A Randomized Double Blind Clinical Trial on a Sabgh Formulation for Patients With Vitiligo

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Abstract

Background. The cosmetic problem that vitiligo produces affects patients psychologically. Many patients with vitiligo are suggested to cover their white skin patches with cosmetic products. There are formulations in traditional Iranian pharmacy to color these white skin patches. In this study, one of these formulations was compared with a cosmetic formulation. Methods. Two groups of patients were selected. One group used a marketed formulation and other group used a traditional Iranian Pharmacy formulation. The quality of life of the patients was compared based on the Dermatology Life Quality Index Questionnaire. Results. Both interventions were associated with statistically improved Dermatology Life Quality Index scores over the 8-week intervention (P < .05), although the difference between the 2 was not statistically significant (P = .436). Conclusion. Traditional Iranian Pharmacy formulation is effective in increasing the quality of life in vitiligo patients.

Keywords

traditional medicine, vitiligo, cosmetics

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Introduction

Vitiligo is an acquired skin depigmentation disorder, which is often progressive. It occurs due to the loss of epidermal melanocytes.¹ The incidence of vitiligo varies from 0.1% to 2% of the population worldwide.² Vitiligo presents itself by forming white macules skin patches as its notable symptom.³ The etiology of vitiligo is unknown; however, research suggests few possibilities such as autoimmune, genetic, neural, growth factor deficiency, and viral factors as the probable causes.⁴

So far the suggested treatments for vitiligo remain ineffective. One of the methods of treatment is topical application of steroids or calcineurin inhibitors. These treatments are proven to be partially successful but they show various side effects. Another approach is phototherapy, or in some cases photochemotherapy. Phototherapy and photochemotherapy are often used for treating symmetrical types of vitiligo. In selected cases, depigmenting treatments and possibly surgical approaches may be considered.⁵

Vitiligo is not life threatening or contagious but the cosmetic problem affects the well-being of a patient psychologically.⁶ Vitiligo is more disfiguring in darker skin tones.¹ Therefore, the initial approach to a patient who is diagnosed with vitiligo is psychological support and symptom treatments such as the use of camouflage cosmetics and sunscreens. In some of the cases, after consulting and discussion, the option of no treatment is chosen.⁵ Research has proven that covering skin patches with cosmetic camouflage can improve the quality of life in patients suffering from vitiligo.⁷

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In traditional Iranian medicine, there are 2 medical terms whose descriptions match vitiligo, namely white Bahaq and white Baras. Ibn sina, like other traditional Iranian medicine scholars describes white Bahaq as superficial, soft, glistening white spots on the surface of the skin. He states that these white spots do not penetrate below the surface of the skin or are only very slightly dispersed below the superficial skin layer. Ibn sina explains that despite the white spots the skin is healthy in all other aspects. He describes white Baras as superficial shining white, skin spots that are smooth. He says that unlike white Bahaq the color of hair arising from white spots in patients suffering from Baras are always white. In one of the Qarabadin books of traditional Iranian pharmacy, the writer mentions that if white Baras is chronic it is not curable therefore it is necessary for the patient to color the white spots. For this purpose, there were formulations introduced and designed by the traditional Iranian medicine physicians and pharmacists. These formulations were called Sabigh, which were defined as formulations to color the skin and cover scars and pigmentation problems. One of the ways to evaluate the quality of life of vitiligo patients is the use of Dermatology Life Quality Index questionnaire, which was designed at Cardiff University. This questionnaire is designed to be used in patients older than 16 years. Dermatology Life Quality Index questionnaire is self-explanatory and can simply be handed to the patient with no need for any further explanation.

In this study, one of the most popular Sabigh formulations was prepared based on traditional medical text books. Two groups of patients were selected. One group was provided with the marketed camouflage cosmetic formulation. The other group was provided with the prepared Sabigh formulation. The quality of life of the patients in 2 groups was compared based on the Dermatology Life Quality Index questionnaire.

Materials, Methods, and Patients
Choosing the Formulation
The 4 terms “white Baras,” “white Bahaq,” “Sabgh,” and “Sabgh” were searched in 11 of the most famous traditional Iranian pharmacy textbooks. The books that were searched for this research were written by Iranian scholars from 5th to 19th century. All the ingredients of these formulations were categorized and identified. One semisolid formulation out of 33 listed formulations was selected and prepared in Shiraz Faculty of Pharmacy. The selection was based on the availability and safety of ingredients and number of times the formulation was repeated in the reference books. The most frequent formulation was chosen for this study.

Studied Sabgh Formulation
The formulation we studied contained 7 ingredients. Three of these were herbal, namely Commiphora myrrha (Nees) Engl (family: Burseraceae), Rubia tinctorum L (family: Rubiaceae), vinegar, and 4 mineral components, which were alum, potassium nitrate, Armenian bole, and khobs al-hadid. The formulation as a semisolid dosage form was prepared based on traditional knowledge and its standardization was performed by modern techniques and methods. A hue was prepared using the colorful ingredients of our formulation, which are madder root, khobs al-Hadid, and Armenian bole. Alum was used as a mordant and potassium nitrate as preservative. The solvent that was used to prepare the hue was vinegar. The hue was then added to the powdered myrrh gum and triturated to obtain a homogeneous paste. The myrrh gum was standardized according to its essential oil by gas chromatography. The pharmaceutical aspects of the traditional Iranian medicine formulation were also evaluated before clinical trial.

Cosmetic Camouflage
We compared the prepared Sabgh formulation with a marketed camouflage cosmetic formulation on the basis of Dermatology Life Quality Index scores for quality of life of the patients. The product that was used in this research is a color cosmetic called Exuviance. Its active ingredient is titanium dioxide, the amount of which varies by shade. The shade that we used was 8729.

Packaging the Cosmetic Camouflages for 2 Groups
The prepared Sabgh formulation and Exuviance formulation were placed in opaque and sealed packages with same appearance and labeled by numbers in both groups. Same numbers were placed on Dermatology Life Quality Index forms.

Statistical Methods
For this study 14 patients needed to be enrolled to have a power of 90% for a 2-sided test with a type I error rate of 0.05 to detect a 6.4 difference in the change in Dermatology Life Quality Index score between the 2 groups. To calculate the number of patients, the following formula was applied:

\[ n = \left( \frac{Z_{1-\alpha/2} + Z_{1-\beta}}{\sigma_1^2 + \sigma_2^2} \right)^2 \times \frac{\left( \mu_1 - \mu_2 \right)^2}{(\alpha_1 - \beta_2)} \]

where \( \alpha = 0.05 \) type I error, \( \beta = 0.1 \) power 90%, \( \sigma_1 = 6.57, \sigma_2 = 3.6, \mu_1 = 9.9, \mu_2 = 3.49, n = 14, \) and \( d = 6.4 \).

For this study, \( t \) test and paired \( t \) test were performed to compare quantitative variables (age, duration of the disease, Dermatology Life Quality Index scores) between and within groups respectively. Fischer’s exact test was used to compare sex of the patients.

Clinical Trial
This study was performed from April to September 2012 in Shiraz University of Medical Sciences. It was an 8-week, randomized, double-blind study conducted on patients with vitiligo. The patients were randomized into 2 groups (Sabgh group= 18 and Exuviance group = 16). Randomization was performed through blocked randomization by the use of the table of random numbers. One group received a marketed formulation (Exuviance cover cosmetic formulation) and the other group received traditional Iranian medicine Sabgh formulation. Thirty patients completed the study (patients who received Sabgh formulation = 15 and patients who used Exuviance formulation = 15). Four patients were lost to follow-up as they did not attend in the follow-up session (lost to follow-up in Sabgh population = 3 and lost to follow-up in Exuviance population = 1; Figure 1). A nurse was asked to hand out the formulations and forms to the patients not being aware of the nature of the formulations. The patients were not also aware of the nature of formulation handed to them. Eligible patients were those who were older than 16 years and had vitiligo depigmented areas on their hands. The patients had received vitiligo
treatments but at the time of study were not under any medication or treatments for vitiligo, and there were both male and female patients. Exclusion criteria were pregnancy, age less than 16 years, chronic skin diseases, and current vitiligo treatments at the time of study. Patients signed written informed consent prior to application of the formulations. They were asked to fill in the Dermatology Life Quality Index questionnaire. It contains 10 questions. The questions are categorized into 6 headings: The first 2 questions concern symptoms and feelings, questions 3 and 4 are about daily activities, questions 5 and 6 are regarding leisure, and questions 8 and 9 are about personal relationships. Each item has a maximum score of 6. Question 7 asks about work and school and question 10 is about treatment, and each of these questions has a maximum score of 3. Quality of life is calculated from this questionnaire by summing the score of each question. This would result in a maximum number of 30 and a minimum of 0. The higher is the score, the more impaired is the quality of life. This questionnaire has been translated to many languages, including Farsi. The reliability and validity of this questionnaire in an Iranian population with vitiligo has been confirmed in the Dermatology Department of Shiraz University of Medical Sciences. Reliability of the Farsi version of Dermatology Life Quality Index questionnaire was obtained in that study by Cronbach’s α coefficient (α = .77). The scaling success rate of 100% was obtained for convergent validity of each scale. Factor analysis was also performed by Aghaei et al. to determine that the Persian version of Dermatology Life Quality Index is a 2-dimensional measure, which includes social and psychological parameters. Permission to use this questionnaire was obtained from Cardiff University before this study. For this research, the Farsi version of Dermatology Life Quality Index was used. Patients were asked to fill in the Dermatology Life Quality Index questionnaire prior to the use of the cosmetic camouflage on their hands and 8 weeks after topical application of the formulation. Patients in each group were asked to apply the formulation in each group twice daily. After 8 weeks they were followed and asked to fill in the Dermatology Life Quality Index questionnaire again. In both groups the score was compared before and after the application of the formulations. The data were collected from the questionnaires and patients’ quality of life was obtained and compared based on statistical analysis of t test and paired t test. The trial was registered in the Iranian Registry of Clinical Trials (No. IRCT201205029618N1). Approval for this study was obtained from the Ethics Committee of the Shiraz University of Medical Sciences. The code number issued for this clinical trial by the committee of ethics is CT-90-5958. The Dermatology Life Quality Index scores were calculated before and after the use of the formulations. The data were analyzed by SPSS statistical software. The numerical variables are described by mean and standard deviation.
**Table 1.** Demographic variables (sex, age and duration of the disease) between the two randomized vitiligo patient groups who received Sabgh (Sabgh group) and Exuviance formulation (Exuviance group).

<table>
<thead>
<tr>
<th>Quantitative Variables</th>
<th>Sabgh Group</th>
<th>Exuviance Group</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, Count (% within group)</td>
<td>Female</td>
<td>12.00 (80.00)</td>
<td>13.00 (86.70)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>3.00 (20.00)</td>
<td>2.00 (13.30)</td>
</tr>
<tr>
<td>Age, years</td>
<td>Mean</td>
<td>38.93</td>
<td>41.06</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>12.97</td>
<td>11.82</td>
</tr>
<tr>
<td>Duration of the disease, years</td>
<td>Mean</td>
<td>10.20</td>
<td>9.70</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>10.55</td>
<td>5.71</td>
</tr>
</tbody>
</table>

Fisher’s exact test.

**Table 2.** DLQI statistics and differences between two randomized vitiligo patient groups before and after the use of Sabgh (Sabgh group) or Exuviance formulation (Exuviance group).

<table>
<thead>
<tr>
<th>Dermatology Life Quality Index Scores</th>
<th>Sabgh Group, Mean (SD)</th>
<th>Exuviance Group, Mean (SD)</th>
<th>t</th>
<th>df</th>
<th>t Test</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before use of formulation</td>
<td>12.93 (5.68)</td>
<td>12.80 (7.22)</td>
<td>0.06</td>
<td>28</td>
<td>.95</td>
<td></td>
</tr>
<tr>
<td>After use of formulation</td>
<td>9.60 (4.32)</td>
<td>10.26 (6.18)</td>
<td>-0.34</td>
<td>25.05</td>
<td>.73</td>
<td></td>
</tr>
<tr>
<td>t</td>
<td>5.29</td>
<td>3.19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>df</td>
<td>14</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paired t test P value</td>
<td>&lt;.001</td>
<td>.006</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference in scores before and after the use of formulations</td>
<td>3.33 (2.43)</td>
<td>2.53 (3.06)</td>
<td>.79</td>
<td>28</td>
<td>.43</td>
<td></td>
</tr>
</tbody>
</table>

Results

The range of age in the Sabgh population was 17 to 60 years and in Exuviance population 26 to 60 years. Normality of demographic variables (age, sex, and duration of the disease) between the 2 groups who received Sabgh and Exuviance formulation was confirmed by Kolmogorov–Smirnov test (Table 1). The mean Dermatology Life Quality Index score of the 2 studied populations before the use of camouflage formulations were 12.93 in the group who received Sabgh formulation and 12.80 in the patients who received Exuviance cover cosmetic. After 8 weeks of using the cover cosmetics twice daily in the 2 groups, the Dermatology Life Quality Index scores were 9.60 and 10.26. The differences in the Dermatology Life Quality Index scores in the 2 groups were compared before and after the use of the camouflage. The difference in the mean Dermatology Life Quality Index scores of the 2 groups was compared. There was no significant difference between the 2 groups. The results are summarized in Table 2.

Discussion

There are patients who have been disappointed with vitiligo treatments, in which case camouflage can be recommended to hide their white skin patches. Research has shown that use of camouflage cosmetics can reduce the Dermatology Life Quality Index scores in patients, which means it can improve their quality of life. The higher Dermatology Life Quality Index scores show that the quality of life of patients are more impaired. There are topical colored formulations mentioned in traditional Iranian medicine to cover white skin patches in vitiligo patients. The oldest lists of pharmaceutical registries that are available today were created by Iranian and Muslim scholars. This category of books is called Qarabadin books, which contain medical formulations. These formulations have been used since ancient times. Despite their popular use by the patients, these remedies were once called out-of the-way formulations in the 19th century since at the time there were no analytical techniques for their standardization. Today with our modern armamentarium, standardization of these formulations is possible. We prepared a formulation based on traditional Iranian knowledge at the Shiraz Faculty of Pharmacy and compared its effect on quality of life in vitiligo patients. The mean Dermatology Life Quality Index score in the population of this study is higher compared with the study performed by Dolatshahi et al. (8.16); Finlay and Khan (7.2), and Kent and al-Abadie (4.82). Generally, the reported Dermatology Life Quality Index in dermatological studies ranges from 4.8 to 15. After 8 weeks of application of the formulation, the mean Dermatology Life Quality Index score was reduced to 9.60 in Sabgh population and to 10.26 in the patient group that received Exuviance formulation. There have been studies performed on the positive psychosocial effect of camouflage cosmetics for vitiligo patients. In our study, we compared Dermatology Life Quality Index scores in 2 groups—one group received the formulation that we prepared with Iranian
ingredients and based on traditional Iranian science and the second group received a marketed formulation. The mean Dermatology Life Quality Index score showed a significant difference in both groups before and after application of study interventions. This means that the use of cosmetic would improve the quality of life in patients with vitiligo. The difference in the mean Dermatology Life Quality Index scores of the 2 groups in our study was not statistically different when the 2 groups were compared with each other. This can indicate that both formulations were equally effective. However, the reduction in DLQI score was more in case of the Sabgh group.

Conclusion
This study indicates that the use of camouflage cosmetic improve the quality of life in patients with vitiligo as both interventions were associated with improved quality of life. We can conclude that the traditional Sabgh formulation, which is based on traditional Iranian medicine knowledge is also effective in increasing the quality of life in patients with vitiligo when compared with the marketed and prescribed formulation.

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Author Contributions
AH wrote the draft, contributed in gathering the data, and wrote the final version of the article. HM rewrote the draft also supervised and contributed in preparation of the formulation. MS contributed in the process of data gathering and clinical trial. AM contributed toward the guidance, revision, and correction of the draft and final article. HS rewrote the first version of the paper and contributed in data gathering and writing the final version of the article. HA-J contributed toward the guidance of the process of the clinical trial.

Declaracion of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval
This clinical trial was approved by the Committee of Ethics of Shiraz University of Medical Sciences.

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