Serum Levels of Vitamin B_{12} and Folate in Korean Patients with Vitiligo

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Sir,

Vitiligo is a common pigmentary disorder characterized by well-demarcated depigmented patches or macules caused by the destruction of melanocytes. Vitamin B_{12} deficiency induces pernicious anaemia, which is caused either by the absence of intrinsic factor from atrophy of the gastric mucosa or by autoimmune destruction of parietal cells of the stomach (1, 2). Vitamin B_{12} facilitates the conversion of folate to tetrahydrofolate, which is essential in various enzyme reactions. Folate is composed of pteridine, para-aminobenzoic acid and L-glutamate, and the former two components are known to play a role in pigmentation (3, 4).

There have been several conflicting reports on the blood levels of vitamin B_{12} and folate in vitiligo (5–7). This study was designed to elucidate the relationship between the blood levels of these vitamins and vitiligo.

MATERIALS AND METHODS

Patients and controls

Seventy-seven Korean patients with vitiligo (32 men and 45 women, mean age 34.5 ± 18 years, range 5–66) were evaluated at the Department of Dermatology of Kyunghee Medical Center. None of the patients had other coexisting chronic diseases, and patients with a history of treatment using either systemic or topical modalities within the 4 weeks preceding examination were excluded.

The patients were classified according to sex, distribution of lesions, duration of disease, age of onset and stability of disease. In terms of lesional distribution, 40 were of the localized type and 37 were of the generalized type. The duration of vitiligo was <1 year in 24 patients and >1 year in 53 patients. The age of onset was below 15 years in 25 patients and in 52 patients it was detected after 15 years of age. In terms of stability of disease, 51 had active lesions — enlargement of extent of lesions during the month prior to examination or positive for the Koebner phenomenon — and 26 had inactive lesions. As control, blood samples were obtained from 35 men and 45 women (mean age 35.8 ± 11.8 years, range 23–65) who had no clinical evidence of vitiligo, had no other chronic illness, and were not on any medication. Blood samples from both the patient and control groups were obtained after 12 h of fasting. SimulTRAC-SNB Radioassay Kit (ICN Pharmaceuticals, Costa Mesa, NY, USA), which utilizes [^{57}Co] and [^{123}I] as tracers, was used to determine the levels of vitamin B_{12} and folate.

The study was approved by the ethics review committee of the Kyung Hee University Medical Center, Seoul, South Korea.

Statistics

Results from the patient and control groups were compared using the two-sample *t*-test, results from the subgroups were also compared using the two-sample *t*-test. A p value <0.05 was considered to indicate statistical significance.

RESULTS

Comparison between patients and control groups

The serum levels of vitamin B_{12} and folate in the patients were all within the normal ranges; however, the mean level of vitamin B_{12} in the patient group was lower (668 ± 290 pg/ml) than that of the control group (875 ± 302; $p<0.05$). The mean level of folate did not differ between the control and patient groups.

Comparisons between patient subclasses

A genderwise comparison revealed that the level of vitamin B_{12} was higher in women (747 ± 312 pg/ml) than in men (558 ± 214; $p<0.05$); however, the level of folate did not differ between men and women. The levels of vitamin B_{12} and folate in patients with generalized vitiligo (651 ± 236 pg/ml and 6.4 ± 2.7 ng/ml) were lower than in those with localized vitiligo (685 ± 334 pg/ml and 7.7 ± 4.2 ng/ml; $p<0.05$ for both). Comparisons between other patient subclasses revealed no statistically significant differences.

DISCUSSION

The incidence rate of pernicious anaemia in patients with vitiligo is 3.7%, which is thirty times higher than

that observed in the general population (1). It can be corrected by appropriate vitamin B_{12} replacement therapy (2). Vitamin B_{12} acts as a coenzyme in the folate-dependent synthesis of pyrimidines and purines. Vitamin B_{12} and folate influence each other in biochemical processes in such a way that the processes involving these cofactors will not proceed in the absence of either one. Animal products are the main source of vitamin B_{12}, and vegetables constitute the primary dietary source of folate (2).

Folate (pteroylmonoglutamic acid) consists of pteridine, para-aminobenzoic acid and L-glutamic acid. Pteridine is the coenzyme involved in the enzymatic hydroxylation of phenyalanine to tyrosine (3). Thus, folate deficiency may lead to tyrosine deficiency and a reduction in melanin formation. It has been suggested that folate and vitamin B_{12} supplementation may have indirect effects on vitiligo and homocysteinuria (7). It has also been suggested that folate may play a role in the melanin synthesis pathway through the activity of its components, pteridine and para-aminobenzoic acid, and through vitamin B_{12}-dependent formation of methionine (8). However, there is a contradictory report of a case in which reversible hyperpigmentation of skin and nail and whitening of hair occurred concurrently in vitamin B_{12} deficiency (9). Another study revealed hyperpigmentation in folate deficiency (4).

Montes et al. (5) reported that the level of folate was decreased in 11 of 15 vitiligo patients, the level of vitamin B_{12} was decreased in 5, and the level of vitamin C was decreased in 4. They treated patients with oral folate (4 mg/day), oral vitamin C (1 g/day), and intramuscular injection of vitamin B_{12} (200 mg/week). The progression of disease was reported to have stopped within weeks; significant repigmentation was observed 3 months later and 80–100% improvement after 2 years. Juhlin & Olsson (6) reported a study involving 100 patients with vitiligo who received folate (10 mg/day) and vitamin B_{12} (2 mg/day) orally and recommendation for exposure to sunlight for 6 months. Repigmentation was observed in 52 patients and suppression of spreading of lesions in 64. Patients <26 years of age and with a disease duration <10 years responded more dramatically to therapy, regardless of disease activity. However, the authors suggested that vitamin B_{12} and folate might not be the main aetiological factors in vitiligo, because the serum levels of these vitamins were within the normal range.

Tjioe et al. (8) compared the efficacy of narrowband UVB therapy with that of a combination therapy involving UVB and folate (5 mg/day) plus vitamin B_{12} (1 mg/day). They observed no difference in the maximum repigmentation rate between these treatments.

The present study showed a significant decrease in the serum level of vitamin B_{12} in vitiligo patients ($p<0.05$), although the levels were within the normal range. The level of vitamin B_{12} was higher in female patients than in male patients. However, this difference was also observed in the control group (777 ± 228 pg/ml in men and 972 ± 336 pg/ml in women, $p<0.05$), and this finding has been made in healthy people in a previous report (10). A comparison between the subclasses divided according to the distribution of lesions showed that the levels of vitamin B_{12} and folate were significantly lower in the generalized type of the disease than in those with the localized type ($p<0.05$). These results seem to imply that decrease in the serum levels of vitamin B_{12} and folate may play a role in the depigmentation process, especially in generalized vitiligo.

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