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Assessment of Role of Latanoprost in Management of Vitiligo: Review Article

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ABSTRACT
Background: One of the PGF2 α analogues, latanoprost solution is applied topically to the eye to lower intraocular pressure and treat glaucoma. Latanoprost has been examined for the treatment of cutaneous hypopigmentation since evidence of its periocular and pigmentation adverse effects emerged. It has been found to be useful, especially when combined with other medications. It has been reported that topical latanoprost is effective as a monotherapy for vitiligo.
Objective: This study aimed to **a**ssess the possible role of latanoprost in management of vitiligo.
Methods: We searched PubMed, Google Scholar, and Science Direct for information on vitiligo with latanoprost. However, only the most current or comprehensive study from November 2001 to May 2021 was considered. The authors also assessed references from pertinent literature. Documents in languages other than English have been disregarded since there aren't enough resources for translation. Unpublished manuscripts, oral presentations, conference abstracts, and dissertations were examples of papers that weren't considered to be serious scientific research.
Conclusion: According to some studies, using latanoprost in conjunction with other treatments for vitiligo is more beneficial than using latanoprost alone.
Keywords: Latanoprost, Management of vitiligo.

INTRODUCTION

Milky white macules and patches appear on the skin and mucous membranes of people with vitiligo, an inherited, progressive depigmenting illness that results from a significant loss of epidermal and, in some cases, hair follicle melanocytes [(1)]. Between half a percent and one percent of the population may have vitiligo [(2)].
The exact aetiology is not well understood, but it is known to be complex and include the interaction of several variables. Most notably, the autoimmune process has been thoroughly documented. Anyone of either gender can develop vitiligo at any time [(3)].

Generalized vitiligo:

Macules or patches of skin without pigmentation that appear at random locations all over the body and are usually bilateral and symmetrical. This condition typically manifests in parts of the body that are frequently subjected to stressors including rubbing, squeezing, and bruising. It can start at any age, from childhood to young adulthood [(4)].

In **acrofacial vitiligo,** macules with missing pigmentation that appear only on the hands, feet, and/or face. Depigmentation of the extremities, such as the fingers and the orifices of the face, is a defining characteristic. As time goes on, it could spread to other parts of the body, at which point it would be more accurately described as systemic or even global [(5)].

In **mucosal vitiligo,** normal mucosal surfaces, such as those in the mouth and genitalia, are frequently affected. It might be an isolated occurrence or part of a more widespread case of vitiligo. Unclassified mucosal vitiligo is characterized as persistent, isolated vitiligo that has been present for at least 2 years [(5)].

In **vitiligo universalis,** full or near-full depigmentation (80-90% of the body's surface). Typically, it begins with widespread vitiligo and advances to whole or nearly total skin and hair depigmentation [(5)].

Regarding **focal vitiligo,** a little, single, depigmented lesion that hasn't spread or changed much over the course of two years. Possible future states include SV and NSV [(5)].

In Mixed vitiligo, simultaneous presence of both SV and NSV. Wood lamp examination rules out nevus depigmentosus at birth and within the first year of life; (2) SV is followed by NSV with a delay of at least 6 months; (3) SV affects at least 20% of the dermatomal segment or presents a definite Blaschko linear distribution; (4) SV responds poorly to conventional narrow-band ultraviolet B (NB-UVB) treatment compared to NSV (good response). Patients with SV who present with leukotrichia or halo nevi at presentation are at increased risk of developing MV [(4)].

In Punctate vitiligo, macules that are between 1 and 1.5 millimeters in diameter and are completely depigmented at their borders. In the absence of conventional vitiligo macules, these spots should be called leukoderma punctata [(6)].

Hypochromic vitiligo or vitiligo minor, indicated by the appearance of hypopigmented macules across the trunk and scalp, as well as a seborrheic distribution of these lesions across the face and neck. It appears to affect only those with dark complexion [(7)].

Follicular vitiligo, manifests as leukotrichia without accompanying epidermal depigmentation [(8)].

Segmental vitiligo, fast onset and segmental distribution of depigmented macules are hallmarks of leukotrichia. The macule-like lesion is a clinical hallmark of NSV. A macule that is completely devoid of melanin and is white,

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non-scaly, and has clear borders [4]. Depigmented macules ranging from a few millimeters to several centimeters in diameter are the most prominent clinical feature of NSV. These lesions often appear on both sides of the body and have a symmetrical distribution pattern. Localized patches of grey or white hairs may appear if the scalp and other hair-bearing areas are affected [5].

Current therapy methods attempt to improve melanocyte shape and function by either increasing melanocyte proliferation or blocking inflammatory variables that affect melanocyte structure and function. There isn't yet a tried-and-true remedy that reliably helps while having few if any negative effects [2].

Prostaglandins are potent lipid hormones that regulate cellular development, differentiation, and death through a variety of routes. Hormones called prostaglandins (PGs) are produced by keratinocytes following UV exposure and can also be found in chronic inflammatory skin lesions [9].

UV light triggers melanogenesis by triggering the breakdown of membrane phospholipids via the COX enzyme's action on arachidonic acid. Melanogenesis may be activated by one or both of the phospholipase A2 (PLEA2) and cyclooxygenase-2 (COX-2) products, PGE2 and PGF2, which are themselves induced by UVR. Melanocytes have been shown to express a variety of receptors for these PGs, including PGE2 receptors (EP1, EP2, and EP3), PGF2 α receptors (FP), and others [10].

Latanoprost role in treatment of vitiligo:

One of the analogues of transforming growth factor beta (TGF), latanoprost solution is applied topically to the eye to treat ocular hypertension by lowering intraocular pressure, a symptom of glaucoma. Latanoprost has been explored for the treatment of cutaneous hypo-pigmentation since proof of its periocular and iridal pigmentation adverse effects arose (e.g: phototherapy) [11].

The role of PGs in melanogenesis and mechanism of action:

Stimulating or inhibiting proliferation, encouraging differentiation, and controlling apoptosis are just a few of the many impacts that PGs have on keratinocytes. The diversity of PGs receptors helps explain why the keratinocyte response to PGs is so complicated [11].

Stimulation of the FP receptors that mediate PGF2 α effects results in the activation of the turnover of phospholipase C-induced phosphoinositide, intracellular Ca^{2+} mobilization, activation of mitogen-protein kinase, and activation of protein kinase C [11].

PGF2, and to a lesser extent PGE2, have been demonstrated to be strong stimulators of dendricity in human melanocytes. Tyrosinase activity in human melanocytes was found to be stimulated by latanoprost, but it did not influence melanocyte proliferation [11]. Furthermore, it has been found that PGE2 and PGF2 do not elevate adenosine monophosphate in human melanocytes (cAMP). Even though the cAMP/protein kinase A (PKA) pathway has been shown to have the largest role in melanocyte dendrite formation, the mechanism used to induce dendritic formation via PGE2 and PGF2**α** is cAMP-independent [12].

Human platelets have been demonstrated to signal through phospholipase C (PLC) when exposed to EP1, EP3, and FP receptors. Thus, prostaglandin E2 and PGF2 can control melanocyte dendricity via the PLC-protein kinase C pathway [13]. In contrast, the melanocyte dendricity can be mediated by the second messenger system, which regulates cytoskeletal proteins and includes endothelin 1, a potent triggering factor for melanocyte dendricity via increased intracellular Ca^{2+}. Potentially, PLC-dependent processes are activated by the receptors EP1/EP3 and FP to increase melanocyte dendricity. This pathway is activated when PLC catalyses the conversion of the membrane lipid phosphoinsototide 4, 5-bisphosphate (PIP2) to the smaller lipids inositol 1, 4, 5-trisphosphate (IP3) and diacylglycerol (DAG). Due to PIP2's role as a binding site for proteins that bind and/or change actin, hydrolysis of PIP2 enables actin-binding proteins to be translocated from PIP2 and incorporated into the cytoskeleton in regions of active actin rearrangement, a process that is crucial for dendricity [11].

Post-translational activation of the enzyme, such as phosphorylation and N-linked glycosylation, can modify enzyme activity or stability by increasing enzyme expression at the mRNA level, or both [11].

One alternative probable reason for the observed upsurge in tyrosinase activity and expression after latanoprost is based on the tumor suppressor p53. UV-dependent p53 upregulation has been shown to boost tyrosinase production [14].

Repigmentation following vitiligo may be aided by all of the aforementioned methods. Latanoprost was also shown to increase PGE2 production, and as PGE2 is a melanogenic stimulant, it is likely that this compound plays a role in inducing repigmentation. Keratinocytes produce more tonofilaments and keratohyalin when exposed to prostaglandin E2, and the processing/presenting function of cutaneous Langerhans cells is inhibited [14].

The effectiveness of latanoprost, tacrolimus ointment, and both of these in combination with NBUVB and microneedling was compared in a trial of 24 individuals with vitiligo vulgaris. There were no reported adverse effects, and latanoprost appeared to stimulate pigment formation in the treated lesions more effectively than tacrolimus ointment, even if this did not show a statistically significant difference. The percentage of latanoprost-treated lesions with pigment production of 75% or more was substantially higher than that of control lesions at treatment's end [11].

It has been reported that topical latanoprost is effective as a monotherapy for vitiligo, **Anbar *et al.*** [14] conclusively demonstrated that the combination of NB-

UVB and 0.005% latanoprost solution produces a better outcome than either treatment alone.

The effectiveness of latanoprost in treating vitiligo has been shown to increase when used in conjunction with other therapies. Thirty patients with vitiligo were treated with a combination of the Fraxel Herbium laser, topical latanoprost solution, and focused UVA1 laser, and the outcomes were positive in terms of repigmentation rate and side effects. The patients were pleased with the protocol treatments because of the cosmetic outcomes and the efficiency with which they were administered [15].

Nowroozpoor and colleagues [16] showed that latanoprost was more effective than placebo in treating the ailment and restoring pigmentation. None of the groups given it experienced any serious complications or side effects. However, **Kim and colleagues** [17] have brought out latanoprost's potential skin side effects, such as diffuse face hyperpigmentation.

CONCLUSION

Combining latanoprost with various treatments for vitiligo has been shown to be more beneficial than using latanoprost alone.

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