THERAPEUTIC UPDATE

Therapeutic Update on Vitiligo

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Vitiligo is a common acquired skin disease of unknown etiology that results in depigmentation. It is clinically characterized by the development of white macules due to selective loss of melanocytes. Lesions typically develop in areas of friction, reflecting koebnerization. Depigmentation, while asymptomatic, may lead to diminished quality of life and severe psychological stress due to cosmetic concerns.[1] There is increasing evidence that vitiligo is an autoimmune disorder that shows a genetic predisposition in about 18% of cases.[2] It occurs in approximately 1% of the U.S. population with equal frequencies between men and women; half of all patients manifest the disease before 20 years of age.

The course of the disease is unpredictable – it may be localized, generalized, or universal. Treatment must be individualized, and a combination of several therapies is often more successful than monotherapy. It is often acknowledged that the diagnosis of vitiligo is quite easy; however, the successful treatment of the disease is quite difficult. There are many medical and surgical treatments aimed at repigmentation. No single therapy produces predictably good results in all patients.

Medical Treatments

Topical Steroids

Topical steroids are the most effective monotherapy and produce the best clinical outcomes when combined with light therapy. Commonly prescribed steroids are clobetasol, betamethasone, and fluocinonide. Head and neck lesions have the best response rate. Potential side effects are skin atrophy and systemic absorption leading to immunosuppression; consequently, topical steroids are typically used for short periods of time or alternated with other medications to decrease the incidence of side effects.

Calcineurin Inhibitors (tacrolimus = Protopic pimecrolimus = Elidel®)

These prescription immunomodulators suppress the immune system where applied, allowing melanocytes to return. They are most effective on the face and less so on the hands and feet. Topical calcineurin inhibitors provide similar to slightly inferior results compared to topical steroids. They have been shown to enhance the effect of laser or light therapy. Side effects may include stinging, burning or itching of treated skin. Both immunomodulators are used twice a day. In most cases, these topical agents have very little systemic absorption, so in a sense, they are safer than topical steroids. Nevertheless, there is a black box warning from the FDA concerning the extremely rare possibility of developing lymphoma.

Vitamin D Analogues

Calcipotriol, also known as calcipotriene, (Dovonex®) is a topical Vitamin D_3 analog with immunomodulatory effects that promote melanocyte development and melanogenesis. Compared to topical steroids, calcipotriol has lower repigmentation rates; however, it has been shown that when combined with steroids, repigmentation rates increase.[3] The onset and repigmentation occurs sooner, and there is a greater stability of repigmentation compared with either agent used alone.[3,4] Off-label use of the topical fixed-combination calcipotriene 0.005% and betamethasone 0.05% (Talconex®) once a day is a popular treatment. There are no serious side effects of using Vitamin D analogues topically; mild irritation, stinging or burning has occasionally been reported.[3,5]

Systemic Steroids

There are few large studies that have evaluated the safety and efficacy of systemic steroids, but in some cases, systemic steroids have been known to help halt disease progression and induce repigmentation. Combining oral or topical steroids with light therapy appears to enhance results. Long-term side effects of oral steroids limit prolonged treatment.

Vitamins

People with vitiligo are often deficient in folic acid, Vitamin B12, zinc and copper. Some studies have shown that a combination of folic acid, Vitamin B12 and sun exposure can help repigment the skin.[6] Topical and oral antioxidants may have a role

in protecting melanocytes from destruction by reactive oxygen species.[7] Vitamin E, Vitamin C, alpha-lipoic acid, ginkgo biloba, topical catalase, superoxide dismutase, and polypodium leucotomos have been used in vitiligo. There is good evidence to support use of oral antioxidants as an adjunct to narrow-band UVB phototherapy for enhanced efficacy.[7] Additional research is needed to define dosing parameters and side effect profiles of vitamin supplements.

Narrowband UVB (NB UVB)

Narrowband UVB (in the 311-312 nm wavelength range) is now considered the gold standard of treatment for vitiligo involving greater than 20% of the body's surface area. NB UVB is usually administered three times a week; some repigmentation is typically noted after 30-60 treatments. Conventional broadband UVB lamps emit a variety of wavelengths between 280-330 nm. However, wavelengths below 300 nm can cause intense erythema, severe burning and increased risk of skin cancer. NB UVB eliminates superfluous and dangerous UV exposure by emitting only wavelengths of 311-312 nm for optimum safety and efficacy.

PUVA

Psoralen plus UVA, known as PUVA, has mostly been surpassed by NB UVB, since the latter is safer and just as effective. The psoralen is typically taken orally, but can also be applied topically. PUVA is usually administered three times a week. Side effects include cataracts, burning, gastrointestinal disturbances and increase risk of skin cancer.

Laser Therapy

The nonablative xenon chloride monochromatic excimer laser emits a 308 nm wavelength, very similar to the 311 nm wavelength of NB UVB phototherapy. Localized areas of stable vitiligo (limited to less than 30% of the body surface) are treated two to three times a week for an average of 24-48 sessions. Potential side effects include burning, erythema and pruritis.[8] It usually takes 11-22 sessions to see repigmentation.[9,10] The face and neck respond better than the hands and feet with less total irradiation.[9-13] In contrast to conventional light therapy, higher Fitzpatrick skin types achieve better results.[9,12]

Camouflage

Temporary make-up, semi-permanent self-tanning agents containing dihydroxyacetone, or permanent micropigmentation (tattooing) can improve appearance and quality of life. Permanent micropigmentation is most useful for mucosal lesions and in patients with darker complexions. Potential side effects include koebnerization, imperfect color matching or allergic reactions to the tattoo pigment.[7]

Depigmentation Therapy

In selected patients when repigmentation therapy has failed or in those with widespread vitiligo (> 50% depigmentation or extensive depigmentation on the face or hands) depigmentation of "normal" skin should be considered. A 20%-40% cream of monobenzylether of hydroquinone is applied twice a day for 3-12 months to depigment the remaining normal skin. Burning or itching may occur; the results are usually permanent.[14] The cream has a systemic effect, so even areas where it has not been applied will still depigment. Patients treated in this way must be very careful about sun exposure due to increased risk of burning.

Surgical Treatments

Surgical treatments are best suited for cosmetically sensitive sites in patients with stable vitiligo and no koebner phenomenon.[7]

Punch Minigrafting

Tiny full-thickness skin grafts are transplanted into the depigmented area. Repigmentation occurs in four to six weeks; the main drawback is the cobblestone effect.

Suction Blister Grafting

Epidermal grafts can be obtained by creating blisters with vacuum suction that cleaves the epidermis from the dermis. These grafts are transferred to the recipient sites of vitiligo, which have been prepared by prior dermabrasion.

Thin Dermoepidermal Grafts (Split-thickness Skin Grafts)

Very thin dermoepidermal sheets are harvested with a dermatome and grafted on to denuded vitiligo recipient sites.

Non Cultured Epidermal Suspensions

After the epidermis is removed from the depigmented areas, an epidermal suspension containing melanocytes and keratinocytes (prepared by trypsinization of normally pigmented donor skin) is spread on to the denuded areas of vitiligo.[15]

Cultured Epidermis and Melanocytes

After denuding depigmented skin using a CO_2 laser, cryosurgery, or superficial dermabrasion, very think sheets of cultured epidermis are spread on to the denuded surface.[16] Expanding the autologous cells in tissue culture prior to grafting facilitates the treatment of larger areas.

Conclusion

There are numerous treatment options for vitiligo, but to date there is no cure. Further studies, combining new technology and existing medical and surgical modalities, are warranted to improve the safety and efficacy of treatment.

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