Psoriasis vulgaris (PV) is a common chronic autoimmune disease manifesting as thick scaly red plaques on the skin. It is often triggered by an infection or stress, however the antigen that triggers the abnormal immune cycle is unknown. Patients with psoriasis are more prone to other autoimmune diseases, cardiovascular disease, diabetes, obesity, and metabolic syndrome. Patients with psoriasis live approximately four years less than the general population. Although many susceptibility genes have been identified, there is still no cure. Over the last several years, researchers have learned more about vitamin D, its role in the immune system and its role in psoriasis. Ahead, we will review these findings and elucidate implications for care.

**Vitamin D**

Vitamin D is thought to play an important role in the regulation of the immune system, based upon the findings of vitamin D receptors (VDRs) and CYP27B1, an enzyme responsible for 25-hydroxyvitamin D (25-(OH)D) synthesis, in various tissues. At least 60 cell types are known to express the VDR and more than 200 genes appear to be modulated by vitamin D. Importantly, VDRs are found on activated T lymphocytes, and evidence suggests that vitamin D plays a role in modulating dendritic cell function and regulating keratinocytes and T cell function.

Epidemiologic data have shown that vitamin D deficiency may be a risk for development of several autoimmune diseases, including rheumatoid arthritis (RA), multiple sclerosis (MS), systemic lupus erythematosus (SLE), and Crohn’s disease (CD). In psoriasis, the prevalence of vitamin D deficiency varies with latitude. It is highest among residents near the poles and decreased in the tropical latitudes. Thus, there is some epidemiological evidence of a relationship between prevalence and latitude that may be related to sun exposure and vitamin D levels. Clinically, some patients with psoriasis respond to topical vitamin D analogs, which also suggests a role for the vitamin in managing the disease. Most autoimmune treatments are expensive and require monitoring for side effects, while others cannot be used in pregnancy. Therefore, it would be of value to know if correcting a vitamin D deficiency would have a positive clinical effect in this population.

Vitamin D deficiency as a risk factor

Vitamin D deficiency may be a risk for development of several autoimmune diseases:
- Rheumatoid arthritis (RA)
- Multiple Sclerosis (MS)
- Systemic Lupus Erythematosus (SLE)
- Crohn’s Disease (CD)
- Psoriasis?
had higher tender joint counts and CRP levels. The few randomized controlled trials (RCTs) are small and do not show a dose-response relationship. Wang, et al. found that vitamin D deficiency is linked to CD. They found that 1,25-dihydroxyvitamin D acts directly on the beta defensin 2 and NOD2 genes, which have both also been linked to CD. A Danish cross-sectional study was recently published with 183 CD and 62 healthy controls. It showed that active CD was associated with decreased 25-(OH)D, and vitamin D supplementation can decrease CD activity.

**THE ROLE OF VITAMIN D IN PSORIASIS**

A year-long cross-sectional study in Italy followed 145 patients with psoriasis, 112 with RA, and 141 healthy controls (family members of cases to reduce the influence of variations in diet intake). Researchers measured vitamin D, parathyroid hormone (PTH), and serum calcium. Among patients with psoriatic disease, 57.8 percent were found to be vitamin D deficient all year long, versus 37.5 percent in the RA group, and 29.7 percent of controls. In winter months, the prevalence rose to 80.9 percent in the psoriasis group, as compared to 41.3 percent in RA patients, and 30.3 percent in healthy controls. Prevalence of 25-(OH)D deficiency was statistically significant in those with psoriasis versus RA (p<0.01) and healthy controls (p<0.001). Additionally, there was no difference in prevalence of deficiency whether patients had psoriasis or both psoriasis and psoriatic arthritis. There was no significant linear correlation between disease severity and 25-(OH) levels.

The study also found that psoriasis patients were younger, more likely to smoke, and had higher BMIs than those with RA or healthy controls. In the logistic regression analysis, vitamin D deficiency was associated with PV with odds ratio 2.5 (95% confidence interval 1.18-4.89; p=0.038) from NB-UVB therapy than those heterozygous for the allele (p =0.026) and those homozygous for the T allele (p=0.013). The odds ratio was 2.89 (with 95% confidence intervals 1.02-7.64, p<0.03) for vitamin D deficiency. The only significant negative correlation was found between 25-(OH)D levels and BMI (r = -0.30, p=0.005). In addition, psoriatic patients with BMI above 27 had higher risk of vitamin D deficiency with sensitivity of 82.3 percent and specificity of 51.7 percent. Importantly, there was no correlation between BMI and hours of daily sun exposure. It is possible to have normal vitamin D blood levels, but if there is a receptor dysfunction, abnormal cell function may arise. This can be true for any cell that has abnormal VDRs, including keratinocytes, T cells, and dendritic cells. Clinical response to topical vitamin D analogs correlates with upregulation of VDR mRNA expression in psoriatic plaques.

Polymorphisms of VDR genes may influence this. Patients homozygous for the Taq1 T allele had a higher rate of non responsiveness to topical calcipotriol. The patients homozygous for the C allele of the Taq1 VDR are associated with decreased activity of the VDR. These patients had a shorter remission duration (p = 0.038) from NB-UVB therapy than those heterozygous for the allele (p =0.026) and those homozygous for the T allele (p=0.013). The parameters of normal levels have also been debated. By definition, vitamin D deficiency is the level which causes bone disease, usually representing a 25-(OH)D level <10-20ng/ml. The levels required to prevent or possibly help treat autoimmune diseases are unknown.

**WHAT CONSTITUTES VITAMIN D DEFICIENCY?**

Much debate has taken place over what constitutes “normal” levels of vitamin D and whether patients with autoimmune diseases would benefit from supplementation. Physician orders for testing of vitamin D levels had increased by more than 50 percent in 2009, and vitamin D sales increased from $40 million to $550 million from 2001-2010. The parameters of normal levels have also been debated. By definition, vitamin D deficiency is the level which causes bone disease, usually representing a 25-(OH)D level <10-20ng/ml. The levels required to prevent or possibly help treat autoimmune diseases are unknown.

**CONCLUSIONS**

Vitamin D deficiency is prevalent in the psoriatic population. Due to the disabling nature and the difficulty controlling these diseases, it would be beneficial to know whether a cost effective therapy such as vitamin D supplementation would improve the disease. Observational studies in large cohorts have shown significant associations between low levels of 25-(OH)D and increased risk of diabetes, metabolic syndrome, and cardiovascular mortality. As psoriasis is an independent risk factor for cardiovascular disease, a therapy that could reduce these risks would be of benefit. Severity of psoriasis is known to correlate with elevated BMI, and BMI is negatively correlated with vitamin D deficiency. It has also been proposed...
that there may be reduced bioavailability of vitamin D as a result of sequestration in fat.\(^1\)

The current data show that vitamin D deficiency is common in the psoriasis population, but large randomized controlled trials need to be implemented to confirm if correction of deficiency would result in a statistically significant clinical improvement, adjusting for confounding factors, such as BMI. Better knowledge of vitamin D receptor polymorphisms may also allow us to understand differential responsiveness to treatments, and even allow development of new treatments that correct the abnormal protein transcription from defective receptors.

Dr. Prussick has served as a consultant, speaker, trainer or investigator for Abbott, Allergan, Amgen, Gene Logic, Janssen, Leo, L’Oreal, Pharmaderm, Medicis and Medimetriks.

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