

Vitamin d deficiency in psoriatic patients -A case control study

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Abstract

Introduction: Many studies have shown that vitamin D deficiency have been associated with multiple autoimmune conditions like psoriasis, rheumatoid arthritis, diabetes mellitus.

Objective: The main purpose of this study was to analyze vitamin D status of psoriasis patients in comparison to healthy controls.

Materials and Methods: The study comprised of 50 (30 male & 20 female) clinically confirmed cases of chronic plaque psoriasis of age group (20-60 years) attending outpatient department of Dermatology, venereology, leprosy, Vinayaka Mission's Medical College & Hospital, Karaikal from 2012 to 2014. At the same time 50 healthy individuals without psoriasis were also investigated (age & sex matched).

Results: The mean serum 25-OHD levels in psoriatic patients and controls were 22.308+₋2.974 and 33.726 +₋2.688 ng/ml respectively. The difference was statistically significant (P=<0.0001).

Limitations: Additional studies with bigger numbers of patients are essential to evaluate the pathogenic mechanisms associated with psoriasis and vitamin D.

Keywords: Psoriasis, Autoimmunity, Psoriasis Area and severity index, 25-hydroxy vitamin D.

Introduction

Psoriasis is a chronic, non-contagious skin disease characterized by red, inflamed cutaneous lesions covered with silvery-white scale. It involves the innate immunologic system (keratinocytes, dendritic cells, histiocytes, mastocytes and endothelial cells) and acquired immunologic system (T lymphocytes).¹ Psoriatic plaques are defined histologically by epidermal hyperplasia, epidermal and dermal infiltration by leukocytes and changes in dermal microvasculature.²

Psoriasis affects both genders equally and can occur at any age, although it most commonly appears for the first time between the ages of 15 and 25. The disease affects the skin and potentially the joints. The prevalence of psoriatic arthritis in psoriasis patients is estimated to be between 25-31%.

Vitamin D performs different functions besides its well-known role in calcium phosphorus metabolism, as indicated by the presence of vitamin D receptors (VDRs) and CYP27B (enzyme responsible for 25-hydroxyvitamin D [25-OHD] synthesis) in different tissues.³⁻⁶ An important regulatory role for vitamin D in the immune system is suggested by the presence of VDRs on activated T lymphocytes^{7,8}, the suppressive or inhibiting effect of 1, 25 dihydroxyvitamin D in different autoimmune diseases, and in vitro and in vivo findings of vitamin D – induced changes in immune functions. The observations that keratinocytes and T cells express VDR and that 1,25(OH)₂ D is a potent stimulator of keratinocyte differentiation provided a reasonable basis for the clinical use of VDR ligands for the treatment of psoriasis.^{9,10}

It promotes the differentiation of monocytes into macrophages thus increasing their cytotoxic activity; reduces the antigen-presenting activity of macrophages to lymphocytes; prevents dendritic cell maturation; inhibits T

lymphocyte-mediated immunoglobulin synthesis in B cells and inhibits delayed-type hypersensitivity reactions.¹¹⁻¹³ In contrast, vitamin D exerts an antiproliferative effect on activated lymphocytes while suppressing the generation and activity of new NK cells.^{14,15} Furthermore vitamin D has been reported to down regulate the production of several cytokines: IL-2, IL-6 and IL-12, IFN- γ , TNF- α and TNF- β .^{13,16}

With this background, we further investigate the association between psoriasis and vitamin d levels between patients with psoriasis and control subjects without psoriasis to look into the fact that psoriasis is an inflammatory disease and whether vitamin d has any role in its treatment.

Materials and Methods

Patients and control subjects

This Prospective clinical case -control study comprised of 50 (30 male & 20 female) clinically confirmed cases of chronic plaque psoriasis of age group (20-60 years) and 50 healthy individuals without psoriasis were also investigated (age & sex matched), who attended outpatient department of Dermatology, venereology, leprosy, Vinayaka Mission's Medical College & Hospital, Karaikal from 2012 to 2014.

In our study a case of psoriasis was defined and diagnosed clinically as erythematous plaque lesions involving symmetrically the extensor aspects with positive Grattage test and Auspitz sign.

Inclusion criteria

All Cases were recruited if aged > 20 years who have diagnosed clinically as having chronic plaque psoriasis independently of the actual psoriasis area and severity index (PASI) score with absence of systemic or topical ant psoriatic treatments, including phototherapy and topical vitamin D derivatives.

Inclusion criteria for control subjects were the same as for cases except for the absence of psoriasis.

Exclusion Criteria

Non consenting Patients with less than 20 years of age with other types of psoriasis (guttate Erythrodermic, and pustular psoriasis), those with concomitant inflammatory bowel disease (ie crohns disease and ulcerative colitis), lupus erythematosus, cutaneous lymphoma, non melanoma skin cancer, RA, IIDM, MS and those receiving therapeutic interventions that might influence vitamin D status, including bisphosphonates, systemic corticosteroids, vitamin D and calcium supplements where excluded.

The study was approved by the Ethics committee of Vinayaka Mission's Medical College & Hospital and written informed consent was obtained from all patients and control subjects.

Clinical and laboratory parameters

A detailed history of the patients with complaints, duration, and evolution with treatment history for the psoriasis taken previously and Morphology of lesion, sites of involvement were noted. Family history of psoriasis, diabetes mellitus, hypertension, obesity hyperlipidemia taken.

Body mass index was calculated according to formula weight/height² in centimeter and obesity has interpreted if BMI is > 25. PASI score was calculated according to the formula 0.1(Eh+Ih+Dh) Ah+ 0.2 (Eu+Iu+Du) Au + 0.3 (Et+It+Dt) At + 0.4 (El+Il+Dl) Al. PASI score < 3 is taken as mild, moderate – 3-15 and severe as > 15. Vitamin D was

measured using competitive enzyme- immunoassay technique with a selected monoclonal antibody recognizing 25-hydroxy (OH) vitamin.

Vitamin D insufficiency was defined as <30ng/ml and deficiency as <20ng/ml. Blood pressure levels > 130/86 were taken as hypertensive. Fasting blood sugar levels greater than 100 mg /dl were taken as abnormal. HDL: 30 - 70 mg/dl and TGL: 40 -160 mg/dl were taken as normal.

Results

Of the 50 psoriatic patients in this study, there were 20 female (40%) and 30(60%) male participants. About 20 (40%) cases were in the age of 41-50 years. Of these 19 patients with psoriasis (38%) had associated comorbidities such as systemic hypertension and 32% with elevated triglycerides.

The control group consisted 50 participants (20 female and 30 male) without psoriasis. The two group did not significantly differ in age, gender. (Table-1). 42% of control group had (>50 ng/ml) of vitamin D.

Vitamin D deficiency (<20 ng/mL) was detected in 10% of cases and 3% of controls. Vitamin D insufficiency (<30 ng/ml) was observed in 40% of cases and 5% of control. 24% had 11-15 years of duration of psoriasis. 60% had a moderate PASI value (3-15).

The mean serum 25-OHD concentration was found to be significantly reduced in psoriatic patients than in control participants (22.308 +_2.974 Vs 33.726 +_ 2.688; P= <0.0001) (Table 5)

Table 1: Comparison of cases and controls according to Socio demographic variable and co-morbidities.

| S. No | Variable | Cases (50) n (%) | Controls (50) n (%) |
|-------|-----------------------|------------------|---------------------|
| 1 | Age in years | | |
| | 21-30 | 8 (16) | 8 (16) |
| | 31-40 | 12 (24) | 12 (24) |
| | 41-50 | 20 (40) | 20 (40) |
| | 51-60 | 10 (20) | 10 (20) |
| 2. | Gender | | |
| | Female | 20 (40) | 20(40) |
| | Male | 30 (60) | 30 (60) |
| 3. | Co-morbidities | | |
| | HTN | 19 (38) | 15 (30) |
| | DM | 9 (18) | 15 (30) |
| | BMI | 8 (16) | 8 (16) |
| | HDL | 17 (34) | 10 (20) |
| | TGL | 16 (32) | 15 (30) |

Table 2: Severely psoriasis estimated according to PASI.

| Severely Psoriasis | Frequency | Percentage |
|--------------------|-----------|------------|
| Mild (<3) | 10 | 20% |
| Moderate (3-15) | 30 | 60% |
| Severe (>15) | 10 | 20% |
| Total | 50 | 100% |

Table 3: Duration of psoriasis of the patients.

| Duration | Frequency | Percentage |
|--------------|-----------|------------|
| 0 – 5 yrs | 10 | 20% |
| 6 – 10 yrs | 16 | 32% |
| 11 – 15 yrs | 12 | 24% |
| 16 – 20 yrs | 8 | 16% |
| 21 – 25 yrs | 4 | 8% |
| Total | 50 | 100% |

Table 4: Comparison of cases and controls according to 25 OHD (ng/ml).

| 25 OHD (ng/ml) | Cases n(%) | Controls n(%) |
|----------------|------------|---------------|
| <10 | 0 | 0 |
| 11 – 20 | 10 | 3 |
| 21 – 29 | 40 | 5 |
| >50 | 0 | 42 |
| Total | 50 | 50 |

Table 5- Comparison of 25 OHD in case and controls.

| 25 OHD | Mean | SD | 95% confidence interval of difference | | P Value |
|---------|--------|-------|---------------------------------------|--------|---------|
| | | | Lower | Upper | |
| Case | 22.308 | 2.974 | 21.288 | 22.936 | <0.0001 |
| Control | 33.726 | 2.688 | 32.143 | 33.924 | |

P value <0.05, so P value considered significant

Statistical Analysis

Statistical analysis was done using t –test.

Discussion

The purpose of the study was a clinical case control study estimation of vitamin D levels in chronic plaque psoriasis. The association between vitamin D in sufficiency and psoriasis was confirmed independently of age, sex, BMI, PASI score.

The finding of vitamin D deficiency in psoriatic patients could be relevant for several reasons as its a risk factor for osteoporosis and increases the risk of falling in the elderly which has been addressed in a large population based case-control study conducted in Israel. Also its observed that low levels of vitamin D may also have important implications in the pathogenesis of psoriasis and its also associated with cardio metabolic comorbidities, cardiovascular mortality and Diabetes mellitus.

Vitamin D undergoes metabolism in the liver to 25(OH)D, and then in the kidney to a number of metabolites, the most important of which is 1,25(OH)₂D. This is the classical pathway and quantitatively the most important for producing 1,25(OH)₂D. However, the keratinocyte is fully capable of producing its own 1,25(OH)₂D.

Keratinocytes are capable of producing a variety of vitamin D metabolites, including 1,25(OH)₂D, 24,25(OH)D, 1,24,25(OH)₃D from exogenous and endogenous sources of 25(OH)D. Production of 1,25(OH)₂D regulates itself in the cell through a negative feedback loop which is similar to that observed in the kidney, but differs from that seen in the macrophage where this feedback is missing. An important difference between keratinocytes and renal cells

in the regulation of 25(OH)D metabolism by 1,25(OH)₂D is that the concentration of 1,25(OH)₂D required to inhibit the 1 α -hydroxylase and induce 24-hydroxylase in renal cells appears to be several times greater than that required to achieve comparable effects in keratinocytes. Thus, 1,25(OH)₂D production by keratinocytes is extremely sensitive to exogenous calcitriol. Cutaneous production of 1,25(OH)₂D may regulate growth, differentiation, apoptosis and other biological processes in the skin.

The main form of circulating 25(OH)D is presented in a complex with vitamin D binding protein (DBP) with only a very small amount (0.03%) available as the free form. Furthermore, the deeper layers of the epidermis are not vascularised, which further impairs the passage of the 25(OH)D₃ – DBP complex from blood to epidermal keratinocytes.

The 1,25(OH)₂D molecule and its analogues, as well as UVB phototherapy, exert antiproliferative, prodifferentiative, and immune modulatory effects on keratinocytes that are of particular importance for the therapy of hyperproliferative skin diseases such as psoriasis vulgaris.

Vitamin D₃ acts mainly on the vitamin D receptor to regulate keratinocyte growth and differentiation, but also has an influence on immune functions of dendritic cells and T lymphocytes. Vitamin D₃ inhibits production of interleukin (IL)-2 and IL-6, blocks transcription of interferon γ and granulocyte – macrophage colony stimulating factor mRNA, and inhibits cytotoxic T cells and natural killer cell activity. Topical Vitamin D derivatives, including calcipotriol (calcipotriene) and calcitriol, have immunomodulatory effects on monocytes, macrophages, T cells and dendritic cells.

Indeed, topical vitamin D derivatives are extensively used as monotherapy or in combination with steroids for the topical treatment of psoriasis. Moreover, phototherapy increases the levels of serum 25(OH)D in patients with psoriasis and it has been proposed that narrowband ultraviolet (UV) B radiation may mediate its beneficial effect on psoriasis also by increasing endogenous vitamin D levels. The recent finding of a resolution of adalimumab-induced psoriasis in a woman with RA after the use of high vitamin D does for the treatment of vitamin D deficiency raises the interesting question on the possible use of vitamin D in the treatment of psoriasis. However, it is clear that more definitive evidence is required to demonstrate that a serum level of 25 (OH)D $<20 \text{ ng mL}^{-1}$ in psoriasis is pathologically low, and that clinical benefit would be gained from vitamin D supplementation.

In general for every 100 IU of vitamin D taken in, there is an increase of roughly 1 ng mL^{-1} (3 nmol L^{-1}) in the serum level of 25(OH)D. Toxicity from vitamin D supplementation is very rare and consists principally of acute hypercalcaemia, which usually results from doses that exceed 10000IU per day. The tolerable upper level of daily vitamin D intake recently set by the Institute of Medicine is 4000 IU.

This study has some limitations, we did not assess daily vitamin D intake in foods; however we excluded from the study patients receiving oral supplementations of vitamin D or drugs that interfere with calcium metabolism. Furthermore, we decided to choose the partners of patients with psoriasis as a control group in order to minimize differences due to different dietary intake of vitamin D.

In conclusion, vitamin D deficiency may be common in psoriasis patients. Considering the fact that psoriasis is an inflammatory autoimmune disease and vitamin D has protective role in such diseases, psoriasis patients could be routinely screened for vitamin D insufficiency and oral supplementation with vitamin D might benefit them.

Conflicts of Interest: None.

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