250mg[19]. Although vitamin D toxicity is very rare due to wide gap between therapeutic and toxic doses[20,21],but most of the patients with back pains,joint pains,fractures, diabetes mellitus,etc take huge amounts of vitamin D supplements putting themselves at risk of toxicity. As of above fact, enough literature on vitamin D toxicity is lacking but sporadic reports are there[22].

Clinically vitamin D toxicity presents with manifestations involving most of the body systems due to universal presence of the vitamin D receptor CYP27B1[23],also it leads to exaggeration of vitamin D signal transduction processes and gene expression(transient receptor potential cation channel V6,calbindins,CaATPase,receptor activator of NF-KB ligand)[24] which collectively leads to hypercalcemia and to some extent hyperphosphatemia, the symptoms of which are nausea, vomiting, dehydration, renal failure,etc[25].Adverse effects of vitamin D toxicity is more likely to occur in high risk patients like those with renal failure, primary hyperparathyroidism or in elderly[20,21].Symptomatic vitamin D toxicity can be treated with saline dieresis,bisphosphonates,calcitonin and glucocorticoids while asymptomatic hypercalcemia needs observation and discontinuation of vitamin D.

II. MATERIALS AND METHODS

The present prospective study was conducted in post-graduate department of orthopaedics, government medical college Srinagar in collaboration with department of medicine, government medical college Srinagar, J&K. A total number of 11 patients were studied from july 2013 to January 2016.Patients

were diagnosed by means of their clinical features and investigations.

III. RESULTS

(Table 1)In our study,a total of 11 patients with 6 females(54.54%) and 5 males(45.45%) in the age group of 23-70 years with a mean of 53 years were found. Patients had vauge symptoms in the form of weakness, fatigue, nausea, vomiting, excessive thirst, constipation, weight loss, etc which were attributed to hypervitaminosis D,due to the fact that all patients had very previously normal with no significant past medical history(only for two patients who were diabetics on oral hypoglycemics with all normal parameters as per their reports) except for excess intake of vitamin D in the form of injections or sachets for back pain, osteoporosis, joint pains, muscle aches, etc. Serum calcium was found elevated in most of the patients in the range of 11.01-15.2 mg/dl with a mean of 12.35.Serum phosphorus was found in normal range or elevated in most of the patients with a mean of 4.14mg/dl(2.84-6.1) while 25-hydroxy vitamin D levels were in the range of 258-410ng/ml with a mean of 319.09.Serum urea was found in the range of 18-76mg/dl with a mean of 49.63 and creatinine levels were in the range of 1.13-3.77mg/dl(mean of 2.14).Serum albumin and alkaline phosphatase levels were in the range of 3.3-3.9g/dl(mean of 3.66) and 114-419U/L(mean of 217.54).All the patients were treated conservatively where further vitamin D and calcium intake was stopped and were given saline diuresis, steroids and bisphosphanates except one patient who need dialysis. All patients improved clinically as well as by their biochemical parameters over period of few weeks.

Table 1 Showing Results of all Patients

S.No.	Age(years)	Sex	Symptoms	Vitamin D intake	Sr.Ca^{2+}(mg/dl)	Sr.P(mg/dl)	25-OH-D(ng/ml)	PTH(pg/ml)	Sr.urea (mg/dl)	Sr.creatinine(mg/dl)	Sr.albumin(g/dl)	Sr. A.P(U/L)
1.	60	M	Knee pains, oliguria, constipation, weakness	Multiple vitamin D 6 lac IU injections over 2 years	15.2	3.37	375	_	36	1.77	3.6	152
2.	23	M	Recurrent vomiting, constipation, polydipsia, irritability	5 injections of vitamin D 6 lac IU over one month	12.29	3.92	338	7.9	76	3.77	3.69	196
3.	38	F	Weight loss, anorexia, weakness	Multiple injections over 5-7 years of vitamin D	12.1	4.85	280	7.2	66	3.6	3.8	412
4.	70	M	Chronic smoker with proximal muscle weakness, nausea, oliguria, fatigue	8 injections of vitamin D 6 lac IU over last 8 months	13.09	5.10	390	_	52	2.79	3.7	155
5.	42	M	Abdominal pain,	30-35 injections	11.1	2.84	258	8.2	18	1.13	3.8	183

			constipation, irritability, polyuria, recurrent urinary tract infections	of vitamin D 6 lac IU as aphrodisiac								
6.	51	F	Type2 diabetes mellitus(controlled) with weakness, polyuria and polydipsia	Multiple injections of vitamin D and multivitamins over 2 years,7 injections ist week and then at regular intervals	11.01	4	299	_	20	1.4	3.3	419
7.	50	F	Polydipsia, anorexia, nausea, vomiting	Vitamin D 6 lac IU injections at 1-2 monthly intervals for last 4-5 years	13.52	6.1	410	8.9	38	2.4	3.7	149
8.	64	F	Constipation, fatigue, weight loss, irritablity	Vitamin d sachets and injections over last 3 years	11.7	3.62	260	_	46	1.3	3.9	172
9.	58	M	Oliguria, weakness, vomiting	Vitamin D multivamin injections at monthly intervals over last 1-1/2 years	12.3	5.17	340	15.8	58	2.1	3.76	249

10.	68	F	Polydipsia, nausea, abdominal pain, constipation	Multiple vitamin D sachets 60000 IU over last 5-10 years at periodic intervals for knee pains	11.25	2.95	268	6.8	72	1.5	3.5	192
11.	59	F	Anorexia, weakness, polydipsia with type2 diabetes mellitus(controlled)	Viatimin D sachets and injections over 3-4 years	12.32	3.72	292	14.2	64	1.8	3.6	114

Sr.=serum,Ca^{2+}=calcium,P=phosphorus,25-OH-D=25-hydroxy vitamin d,PTH=parathyroid hormone,A.P=alkaline phosphatase

IV. DISCUSSION

Vitamin D,although required for many functions of the body is toxic in excess and can be fatal at times. In third world countries, patients take huge amounts of vitamin D and calcium supplements in order to cure their joint pains, generalized weakness, etc and in return it leads to excess which usually goes unrecognized till the stage it leads to severe toxicity, which is due to fact of lack of access to proper health care, follow up, monitoring of various biochemical parameters and also poor economy.

In our study,all the patients had vitamin D toxicity with symptoms of hypercalcemia due to excess intake of vitamin D in the form of injections or sachets (all patients had vitamin D levels beyond 100ng/ml which is much higher than normal levels[17,19]) .All other causes like malignancy and other granulomatus diseases were ruled out.Serum parathyroid hormone levels were on lower or normal side which rules out hyperparathyroidism[17].Dietary excess more than normal recommended intake(400-800IU)[26]was unlikely in our study because there was no such history of consumption of dietary products with excess vitamin D or vitamin D fortified foods,moreso C-1 hydroxylation of vitamin D is so tightly regulated that non-hydroxylated prohormones of vitamin D found in diet are less likely to cause toxicity than hydroxylated active pharmaceutical products of vitamin D,unless dietary products are taken in large doses as in the study of Nussey S et al[28].Elderly and postmenopausal females were the majority of the patients in our study due to decreased renal function in old people and reduced ability to excrete excess calcium,and excess intake of vitamin D and calcium in postmenopausal females for osteoporotic back and other joint pains, leads to vitamin D toxicity as also mentioned by Moushmi Lodh et al[29].As vitamin D is stored in fat, hypercalcemia can develop over a long period and also it can remain for many years[30], as in some of our patients who developed the toxicity over years. Hypercalcemia, normal or high phosphate levels, normal or low levels of alkaline phosphatase, high levels of vitamin D,low parathriod levels and high urea and creatinine levels are found in hypervitaminosis D[31],as also found in our study in majority of patients.

As also mentioned in various studies[32,33,34],advocating higher intake of viatim D and calcium intake for diabetics, pregnant women, lactating women, postmenopausal women, obese, older people, etc without any documentary evidence is unwarranted and does not reflect an evidence based approach which in long term can lead to hypervitaminosis D and hypercalcemia.

V. CONCLUSION

Due to wide therapeutic index and lack of monitoring, many cases of mild vitamin D toxicity go unnoticed, only the cases with serious side effects attend hospitals, thus reducing the actual number of cases of hypervitaminosis D.But inspite of that fact, still hyperviatminosis D is not so common but recommending vitamin D and calcium to patients without any labortary evidence of vitamin D deficiency is not warranted and one should strictly have the documented deficiency before they are prescribed vitamin D supplements to prevent them from serious side effects of vitamin D overdose. Due to lack of enough sunlight, cold climate and being a forest surplus

area, most of the patients in Kashmir are presumed to be vitamin D deficient and are prescribed lot of vitamin D supplements. Also as the custom of cross legged sitting makes osteoarthritis quiet common in kashmiri people, along with cold induced joint and back pains in winter months in these patients, for which they frequently visit different doctors who prescribe the same medications in the form of analgesics, vitamin D and calcium supplements, only changing the trades which ultimately leading to hypervitaminosis D and hypercalcemia.

From the above study we finally conclude that before prescribing vitamin D supplements, we should properly look into the background history of the patient along with biochemical parameters to know the status of vitamin D so that toxicity is prevented.

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