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Application of a pigment measuring device – Mexameter® – for the differential diagnosis of vitiligo and nevus depigmentosus

Eun Sang Park[1,2], Jung Im Na[1,2], Seon Ok Kim[2], Chang Hun Huh[1,2], Sang Woong Youn[1,2] and Kyoung Chan Park[1,2]

[1]*Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea, and* [2]*Department of Dermatology, Seoul National University Bundang Hospital, Kyounggi, Korea*

Background/purpose: Vitiligo and nevus depigmentosus (ND) present similar hypopigmented macules with significantly different prognoses. Although the distinction between the two diseases is important, differential diagnosis relies on medical history and physical examination, which is far from decisive in some cases. The Mexameter® is an objective skin color-measuring device, and has been reported to provide a reproducible and sensitive means of quantifying small skin color differences. In this study, we investigated the usefulness of a Mexameter® for discriminating these diseases.

Methods: A selection of 202 hypopigmented skin lesions (182 from vitiligo and 20 from ND) were the objects of this study. Using a Mexameter, MIs were obtained from lesions and symmetrically located control skin. RMIs, ratios of the MIs of lesional skins to control skins, were calculated.

Results: The mean MIs and RMIs were significantly different for vitiligo and ND. The mean RMI of ND lesions was 74 ± 13, which was significantly higher than that of vitiligo lesions (50 ± 24). No ND lesion had an RMI of <50%.

Conclusion: This study shows that the Mexameter®, an objective pigment-measuring device, can be used to achieve a more accurate diagnosis of hypopigmentary disorders, and that the relative melanin index (RMI), which represents the relative pigment levels, might be a more effective parameter than the melanin index (MI) itself for comparing pigmentation differences.

Key words: Mexameter® – vitiligo – nevus depigmentosus

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VITILIGO, AN acquired pigmentation disorder, is characterized by a loss of melanocytes and results in white skin patches. Nevus depigmentosus (ND) is frequently confused with vitiligo, and is defined as a congenital non-progressive hypopigmented lesion that is stable in terms of size and distribution throughout life (1). A distinction between vitiligo and nevus depigmentosus is important because these disorders have significantly different prognoses and psychological effects.

The typical vitiligo macule has a chalk- or milk-white color, whereas ND is reported to be slightly off-white, but both are accentuated under a Wood's lamp. The diagnosis of generalized vitiligo is straightforward but often the differential diagnosis of segmental vitiligo and ND is not. The commonly used clinical diagnostic criteria for nevus depigmentosus are as follows (2): leukoderma present at birth or with an early onset, no alteration in the distribution of leukoderma throughout life, no alteration in the texture or change in sensation in the affected area, and the absence of a hyperpigmented border. The differential diagnosis of these two diseases depends largely on history and clinical presentation. Wood's lamp examination and the histopathologic detection of melanocytes would be helpful, but they are not definitive because newly developing vitiligo lesions still retain melanocytes (3, 4).

Mexameter® (Courage-Khazaka Electronic, Köln, Germany) is a narrow-band reflectance spectrophotometer, and is designed to measure the intensity of erythema and melanin pigmentation. It has mainly been used for cosmetic research but recently has also been used to evaluate hyperpigmenting disorders like melasma (5, 6). It

has been reported that this instrument is highly discriminative and sensitive enough to detect small differences in skin color, and it has also been mentioned that its measurement reproducibility is satisfactory (6).

The present study represents the first report on the use of this device concerning its applicability for the differential diagnosis of these hypopigmentary disorders.

Material and Methods

Patient selection

Between January and June 2004, patients with depigmented or hypopigmented skin lesions were referred to the vitiligo clinic at Seoul National University Bundang Hospital. All patients were examined by a specialized dermatologist to exclude other hypopigmentary disorders, such as nevus anemicus, pityriasis alba, or postinflammatory hypopigmentation. A diagnosis was made based on medical history-taking, a physical examination, and a Wood's lamp examination based on the clinical criteria proposed by Coupe [2]. The following information was assessed for each patient: age at presentation, family history, involved sites, lesion stability, Koebner phenomenon, preceding skin disease at the affected sites, and if necessary, a KOH smear for detecting fungus. Finally, 80 patients were enrolled; a diagnosis of vitiligo was made in 69 patients and of nevus depigmentosus in 11 patients.

Quantitative measurements of pigment loss

Melanin indexes (MIs) were determined using a Mexameter MX16 (Courage-Khazaka Electronic). This reflectance meter utilizes the optical principle developed by Diffey et al. (7). It measures absorbed and reflected light at wavelengths for hemoglobin (green and red) and for melanin (red and near-infrared). MI is automatically computed from the intensities of absorbed and reflected light at 660 and 880 nm, respectively. The measuring area is 5 mm in diameter (surface 0.20 cm^2) and measurement involves applying a probe to the skin surface (1.54 cm^2) at a constant pressure. For each patient, representative macules were selected and MI was read from the center of the selected lesions (an average of three readings/macule was recorded). One hundred and eighty-two such averages were obtained from the 69 patients with vitiligo and 20 from the 11 patients with ND. Symmetrically located normally pigmented areas were selected as control sites and were also evaluated using the Mexameter. We calculated the relative melanin indexes (RMIs) using

$$\mathrm{RMI}(\%) = \frac{\text{MI of an affected lesion}}{\text{MI of a symmetrically located normally pigmented area}} \times 100$$

All procedures were performed by one investigator under controlled ambient conditions (room temperature 22 °C and relative humidity 42%).

Statistical analysis

SPSS software (version 10.0) was used for the statistical analyses. The vitiligo and ND groups were compared with MI and RMI using Student's *t*-test. The correlation of the MI of an affected lesion with the MI of a symmetrically located control area was tested using Pearson's correlation test. Statistical significance was defined as $P < 0.05$.

Results

Clinical characteristics

Table 1 summarizes the clinical characteristics of the patients with vitiligo and nevus depigmentosus. The ages at initial presentation ranged from 1 to 72 years (mean 30.5 years) in the vitiligo group, and from 1 month to 7 years (mean 3.1 years) in the ND group. The mean disease duration was 42 months in the vitiligo group and 19 months in the

TABLE 1. Demographic profile of patients

Total patients	Vitiligo ($N = 69$)	Nevus depigmentosus ($N = 11$)
No. of lesions	182	20
Age		
Mean (years)	30.5	3.1
Range	1–72 years	3 months–7 years
Sex		
Male	31	6
Female	38	5
Duration		
Median (months)	7	14
Range (months)	1–600	1–60
Type		
Generalized	29 (42%)	–
Localized	40 (58%)	–
Isolated	–	6 (55%)
Segmental	–	5 (45%)

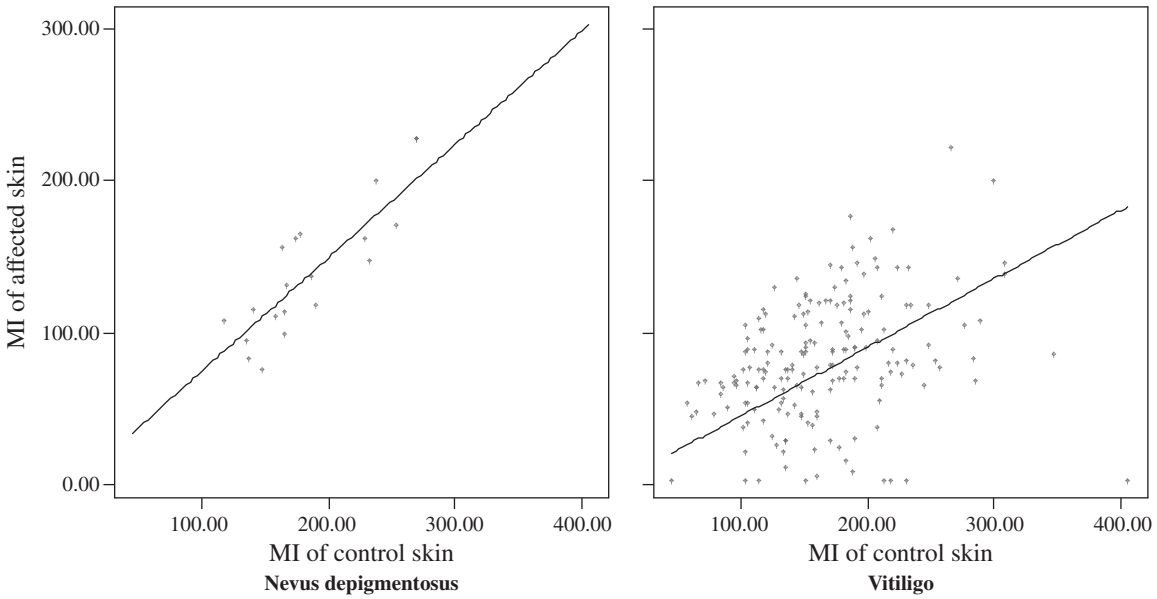

Fig. 1. Correlations of the MI of an affected skin with the MI of a control skin. Significant correlations between the MI of an affected skin and the MI of its control are found in both nevus depigmentosus and vitiligo group. Pearson's correlation coefficient is 0.861 and 0.327, respectively (P = 0.000 in both groups). MI, melanin index.

ND group. The male-to-female ratios of the two groups were almost equal. In the vitiligo group, the localized type was more common than the generalized type. Of the 11 patients with ND, six (55%) had the isolated type and four (45%) had the segmental type.

MIs and RMIs of vitiligo and nevus depigmentosus

The mean MI of ND lesions was 138.17 ± 43.87, which was significantly higher than that of vitiligo lesions (79.11 ± 40.24, $P = 0.000$). However, MIs of affected skin varied according to the level of background pigmentation presented as MIs of symmetric control area. Scatter plots showed a positive correlation in both the ND and the vitiligo groups, and the correlation coefficient was $r = 0.861$ ($P = 0.000$) and $r = 0.327$ ($P = 0.000$), respectively (Fig. 1). In order to eliminate the confounding effect of regional color differences, we utilized RMI. The mean RMI of ND lesions was 74 ± 13 (range 50–95), which was significantly higher than that of vitiligo lesions (50 ± 24, range 0–97, Table 2).

TABLE 2. Comparison of mean MIs and RMIs in nevus depigmentosus and vitiligo

	Vitiligo ($N = 69$)	Nevus depigmentosus ($N = 11$)	*P*-value*
No of lesions	182	20	
Melanin index			
Mean ± SD	79.02 ± 40.38	135.07 ± 43.87	0.000
Minimum	.00	73.33	
Maximum	219.66	225.00	
RMI (%)			
Mean ± SD	50 ± 23	74 ± 13	0.000
Minimum	0	50	
Maximum	97	95	

*Determined by Student's *t*-test. Mean MI and RMI of nevus depigmentosus are significantly higher than that of vitiligo. Note that minimum RMI of nevus depigmentosus is 50, which is much higher than zero of vitiligo. MI, melanin index; RMI, relative melanin index.

Discussion

Vitiligo is an acquired depigmentation disorder, whereas nevus depigmentosus is thought to be a congenital disorder. Reports show that ND presents at various ages, although this is probably owing to delayed detection. Although lesions are present in infants and young children, a color contrast may not be visible until the skin is tanned. A multicenter study performed in Korea showed that 20.2% of NDs are first detected after the age of 3 (8). The clinical criteria have been widely used for the differential diagnosis of vitiligo and ND, and are challenging in some cases, especially in childhood patients or in those with early-stage disease (3, 8, 9). On the other hand, the diagnosis of generalized vitiligo, which is symmetrically distributed, is straightforward. However, focal or segmental vitiligo characterized

by isolated or a few macules resemble ND. Recent studies have shown that segmental variants of ND account for as many as 50% of cases (3, 8). Furthermore, segmental vitiligo tends to have an earlier onset and to be more stable than generalized vitiligo, and to overlap more so with the clinical features of ND. Because these hypopigmentary disorders have quite different prognoses and psychological impacts, their differential diagnosis is of importance. A biopsy may be helpful, but the presence of melanocytes cannot be assumed to exclude a diagnosis of vitiligo because early (6 months) and repigmenting macules of vitiligo also contain melanocytes (4, 10). In addition, the presence of melanocytes even in long duration vitiligo lesions has been reported (11). These findings demonstrate that the presence or absence of melanocytes cannot be taken as a differential point in the diagnosis of hypopigmentary disorders.

Recently, several devices have been introduced to measure melanin pigment in the skin, especially for cosmetic research purposes. However, these devices are rarely used in clinical practice. In the present study, we used a Mexameter MX16 (Courage-Khazaka Electronic) and investigated whether this device is useful for the differential diagnosis of these hypopigmentary disorders. Our results show that MI as measured using a Mexameter® is significantly higher in ND (138.17 ± 43.87) than in vitiligo (79.11 ± 40.24). However, all types of vitiligo and ND were included in the present study, regardless of previous treatment and response to therapy. In addition, MI is dependent on skin type and body site even in a single individual (12). Moreover, our study shows that the MIs of vitiligo lesions overlap with those of ND, possibly because of the presence of residual melanocytes in vitiligo lesions and other factors such as skin type and site variations. Thus, we introduced RMI, which represents the ratio of pigmentation at a lesion site relative to that of symmetrically disposed normal skin. As was expected, the mean RMI (50 ± 24) of vitiligo lesions was also significantly lower than that in ND (74 ± 13), but the RMI measure was associated with a much lower standard deviation (SD) than MI, especially for ND lesions. This means that considerations of skin color are important in the diagnosis of hypopigmentrary disorders.

Our results suggest guidelines for the differential diagnosis of ND and vitiligo. Variations of skin color in vitiligo have made the establishment of guidelines difficult, but based on our findings, an RMI of $>74\%$ can be suspected as ND [odds ratio (OR) = 4.697, 95% confidence interval (CI) = 1.779–12.404]. In addition, another important finding of the present study was that all ND lesions had an RMI of $>50\%$. Thus, our findings suggest that vitiligo is indicated for any lesion with an RMI of $\leq 50\%$. These findings may mean that RMIs determined at several sites could help clinicians make a differential diagnosis in these hypopigmentary disorders. However, it should be noted that our sample size was small, and thus more extensive study is necessary to confirm the results and to set guidelines.

In conclusion, despite the limitation of small numbers, our findings indicate that the current commercially available Mexameter® provides a clinically accessible and straightforward means of increasing diagnostic accuracies in hypopigmentary disorders.

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Address:
Kyoung-Chan Par
Department of Dermatology
Seoul National University Bundang Hospital
300 Gumi-dong
Bundang-gu
Seongnam-si
Kyounggi-do, 463-707
Korea

Tel: +82 31 787 7311
Fax: +82 31 787 4058
e-mail: gcpark@snu.ac.kr