

Original Article

The Influence of Insufficient Exposure to Sunlight on Vitamin D Deficiency and Related Symptoms among Women in the State of Kuwait

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ABSTRACT

Objectives: To study Vitamin D deficiency as a cause of osteomalacia in young women and to assess the therapeutic effects of high dose vitamin D and sunlight exposure

Design: Prospective

Setting: Al-Jahra hospital, Kuwait

Subjects: Twenty four consecutive patients with osteomalacia presenting to the endocrinology clinic

Intervention: High dose vitamin D, calcium supplements, sunlight exposure and increased consumption of dairy products

Main outcome measure: We confirm that adequate sunlight exposure is an essential factor in the prevention of osteomalacia.

Results: All the 24 patients were female and their mean age and standard deviation (SD) was 23.08 ± 9.14 years. The means and SD of initial biochemical parameters and

during treatment respectively were: serum calcium = 2.12 ± 0.14 , 2.24 ± 0.37 mmol/l (N = 2.2 - 2.6), serum phosphate = 0.88 ± 0.26 , 1.28 ± 0.24 mmol/l (N = 0.8 - 1.6), alkaline phosphatase = 413.1 ± 292.2 , 220.7 ± 186.0 mmol/l (N = 95 - 200), urinary calcium = 1.26 ± 0.95 , 2.16 ± 1.67 mmol/24 hr (N = 0.33 - 7.5), urine phosphate = 8.10 ± 6.14 , 8.52 ± 8.87 mmol/24 hr (N = 13 - 42), serum PTH = 38.68 ± 23.43 , 10.85 ± 4.49 pmol/l (N = 0.7 - 5.6), 25(OH)D = 8.10 ± 8.05 nmol/l (N = 23 - 113) and bone densitometry scan = -2.086 ± 0.91 .

Conclusion: Osteomalacia due to insufficient sunlight exposure and inadequate dairy product consumption is not uncommon even in a sunny climate. The patients improved after treatment with high dose of vitamin D, adequate sunlight exposure and consumption dairy products.

KEYWORDS: health education, high dose vitamin D, sunny climate, osteomalacia

INTRODUCTION

Since 1920, rickets has almost disappeared in the western world because of the use of cod liver oil or vitamin D preparations and by adequate exposure to sunshine^[1,2]. In 1967 it was recognized that osteomalacia was more common than expected especially in elderly women^[3]. The major role of vitamin D is to increase the absorption of calcium and phosphate for the mineralization of the skeleton. Vitamin D deficiency results in failure of mineralization of a growing or a mature bone causing rickets in children or osteomalacia in adults respectively. Vitamin D3 or cholecalciferol, is synthesized in the skin from conversion of the precursor, 7-dehydrocholesterol by the ultraviolet (UV) light of the sun. UV radiation passes through glass and most plastics but not through heavy clothing and sunscreens^[1].

Vitamin D is hydroxylated in the liver into 25-hydroxyvitamin D [25(OH)D], which is the major

circulating metabolite^[4]. Further hydroxylation into 1, 25-dihydroxyvitamin D [$1,25(\text{OH})_2\text{D}$] occurs primarily in the kidney. The hydroxylation in the kidney is stimulated by parathyroid hormone (PTH) and suppressed by phosphate. $1,25(\text{OH})_2\text{D}$ is the most active metabolite stimulating the absorption of calcium and phosphate from the gut, whereas 25(OH)D has limited biological activity. Vitamin D binding protein (DBP) binds vitamin D and its metabolites and transports them in the bloodstream. Some nutrients also contain vitamin D3, e.g., fatty fish, eggs and fortified dairy products. Vitamin D deficiency causes stimulation of the parathyroid glands, which may lead to high bone turnover, bone loss, and hip fractures. Vitamin D deficiency was suspected in patients with symptoms of bone pain and muscle weakness and was diagnosed by low serum calcium and phosphate levels and elevated alkaline phosphatase activity. In this study, we reviewed the cause of

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vitamin D deficiency in patients with osteomalacia that was complicated with osteoporosis in some of them in a place with sunny climate (Kuwait) and assessed the clinical and biochemical effect of high doses of vitamin D in the treatment of osteomalacia.

SUBJECTS AND METHODS

From July 2002 to June 2003, we recruited 24 consecutive patients with osteomalacia. Patients were referred to the metabolic bone disease clinic in Al-Jahra hospital, Kuwait, from orthopedic or medical outpatient clinics for evaluation of osteomalacia. They presented with symptoms of bone pain, fatigue, proximal muscle weakness, biochemical findings and/or radiological images suggestive of osteomalacia. Other causes of rickets and osteomalacia apart from vitamin D deficiency such as inadequate dietary ingestion or insufficient sunlight exposure were excluded by appropriate clinical and laboratory investigations. The clinical parameters recorded were: age, sex, exposure to sunlight (exposure of the uncovered face and arms or lower legs to sun light at least 10 minutes daily), diet that contain at least 1 g of calcium per day, and symptoms of generalized weakness, numbness, bone pain, and signs of proximal myopathy. The biochemical parameters recorded initially and after treatment with high dose vitamin D were: serum calcium, phosphate, alkaline phosphatase, urinary calcium and phosphate, PTH and 25(OH)D levels.

The bone mineral density of the lumbar and femoral sites was performed in most patients using a DEXA scan. Osteopenia is defined according to the WHO as T- Score = -1 and > -2.5 and osteoporosis as T-score < -2.5. Complete blood count, liver and renal profiles were performed in all patients. Patients were treated with oral vitamin D (ergocalciferol) 600,000 U per week for two weeks, then every other week for two doses then once monthly for three months. They were also given oral calcium 1.5 g per day in the form of calcium carbonate or citrate. Symptoms of hypercalcemia if any, such as lethargy, fatigue, confusion, nausea, vomiting, constipation, polyuria, polydipsia and abdominal pain were noted. Health education in the value of sunlight exposure for at least 10 minutes daily of the uncovered skin such as the face, arms and/or legs and consumption of at least 1 g of calcium daily from dairy product, green vegetables and/or fish consumption was given to the patients verbally in the clinic. Exclusion criteria included patients with liver, gastrointestinal or kidney disease and those on any medication that interferes with vitamin D metabolism such as antiepileptic drugs.

RESULTS

All the 24 patients diagnosed with osteomalacia

Table 1a: Pre-treatment biochemical values of patients with osteomalacia

Patient No.	Calcium (mmol/l)	Phosphate (mmol/l)	Alkaline phosphatase (mmol/l)	Urinary Calcium (mmol/24hr)	Urinary phosphate (mmol/24hr)	PTH25 (pmol/l)	(OH)D level (nmol/l)
1	2.24	0.9	738	0.87	9.6	32.4	<5
2	2.23	1.6	455	0.5	8	24.7	7
3	1.96	0.75	257	0.5	1.7	68.7	<5
4	2.15	0.49	410	0.3	6.87	58.3	<5
5	2.06	0.68	221	2.01	14.1	24.8	6
6	2.17	0.61	144	0.84	18.9	22.5	10
7	2.28	0.89	228	0.46	2.4	61.2	<5
8	2.17	0.59	285	0.68	6.3	48.5	6
9	2.07	0.62	153	0.49	7.22	15	15.8
10	2.02	0.73	329	1.46	10.36	16.2	7.1
11	2.23	0.95	231	1.02	4.21	59.4	<5
12	1.91	0.88	136	0.77	6.68	55.5	<5
13	2.02	0.81	399	0.49	7.33	83	<5
14	2.2	1.81	82	2.43	1.04	4	<5
15	2.3	1.28	217	0.92	0.33	40.3	6.4
16	2.26	0.91	103	1.68	6.44	4	22.4
17	2.07	0.8	302	1.02	8.11	48.4	<5
18	1.81	0.85	186	0.55	13.9	23.5	<5
19	2.2	0.71	191	0.7	5.64	55.4	9.6
20	2.2	0.97	305	0.3	4.87	39.8	<5
21	2.18	0.58	206	1.5	1.6	3.6	24.8
22	2.1	0.6	637	1.23	3.05	17.4	2.1
23	1.99	0.82	344	0.4	5.7	82	<5
24	2.03	0.72	250	1.32	2.78	18	<5

due to vitamin D deficiency were female and the mean age and standard deviation (SD) was 23.08 ± 9.14 years. Diffuse bone pain and generalized weakness were the most common presenting symptoms while proximal myopathy was the most common presenting sign. Inadequate dairy product intake (less than 500 mg of calcium per week in any form of calcium containing products such as dairy products, green vegetables or fish was reported by most of the patients) and insufficient sunlight exposure (less than 10 minutes per week due to almost complete covering of the skin by wearing a traditional and/or religious clothing, (for e.g., long dress hejab, niqab, abaya and gloves and socks) were an obvious cause of vitamin D deficiency. Only one patient had symptoms of hypocalcemia (numbness in the fingers and around the mouth); physical examination showed mild positive Chvostek's sign but negative Trousseau's sign. The corrected serum calcium was 1.81 mmol/l. The mean \pm SD of the initial biochemical parameters and during treatment (Table 1a and Table 1b) respectively were: serum calcium = 2.12 ± 0.14 , 2.24 ± 0.37 mmol/l (normal = 2.2-2.6), serum phosphate = 0.88 ± 0.26 , 1.28 ± 0.24 mmol/l (normal = 0.8-1.6), alkaline phosphatase = 413.1 ± 292.2 , 220.7 ± 186.0 mmol/l (normal = 95-200), urinary calcium = 1.26 ± 0.95 , 2.16 ± 1.67 mmol/24hr (normal = 0.33-7.5), urine phosphate = 8.10 ± 6.14 , 8.52 ± 8.87 mmol/24

Table 1b: biochemical values post-treatment with high dose of vitD.

Patient No.	Calcium (mmol/l)	Phosphate (mmol/l)	Alkaline phosphatase (mmol/l)	Urinary Calcium (mmol/24hr)	Urinary phosphate (mmol/24hr)	PTH25 (pmol/l)	(OH)D level (nmol/l)
1	2.51	1.32	273	7.1	2.68	4.7	102
2	2.29	1.71	126	0.9	4.7	1.2	120
3	2.36	1.22	72	3.49	10.1	5.9	78
4	2.34	1.57	144	6.2	9.4	4.4	112
5	2.17	1.01	224	2.33	8.43	10.1	155
6	2.18	0.92	119	3.32	12.3	5.5	222
7	2.32	1.67	34	1.04	21.4	2.8	80
8	2.04	1.32	85	4.12	4.5	16.3	96
9	2.4	1.39	469	3.66	16.3	19.1	109
10	2.6	1.22	122	2.46	7.92	17.4	65
11	2.26	1.77	272	2.8	9.4	6.1	194
12	2.4	1.44	360	2.61	8.8	12.6	90
13	2.35	1.34	215	1.99	1.01	4.61	50
14	2.4	1.47	68	3.21	5.96	2.33	141
15	2.32	1.35	166	1.86	6.73	5.5	—
16	2.31	1.19	93	1.02	8.7	4.93	78
17	2.09	1.12	219	1.82	0.27	6.22	89
18	2.34	1.35	122	2.0	5.4	3.8	—
19	2.3	1.41	96	0.98	4.2	2.15	39
20	2.61	2.44	112	3.21	4.47	5.2	120
21	2.4	1.33	147	—	—	—	75
22	2.2	1.04	401	2.31	6.11	7.01	81
23	2.19	1.02	213	1.97	9.01	5.7	65
24	2.41	1.23	89	3.12	.95	4.3	91

— = data not available

hr (normal = 13-42), serum PTH = 38.68 ± 23.43 , 10.85 ± 4.49 pmol/l (normal = 0.7-5.6), 25(OH)D = 8.10 ± 8.05 nmol/l (normal = 23-113) and skeletal X-ray showed pseudofractures (looser's zones, which are nearly pathognomonic features of rickets and osteomalacia) in some of our patient and pathological fracture in one patient. Bone densitometry scan showed osteopenia and osteoporosis in most patients and the mean T-Score was -2.086 ± 0.91 . All symptoms and signs improved dramatically during treatment with high dose of vitamin D and calcium. Health education that helped in greater exposure to sunlight (at least 10 minutes daily) and an increase in the consumption of dairy products to obtain approximately 1 g of calcium daily had an important role in the management. There were no reported symptoms or biochemical finding of hypercalcemia.

DISCUSSION

In our study, we found that patients in a sunny climate like Kuwait may still present with osteomalacia due to vitamin D deficiency as a result of insufficient sunlight exposure and inadequate dairy product intake. Almost all our patient (96%) consumed less than 1,000 mg of calcium per week, while the daily requirement is about 1,200 mg. Also some of our patients were from the low socioeconomic status and lived in houses where

little if any sunlight was allowed to enter. They were also ignorant about the value of vitamin D and calcium for the process of bone mineralization. They were eating very minimal amounts of calcium containing products (because they did not like milk and/or dairy products) and they were wearing traditional or religious clothing that covered all the body except the eyes (long dress hejab, niqab, abaya, gloves and socks). This resulted in inadequate exposure to sunlight required for vitamin D synthesis. These overclothing style among women as young as eight years old may lead to vitamin D deficiency. This also explains why all our patients were female since this clothing habit is exclusive to women. This is in agreement with a previous study which concluded that vitamin D deficiency in the Middle East was due to clothing habits⁶¹. It is also known from previous studies that UV radiation passes through glass and most plastics⁶¹ but not through clothing and sunscreen^{6,71}.

The prevalence of osteomalacia due to vitamin D deficiency is unknown in Kuwait and an epidemiological study is required.

Almost all of our patients presented with typical non-specific symptoms of osteomalacia such as lethargy, proximal muscle weakness, and diffuse bone pain. We noticed that proximal muscle weakness is so prominent among our patients that it can be used as a good indicator of improvement followed by other symptoms like diffuse bone pain and the feeling of lethargy. On presentation one patient had symptoms of hypocalcemia (numbness and tingling sensation around the mouth and corrected serum calcium found to be low (1.8 mmol/l) and another had a pathological fracture due to severe osteoporosis which is a known complication of severe osteomalacia.

The clinical diagnosis of osteomalacia is based on the findings of low levels of 25(OH)D, serum calcium, serum phosphate, urinary calcium and phosphate and increased levels of alkaline phosphatase, PTH. These abnormal biochemical findings result from vitamin D deficiency which results in decreased intestinal absorption of calcium and phosphate that consequently lead to secondary hyperparathyroidism. The cornerstone in the diagnosis of osteomalacia is the demonstration of a reduction in the mineral apposition rate, mineralization surface, and bone formation rate, which can be measured after the administration of double tetracycline labels before the bone biopsy. The diagnosis of osteomalacia in our patients was obvious from the clinical presentation, biochemical finding and radiological images. Therefore, there was no need for an invasive procedure like transcortical bone biopsy to establish the diagnosis.

We treated our patients with oral vitamin D (Ergocalciferol) 600,000 U per week for two weeks; then every other week for two doses and then once monthly for three months. We closely observed them for clinical features or biochemical finding of vitamin D intoxication such as bone resorption, hypercalcemia, hypercalciuria, and/or renal functional impairment. We did not encounter any complication when using such large doses of vitamin D in healthy young patients. Hypercalcemia due to high dose of vitamin D has been reported in few previous studies, where hypercalcemia was observed in older patients with a dose of 2000 IU/day and in one patient receiving a single oral dose of 600,000 IU. We did not have this complication possibly because our patients were young, healthy and without renal impairment and we treated them for short period of time. The occurrence of vitamin D intoxication is rather unpredictable, and it may occur even after years. Although practical, high doses may not be as safe as low doses.

We also treated our patient with 1-3 g of elemental calcium per day. Serum calcium was normal in 87.5% of patients and that was due to compensatory secondary hyperparathyroidism. Calcium deficiency has been suggested as a cause of rickets in children with apparently good exposure to sunlight in Nigeria and Bangladesh^[8,9]. Another study also showed that a very low dietary calcium intake might cause histological osteomalacia^[10].

Results of treatment of patient with vitamin D may be judged by monitoring the improvement in clinical features, biochemical tests such as increase of serum 25(OH)D, the decrease of serum PTH, decrease of markers of bone turnover, increase in BMD and decreased incidence of fractures.

Prevention of vitamin D deficiency by supplementation with a daily dose of 400-800 IU or consumption of milk fortified with vitamin D3 (400 IU/ quart or 400 IU/ liter) is very effective but may be impractical^[11]. Higher doses are seldom necessary, but 100,000 to 300,000 IU by mouth or by intramuscular injection have been used once every six months or once yearly because of the ease of administration, obviating the need of checking compliance^[5-7]. In these studies, hypercalcemia was not observed.

Health education in the value of sunlight exposure for at least 10 minutes daily of the uncovered skin e.g., face, arms and legs and consumption of at least 1 g of calcium daily from dairy product, green vegetables and/ or fish consumption should be widely recommended.

CONCLUSION

Osteomalacia due to vitamin D deficiency secondary to insufficient sunlight exposure and inadequate dairy product consumption is not uncommon in women of Jahra region of Kuwait in spite of the sunny climate. They improved symptomatically and biochemically, without ill effects, after treatment with high dose of vitamin D, and after health education that helped in greater exposure to sunlight and an increase in the consumption of dairy products to obtain approximately 1 g of calcium daily.

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