

# Mequinol 2%/Tretinoin 0.01% Topical Solution for the Treatment of Melasma in Men: A Case Series and Review of the Literature

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*Melasma is a common hyperpigmentation disorder that typically affects women, though up to 10% of white individuals seeking treatment for melasma are men. Melasma can be a source of embarrassment for men because of its association with women and pregnancy. We performed a case series assessing the use of mequinol 2%/tretinoin 0.01% topical solution in 5 men with melasma. Four of 5 patients achieved complete clearance of melasma at 12 weeks, and 1 patient showed moderate improvement. Side effects were minimal and consisted of stinging in one patient. All patients maintained results at the 16-week follow-up visit. Mequinol 2%/tretinoin 0.01% topical solution was an effective and well-tolerated treatment of melasma in men. The vehicle resulted in good compliance and minimal adverse effects in patients. This is the first report describing the use of mequinol 2%/tretinoin 0.01% topical solution for the treatment of melasma in men; there are no reports in women.*

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## Case Series

In our experience in southern Florida, men frequently seek treatment for melasma. When discussing treatment options with these patients, they generally prefer using a solution formulation rather than a cream or ointment. As a result, we conducted a case series of 5 healthy men aged 30 through 45 years treated with nightly application of mequinol 2%/tretinoin 0.01% topical solution for 12 weeks. We chose this combination product because of the preference for a solution formulation in men, as well as its effectiveness as a bleaching agent in other hyperpigmentation disorders, ease of application, and ethanol-based fast-drying properties. Three patients were Hispanic and 2 patients were white. Three patients had centrofacial melasma, while 2 patients had mandibular melasma. Zinc oxide 6% sunblock was suggested for use every morning, with reapplication every 2 hours during continuous sun exposure. Follow-up assessments were conducted at 2, 4, 8, 12, and 16 weeks, and standardized photographs were taken.

All 5 patients had a history of chronic sun exposure, melasma duration of more than one year, and a family history of melasma. No personal skin care products were consistently used by most patients. No changes in facial shaving practices were instructed or observed. There was no history of regularly used prescription or over-the-counter oral medications. Additionally, all of the patients had no success with prior treatment with hydroquinone 4%, and one patient had no success with the triple combination therapy of fluocinolone acetonide 0.01%, hydroquinone 4%, and tretinoin 0.05% cream.

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**Figure 1.** A 32-year-old man with centrofacial melasma at baseline (A) and after 12 weeks of therapy with mequinol 2%/tretinoin 0.01% topical solution (B).

It was observed that melasma in 4 of 5 patients completely cleared at 12 weeks. Results were seen as early as 4 weeks, with maximum efficacy noted at 12 weeks. The mequinol 2%/tretinoin 0.01% topical solution was discontinued at 12 weeks and results were maintained at a 16-week follow-up visit. A 32-year-old man with centrofacial melasma at baseline demonstrated substantial improvement at the 12-week follow-up visit (Figure 1). Noticeable improvement of the extensive involvement of facial dyspigmentation was seen at 4 weeks of therapy, with complete clearance at the 12-week follow-up visit (Figure 2). It was observed that 3 of 4 remaining patients completely cleared at 12 weeks and 1 patient showed only moderate improvement. One patient complained of stinging after use, but it was not severe enough for him to discontinue therapy. We were able to contact 3 of 5 patients at one year posttherapy. The patient described above stated that his facial pigmentation had not returned, though 2 patients stated that their melasma had returned to baseline levels. These patients with recurrent melasma admitted to noncompliance with daily sunscreen use posttherapy.

### Comment

Melasma is a common hyperpigmentation disorder that typically affects women. However, it has been reported that up to 10% of white individuals seeking treatment for melasma are men.<sup>1</sup> Little is known about the etiology of melasma in men. In a review of the literature of *Index Medicus* journals, there have been only 4 reports of melasma in men.<sup>2-5</sup> None of these reports described effective treatment of these patients. The disorder can be a source of embarrassment for men because of its unsightly appearance

and the social stigma of being categorized as a disease in pregnant women, which results in a negative impact on quality of life, much like women affected with hyperpigmentation disorders.<sup>6-8</sup>

There are several theories describing the etiology of melasma in men. Chronic sun exposure seems to be the most likely cause in most cases or at least the most important exacerbating factor. Vázquez and colleagues<sup>2</sup> researched the etiology of melasma in 25 Puerto Rican and 2 South American men. In this study, 81.4% (22/27) of patients had a history of chronic sun exposure and 66.6% (18/27) noticed worsening of their condition with sunlight exposure.<sup>2</sup> Sarkar et al<sup>4</sup> discussed the etiology of melasma in 31 Indian men. Approximately 58% (18/31) of the men were outdoor workers with frequent sun exposure.<sup>4</sup> These findings correlated with our case series, with all men having a notable history of either work-related or recreational chronic sun exposure. Sunscreen with sun protection factor 30 or higher must be used in the treatment of melasma as well as other disorders of hyperpigmentation affecting either men or women.

Hormonal influences are known to cause melasma in women, as seen in pregnant women and women taking oral contraceptives. Hormonal changes, although different than women, may play a role in the development of melasma in men. Sialy and colleagues<sup>3</sup> assessed serum levels of luteinizing hormone, follicle-stimulating hormone, and testosterone in 15 men aged 20 to 40 years with melasma. Statistically significant higher levels of luteinizing hormone and lower levels of testosterone were found when compared with 11 age-matched controls



**Figure 2.** A 32-year-old man with centrofacial melasma at baseline (A). Noticeable improvement of the extensive involvement of facial dyspigmentation was seen at 4 weeks of therapy with mequinol 2%/tretinoin 0.01% topical solution (B), with complete clearance at the 12-week follow-up visit (C).

( $P < .05$  and  $P < .002$ , respectively). The authors used the term *subtle testicular resistance* as a possible cause of melasma in men.<sup>3</sup>

Genetic predisposition also may play a role in the etiology of melasma in men. Vázquez and colleagues<sup>2</sup> reported that 70.4% (19/27) of men in their study had a family history of melasma in first- or second-degree relatives, though none of the men reported melasma in their fathers. In contrast, Sarkar and colleagues<sup>4</sup> found that only 16.1% (5/31) of Indian men with melasma had a family history of the disease. In our patients, genetic predisposition seemed to correlate with the development of melasma. All patients had a family history of melasma in a first- or second-degree female relative, while 2 patients acknowledged having an affected male relative.

Other less prevalent etiologies of melasma in men also have been described. In Indian men, those who used vegetable oils, most notably mustard oil on the face after bathing, described the onset of melasma with concurrent sun exposure.<sup>4</sup> No personal skin care products stood out as being used by most of our patients. Medications have been mentioned as a possible etiology in some men. Men receiving diethylstilbestrol therapy for prostate cancer have developed melasma as a side effect.<sup>3</sup> However, the melasma is most likely hormonally induced secondary to the drug being an estrogen derivative. Melasmalike pigmentation also is a known side effect of phenytoin therapy.<sup>4</sup> Sarkar and colleagues<sup>4</sup> reported that 2 of 31 Indian men in their study had received phenytoin therapy. None of our patients had a history of regular use of any oral medications.

Our case series is the first report of mequinol 2%/tretinoin 0.01% topical solution for the treatment of melasma in men; no reports in women exist. Mequinol is a potent bleaching agent that is a phenolic derivative of hydroquinone. The mechanism of action of mequinol as a bleaching agent is largely unknown. Possible theories include inhibition of melanin synthesis, direct melanocyte cytotoxicity, and secondary cytotoxicity via products derived from tyrosinase oxidation.<sup>9-12</sup> Tretinoin is known to have an inhibitory effect on tyrosinase by decreasing melanin synthesis and affecting melanin transfer to keratinocytes.<sup>13,14</sup> An additional synergistic effect of tretinoin is its ability to increase penetration of bleaching agents.<sup>15,16</sup> Tretinoin also accelerates epidermal turnover, leading to faster desquamation of melanin pigment within the epidermis.<sup>17</sup>

Currently, mequinol 2%/tretinoin 0.01% topical solution is approved by the US Food and Drug

Administration for the treatment of solar lentigines. It has been described as an effective treatment for solar lentigines<sup>18-23</sup> and has been shown to be superior to either of its components alone.<sup>18</sup> Compared with hydroquinone 3%, mequinol 2%/tretinoin 0.01% topical solution was more efficacious for lentigines on the forearms, with similar results on the face.<sup>19</sup> The side-effect profile of mequinol 2%/tretinoin 0.01% topical solution is favorable compared with other agents. In animal studies, mequinol was less irritating than hydroquinone.<sup>24</sup> In the literature, the most common adverse reaction reported was stinging, as was reported in one of our patients. Other adverse reactions include erythema, desquamation, and pruritus.<sup>18-21,25</sup> The stinging sensation partly may be due to the high ethanol content (77.8% by volume),<sup>25</sup> which can be problematic, particularly if men use this product after shaving. Transient hypopigmentation also has been reported in a minority of patients.<sup>19,22</sup> Mequinol as a phenolic derivative also has the potential to cause exogenous ochronosis, though it has not been reported. Mequinol 2%/tretinoin 0.01% topical solution is contraindicated in pregnancy and should be used with caution in patients taking photosensitizing medications.<sup>25</sup>

### Conclusion

Mequinol 2%/tretinoin 0.01% topical solution is an effective therapy for melasma in men. It is likely that several courses of therapy or therapy for more than 12 weeks is needed for good long-term results. Concomitant sunscreen use is imperative and must be addressed with all patients during therapy and posttherapy. The product is fast drying because of its high ethanol content, making it easy to use, which leads to increased compliance in most cases, though the potential to cause irritation exists.

It is important that efficacious treatments are available for men with hyperpigmentation disorders. To put this into perspective, 80% of the world's population is described as having skin of color.<sup>26</sup> It has been estimated that 50% of the US population will have skin of color by the year 2050, and the men of this population have a higher risk for developing melasma and other hyperpigmentation disorders.<sup>27</sup> Men are already becoming a rapidly growing sector seeking treatment for these disorders and this trend is expected to continue in the future. Hyperpigmentation disorders can be a source of embarrassment and can negatively impact the quality of life for both men and women. Additional research is needed

to evaluate existing and potential therapies for melasma and other hyperpigmentation disorders in men.

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