Double-blind randomized trial of once a week narrowband ultraviolet B (NB-UVB) phototherapy in vitiligo

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Abstract

Background: Vitiligo is a skin pigmentation disorder, affecting approximately 1-2% population worldwide. Currently, there are wide varieties of treatment to achieve re-pigmentation, and phototherapy is one of the effective treatments. Narrowband ultraviolet B (NB-UVB) is administered twice a week according to the phototherapy protocol for vitiligo. Some vitiligo patients have difficulty following this schedule, leading to decrease of patient’s compliance. Therefore, we performed study comparing the efficacy of phototherapy frequency, once a week and twice a week NB-UVB in vitiligo.

Methods: This preliminary study divided 10 patients into 2 groups of 5 patients each with randomized, double-blind method. Group A was scheduled for NB-UVB phototherapy twice a week while Group B was scheduled for once a week. All patients received topical desoxymetasone cream once daily. Re-pigmentation were compared using Vitiligo Area Scoring Index (VASI). VASI was graded as good (≥25%), moderate (10-24%), and poor (<10 %) responses. Evaluation for melanin index for each lesion was assessed by Mexameter® and cumulative doses of phototherapy were compared.

Results: Thirty-seven lesions were treated on face and neck, trunk and extremities. Good responses were obtained in 14.29% group A patients and 13.04% group B patients. The mean of cumulative doses phototherapy in group A was 850 mJ/cm², whereas group B was 800 mJ/cm². There was no significant differences (p>0.05) between both groups in terms of re-pigmentation, cumulative doses of phototherapy, and melanin index.

Conclusion: In vitiligo, once a week NB-UVB phototherapy appears to be as efficacious as twice a week treatment schedule.

Keywords: melanin index, narrowband ultraviolet B, phototherapy, vitiligo, vitiligo area scoring index.

Background

Vitiligo is a skin pigmentation disorder characterized by white depigmentation patches. The prevalence affects approximately 1-2% world population. This disorder often causes cosmetic issue which can affect both psychological and social aspects in vitiligo patients. Treatment of vitiligo is based on references: to control the progression of the disease and to achieve re-pigmentation of the lesions. There is no definitive therapy to cure vitiligo. Nowadays, wide variety of therapeutic modalities are used to achieve re-pigmentation of vitiligo lesions and to stabilize the de-pigmentation process. Phototherapy is one of the effective treatments for vitiligo. Since psoralen with ultraviolet had been used, phototherapy for vitiligo had been developed into psoralen with ultraviolet A, narrowband ultraviolet B, combination therapy with topical treatment, and targeted phototherapy with laser and ultraviolet. Targeted phototherapy is one of the most effective treatments for vitiligo, particularly for patients with localized vitiligo. In accordance with the term, targeted phototherapy specifically targets the lesion, while normal skin around the lesion remains unexposed. Therefore, normal skin remains protected, while the lesions are exposed to high energy, which will enable faster therapeutic effect.
Several targeted phototherapy devices, which have been used for vitiligo, are xenon-chloride excimer laser, excimer lights, and targeted ultraviolet devices which provide broadband ultraviolet B or narrowband ultraviolet B. Targeted phototherapy uses non-coherent conventional ultraviolet light, which is exposed on vitiligo lesions area through optic fiber. Targeted phototherapy such as targeted ultraviolet B phototherapy (T-UVB) is commonly performed twice or thrice a week. The phototherapy dose is gradually increased until mild erythema or perifollicular pigmentation appears. One of targeted ultraviolet B phototherapy’s weaknesses is that the patient had to come twice or thrice a week for treatment. For some patients, this is considered interfering their daily schedule, making it difficult for them to continue the treatment. Once a week phototherapy is considered less interfering patient’s daily schedule, therefore it is expected to improve patient’s compliance.

Previous similar study was conducted by Majid et al. in India. This study was also conducted in Indonesia due to non-compliance expressed by some of our vitiligo patients who had phototherapy. The factor influencing patients’ non-compliance included busy schedule, far distance which they had to travel at least 2-3 times per week for a prolonged period, time efficiency, as well as expense that patients had to spend for every visit. Commonly, patients preferred the minimum duration for a visit. This study was performed to compare the efficacy of once a week and twice a week narrowband ultraviolet B phototherapy for vitiligo treatment. This study is distinctive from other studies because the measurement of extent re-pigmentation in this study was performed by Vitiligo Area Scoring Index (VASI) which is semi-objective measurement, and the measurement of melanin index for the vitiligo lesion was performed by Mexameter device which is objective measurement.

Methods

Ten vitiligo patients were chosen for the study, with vitiligo areas on face and neck, trunk, and extremities. They were randomized and divided into 2 groups, each group consisted of 5 patients. Group A received twice a week narrowband ultraviolet B phototherapy, while group B received once a week narrowband ultraviolet B phototherapy. All patients in both groups came twice weekly for phototherapy and their eyes were covered when the phototherapy was performed. For the second visit of group B patients, the device was only put on their skin with lights off, and both author and patients didn’t know whether they were in group A or B. The co-authors performed all phototherapy in both groups and then the assessment was performed by author. The patients’ age ranged from 14 to 47 years old. All patients were outpatients of dermatology clinic in dr. Moewardi General Hospital, Surakarta, Indonesia. The study was conducted for 5 weeks from March 2016 until April 2016. All patients signed informed consents prior to the study. The exclusion criterion was pregnancy. All protocols for this study had been approved by Ethics Committee of our institution.

All patients were treated with narrowband ultraviolet B device named Dermapal® (Daavlin Company, Canada). The melanin index of each lesion was measured with Mexameter® (MDD4, Courage and Khazaka), and Vitiligo Area Scoring Index (VASI) was measured before and after phototherapy. In both groups, the dosage of phototherapy was increased 50 mJ/cm² gradually after phototherapy had been performed for 3 times. All the patients in both groups also received same topical steroid therapy that was applied once daily.

Group A received twice a week phototherapy with interval of 2-3 days in between doses while group B received once a week phototherapy on a fixed schedule. Response to phototherapy was monitored clinically and photographically, which was graded as good response (≥25% re-pigmentation), moderate response (10-24% re-pigmentation), and poor response (<10% re-pigmentation). The primary outcome was the extent of re-pigmentation measured by VASI. This was calculated for each location of the lesions, divided into 3 parts (face and neck, trunk, and extremities); which was later compared in both groups. In addition, the melanin index of each lesions was measured by Mexameter® and the cumulative doses of phototherapy were also compared in both groups. The independent sample t-test was used to assess the statistical significance of these comparisons and p<0.05 was considered as statistically significant.

Results

The patients’ age in group A (twice a week) ranged from 14 to 47 years old with mean of 29.4 years old, whereas patients’ age in group B (once a week) ranged from 11 to 71 years old with mean of 53 years old. There were 3 male patients and 2 female patients in both groups.
Total of 37 lesions were treated, 14 lesions in group A (4 lesions on face and neck, 10 lesions on extremities), and 23 lesions in group B (8 lesions on face and neck, 8 lesions on trunks, 7 lesions on extremities). The extent of repigmentation was measured by VASI. Good response (≥25% repigmentation) were achieved in 13.51% (5/37) lesions, moderate response (10-24% repigmentation) were achieved in 54.1% (20/37) lesions, and poor response (<10% repigmentation) were achieved in 32.43% (12/37) lesions. By comparing results of both groups, 2 out of 14 lesions (14.29%) showed good response in group A, while 3 out of 23 lesions (13.04%) showed similar results in group B (Table 1). Comparing results in both groups, patients showed a good response in group A only on extremities in 20% (2/10) lesions, while in group B showed a good response only on trunks in 37.5% (3/8) lesions (Table 1).

Data was analyzed using statistical package for social science (SPSS) software program for Mac, and independent sample t-test to assess the statistical significance of the results. There were no significance differences between the repigmentation achieved by both groups on lesions area (p=0.860) (Table 1). The mean and standard deviation for duration of vitiligo in group A were 10.8 ± 8.64 (range of 3 – 24 months), whereas in group B were 14.8 ± 9.34 (range of 2 – 24 months) (Table 2). The cumulative doses of narrowband ultraviolet B phototherapy given in group A ranged 450-1600 mJ/cm², with mean of 850 mJ/cm². In group B, the cumulative doses ranged 450-1200 mJ/cm², with mean 800 mJ/cm². There was no significance difference between both groups based on statistical analysis with independent sample t-test (p=0.840) (Table 2). In the assessment, comparison for melanin index of each lesions by Mexameter® also showed no significance differences between both groups (p=0.628) (Table 2).

**Figure 1.** Group A (a) Vitiligo with twice a week narrowband ultraviolet B phototherapy (b) Good response

**Figure 2.** Group B (a) Vitiligo with once a week narrowband ultraviolet B phototherapy (b) Good response
Table 1. Comparison of re-pigmentation achieved in the group A (twice a week) and group B (once a week) by VASI

<table>
<thead>
<tr>
<th>Site of Lesion</th>
<th>Good response (≥25% re-pigmentation)</th>
<th>Moderate response (10-24% re-pigmentation)</th>
<th>Poor response (&lt;10% re-pigmentation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (twice a week)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face and neck</td>
<td>-</td>
<td>4/4(100%)</td>
<td>-</td>
</tr>
<tr>
<td>Trunk</td>
<td>-</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Extremities</td>
<td>2/10 (20%)</td>
<td>3/10 (30%)</td>
<td>5/10 (50%)</td>
</tr>
<tr>
<td>Total</td>
<td>2/14 (14.29%)</td>
<td>7/14 (50%)</td>
<td>5/14 (35.71%)</td>
</tr>
<tr>
<td>Group B (once a week)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face and neck</td>
<td>-</td>
<td>5/8 (62.5%)</td>
<td>3/8 (37.5%)</td>
</tr>
<tr>
<td>Trunk</td>
<td>3/8 (37.5%)</td>
<td>5/8 (62.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Extremities</td>
<td>-</td>
<td>3/7 (42.86%)</td>
<td>4/7 (57.14%)</td>
</tr>
<tr>
<td>Total</td>
<td>3/23 (13.04%)</td>
<td>13/23 (56.5%)</td>
<td>7/23 (30.43%)</td>
</tr>
<tr>
<td>Total</td>
<td>5/37 (13.51%)</td>
<td>20/37 (54.1%)</td>
<td>12/37 (32.43%)</td>
</tr>
</tbody>
</table>

p=0.860, independent sample t-test

Table 2. Comparison of other variables between group A and group B

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of vitiligo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A (twice a week)</td>
<td>14</td>
<td>10.8</td>
<td>8.643</td>
<td>0.502</td>
</tr>
<tr>
<td>Group B (once a week)</td>
<td>23</td>
<td>14.8</td>
<td>9.338</td>
<td></td>
</tr>
<tr>
<td>Cumulative dose of narrowband UVB phototherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A (twice a week)</td>
<td>14</td>
<td>850</td>
<td>438.748</td>
<td>0.840</td>
</tr>
<tr>
<td>Group B (once a week)</td>
<td>23</td>
<td>800</td>
<td>310.242</td>
<td></td>
</tr>
<tr>
<td>Melanin index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A (twice a week)</td>
<td>14</td>
<td>-0.13</td>
<td>0.447</td>
<td>0.628</td>
</tr>
<tr>
<td>Group B (once a week)</td>
<td>23</td>
<td>-0.0674</td>
<td>0.223</td>
<td></td>
</tr>
</tbody>
</table>

p value was calculated using independent sample t-test.
SD: standard deviation

Discussion

There are many clinical studies showing the efficacy of targeted phototherapy, including targeted ultraviolet B phototherapy for vitiligo. In addition, a number of topical treatment options have been shown to have synergistic effect with phototherapy. Several clinical studies have demonstrated that the efficacy of targeted phototherapy, including targeted ultraviolet B, is site dependent in vitiligo lesions, it was stated that the area of vitiligo lesions on face and neck responded better than other body sites, and extremities lesions responded the least against phototherapy.

In most clinical studies of targeted phototherapy, treatment schedule of twice a week was most commonly conducted with excimer laser, broadband ultraviolet B or narrowband ultraviolet B. There were only few clinical studies which compared different treatment schedules using targeted phototherapy devices for vitiligo. Hofer et al. (2005) compared the efficacy of targeted phototherapy with excimer laser for vitiligo with different schedule regimens. They found almost similar results in once a week, twice a week, and thrice a week phototherapy. It was mentioned that the re-pigmentation started earlier in group of patients who were treated with twice a week and three times a week excimer laser treatment, compared to once a week group. The result of re-pigmentation extent was achieved almost similarly in all groups. This study concluded that the re-pigmentation achieved depended entirely on the total number of treatments, not treatment frequency.

Another study by Shen et al. in China reported observations with 4 different treatment schedules with laser. The patients in this study were treated with excimer laser for vitiligo lesions on the face and neck. The final re-pigmentation was achieved almost similarly in all groups which were treated for once, twice, and thrice a week; whereas the group who was treated with one exposure every two
weeks could not achieve the same level of re-pigmentation. The re-pigmentation occurred more rapidly in the group who was treated with two and three exposure every week. However, the final re-pigmentation was achieved in two latter groups similarly with the group who was treated with once a week exposure.\textsuperscript{20}

There was one clinical study reported to have successful result by using targeted ultraviolet B device, which was conducted once every two weeks. This study reported >75\% re-pigmentation in 69.5\% of 734 patients treated for 12 months. There were 112 patients (15.3\%) who achieved complete re-pigmentation in 734 vitiligo patients. The device used in this study was Bioskin\textsuperscript{®} which was narrowband ultraviolet B with emission spectrum of 300 – 320 nm and peak of 311 nm.\textsuperscript{16}

The other research by Majid et al. in India compared targeted narrowband ultraviolet B phototherapy in vitiligo with once-weekly and twice-weekly treatment regimens. The study concluded that there was no significance difference between the two regimens.\textsuperscript{4} The underlying research conducted similar research in Indonesia.

Targeted phototherapy is considered as a therapy for vitiligo patients. The most important factor which affects the choice for this therapy is the ability of the patients to comply with the treatment schedule. If given choices, most patients will prefer an option that interferes the least of their daily activities. Visiting phototherapy clinic twice a week is a difficult choice for most patients. This is the primary reason for the limited use of targeted phototherapy in vitiligo, therefore most patients are not able to get the benefit from this therapeutic modality.\textsuperscript{4}

In this study, we treated vitiligo lesions on face and neck, trunk, and extremities. Good response of re-pigmentation was achieved in 13.51\% of all treated vitiligo lesions. Lesions on face and neck, also trunk showed more moderate response, while lesions on extremities showed the lowest response to the therapy. The comparison of re-pigmentation achieved by both groups showed no statistical significance differences.

Assessment of melanin index measured by Mexameter\textsuperscript{®} also showed no significance difference between both groups. The cumulative doses of narrowband ultraviolet B phototherapy did not differ in both groups, which there was also no statistical significance difference. This means that patients do not require higher cumulative doses when the frequency of narrowband ultraviolet B phototherapy is once a week. It also provides indirect evidence that the efficacy of phototherapy remains the same in either once a week or twice a week schedule.

**Conclusion**

From this study and supported by previous studies, we conclude that compliance of the vitiligo patient to the treatment, particularly phototherapy, can be greatly improved if once a week treatment schedule becomes an option for phototherapy treatment schedule.

The results of this study indicate that the therapy’s success is not subsided by once a week treatment schedule for phototherapy. If the selection treatment schedule of once a week is offered to vitiligo patients, it is likely that more vitiligo patients will be willing to choose that optional schedule because their daily life will be less interfered. Therefore, it is expected to be able to improve the compliance of vitiligo patients, furthermore their phototherapy treatment will be more likely to be completed.

**References**