Painting a More Colorful Picture: A Review of Recently Proposed Vitiligo Treatments

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Abstract

Vitiligo is a depigmentation disorder of the skin with profound physical and psychological effects. Several techniques have been developed over the years to treat this disorder, including combinations of topical treatments, oral medications, light therapies, and laser treatments. The current mainstay for treatment is narrow-band ultra-violet B (NB-UVB), topical calcineurin inhibitors, and topical corticosteroids. Still, many patients today continue to suffer from the effects of this disorder. This paper aims to present new, promising treatments for vitiligo that has been presented in the literature of late.

Keywords: Vitiligo; Topical treatments; Narrow-Band Ultra-Violet B (NB-UVB); Laser treatments

Introduction

Vitiligo is a hypomelanotic disorder of the skin that results from loss of functional melanocytes in the skin [1]. The disorder affects people of all ages, races, and sexes, with a prevalence of 1-2%, and half of people with vitiligo have disease onset before the age of 20 years [1]. Vitiligo can lead to stress and embarrassment, particularly in darker-skinned individuals where the loss of pigment leads to a stark contrast in color [2,3]. To date, there is no universally accepted safe and efficacious treatment for vitiligo. Relapse is very common and complete repigmentation is rare [4].

The main histopathological finding in vitiligo is the total absence of functioning melanocytes in the lesions. The main inflammatory cells most commonly found on the edges of these lesions are CD4+ and CD8+ T lymphocytes [5]. Based on this principle, commonly used treatment strategies have focused on control of the autoimmune damage as well as stimulation of melanocyte migration from the unaffected edges of the lesions to the affected skin [5]. Currently, treatment for vitiligo can be categorized into three basic groups: pharmacological (both topical and systemic) treatment, physical treatment, and surgical treatment [5]. Examples include topical and systemic corticosteroids, topical calcineurin inhibitors, NVUUB therapy, phototherapy with UVA and psoralens (PUVA), and surgical transplantation of melanocytes [5]. Again, it is well known that all of these treatments have major setbacks and that complete repigmentation is uncommon.

Recently, the literature has suggested various novel treatments for vitiligo. This paper will aim to present several new treatments proposed in the literature over the past year.

Discussion

Intralesional corticosteroids

Topical steroids are frequently used in the treatment of vitiligo. Literature has shown varying levels of efficacy with topical steroids and high rates of relapse upon tapering the topical steroids [6]. Topical steroids also carry the risk of atrophy, telangiectasias, and striae, as well as systemic side effects, and are therefore best used in localized areas [6]. Interestingly, a meta-analysis in 1998 showed that class 3 topical steroids were most effective in treating localized vitiligo compared to class 4 topical steroids, while patients using class 4 drugs also demonstrated higher rates of atrophy [5,7]. This difference in efficacy may suggest that achieving a particular milieu for normal cell function is the ultimate goal.

A treatment modality not yet commonly used for vitiligo is intralesional corticosteroid injections [8]. For the first time in 30 years, new literature shows that intralesional corticosteroid injections are a safe and very effective treatment for vitiligo [8-11]. Wang et al. followed nine adult females with vitiligo from 2009 to 2013 and treated them with intralesional triamcinolone injections to vitiligo patches every four to six weeks [8]. Of these patients, six were treatment-resistant and three were treatment-naïve. Those who were being treated with inadequate NBUUVB and/or topical corticosteroids had the medications continued. Remarkably, all nine patients responded to the intralesional corticosteroid injections with 80-90% repigmentation. The average duration of treatment was four months, with the longest duration being only seven months [8]. The article demonstrates that some patients repigmented up to 75% from just one treatment. Average start time to repigmentation was one month, and the earliest repigmentation was seen at three weeks [8]. The untreated vitiliginous patches did not show any repigmentation. This study was also remarkable in that most patients maintained their pigmentation for years after cessation of injections. Furthermore, in the patients that did lose pigment, no more than 15% depigmentation was seen [8]. At this point, one may ask about the side effects of the injections. Astoundingly, complications in this study were minimal, with skin atrophy seen in only one patient. Two of the women showed menstrual irregularities, but resumed normal cycles after cessation of treatment [8]. This study demonstrates that more research must be conducted on a larger scale to see if intralesional corticosteroid injections should be used more often in the treatment of vitiligo.

A famelanotide and narrowband UVB phototherapy

A recent study by Lim et al. proposed utilizing the body’s cutaneous melanocortin system to help treat vitiligo. This system contains α-melanocyste-stimulating hormone (α-MSH), an important protein that stimulates melanogenesis and melanocyte proliferation [12]. Lim et al. used afamelanotide, a potent synthetic analogue of α-MSH in a controlled-release formulation, in combination with NBUBV

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Received: October 20, 2014; Accepted: October 22, 2014; Published: October 27, 2014


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These results suggest that EGCG may have protective effects against vitiligo, and that it could contribute to suppression of activation of CD8+ T cells and inflammatory mediators [14].

Based on these results, Zhu et al. conducted further studies on these mice by investigating the gene-expression profile of this model in relation to EGCG [14]. Using whole genome oligo-microarray assay, 1264 down-regulated genes and 1332 up-regulated genes were recorded in the EGCG group compared with the model group, and selected genes were validated by real-time polymerase chain reaction [14]. Remarkably, the genetic study demonstrated that EGCG administration was significantly associated with a decreased risk of vitiligo [14]. Therefore, based on these results, EGCG could be considered a new preventive agent against vitiligo in the clinical setting [14]. This model demonstrates the need for further research into antioxidants and their effects on vitiligo, especially given their qualities of benign nature, easy accessibility, easy administration, and cost-efficiency.

**T-regulatory cells and control of vitiligo**

As discussed earlier, immunology likely plays a role in the pathogenesis of vitiligo. Dwivedi et al. recently published an excellent review of the various immunotherapies currently being studied for treatment of vitiligo [17]. Dependent on the fact that regulatory T-cells (Tregs) are critical to the development of self-tolerance, they can be considered a major focus in studying the autoimmune pathogenesis of vitiligo [17]. In this review, Dwivedi discusses the autoimmune pathogenesis of vitiligo, and goes on to discuss current therapeutic options being studied based on these principles. An interesting animal study in particular was performed by Catterjee et al. using transgenic mice. The mice carry T-cells with human leukocyte antigen (HLA)-A2-restricted human tyrosinase peptide-reactive T-cell receptor and develop vitiligo from an early age [17,18]. Tregs were adoptively transferred into these mice and were found to induce a lasting remission of vitiligo when transferred at the onset of the disease, and also when transferred during established disease [18]. The study showed that reduced regulatory responses were critical to the development of vitiligo in disease-prone mice, and suggested that an increase in the Treg cell population might benefit vitiligo patients with active disease [18]. This was the first animal study of its kind [17,18]. These fascinating results, as well as other studies reviewed by Dwivedi et al., call for further study of Tregs and their role in the therapeutics of vitiligo.

**Conclusions**

Though vitiligo still remains a difficult disease to treat, recent progress in its research has presented a rainbow of various therapeutic options for the future. With continued focus on immunology, genetics, and melanogenesis, perhaps scientific advances will bring more hope and improved quality of life to vitiligo patients going forward.

**References**