

**The Prescribing Trends of Vitamin D Supplements and the Concurrent Use of
Medicines for Chronic Conditions**

ABSTRACT

Aim: This study aims to determine the prescribing patterns of vitamin D supplements in a public hospital in Al-Kharj.

Methodology: This cross-sectional drug utilization study was conducted at a public hospital in Al-Kharj that included a review of the outpatient electronic prescriptions in 2018.

Results: In 2018, 311 patients were received Alfacalcidol. Most of the patients who received Alfacalcidol were females (76.21%), aging 40-69 (58.85%). The majority of Alfacalcidol drugs were prescribed by Internal Medicine department (56.91%). In 2018, 127 patients were received Cholecalciferol. Most of the patient were females (79.53%), in the age level between 30-39 (21.26%) followed by patients less than 10 years (18.90%). The majority of Cholecalciferol drugs were prescribed by Internal Medicine department (30.71%).

Conclusion: Vitamin D supplements were used frequently with other medicines for chronic conditions. More studies are needed to know the effect of Vitamin D supplements in the prevention or treatment of chronic diseases. Moreover, in order to use vitamin D supplements correctly, it is important to know the prescribing trends of these supplements.

Keywords: *Prescribing, Trends, Vitamin D, Chronic conditions.*

INTRODUCTION

Vitamin D is a fat-soluble vitamin that plays an important role in calcium homeostasis and bone metabolism [1]. Dermal synthesis and dietary intake (fatty fish livers, fortified food) are the major sources of ergocalciferol (D₂) and

cholecalciferol (D3), both of which are converted to 25-hydroxy-vitamin D2 (25-OH-D2) and 25-hydroxy-vitamin D3 (25-OH-D3) respectively in the liver by the enzyme hepatic enzyme 25-hydroxylase. Both 25-OH-D2 and 25-OH-D3 are then converted to the most active form of vitamin D (1,25 dihydroxyvitamin D) by the enzyme 1-alpha-hydroxylase in the kidneys [2].

Several preparations of vitamin D are available. Vitamin D3 (cholecalciferol), when compared with vitamin D2 (ergocalciferol), has been shown to be more efficacious in achieving optimal 25-hydroxyvitamin D levels, thus favoring vitamin D3 as a treatment of choice [3].

Vitamin D deficiency has been linked with significant complications such as cardiovascular events, obesity, metabolic syndrome, type 2 diabetes, various types of cancer, immune disorders, increased mortality and adverse pregnancy outcomes [4-6].

Prescription Patterns explain the extent and profile of drug use, trends, quality of drugs, and compliance with regional, state or national guidelines like standard treatment guidelines, usage of drugs from essential medicine list and use of generic drugs [7]. Investigating the prescribing trend of medications is very important to improve rational prescribing [8].

Pavani et al stated that defining drug prescription and consumption pattern provides advantageous feedback to prescribers in order to improve their prescribing behavior. Prescription analyzing studies help the policymakers to set the priorities to promote the rational use of medicines nationwide [9]. This study aims to determine the prescribing patterns of vitamin D supplements in a public hospital in Al-Kharj.

METHODOLOGY

This cross-sectional drug utilization study was conducted at a public hospital in Al-Kharj that included a review of the outpatient electronic prescriptions in 2018. Therefore, inclusion criteria included the outpatient prescriptions that contain Vitamin D supplement in 2018.

The multivitamin products that contain only low-dose vitamin D were excluded. Moreover, inpatient electronic prescriptions and the prescriptions before or after 2018 were excluded from the study.

The data were collected after the approval of the study by Institutional Review Board (IRB) ethical committee.

The data were collected using Microsoft Excel® and the descriptive data were represented as numbers and percentages. These data include the prescribing pattern of Alfacalcidol and Cholecalciferol (gender, age and nationality of patients receiving Vitamin D supplement in addition to the departments which prescribed it and the level of physicians who prescribed these supplements).

RESULTS and DISCUSSION

In 2018, 311 patients were received Alfacalcidol. Most of the patients who received Alfacalcidol were females (76.21%), aging 40-69 (58.85%). The majority of Alfacalcidol drugs were prescribed by Internal Medicine department (56.91%) followed by Orthopedic (21.86%). Furthermore, most of the prescribers were residents (72.67%). Table 1 shows the prescribing pattern of Alfacalcidol in 2018.

Table 1. The prescribing pattern of Alfacalcidol in 2018.

Variable	Category	Number	Percentage
Gender	Male	74	23.79%
	Female	237	76.21%
Age	Less than 10	4	1.29%
	10-19	14	4.50%
	20-29	27	8.68%
	30-39	39	12.54%
	40-49	70	22.51%
	50-59	62	19.94%
	60-69	51	16.40%
	More than 69	42	13.50%
Nationality	Saudi	254	81.67%
	Non-Saudi	57	18.33%
Prescribing Department	Rheumatology	1	0.32%
	Orthopedic	68	21.86%
	Ophthalmology	1	0.32%
	Neurology	2	0.64%
	Neuro Surgery	6	1.93%
	Nephrology	27	8.68%
	Internal Medicine	177	56.91%
	Gastroenterology	14	4.50%
	Emergency	9	2.89%
	Dermatology	1	0.32%
	Cardiology	3	0.96%
	Pediatrics	1	0.32
	General Surgery	1	0.32
Physician level	Consultant	36	11.57%
	Resident	226	72.67%
	Specialist	49	15.76%

In 2018, 127 patients were received Cholecalciferol. Most of the patient were females (79.53%), in the age level between 30-39 (21.26%) followed by patients less than 10 years (18.90%). The majority of Cholecalciferol drugs were prescribed by Internal Medicine department (30.71%) followed by Orthopedic (20.47%). Furthermore, most of the prescribers were residents (65.35%). The prescribing pattern of Cholecalciferol in 2018 is shown in table 2.

Table 2. The prescribing pattern of Cholecalciferol in 2018.

Variable	Category	Number	Percentage
Gender	Male	26	20.47%
	Female	101	79.53%
Age	Less than 10	24	18.90%
	10-19	7	5.51%
	20-29	21	16.54%
	30-39	27	21.26%
	40-49	19	14.96%
	50-59	17	13.38%
	More than 59	12	9.45%
Nationality	Saudi	109	85.83%
	Non-Saudi	17	14.17%
Prescribing Department	Rheumatology	16	12.60%
	Orthopedic	26	20.47%
	Neurology	3	2.36%
	Urology	2	1.57%
	Internal Medicine	39	30.71%
	Obstetrics & Gynecology	13	10.24%
	Emergency	9	7.09%
	E.N.T	1	0.79%
	Pediatrics	18	14.17%
Physician level	Consultant	27	21.26%
	Resident	83	65.35%
	Specialist	17	13.39%

Vitamin D supplements were prescribed mainly by internal medicine department and orthopedic department and this is rational because Internal medicine department include patients with different diseases that affect vitamin D level in the body or treated by a treatment approach that include vitamin d supplement such as allergy, heart diseases, endocrine diseases, hormone disorders, blood disorders, infectious diseases, diseases of the gastrointestinal gut, kidney diseases, cancers, lung disorders, arthritis and musculoskeletal disorders [10]. Moreover, vitamin D is used commonly to prevent or treat different diseases in orthopedic department specially osteoporosis.

The use of Vitamin D supplement in hypertensive patients

In the present study, alfacalcidol was prescribed for 55 hypertensive patients. Some of these patients use 1 antihypertensive agent and others used more than 1 drug. Generally, the 55 hypertensive patient who received Alfacalcidol used 73 drugs (28 CCBs, 14 ARBs, 12 diuretics, 11 BBS and 8 ACEIs). Out of the patients who received cholecalciferol, only 6 patients used an antihypertensive drug (3 CCBs, 2 ACEIs, 1 diuretic). Therefore, in the present study 13.93% of patients who received vitamin D were suffering from hypertension.

Several studies have reported that Vitamin D also play a role in the regulation of blood pressure and in heart health [11, 12]. Rostand observed that cases of high blood pressure increase in the places that are far away from the equator and during winter, there is a decrease in available sunlight in both situations leads to decrease the production of vitamin D [13].

The use of Vitamin D supplement in patients with other cardiovascular diseases

Out of the patients who received cholecalciferol, 2 patients used an antiplatelet agent and 1 patient used an anticoagulant agent. Furthermore, regarding the patients who used alfacalcidol, 30 patients used an Antiplatelet agent, 3 patients used an anticoagulant drug, 19 patients used statins and 1 patient used an antiarrhythmic. 7.31 % of the patients used an antiplatelet and 4.34% used statins.

Kendrick et al reported that individuals surveyed in The National Health and Nutritional Examination Surveys 1988–1994 who had vitamin D deficiency had higher prevalence of self-reported myocardial infarction, angina and heart failure compared with individuals with higher levels of vitamin D [14]. In the most recent National Health and Nutritional Examination Surveys 2000–2004 survey, vitamin D deficiency was related to increased prevalence of self-reported coronary heart disease, peripheral vascular disease and heart failure [15].

The use of Vitamin D supplement in diabetic patients

In the present study, 7 patients who received cholecalciferol was also used antidiabetic agent (1 insulin and 6 other drugs). Moreover, 49 patients who used alfacalcidol was also used antidiabetic agent (24 insulin and 30 other antidiabetic drugs). So in the present study 12.79% of patients who used vitamin D were suffer from diabetes, mainly type 2.

One study showed that providing vitamin D supplements to infants in North Europe, where daylight hours are shorter than in other countries, decreased the risk for new-onset type 1 DM [16]. Another study reported significant effects of vitamin D administration on maintaining β -cell function after the development of type 1 DM [17]

A previous study was conducted in the United Kingdom showed that baseline 25-hydroxycholecalciferol concentrations in patients without diabetes were inversely related with the risk for insulin resistance and hyperglycemia at 10 years of follow-up visits [18]. Moreover, another study reported that low 25-hydroxycholecalciferol levels were a risk factor for type 2 DM [19].

The use of Vitamin D supplement in patient suffered from osteoporosis

Several patients who used vitamin D were used Calcium supplement to treat osteoporosis or osteopenia. Out of the patients who received alfacalcidol or cholecalciferol, 51 patients used calcium carbonate supplement (11.64%). Moreover, some patients used other drugs to treat osteoporosis such as alendronate (used by 1 patient), teriparatide (used by 1 patient), paricalcitol (used by 5 patients) and denosumab (used by 2 patients).

Clinical trial data support skeletal benefits of vitamin D supplementation in persons with circulating 25-hydroxyvitamin D levels of less than 30 nmol/L and that vitamin D supplementation benefit is only seen in the treatment of vitamin D deficiency [20,21]. Bischoff-Ferrari et al reported that serum levels of 25 hydroxy vitamin D were directly related to bone mineral density in Black, White and Mexican-American women and men [22].

The use of Vitamin D supplement in patient suffered from neurological or psychiatric disorders.

Among patients who used cholecalciferol, 1 patient used carbamazepine, 1 patient used gabapentin and 1 patient used benzhexol. Regarding patients who received alfacalcidol, 3 patients used amitriptyline, 2 used pregabalin, 1 used carbidopa/levodopa, 1 used diazepam, 1 used carbamazepine, 1 used escitalopram, 1 used lamotrigine, 1 used sodium valpoate, 1 used haloperidol, 1 used phenobarbital and 1 patient used gabapentin. Accordingly, more than 3% of patients who received vitamin D suffer from neurological or psychiatric disorders.

In the United States, more than 50% of psychiatric inpatients have vitamin D deficiency [23]. Moreover, Somma et al stated that the association between low levels of hydroxyl vitamin D and a wide spectrum of neurodegenerative conditions such as Parkinson's disease, multiple sclerosis, Alzheimer's disease and neurocognitive disorders is supported by in vivo and in vitro data [24].

The use of Vitamin D supplement in patient suffered from thyroid diseases

Among patients who used vitamin D, 23 patients used levothyroxine for the treatment of hypothyroidism and 1 patient used carbimazole for treating hyperthyroidism. So 5.25% of the patients used a drug for thyroid diseases.

Kim reported that recent evidence has found an association between low vitamin D status and autoimmune thyroid diseases such as Graves' disease and Hashimoto's thyroiditis. He also stated that impaired vitamin D signaling has been reported in thyroid cancers [25].

In addition to that some patients who used vitamin D received also bronchodilators for asthma; several patients used rheumatoid arthritis medications. Additionally, some patients used vitamin d with other vitamins and other elements especially pregnant females or patients with chronic kidney diseases.

CONCLUSION

Vitamin D supplements were used frequently with other medicines for chronic conditions. Previous studies showed that vitamin D deficiency is associated with several chronic diseases, the treatment of these diseases is not curative, and so more studies are needed to know the effect of Vitamin D supplements in the prevention or treatment of chronic diseases. Moreover, in order to use vitamin D supplements correctly, it is important to know the prescribing trends of these supplements.

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