

Serum Levels of Folic Acid and Vitamin B₁₂ in Korean Patients with Vitiligo

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Abstract

The association of vitiligo and pernicious anemia has been previously documented. The low levels of folic acid and vitamin B₁₂ were thought to be related to vitiligo. To date, there have been very few reports about the serum levels of folic acid and vitamin B₁₂ in patients with vitiligo. Using radioimmunoassay, we measured the serum levels of folic acid and vitamin B₁₂ in 100 Korean patients with vitiligo. The mean serum levels of folic acid and vitamin B₁₂ were 6.31 ± 2.82 ng/ml and 630.25 ± 230.94 pg/ml, respectively, in patients with vitiligo. These levels showed no significant difference compared to the normal control group, suggesting that folic acid and vitamin B₁₂ do not appear to play a role in the pathogenesis of vitiligo.

Key Words: Folic acid, vitamin B₁₂, vitiligo

INTRODUCTION

Vitiligo is an acquired, idiopathic, hypomelanotic disease characterized by circumscribed depigmented patches. It affects approximately 1–4% of the world's population.¹ The causes of vitiligo remain to be elucidated. Vitiligo may be an autoimmune disease and it is associated with other disorders such as thyroiditis, pernicious anemia, polyglandular autoimmune endocrinopathy, Addison's disease, hypoparathyroidism, and diabetes mellitus, which may also arise due to an autoimmune mechanism.^{2,3}

Vitiligo has been reported in 1.6 to 10.6% of patients with pernicious anemia.^{4,5} From a total of 135 Danish patients with vitiligo, five (3.7%) had pernicious anemia.⁵ Although the association of vitiligo with pernicious anemia has been documented, there have been very few reports evaluating blood levels of folic acid and vitamin B₁₂ in patients with vitiligo. Montes et al. showed diminished serum levels of folic acid in 11 of 15 patients, and vitamin B₁₂ in 5 of

15 vitiligo patients in Buenos Aires.⁶ He also reported that supplements of folic acid, vitamin B₁₂ and vitamin C induced repigmentation in vitiligo. Juhlin and Olsson treated 100 patients with vitiligo using oral folic acid, vitamin B₁₂ and sun exposure.⁷ Clear repigmentation occurred in 52 patients and the spread of vitiligo stopped in 64% of patients.

In this study, the serum levels of folic acid and vitamin B₁₂ were measured in 100 Korean patients with vitiligo to investigate whether the deficiency of these vitamins may be related to the pathogenesis of vitiligo.

MATERIALS AND METHODS

One hundred Korean patients with vitiligo registered at Severance Hospital, Yonsei University College of Medicine were evaluated. Fifty patients were male and 50 were female. The age of patients varied from 6 to 61 years and their mean age was 31. Eighty-seven patients had spreading vitiligo and 13 were stable. In regard to the type of vitiligo, 19 patients were segmental, 14 were focal, 62 were vulgaris, 1 was universalis, and 4 were mixed type. Among the patients with vitiligo, 17 had other diseases such as atopy, halo nevi, alopecia, hyperthyroidism, diabetes mellitus, and premature graying hair. They were included in this study because those

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Table 1. The Mean Serum Levels of Folic Acid

Groups	Mean (ng/ml) \pm Standard deviation
Control*	6.11 ± 3.11
Patients with vitiligo*	6.31 ± 2.82

* $p > 0.05$, as compared with two-sample t-test.

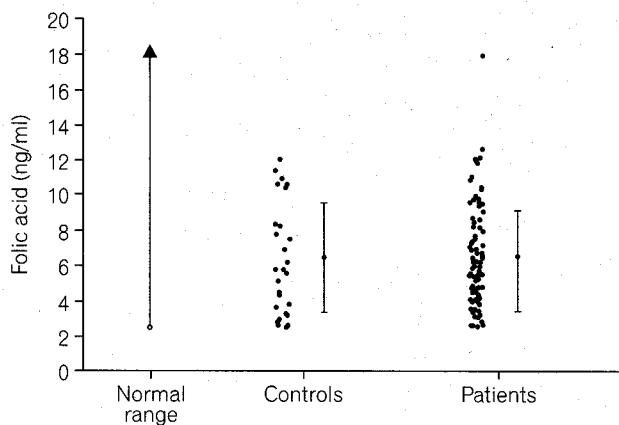


Fig. 1. Serum levels of folic acid of normal range (>2.5 ng/ml), from controls (6.11 ± 3.11 ng/ml) and patients with vitiligo (6.31 ± 2.82 ng/ml).

diseases do not influence the serum levels of folic acid and vitamin B₁₂. Thirty age and sex-matched healthy individuals were chosen as a control group (mean age; 29 years old, 14 males and 16 females).

Using radioimmunoassay, the serum levels of folic acid and vitamin B₁₂ were measured in patients with vitiligo and the control group. KODAK folic acid and vitamin B₁₂ Radioassay Kit were used. By this method, the serum levels of folic acid and vitamin B₁₂ were determined simultaneously in a single tube. Master tracer isotopes were cobalt 57 and iodine 125. The normal range of the level for serum folic acid was above 2.5 ng/ml, while for vitamin B₁₂ it was 180–710 pg/ml.

We compared our results statistically by the two-sample t-test and one-way ANOVA method (significance level; 0.05) between patients and the control group, male and female, children (under 15 years of age) and adults, vitiligo with and without other diseases, spreading and stable vitiligo, segmental and non-segmental type, and among focal, vulgaris, and universal type.

Table 2. The Mean Serum Levels of Vitamin B₁₂

Groups	Mean (pg/ml) \pm Standard deviation
Control*	627.16 ± 251.35
Patients with vitiligo*	630.25 ± 230.94

* $p > 0.05$, as compared with two-sample t-test.

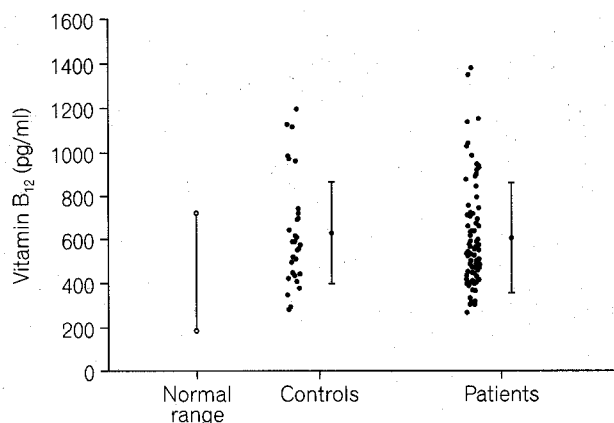


Fig. 2. Serum levels of vitamin B₁₂ of normal range (180–710 pg/ml), from controls (627.16 ± 251.35 pg/ml) and patients with vitiligo (630.25 ± 230.94 pg/ml).

RESULTS

In the control group, the mean serum levels of folic acid and vitamin B₁₂ were 6.11 ± 3.11 ng/ml and 627.16 ± 251.35 pg/ml, respectively. In the group of patients with vitiligo, the mean serum levels of folic acid and vitamin B₁₂ were 6.31 ± 2.82 ng/ml and 630.25 ± 230.94 pg/ml, respectively. Serum levels of folic acid and vitamin B₁₂ didn't show any difference in either group (Table 1 and 2, Fig. 1 and 2). In both cases of folic acid and vitamin B₁₂, there were no statistically significant differences between subgroups, such as children (under 15 years of age) and adults, vitiligo with and without other diseases, spreading and stable vitiligo, segmental and non-segmental type, and among focal, vulgaris, and universal type. Only in the case of folic acid, male patients with vitiligo had lower serum levels than females with statistical significance (Table 3 and 4).

Table 3. Serum Levels of Folic Acid in Patients with Vitiligo

Subgroups	Mean (ng/ml) ± Standard deviation	p-value
Male	5.68 ± 2.18	p < 0.05*
Female	6.94 ± 3.23	
Childhood	6.07 ± 2.95	p > 0.05*
Adult	6.36 ± 2.81	
With other disease	6.32 ± 2.46	p > 0.05*
Without other disease	6.30 ± 4.16	
Spreading vitiligo	6.26 ± 2.87	p > 0.05*
Stable vitiligo	6.63 ± 2.48	
Segmental type	6.94 ± 3.75	p > 0.05*
Non-segmental type	6.17 ± 2.56	
Focal type	6.93 ± 2.90	p > 0.05 †
Vulgaris type	6.27 ± 2.43	
Universal type	2.61	

* two-sample t-test.

† one-way ANOVA.

Table 4. Serum Levels of Vitamin B₁₂ in Patients with Vitiligo

Subgroups	Mean (pg/ml) ± Standard deviation	p-value
Male	580.19 ± 234.87	p > 0.05*
Female	626.31 ± 226.88	
Childhood	627.32 ± 195.26	p > 0.05*
Adult	598.32 ± 238.30	
With other disease	608.06 ± 233.59	p > 0.05*
Without other disease	581.32 ± 223.38	
Spreading vitiligo	598.55 ± 222.35	p > 0.05*
Stable vitiligo	634.68 ± 290.36	
Segmental type	559.72 ± 153.43	p > 0.05*
Non-segmental type	613.46 ± 245.21	
Focal type	631.91 ± 292.18	p > 0.05 †
Vulgaris type	617.08 ± 243.28	
Universal type	528.20	

* two-sample t-test.

† one-way ANOVA.

DISCUSSION

Vitiligo is a very common disorder but its etiology is unknown. It has been considered an autoimmune disorder partly due to the reported frequent association of other autoimmune diseases.³ Alternative theories are autotoxicity, neurohumoral, and exogenous chemical exposure. Several reports have mentioned the association of vitiligo and pernicious anemia.^{2,4,5,8} Grunnet et al. showed that the incidence of vitiligo in pernicious anemia is up to 10 times higher than that occurring in the general population and that pernicious anemia is 30 times more frequent among Danish patients with vitiligo than among the general population.⁵ Pernicious anemia showed that it had a tendency to be more common with late-onset vitiligo.⁹ However, Song et al. reported that there were no cases of pernicious anemia out of 1,088 Korean patients with vitiligo.¹⁰ From this finding, the association of pernicious anemia with vitiligo should be carefully evaluated again with a large population study.

Folic acid contains 3 components; pteridine, para-aminobenzoic acid, and L-glutamic acid. Free pteridine is the coenzyme for the enzymatic hydroxylation of phenylalanine to tyrosin. Para-aminobenzoic acid, when administered in a large dose, resulted in the

darkening of hair.¹¹ Vitamin B₁₂ facilitates the reduction of folic acid to tetrahydrofolic acid, a necessary prerequisite to the participation of folic acid in enzyme reactions. The two substances, folic acid and vitamin B₁₂, require each other's presence in biological reactions that will not proceed in the absence of either one. There have been very few reports evaluating blood levels of folic acid and vitamin B₁₂ in patients with vitiligo. Montes et al. suggested the role of folic acid in pigmentation.⁶ However, our results showed that the levels of folic acid and vitamin B₁₂ in serum were normal, contrary to Montes et al.'s⁶ report.

Supplements of folic acid and vitamin B₁₂ as a treatment of vitiligo have also been introduced. Montes et al. treated 8 of 15 patients for 3 years with oral folic acid (2 mg, twice daily), ascorbic acid (500 mg, twice daily), and vitamin B₁₂ (100 mg, intramuscularly every 2 weeks).⁶ The progression of vitiligo stopped within weeks and significant repigmentation was observed 3 months later. After 2 years, 80–100% of the vitiligo had repigmented. However, this study should be conducted with more patients to give us scientific data. Juhlin and Olsson treated 100 patients with vitiligo with oral folic acid (5 mg, twice daily) and vitamin B₁₂ (1 mg cyanocobalamin, twice daily) for more than 6 months.⁷ They also encouraged

patients to expose their skin to the sun in summer and UVB irradiation in winter. Prior to starting treatment, serum levels of folic acid and vitamin B₁₂ were determined in 53 patients and found to be normal. Clear repigmentation occurred in 52 patients and the spread of vitiligo stopped in 64% of patients. Repigmentation was significantly more common in patients younger than 26 years of age and in patients with vitiligo for less than 10 years, but it was the same in active versus stable vitiligo. Considering the report that 311 nm UVB can cause vitiligo lesions to repigment,¹² the repigmentation may be induced by UVB radiation rather than vitamin B₁₂ and folic acid supplement. Our experience with folic acid and vitamin B₁₂ treatment in vitiligo did not show any significant repigmentation and another researcher's experience showed the same result (personal communication with Dr. Nordlund).

In this study, serum levels of folic acid and vitamin B₁₂ were within normal limits in 100 Korean patients with vitiligo. Folic acid and vitamin B₁₂ do not appear to play a role in the pathogenesis of vitiligo.

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