

## SHORT REPORT

## Seasonal variations in vitamin D levels in melanoma patients: a single-centre prospective pilot comparative study

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### Abstract

**Background** More than 90% of vitamin D synthesis is dependent on UV exposure. Photosensitive disorders such as lupus erythematosus, protoporphyria and xeroderma require strict sun avoidance, and vitamin D deficiency has been demonstrated in these patients. Melanoma patients are also instructed to avoid sun exposure and may hence be expected to be vitamin D deficient.

**Materials and methods** Winter and summer vitamin D levels were compared in a group of melanoma patients ( $n = 61$ ) and age- and phototype-matched controls ( $n = 53$ ) without photosensitive disorders.

**Results** Oral supplementary vitamin D intake was reported in 32.7% of the melanoma patients and in 15.1% in the control group. Despite oral supplementation, only 25% of the melanoma patients and the controls presented with vitamin D levels of 30 ng/mL or higher. In non-supplemented subjects in the melanoma and control groups, respectively, mean winter vitamin D levels were below the recommended threshold at 12.6 ng/mL vs. 13.2 ng/mL, respectively, but not statistically different. These values increased significantly in both groups during the summer to 24.6 and 23.8 ng/mL respectively.

**Conclusion** Unexpected, significant increases in vitamin D levels were seen in melanoma patients during summer, suggesting non-adherence with photoprotective measures and reflecting a heliophilic behaviour. Vitamin D supplementation is recommended in melanoma patients during both winter and summer.

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### Conflict of interest

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### Introduction

Vitamin D deficiency is a common and widespread condition in children and adults.<sup>1,2</sup> Most experts recommend a level of 30 ng/mL or higher.<sup>2</sup> Vitamin D deficiency increases the risk for phosphocalcic disorders such as osteopenia, osteoporosis, osteomalacia, muscle weakness, growth retardation, skeletal deformities and bone fractures.<sup>2,3</sup> Recent research has revealed the importance of vitamin D in a range of conditions such as cardiovascular disease including arterial hypertension,<sup>4</sup> various malignancies,<sup>5</sup> multiple sclerosis,<sup>6</sup> increased susceptibility to some infectious diseases,<sup>7</sup> psychiatric disorders<sup>8</sup> and autoimmune diseases.<sup>2</sup>

UV-B radiation is responsible for meeting 90% of the body's vitamin D requirements.<sup>2,9</sup> Strict photoprotection is recommended for patients with photosensitive disorders, renal transplant recipients,<sup>10</sup> skin cancer patients<sup>10</sup> and for those taking photo-

sensitizing drugs. The same recommendations are valuable for melanoma patients,<sup>11</sup> although some contradiction exists.<sup>12</sup> Consequently, evidence of low vitamin D levels have been found in patients with xeroderma pigmentosum,<sup>10,13</sup> Gorlin's syndrome, lupus erythematosus,<sup>14</sup> HIV-infection, erythropoietic protoporphyria,<sup>15</sup> as well as in renal transplant recipients.<sup>17</sup> Low vitamin D levels may also be expected in melanoma patients.

This prospective, single-centre study compared the seasonal variations of vitamin D levels in melanoma patients with those in healthy, age-matched, non-photosensitive controls.

### Materials and methods

The study was performed according to the Helsinki Protocol (2000) and approved by the local ethics committee. Outpatient melanoma patients ( $n = 61$ ) were included irrespective of their

**Table 1** Patient distribution

Patient categories	Mean age (years)	Number	Winter, mean (SD)	Summer, mean (SD)
Melanoma with vit D3	63.7	<i>n</i> = 20	25.4	ND
Melanoma without vit D3	43.7	<i>n</i> = 41	12.6 (5.0)	24.6 (8.8)
Controls with vit D3	59.6	<i>n</i> = 12	29.8	ND
Controls without vit D3	47.2	<i>n</i> = 41	13.2 (5.7)	23.8 (8.9)

ND, not determined.

melanoma staging. The healthy control group (*n* = 53) comprised age- and phototype-matched subjects. Patients with photosensitive diseases, including discoid lupus erythematosus, subacute cutaneous lupus, chronic actinic dermatitis, polymorphous light eruption, actinic prurigo and porphyria cutanea tarda, and patients receiving phototherapy or photosensitizing drugs were excluded. Oral supplementary vitamin D intake and phototype was recorded. Vitamin D levels were measured during the winter period (January and February) and during the summer period (August and September). Levels of 25-OH vitamin D were determined using the Liaison 25-OH vitamin D total method (Diasorin, Stillwater, MN, USA). In this study, the 30 ng/mL vitamin D threshold was used.

## Results

All melanoma patients and controls presented with phototypes II or III. Oral supplementary vitamin D intake was reported in 32.7% (20/61) of the melanoma patients and in 15.1% (8/53) of subjects in the control group. Irrespective of season, only 25% of the orally supplemented melanoma patients and controls presented with vitamin D levels  $\geq 30$  ng/mL. Table 1 summarizes the different patient categories, mean age, the number of patients, and winter and summer vitamin D levels. The mean age of vitamin D-supplemented melanoma patients and controls was higher compared with non-supplemented patients at 63.7 and 59.6 years vs. 43.7 and 47.2 years, respectively.

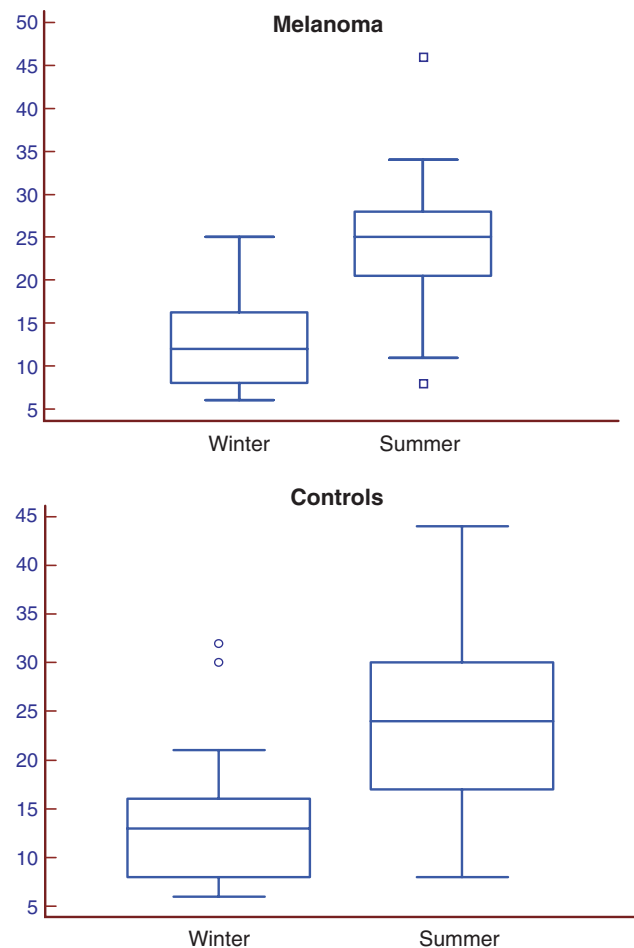
Winter and summer vitamin D levels were below recommended levels (30 ng/mL) in non-vitamin D-supplemented and in vitamin D-supplemented melanoma patients and controls (Fig. 1). No statistical significant difference was observed between non-supplemented melanoma patients and controls with respect to vitamin D levels ( $P < 0.0001$ ). Vitamin D levels were higher in melanoma patients and controls on oral vitamin D supplementation than in non-supplemented subjects. Vitamin D levels increased significantly during the summer period in non-supplemented melanoma patients and controls. The mean increase in melanoma patients was 12.0 ng/mL compared to 10.6 ng/mL in controls. The changes in vitamin D levels are shown in Fig. 1.

## Discussion

The low vitamin D levels observed in both melanoma patients and healthy controls, irrespective of oral vitamin D supplementation status, reflect the prevalence of vitamin D deficiency in the general population. Oral vitamin D intake was reported in 32.7% of the

melanoma patients but only in 15.1% of the control group. This difference probably reflects the increased awareness of the importance of vitamin D intake among both melanoma patients and/or their doctors. Furthermore, supplementary vitamin D intake was more prevalent in higher age groups, probably as a result of an increased awareness of phosphocalcic disorders in this age group.

Vitamin D levels were expected to be low in the melanoma patients, as commonly observed in patients with increased photosensitivity.<sup>10,13,14</sup> Surprisingly, there was a significant increase in vitamin D levels during summer in the melanoma patients. These differences could not be explained by high dietary intake of



**Figure 1** Winter and summer vitamin D levels in melanoma patients and healthy controls.

vitamin D,<sup>1,2</sup> nor by sun exposure of the face and the dorsum of the hands only.<sup>16</sup> An increase of this magnitude is most probably due to full-body UV exposure.<sup>17</sup> This suggests that melanoma patients still display a heliophilic behaviour after diagnosis, although patients usually deny this. The diagnosis of melanoma has been shown to be associated with increased sun awareness and protection.<sup>17</sup> The use of sunscreen and protective clothing increased and sunbed use decreased dramatically.<sup>18</sup> However, in the healthy population, health campaigns on photoprotection seem to have had little impact on attitudes to sun exposure.<sup>18</sup>

Awareness of the risks of sun exposure is not always associated with effective use of sun-avoiding measures. Only 54% of renal transplant recipients recalled receiving advice on photoprotection and only 30% were aware of the risks of photo exposure.<sup>19</sup> Furthermore, sun-protective measures were inadequate and the use of sun barrier creams was inappropriate. Many patients fail to apply sunscreen in adequate dosages, irrespective of body area. The effective level of protection achieved is lower than the labelled SPF, roughly by a factor of four.<sup>20</sup> This study also showed that adherence to photoprotection cannot be reliably assessed merely by questioning the patients and suggested that vitamin D levels could serve as indirect markers of compliance with sun-protective measures in non-vitamin D-supplemented melanoma patients.

The results of this study provide a case for increased educational efforts by dermatologists, healthcare professionals and public health organizations to reduce heliophilic behaviour in melanoma patients. Photoprotection should be adequate and adherence assessed at every clinic visit.

Interestingly, significantly higher survival rates were reported in a group of melanoma patients disrespecting anti-UV measures compared with strictly sun-avoiding patients.<sup>21</sup> Other recent reports toned down the importance of UV radiance in melanoma patients.<sup>12</sup> The antiproliferative, antiangiogenic, antimetastatic and apoptotic functions of vitamin D, mediated through VDR gene encoded receptors, may account for the improved survival rate. Nonetheless, guidelines for melanoma patients currently maintain the recommendation of sun avoidance and oral vitamin D supplementation.<sup>2</sup> Vitamin D deficiency caused by sunscreen use should not preclude adequate photoprotective behaviour.<sup>21</sup> Indeed, this study has shown that despite oral vitamin D supplementation, only 25% of melanoma patients and controls presented with vitamin D levels  $\geq 30$  ng/mL. In at-risk groups, a large dose should be administered initially to restore vitamin D levels, followed by a maintenance dose of 800 IU/day.<sup>2</sup>

## Conclusion

This study showed an unexpected increase in vitamin D levels during the summer period in non-vitamin D supplemented melanoma patients. This may reflect a persistent heliophilic behaviour or inadequate use of sun-protective measures. Oral vitamin D supplementation should be recommended and monitored in melanoma patients.

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