Dermatology Case Reports

Short Communication Open Access

The Puzzle of Vitiligo, Oxidative Stress and Narrow Band Ultraviolet-B

Christian Diehl*

Department of Dermatology, University Degli Studi Guglielmo Marconi, Rome, Italy

Short Communication

We all know about vitiligo, a common chronic acquired disease of pigmentation. We are still in limbo regarding its exact aetiology, despite lots of works and significant progress accomplished over the past decades.

Obviously, vitiligo is a multifactorial disease, and at this stage, we all accept that the autoimmune theory, the adhesion defect theory and the biochemical theory based on oxidative stress are the mainstays of our current knowledge about the aetiology of the disease. The presence of an imbalance in the anti-oxidant system in vitiligo melanocytes was assessed early, providing support for a free radical-mediated damage as an initial pathogenic event in melanocyte degeneration in vitiligo [1,2]. Since then, it was demonstrated that vitiligo patients had an increased epidermal level of H_2O_2 but also an increased superoxide dismutase (SOD) activity, especially in active lesions [3,4]. Not surprisingly, systemic antioxidants provide a helpful adjuvant in the treatment of vitiligo, as well as topical antioxidants, among them combinations of SOD and catalase (CAT) whose activity has been reported as similar to that of 0.05% betamethasone [5].

Among available therapies, Westerhof and Nieweboer-Krobotova introduced in 1997 narrowband ultraviolet B (NB-UVB) in the treatment of vitiligo, which has effectively replaced psoralen with ultraviolet A (PUVA) therapy due to its superior efficacy and better side effect profile [6]. However, at this stage, more studies are needed to establish the dosage, safety, and long-term efficacy of NB-UVB monotherapy in treating vitiligo.

In particular, the possibility of long-term skin damage and possible skin cancer following prolonged UV treatment for vitiligo needs to be researched [7]. Narrowband ultraviolet B may exert its effects in vitiligo in a two-step process. Both steps may occur simultaneously, the first being stabilization of the depigmenting process and the second, stimulation of residual follicular melanocytes [8]. The well-documented immunomodulating effects of UV radiation can explain the stabilization of the local and systemic abnormal immune responses, thereby stabilizing depigmentation [9]. It is also likely that NB-UVB, similar to PUVA therapy, stimulates the dopa-negative, amelanotic melanocytes in the outer hair root sheaths, which are activated to proliferate and migrate outward to adjacent depigmented skin resulting in perifollicular repigmentation and subsequently these melanocytes migrate downward to the hair matrices to produce melanin [10]. Wu et al. demonstrated that NB-UVB irradiation stimulates the release of basic fibroblast growth factor (bFGF) and endothelin-1 (ET-1) from keratinocytes, which induces melanocyte proliferation. They also found that NB-UVB irradiation stimulates the expression of focal adhesion kinase and matrix metalloproteinase-2 (MMP-2) in melanocytes. This leads to enhanced melanocyte migration and overcomes the deleterious effects of vitiligo associated IgG on cell migration, melanin formation, and tyrosinase expression [11,12]. However, since the end of the eighties, thanks to experiments on hairless mice epidermis, it was known that a single exposure to near ultraviolet (>320 nm) was capable to produce oxidative stress, including impairment of cutaneous catalase and glutathione reductase and a decrease in cutaneous tocopherol, ubiquinone and ascorbic acid levels [13]. Further, a decrease of levels of superoxide dismutase was reported in analogous experimental conditions [14].

These results were later confirmed, along with a simultaneous increase of cutaneous lipid hydroperoxides [15], and the pattern of recovery was different for each enzyme, depending on the level of irradiation: SOD recovered full activity by 120 h in the dermis and only 50% of control activity by 120 h in the epidermis, whilst catalase activity in both epidermis and dermis had returned to only 50% of control activity at 120 h [15]. Despite the efficacy of NB-UVB in the treatment of vitiligo, which is beyond any discussion, the property of UVB to generate oxidative stress in the skin may represent an inconvenience, as this is one of the causative factors of the disease.

Probably for this reason, various authors elaborated combination therapies with NB-UVB and systemic or topical antioxidants. In patients treated either with NB-UVB plus oral vitamin E or with NB-UVB, oral vitamin represented a valuable adjuvant therapy, preventing lipid peroxidation in the cellular membrane of melanocytes caused by NB-UVB and increasing the effectiveness of this therapy [16]. In an evaluation of the clinical effectiveness of NB-UVB but also of the repairing of oxidative stress-induced damage, patients with non-segmental vitiligo received, for 2 months before and for 6 months during the NB-UVB treatment, a balanced antioxidant pool (AP) containing alpha-lipoic acid, vitamins C and E, and polyunsaturated fatty acids. It was concluded from this study that oral supplementation with AP containing alpha-lipoic acid before and during NB-UVB significantly improved the clinical effectiveness of NB-UVB, reducing vitiligo-associated oxidative stress [17].

As regards to topical antioxidants used in combination with NB-UVB, topical SOD/CAT appears to be a therapeutic option which should be considered in the management of vitiligo, as various studies reported better results with the combination treatment than with NB-UVB alone [18,19]. Contrarily, pseudocatalase cream does not appear to add any incremental benefit to NB-UVB alone [20]. In conclusion, NB-UVB behaves as a double-edged weapon in the management of vitiligo: by one side, it is giving good results in terms of repigmentation, but on the other side it is increasing the oxidative stress present in vitiligo. It appears that oral intake of antioxidants such as vitamins A, C and E, alpha-lipoic acid and polyunsaturated fatty acids may improve the efficacy of NB-UVB therapy [16,17]. In a similar manner, a combination treatment with topical SOD/CAT (but not pseudocatalase) and NB-UVB therapy appears to improve the effects of the latter [18-20]. For this reason, we should keep in mind, rather than prescribing NB-UVB treatment alone, a combination treatment with NB-UVB plus systemic and/or topical antioxidant which is required to improve the effect of the therapy.

***Corresponding author:** Christian Diehl, Department of Dermatology, University Degli Studi Guglielmo Marconi, Rome, Italy, Tel: 41763992637; E-mail: chdiehl@hotmail.com

Received: March 03, 2016; **Accepted:** October 13, 2016; **Published**: October 20, 2016

Citation: Diehl C (2016) The Puzzle of Vitiligo, Oxidative Stress and Narrow Band Ultraviolet-B. Dermatol Case Rep 1: 113.

References

1. Maresca V, Roccella M, Roccella F, Camera E, Del Porto G, et al. (199) Increased sensitivity to peroxidative agents as a possible pathogenic factor of melanocyte damage in vitiligo. J Invest Dermatol 109(3): 310-313.
2. Schallreuter KU, Moore J, Wood JM, Beazley WD, Gaze DC, et al. (1999) *In vivo* and *in vitro* evidence for hydrogen peroxide (H2O2) accumulation in the epidermis of patients with vitiligo and its successful removal by a UVB-activated pseudocatalase. J Investig Dermatol Symp Proc 4: 91-96.
3. Sravani PV, Babu NK, Gopal KV, Rao GR, Rao AR, et al. (2009) Determination of oxidative stress in vitiligo by measuring superoxide dismutase and catalase levels in vitiliginous and non-vitiliginous skin. Indian J Dermatol Venereol Leprol 75(3): 268-271.
4. Jain A, Mal J, Mehndiratta V, Chander R, Patra SK (2011) Study of oxidative stress in vitiligo. Indian J Clin Biochem 26(1): 78-81.
5. Sanclemente G, Garcia JJ, Zuleta JJ, Diehl C, Correa C, et al. (2008) A double-blind, randomized trial of 0.05% betamethasone vs. topical catalase/dismutase superoxide in vitiligo. J Eur Acad Dermatol Venereol 22(11): 1359-1364.
6. Westerhof W, Nieuweboer−Krobotova L (1997) Treatment of vitiligo with UV−B radiation vs topical psoralen plus UV−A. Arch Dermatol 133: 1525−1528.
7. Whitton ME, Pinart M, Batchelor J, Lushey C (2010) Interventions for vitiligo. Cochrane Database Syst Rev 1:CD003263.
8. Arora AK, Dogra S (2015) Narrowband ultraviolet B and beyond: Evolving role of phototherapy in vitiligo. Pigment International 2(1): 9-15.
9. Fitzpatrick TB (1997) Mechanisms of phototherapy of vitiligo. Arch Dermatol 133: 1591−1592.
10. Cui J, Shen LY, Wang GC (1991) Role of hair follicles in the repigmentation of vitiligo. J Invest Dermatol 97: 410−416.
11. Wu CS, Yu CL, Wu CS, Lan CC, Yu HS (2004) Narrow−band ultraviolet−B stimulates proliferation and migration of cultured melanocytes. Exp Dermatol 13: 755−763.
12. Wu CS, Lan CC, Yu HS (2012) Narrow−band UVB irradiation stimulates the migration and functional development of vitiligo−IgG antibodies−treated pigment cells. J Eur Acad Dermatol Venereol 26: 456−464.
13. Fuchs J, Huflejt ME, Rothfuss LM, Wilson DS, Carcamo G, et al. (1989) Acute effects of near ultraviolet and visible light on the cutaneous antioxidant defense system. Photochem Photobiol 50(6): 739-744.
14. Sasaki H, Akamatsu H, Horio T (1997) Effects of a single exposure to UVB radiation on the activities and protein levels of copper-zinc and manganese superoxide dismutase in cultured human keratinocytes. Photochem Photobiol 65(4): 707-713.
15. Shindo Y, Witt E, Han D, Tzeng B, Aziz T, et al. (1994) Recovery of antioxidants and reduction in lipid hydroperoxides in murine epidermis and dermis after acute ultraviolet radiation exposure. Photodermatol Photoimmunol Photomed 10(5): 183-191.
16. Elgoweini M, Nour El Din N (2009) Response of vitiligo to narrowband ultraviolet B and oral antioxidants. J Clin Pharmacol 49(7): 852-855.
17. Dell'Anna ML, Mastrofrancesco A, Sala R, Venturini M, Ottaviani M, et al. (2007) Antioxidants and narrow band-UVB in the treatment of vitiligo: a double-blind placebo controlled trial. Clin Exp Dermatol 32(6): 631-636.
18. Doghim NN, Hassan AM, El-Ashmawy AA, Gheida SF (2011) Topical antioxidant and narrowband versus topical combination of calcipotriol plus betamethathone dipropionate and narrowband in the treatment of vitiligo. Life Science Journal 8(4): 186-197.
19. Kostović K, Paštar Z, Pašić A, Čeović R (2007) Treatment of vitiligo with narrow-band UVB and topical gel containing catalase and superoxide dismutase. Acta Dermatovenerol Croat 15(1): 10-14.
20. Bakis-Petsoglou S, Le Guay JL, Wittal R (2009) A randomized, double-blinded, placebo-controlled trial of pseudocatalase cream and narrowband ultraviolet B in the treatment of vitiligo. Br J Dermatol161(4): 910-917.