Note

Percutaneous Absorption of Biotin in Healthy Subjects and in Atopic Dermatitis Patients

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Summary The study was designed to test the ability of sequential applications of biotin-containing ointment to increase serum biotin levels. Twenty atopic dermatitis patients (mean age, 20.5 yr) and 11 healthy subjects (mean age, 25.5 yr) volunteered to participate in this study. The diagnosis of atopic dermatitis was established dermatologically. Seven grams per day of ointment containing 0.3% biotin and 1-4 g per day of steroid ointment were both applied sequentially. The healthy subjects applied only biotin ointment. The biotin concentration was determined microbiologically. Before biotin treatment, the average serum biotin level was significantly lower in atopic dermatitis patients than in healthy subjects. The percutaneous application of biotin-containing ointment caused a significant increase in the serum biotin concentration in both healthy subjects (from 41.5 ± 10.0 to 50.2 ± 9.2 nmol/L) and in atopic dermatitis patients (from 27.9 ± 17.4 to 50.7 ± 21.6 nmol/L), especially in patients whose initial level was low, and also could be effective in regulating the atopic allergic response involving eosinophils. In conclusion, biotin appears to be readily absorbed through both normal and dermatitis-affected human skin.

Key Words percutaneous absorption, biotin, atopic dermatitis, eosinophil

There are a few papers dealing with the percutaneous absorption of fat-soluble vitamins, namely vitamin E (1), vitamin D (2), and retinyl palmitate (3). In contrast, there are very few reports about the absorption of water-soluble vitamins. Howe et al (4) investigated the percutaneous absorption of vitamin B12 in the rat and guinea pig. They observed that the topical application of vitamin B12 to weanling rats consuming a vitamin B12-deficient diet prevented body weight loss. This result
indicated that the vitamin was efficiently absorbed in an active form.

Biotin, a water-soluble vitamin, is well known not only to act as a coenzyme with four substrate carboxylases (5), but also to perform some nonprosthetic group functions (6–8). From these reports, it could be concluded that biotin is deeply involved in various kind of cellular functions. Interestingly, in a few human studies, biotin, given per os or intravenously, has been reported to have a beneficial effect on atopic dermatitis (9), pustulosis palmaris et plantaris (10), and psoriasis (11).

We thought that the topical application of biotin might constitute a very easy and effective therapy for the above kinds of dermatitis. Unfortunately, there has been no study on the percutaneous absorption of biotin in such patients. For this reason, we undertook to clarify whether or not biotin can be absorbed percutaneously by atopic dermatitis patients.

Subjects and methods

Twenty patients with atopic dermatitis [11 males and 9 females, 8–34 yr in age (mean, 20.5 yr)] were recruited for the present study.

The diagnosis of each patient’s condition was established dermatologically. The patients had not been treated orally or topically at all with steroidal drugs before this study started. After we had obtained consent to conduct this trial from all of the patients, 7 g per day of ointment containing 0.3% biotin and 1–4 g per day of steroidal ointment (0.02–0.03% diflucortolone valerate or 0.005–0.0075% beclometasone dipropionate) were applied sequentially for 2–12 mo (mean, 4.07 mo). All patients were instructed to apply the ointments to the atopic skin over as wide an area as possible. Blood for biotin and peripheral eosinophil determination was collected from the brachial vein just before and 2–5 mo (mean 3.2 ± 1.07 mo) after the patients had been administered the biotin and steroidal ointments. A control group of 11 healthy subjects [8 males and 3 females, 21–41 yr in age (mean, 25.5 yr)] volunteered to take part in this study. As with the patients, 7 g/d of ointment containing 0.3% biotin was applied sequentially to an area of about 50% of the body surface, but only for 7 d. No steroidal ointment was used. None of the control subjects had any significant past history or any family history of atopic dermatitis. The constituents of the biotin-containing ointment were referred to in a previous paper (12). The blood used for determining the biotin concentration and/or number of peripheral eosinophils was collected on the first and last days of these trials prior to the taking of breakfast.

The biotin concentration in the serum was determined microbiologically (13). The number of eosinophils in the peripheral blood from 18 out of 20 patients was determined microscopically. Smear preparations of peripheral blood were stained with May-Giemsa solution to enable the number of eosinophils per mm³ of peripheral blood to be counted.

Values are presented as means with the standard deviation of the mean (SD). When the difference between two means needed to be statistically evaluated, a Wilcoxon’s test, a paired t-test, or a one-way analysis of variance (ANOVA) with
Fig. 1. Serum biotin concentrations in atopic dermatitis patients and healthy subjects. The broken line indicates the lowest serum biotin concentration found in healthy subjects. Eleven out of 20 patients had serum biotin levels that were below the line (open circles), but the remaining 9 showed normal levels (closed circles).

Results and discussion

The average serum biotin concentration before treatment with biotin was significantly higher in healthy subjects than in patients with atopic dermatitis, (41.4 ± 9.9 vs. 27.9 ± 17.3 nmol/L; p < 0.025, one-way ANOVA). Eleven of the 20 patients had serum biotin levels that were lower than the lowest serum concentration seen in healthy subjects (30.0 nmol/L), while the other 9 patients exhibited values within the range seen in the healthy subjects (Fig. 1). On this basis, the patients were divided into a low biotin (LB) group and a normal biotin (NB) group. The coefficient of variation for the patient group was almost 2.6 times that for the healthy subjects (62.0 and 24.1 nmol/L, respectively).

This seems to indicate that these 11 patients developed atopic dermatitis with a concomitant shortage of biotin, whereas in the remaining 9, it developed without such a shortage. Interestingly, the average serum biotin level of the LB group was strongly increased by the percutaneous application of biotin, whereas that of the NB group was not. This result could conceivably mean that the ability to absorb biotin percutaneously can be affected by the existing level of biotin in the blood, and perhaps in the organs.

Figure 2 shows the serum biotin concentrations before and after the course of percutaneously applied biotin ointment in patients with atopic dermatitis. Sequential percutaneous application of biotin ointment significantly increased the serum biotin concentration of the whole group of patients (p = 0.01; Wilcoxon's test). The average serum biotin concentration increased from 27.9 ± 17.3 to 50.7 ± 21.6 nmol/L, and 18 of the 20 patients (90.0%) showed an increase in their serum biotin concentration.
Fig. 2. Serum biotin concentration in NB and LB atopic dermatitis patients before and after percutaneous application of biotin ointment. Symbols represent the serum biotin concentration before and after application of the ointment in the NB group (closed circles) or LB group (open circles). In the LB group, there is a significant difference between before and after application of the ointment (p<0.01; Wilcoxon’s test), but this was not the case for the NB group.

After biotin treatment, the serum biotin concentration in 15 out of 20 patients (75.0%) reached at least the average value seen in healthy subjects before any application of the biotin ointment. In the LB group, a significant increase in serum biotin was observed (from 14.5±8.4 to 51.6±20.4 nmol/L ± SD: p<0.01; Wilcoxon’s test), but this was not the case for the NB group (from 44.4±8.7 to 49.6±24.2 nmol/L: p=0.374; Wilcoxon’s test). There was no difference in age between the LB group and the NB group (20.4±5.2 and 20.6±8.2 yr, respectively).

Sequential daily percutaneous application (for 1 wk) of biotin ointment significantly increased the serum biotin concentration in the healthy subjects (p<0.05; Wilcoxon’s test). The average serum concentration increased from 41.5±10.0 to 50.2±9.2 nmol/L, and 10 of the 11 subjects (90.9%) showed an increase in serum biotin concentration.

These results clearly indicate that biotin is readily absorbed through both healthy and dermatitis-affected skin. In an earlier report (14), it was demonstrated that 9 mg/d of biotin orally administered to healthy subjects for 3 d increased the serum biotin concentration by about 3-fold. This increase is significantly greater than that seen in the present study. In the former study, in which administration was per os, the vitamin probably appeared almost immediately in the bloodstream at a high concentration. However, when percutaneously applied, the rate of absorption would be expected to be much slower. This conclusion is consistent with previous reports about vitamin B12 (4, 15).

It is well known that blood eosinophilia is common among atopic dermatitis patients (16), without there being infiltration of dermal or epidermal tissue by...
Fig. 3. The number of peripheral eosinophils in NB and LB patients before and after percutaneous application of biotin ointment. Symbols represent the number of peripheral eosinophils before and after application of the ointment in the NB group (closed circles) or LB group (open circles). In the case of all patients and the LB group, there is a significant difference between before and after application of the ointment ($p=0.05$; Wilcoxon’s test), but this was not the case for the NB group.

eosinophils (17). In addition, Leiferman et al (18) demonstrated a high blood level of the major basic protein that has been localized to the crystalloid core of the eosinophil granule in the absence of a pronounced accumulation of eosinophils in the atopic skin. These previous reports indicate that the number of eosinophils in peripheral blood is a useful index of the status of atopic dermatitis.

Figure 3 shows the number of eosinophils in the peripheral blood before and after the course of percutaneously applied biotin ointment in patients with atopic dermatitis. The number of eosinophils decreased significantly in the all patients ($p=0.05$; Wilcoxon’s test), and in the LB group ($p=0.05$; Wilcoxon’s test) but not in the NB group ($p=0.214$; Wilcoxon’s test). The improvement of exanthema was observed in 18 of 20 patients by the treatment of biotin and steroid ointments. However, there was no significant correlation between the degree of dermatological improvement and level of serum biotin concentration (data not shown).

The results of the present study (Figs. 2 and 3) suggest that percutaneously absorbed biotin could be effective in regulating the atopic allergic response involving eosinophils, or at very least, it could enhance the effect of the steroid hormone applied simultaneously to the same patients.

Finally, further study will be needed to clarify the mechanism by which the percutaneous absorption of biotin takes place.

REFERENCES


