

Bupropion: The Antidepressant of Choice for Vitiligo Patients?

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Vitiligo is an acquired depigmentation disorder of great cosmetic importance, which is characterized by loss of melanocytes from the affected skin. Vitiligo patients are at a significantly higher risk of depression compared to healthy individuals. In addition, stress seems to play an important role in the onset and aggravation of vitiligo.^[1]

Several hypotheses including neural, immunological, and impaired redox status theories have been proposed to explain the destruction of melanocyte in vitiligo; however, the exact pathogenesis remains poorly understood.^[2] The neural and immunological hypothesis are detailed below.

NEUROTRANSMITTER CHANGES IN VITILIGO

Studies have shown that a significant number of vitiligo patients experience high amount of depression, anxiety, and stress due to the changes in appearance caused by this skin disorder.^[1]

It has been found that plasma levels of norepinephrine (NE) are elevated in vitiligo patients in comparison to controls.^[2]

Acute or chronic exposure to stressors is known to activate the sympathoadrenal system and increase the synthesis of catecholamines.^[3] Chromaffin cells of the adrenal medulla are innervated by the splanchnic nerve from the sympathetic nervous system. Acetylcholine (ACh), released on stimulation of this nerve, activates neuronal nicotinic ACh receptors (nAChRs) on chromaffin cells, and induces membrane depolarization that triggers catecholamine secretion.^[4]

NE is known for having direct and indirect cytotoxic effects on melanocytes. Direct actions include interacting with cellular sulfhydryl groups, enzyme inhibition, impairing mitochondrial calcium uptake, and forming cytotoxic products including free radicals. The indirect effects include activating α -receptors of the arterioles, causing vasoconstriction, and thereby producing toxic oxygen radicals caused by hypoxia.^[2]

In summary, increased NE level seems to play a significant role in the pathogenesis of vitiligo.

CYTOKINE CHANGES IN VITILIGO

Recent studies support the role of altered cellular immunity and cytokines in the pathogenesis of vitiligo. Immunohistochemical studies of the perilesional area in vitiligo skin detect CD4 and CD8 positive T-cells in the infiltrate, often with an increased CD8/CD4 ratio. Furthermore, an imbalanced cytokine levels in the epidermal microenvironment of lesional vitiligo skin have been demonstrated, which could impair the normal life and function of melanocytes. The production of tumor necrosis factor-alpha (TNF- α), a major inflammatory mediator involved in the pathogenesis of autoimmune diseases, and interferon gamma (IFN- γ) has been demonstrated to be elevated in vitiligo patients.^[5]

BUPROPION AND ITS POTENTIAL THERAPEUTIC ASPECTS IN VITILIGO

Bupropion is an antidepressant, which is as effective as the selective serotonin reuptake inhibitors sertraline, paroxetine, and fluoxetine in alleviating depressive symptoms but was

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not associated with weight gain or sexual dysfunction. Bupropion is an NE and dopamine (DA) reuptake inhibitor, and its efficacy in depression has been attributed to its effects on increasing synaptic concentrations of DA and NE without directly affecting other neurotransmitter systems.^[6]

There are three mechanisms that may explain its potential effectiveness in the treatment of vitiligo:

1. Bupropion is an antidepressant and anxiolytic drug which could be beneficial in alleviating depressive symptoms and stress, as one of the main triggers of vitiligo, in the affected patients and improving their quality of life. While this drug acts as an antidepressant by inhibition of DA and NE reuptake, it has no effect on plasma NE levels, a finding that indicates that it does not have cytotoxic effects on melanocytes induced by NE.^[1,6]
2. Bupropion has been shown to be capable of blocking nAChRs with some degree of selectivity; hence, this drug can decrease the production of NE by adrenal medulla cells.^[7] As stated above, NE has direct and indirect cytotoxic effects on melanocytes; therefore, the blockage of nAChRs on chromaffin cells, with the resultant decreased NE levels, may be the second mechanism supporting our hypothesis.
3. It has been shown that bupropion lowers the levels of pro-inflammatory cytokines such as IFN- γ and TNF- α , which have significant roles in the pathogenesis of vitiligo.^[8] Therefore, the immunomodulatory effects of bupropion may be another justification for the treatment of vitiligo by this agent.

In conclusion, given the antidepressant, anxiolytic, and immunomodulatory effects of bupropion plus its nicotinic

receptor antagonism, we theorized that bupropion could be effective against vitiligo. We encourage conduction of clinical trials on this important subject.

REFERENCES

1. Cupertino F, Niemeyer-Corbellini JP, Ramos-E-Silva M. Psychosomatic aspects of vitiligo. *Clin Dermatol* 2017;35:292-7.
2. Namazi MR. Neurogenic dysregulation, oxidative stress, autoimmunity, and melanocytorrhagy in vitiligo: Can they be interconnected? *Pigment Cell Res* 2007;20:360-3.
3. Axelrod J, Reisine TD. Stress hormones: Their interaction and regulation. *Science* 1984;224:452-9.
4. Sala F, Nistri A, Criado M. Nicotinic acetylcholine receptors of adrenal chromaffin cells. *Acta Physiol (Oxf)* 2008;192:203-12.
5. Ongenaes K, Van Geel N, Naeyaert JM. Evidence for an autoimmune pathogenesis of vitiligo. *Pigment Cell Res* 2003;16:90-100.
6. Stahl SM, Pradko JF, Haight BR, Modell JG, Rockett CB, Learned-Coughlin S, *et al.* A review of the neuropharmacology of bupropion, a dual norepinephrine and dopamine reuptake inhibitor. *Prim Care Companion J Clin Psychiatry* 2004;6:159-66.
7. Slemmer JE, Martin BR, Damaj MI. Bupropion is a nicotinic antagonist. *J Pharmacol Exp Ther* 2000;295:321-7.
8. Brustolim D, Ribeiro-dos-Santos R, Kast RE, Altschuler EL, Soares MB. A new chapter opens in anti-inflammatory treatments: The antidepressant bupropion lowers production of tumor necrosis factor-alpha and interferon-gamma in mice. *Int Immunopharmacol* 2006;6:903-7.

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