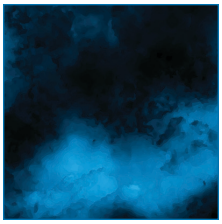

Could α MSH-MIFT Axis and IDH2 be Considered Promising Predictors of Non-segmental Vitiligo Response to NB-UVB Phototherapy?

by KHALED MOHEY EL-DIN MONIB, MD; NEVEEN EMAD SOROUR, MD; NAGLAA FATHY ALHUSSEINI, MD; ASMAA GABER ABDOU, MD; AMAL YOUSIF, MD; and REHAB MOHAMMED SALEM, MD

Drs. Monib and Sorour are Professors of Dermatology and Andrology, Faculty of Medicine at Benha University in Benha, Egypt. Dr. Alhusseini is a Professor of Medical Biochemistry and Molecular Biology, Faculty of Medicine at Benha University in Benha, Egypt. Dr. Abdou is a Professor of Pathology, Faculty of Medicine at Menoufia University, Egypt. Dr. Yousif is a Lecturer of Dermatology and Andrology, Faculty of Medicine at Benha University in Benha, Egypt. Dr. Salem is an Assistant Professor of Dermatology and Andrology, Faculty of Medicine at Benha University in Benha, Egypt.

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BACKGROUND: The search for objective factors that help in predicting the response of vitiligo treatment is very important. **OBJECTIVE:** We sought to evaluate the effect of NB-UVB phototherapy on both the alpha melanocyte stimulating hormone-microphthalmia-associated transcription factor (α-MSH-MIFT) axis, and isocitrate dehydrogenase 2 (IDH2) in non-segmental vitiligo (NSV). **METHODS:** This prospective clinical trial included 50 NSV patients and 50 healthy control subjects. α-MSH tissue levels as well as MITF and IDH2 immunostaining were assessed in normal and vitiliginous skin biopsies before treatment and then in the repigmented areas following 24 NB-UVB phototherapy treatment sessions using ELISA technique and immunohistochemical study, respectively. **RESULTS:** There was a significant negative correlation between baseline VASI scores and the tissue levels of α-MSH (p=0.006) and the expression of both MITF (p<0.00001) and IDH-2 (p= 0.001). The mean α-MSH tissue levels increased significantly after treatment (p<0.001). Tissue expression of both MTIF and IDH-2 was significantly upregulated following treatment (P-value <0.001). The percentage of improvement showed a significant positive correlation with the studied markers (p<0.00001). **CONCLUSION:** α-MSH- MIFT axis and the antioxidant protein IDH2 are promising objective markers of non-segmental vitiligo severity, and are suggested as predictors of vitiligo response to treatment.

Vitiligo is a chronic autoimmune depigmenting skin disease resulting from acquired loss of melanocytes. It is usually associated with a negative impact on the quality of life and marked psychosocial distress.[1]

The exact pathogenesis of vitiligo is not fully understood and many hypotheses have been proposed to explain the etiology of melanocytes loss in the vitiliginous patches. Among the suggested theories for vitiligo development; the toxic effects of the oxidative stress on melanocytes is one of the highly accepted ones. There are multiple natural antioxidant substances in the body. These natural antioxidants can clear the harmful oxidative products which are produced in the body during many processes including melanogenesis. Disturbance in the natural oxidant- antioxidant balance may lead to melanocytes damage and development of vitiligo.[2] Isocitrate dehydrogenase 2 (IDH2) is a mitochondrial enzyme which fights reactive oxygen species (ROS) as one of the endogenous antioxidant proteins by converting NADP+ to NADPH with a subsequent reduction of oxidized glutathione into reduced glutathione.[3]

Melanogenesis is a physiological process that requires an interaction between the melanocytes and its neighboring keratinocytes. Keratinocytes, upon UV exposure release a melanogenesis regulatory product called α-melanocyte-stimulating hormone (α-MSH), which binds to its receptor on the melanocyte cell surface [melanocortin 1 receptor (MC1R)]. The binding between this receptor with its ligand initiates an intracellular cascade of interactions the ends up with activation of the transcription of a variety of downstream targets, including microphthalmia-associated transcription factor (MITF).[4] MIFT is involved in regulating the activity of several enzymes in the synthetic pathway of melanin such as tyrosinase, tyrosinase related protein 1, tyrosinase related protein 2 and melanocytic differentiation markers.[5] MITF is also one of the melanocyte differentiation, proliferation, survival, and activity regulatory factors.[6]

The current study aimed to evaluate the effect of narrow band UVB (NB-UVB) phototherapy on both the α melanocyte stimulating hormone- microphthalmia-associated transcription factor (α-MSH-MIFT) axis, as well as the antioxidant protein IDH2 in vitiliginous patches in non-segmental vitiligo patients.

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CORRESPONDENCE: Rehab Mohammed Salem, MD; Email: rehabsalem122@yahoo.com