Medical and Maintenance Treatments for Vitiligo

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KEYWORDS

• Vitiligo • Medical treatments • Topical steroids • Calcineurin inhibitors • Sytemic steroids • Methotrexate

KEY POINTS

- Medical treatments alone, or in combination with phototherapy, are key approaches for treating nonsegmental vitiligo and, to a lesser extent, for treating segmental vitiligo.
- The treatments can be useful for halting disease progression and have proved effective for inducing repigmentation and decreasing the risk of relapses.
- Although the treatments have some side effects and limitations, vitiligo often induces a marked decrease in the quality of life of affected individuals and in most cases the risk:benefit ratio is in favor of an active approach.
- Systemic and topical agents targeting the pathways involved in the loss of melanocytes and in the differentiation of melanocyte stem cells should provide even more effective approaches in the near future, thanks to the increased knowledge of the pathophysiology of vitiligo.

INTRODUCTION

There are 3 aims needed for the optimal care of vitiligo patients: first, halting the disease progression; then, allowing complete repigmentation of lesional areas; and, finally, preventing relapses. There is still no therapeutic panacea for vitiligo but current options can lead to significant improvement of vitiligo lesions. Some areas, such as the face, usually respond well to therapies whereas they remain mostly ineffective for others, such as hands and feet. Recent advances in the understanding of the pathophysiology of vitiligo foster new therapeutic opportunities. One of the most promising is the demonstration of the key role of the interferon gamma (INF-γ)/Janus kinase (JAK)/CXCL10 pathway in the depigmentation process of vitiligo.[1] Targeting this pathway might provide effective therapeutic approaches, as suggested by recent cases reports (discussed later).[2,3] The immune reaction is absent of complete depigmented lesions, however, and repigmentation may be difficult in lesions of some patients while their vitiligo remains inactive for years. Recent transcriptomic analysis showed an impaired Wnt signaling pathway in vitiligo lesions preventing the differentiation of melanocyte stem cells.[4] Fibroblasts of some areas, such as hands and feet, produce Wnt inhibitors.[5] This might contribute to a defect in melanocyte differentiation and could explain the difficulties for repigmenting those localizations. So far the best way to stimulate the differentiation of melanocytes is ultraviolet (UV) radiation. Recent data have shown that the action of UV on melanocyte stem cells is mediated by Wnt proteins.[6] Thus, stimulating the Wnt pathway by using topical agents might allow repigmenting even difficult-to-treat areas. Although phototherapy and surgery remain useful approaches for vitiligo, systemic or topical medical therapies are important alone or combined for optimal treatment of most vitiligo cases

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and, in light of recent pathophysiologic advances, they offer encouraging options for the near future.

HALTING DISEASE PROGRESSION

The course of vitiligo is unpredictable. An active phase, however, can be clinically detected. Medical history of the vitiligo, reporting a rapid onset and ongoing extension of depigmented lesions, is highly suggestive of active disease. Wood lamp examination is of great importance because it can show blurred and hypochromic borders of lesions that are associated with ongoing depigmenting process.[7] The presence of a confetti sign was recently reported to be also associated with a marked spreading of vitiligo lesions within the following months.[8] Several medical approaches have been proposed for halting or decreasing the progression of active vitiligo.

Systemic Steroids

Systemic corticosteroids (high-dose pulsed therapy, minipulsed regimen, or daily oral low dose) have been reported to rapidly arrest spreading vitiligo and to induce repigmentation.[9] Low-dose oral prednisolone (0.3 mg/kg) taken daily for 2 months[10] and a high dose of intravenous methylprednisolone (8 mg/kg) administered on 3 consecutive days[11] were evaluated in open-label clinical studies. Both regimens were reported to halt disease progression in more than 85% of cases and to induce some repigmentation in more than 70% of cases. Most studies have evaluated oral minipulse (OMP) betamethasone or dexamethasone using 5 mg twice a week on 2 consecutive days usually for 3 months[12] to 6 months.[13] The progression of disease was stopped in more than 85% of cases but a marked repigmentation was observed in less than 7% of cases. Side effects included weight gain, insomnia, acne, agitation, menstrual disturbance, and hypertrichosis. The prevalence of side effects ranged from 12%[12] to 69%.[13] A large retrospective study confirmed these results, showing an arrest of disease activity in 91.8% of cases.[14] Adverse reactions, such as weight gain, lethargy, and acneiform eruptions, were observed in 9.2% of patients. Relapses after discontinuation of the treatment are not rare. In 138 children treated with OMP of methylprednisolone for 6 months, 34.8% had relapses over a period of 1 year. The rate of relapses was higher in children below 10 years of age (47.4%). Thus, systemic corticosteroids seem to halt disease progression in most cases. No prospective randomized trial against placebo, however, has been performed yet. Given the significant potential for side effects and the high rate of relapses, the use of such an approach remains controversial.

Methotrexate

The first case supporting the use of methotrexate in vitiligo was reported in a woman treated with 7.5 mg per week for rheumatoid arthritis. She had a 6-month history of rapidly progressing vitiligo. She stopped developing new lesions after 3 months of treatment.[15] More recently, the efficacy of methotrexate (10 mg per week) was compared with OMP dexamethasone (5 mg per week with 2.5 mg taken on 2 consecutive days) in a prospective randomized open-label study in 52 vitiligo patients.[16] After 6 months of treatment, 6 of 25 patients developed new lesions with methotrexate compared with 7 of 25 patients with OMP. Both groups had also a similar reduction in vitiligo disease activity score. The investigators concluded that both drugs are equally effective in controlling the disease activity of vitiligo. The data evaluating the use of methotrexate in vitiligo, however, remain limited.

Minocycline

Minocycline was proposed for treating vitiligo because of its anti-inflammatory, immunomodulatory, and free-radical scavenging properties. An initial open-label study reported an arrest in disease progression in 29 of 32 patients treated with 100 mg per day of minocycline.[17] The same group further reported a prospective randomized trial comparing OMP (5 mg per week) with minocycline (100 mg per day)[18]; 50 patients with active vitiligo were included. After 6 months of treatment, both groups showed a significant decrease in vitiligo disease activity score from 4.0 to 1.64 $\pm$ 0.86 (P<.001) and from 4.0 to 1.68 $\pm$ 0.69 (P<.001), for minocycline and OMP, respectively. The difference between the 2 groups was not statistically significant (P = .60). Minocycline (100 mg per day) was also compared with narrow-band (Nb)-UVB (twice weekly) in a prospective comparative trial performed in 42 patients with active vitiligo.[19] After 3 months of treatment, only 23.8% of patients still had active lesions with Nb-UVB compared with 66.1% with minocycline (P<.05). Patients in the Nb-UVB group also showed significantly higher repigmentation compared with those in minocycline group. Both studies lacked an untreated group to assess the evolution of vitiligo without treatment. These results need further evaluation, but Nb-UVB seems more important for halting disease progression and has the main advantage of also promoting more efficient repigmentation of vitiligo lesions.