Vitamin D Status in Psoriasis Patients Treated with UVB Therapy

Amra Osmancevic
Department of Dermatology and Venereology, Sahlgrenska University Hospital, Gothenburg, Sweden. E-mail: amra.osmancevic@vgregion.se

Amra Osmancevic defended her doctoral thesis on February 20, 2009 at Sahlgrenska Academy, University of Gothenburg, Sweden. The opponent was Associate Professor Göran Toss, Department of Endocrinology, Linköping University, Sweden and the tutor was Associate Professor Anne Lene Krogstad, Department of Sahlgrenska Academy, Sweden and Department of Dermatology, Oslo University, Norway.

The thesis deals with the effect of ultraviolet B (UVB) on vitamin D production in psoriasis patients during treatment with phototherapy. Vitamin D is an ancient vital molecule that dates back at least 800 million years. During the last decade vitamin D has become a hot topic in medical research and our knowledge of its vital role in health and disease is constantly expanding.

Vitamin D is an essential steroid for calcium homeostasis and skeletal health, for regulation of cellular growth, cell proliferation and cell differentiation. Vitamin D regulates the immune system, controls cancer cell growth and plays a role in the regulation of blood pressure. Therefore, vitamin D insufficiency may cause many chronic diseases that affect both children and adults. Today, most plants and animals exposed to sunlight have the capacity to produce vitamin D. It has been estimated that 90–95% of the world population obtains its vitamin D requirement from sunlight.

Vitamin D3, or cholecalciferol, is produced in the basal epidermis by UVB radiation (290–315 nm) of vitamin D precursor 7-dehydrocholesterol (7-DHC). However, vitamin D is biologically inert. Through hydroxylation in the liver on carbon 25, the major circulating form of vitamin D, 25-hydroxycholecalciferol (25(OH)D) is formed. 25(OH)D is also biologically inert at physiological concentrations. The molecule is further converted to its activated form 1,25dihydroxycholecalciferol (1,25(OH)2D) in the kidney, which represents the most important pathway of production. However, the keratinocytes are also fully capable of producing their own 1,25(OH)2D. Thereby the skin constitutes the only tissue yet known in which the complete UVB-induced pathway from 7-DHC via intermediates (previtamin D3, vitamin D3, 25(OH)D) to the final product 1,25(OH)2D, takes place under physiological conditions.

25(OH)D is used clinically to measure vitamin D status for vitamin D deficiency, sufficiency, and intoxication. A 25(OH)D level of less than 30 ng/ml (75 nmol/l) is considered a sub-

Fig. 1. Amra Osmancevic *(centre)* with opponent Göran Toss, Associate Professor at the Department of Endocrinology, Linköping University, and tutor Anne Lene Krogstad, Associate Professor at the Department of Dermatology, Sahlgrenska Academy and Oslo University Hospital.

optimal vitamin D status (i.e. the minimal level of 25(OH)D necessary to suppress parathyroid hormone secretion). The cut-off level for serum 25(OH)D, which is taken as a diagnostic value for vitamin D deficiency, has varied over the years.

1,25(OH)2D facilitates the regulation of cell growth and maturation, stimulates insulin secretion, inhibits renin production, and modulates the functions of activated T and B lymphocytes and macrophages. It is known that the risk of morbidity or mortality from colon, prostate, breast, ovarian, oesophageal, non-Hodgkin's lymphoma, and a variety of other aggressive cancers is related to living at more northern latitudes and thereby having a higher risk of vitamin D deficiency. Thus, the vitamin D has such important health implications that measurement of 25(OH)D should be part of routine physical examination for children and adults of all ages.

Sun exposure is the strongest factor influencing 25(OH)D levels. The serum concentrations of the 25(OH)D shows clear seasonal variation, with a maximum in late summer and a minimum at the end of winter. The extent of this seasonal varia-

tion depends on the latitude, skin pigmentation, clothing and application of sunscreen. The latitude of Sweden (Stockholm) is 62º north of the equator and in this geographical area UVB is not present in sunlight from October to March. People of darker skin colour are more prone to vitamin D deficiency at northern latitudes. Vitamin D deficiency has been recognized even in some of the sunniest climates, including Saudi Arabia and India. Increased intake of vitamin D fortified foods and fatty fish will help to satisfy the requirement for vitamin D in the absence of exposure to sunlight.

It has been estimated that exposure to sunlight for approximately 5–15 min a day (between 10.00 h and 15.00 h) on the limbs or hands, face and arms in fair-skinned persons during the spring, summer, and autumn (not during the winter unless located below 35° north) provides the required 1,000 IU of cholecalciferol.

A similar wavelength spectrum of UVB (290–315 nm) as that responsible for D vitamin synthesis has been used successfully for years to treat psoriasis and other chronic inflammatory skin disorders. Psoriasis lesions usually deteriorate during the winter period and many patients obtain repeated UVB treatments during this season.

Information about vitamin D status in patients with psoriasis and the effect of phototherapy on vitamin D status in this group is sparse. The aim of this doctoral thesis was to study vitamin D status in psoriasis patients during treatment with phototherapy.

The studies included in the thesis showed that UVB and heliotherapy increased serum 25(OH)D production, reduced serum parathyroid hormone (PTH) concentrations and improved psoriasis, lipid and carbohydrate status in the patients.

Vitamin D production in psoriasis patients increased less with narrowband UVB than with broadband UVB phototherapy. One explanation might be that the optimal wavelength for the vitamin D3 pathway is 300 ± 5 nm, which is part of the broadband UVB range (280–320 nm), but not the narrowband UVB (311 ± 1 nm). The synthesis of vitamin D, however, is stimulated by wavelengths of up to 315 nm. Our results showed that wavelengths of 311 nm induced vitamin D synthesis, but the levels obtained were significantly lower than in the broadband-treated patients. The treatment time correlated strongly with the type of lamp (patients treated with narrowband UVB required four times longer exposure times than patients treated with broadband UVB). This is consistent with other studies demonstrating that the dose response of the erythemal spectra of narrowband UVB should be approximately 4.2 times that of broadband UVB.

Postmenopausal women with psoriasis had higher bone mineral density than age-matched controls; a finding that could be related to their higher body weight, physical activity and UVB exposure. The studies also showed that the production of 25(OH)D did not correlate with the dose of UVB, indicating a complexity in the regulation of the synthesis and metabolism of vitamin D.

It is not known whether skin affected by diseases such as psoriasis or eczema differ in vitamin D production compared with normal skin. Further research is needed to achieve a more comprehensive understanding of the synthesis of vitamin D in the skin. More studies are needed to develop safe recommendations for sun exposure to obtain appropriate vitamin D levels, especially in the Scandinavian population. It is also necessary to establish new recommendations for daily vitamin D supplements in different patient groups. These issues are being investigated in ongoing postdoctoral projects.

This research was team-based, and I would like to thank my supervisor Anne Lene Krogstad, my co-supervisors Kerstin Landin-Wilhelmsen, Olle Larkö, Ann-Marie Wennberg, and co-authors Dan Mellström, Lena Hulthén, Lill Tove Nilsen, Elisabeth Søyland, Peter Abusdal Torjesen, Marit Nenseter and Tor Arne Hagve for excellent and stimulating collaboration.