

## An innoxious combination for depigmentation

Sir,

A 58-year-old man presented to the outpatient department with extensive vitiligo. His symptoms began ten years back and was earlier treated with the aim to induce pigmentation through various treatment modalities such as tacrolimus 0.1% ointment, decapeptide lotion, narrow band ultraviolet B therapy, oral steroids and other immunosuppressants for several months. Later he was lost to follow-up. Now he presented with extensive vitiligo which was interspersed

with multiple pigmented macules on sun exposed areas such as face, neck, anterior chest and dorsum of hands. These pigmented macules had increased after working in sunlight for past one month [Figures 1-3]. Apart from vitiligo he was in good health. He was mainly concerned about the multiple areas of repigmentation on the face with significant contrast to the depigmented vitiligo patches and hence he desired depigmentation therapy for his pigmented areas. On examination, more than 80% of the body surface area was



**Figure 1:** Before and after retinoic acid-monobenzyl ether of hydroquinone combination treatment. Note the marked lightening of pigmented macules over the dorsum of hands.



**Figure 2:** Before and after photos of retinoic acid-monobenzyl ether of hydroquinone combination treatment. Note the marked lightening of pigmented macules over face and neck.



**Figure 3:** Before and after photos of retinoic acid-monobenzyl ether of hydroquinone combination treatment. Note the marked lightening of pigmented macules over posterior aspects of neck, arms and upper back.

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affected with vitiligo. The patient was photographed for documentation after taking his consent. He was given two tubes; one of monobenzyl ether of hydroquinone (MBEH) 20% and the other of retinoic acid (RA, tretinoin 0.025%). He was instructed to mix equal volumes of both and apply at night to pigmented areas of dorsum of hands with good sun protection measures during daytime. He experienced mild itching and stinging sensation which were not troublesome, so continued the application and within a week these symptoms subsided without any additional treatment. After eight weeks, noticeable lightening had occurred. Then the treatment was extended to other sites and patient was followed up every four weeks. At the end of 24 weeks, depigmentation was extremely satisfactory matching the vitiliginous [Figures 1-3].

Monobenzyl ether of hydroquinone is a phenol derivative that is United States Food and Drug Administration approved drug for depigmentation in patients with extensive vitiligo.<sup>1</sup> It reacts with the key enzyme tyrosinase to form reactive oxygen species which induces the specific T cell response against melanocytes.<sup>1</sup> Nair *et al.*<sup>2</sup> have proposed that the retinoic acid enhances the absorption of monobenzyl ether of hydroquinone by melanocytes through the inactivation of their glutathione-dependent defense mechanisms. In a study by Kasraee *et al.*,<sup>3</sup> it was observed that the treatment of black guinea pigs with monobenzyl ether of hydroquinone (10%) produced mild-to-moderate depigmentation and the retinoic acid (0.025%) – monobenzyl ether of hydroquinone (10%) combination, however, produced a complete degree of depigmentation in the majority of treated sites after ten days of application. Side effects of monobenzyl ether of hydroquinone include skin irritation, contact dermatitis, exogenous ochronosis, unmasking of telangiectasia on the lower extremities, pruritus, xerosis, erythema, rash, edema, conjunctival melanosis and distant depigmentation.<sup>1,4</sup> Risk of carcinogenesis of monobenzyl ether of hydroquinone cannot be ruled out, while the side effects of retinoic acid include sensation of warmth, stinging, redness and scaling. We observed that the combination of retinoic acid-monobenzyl ether of hydroquinone was safe with minimal adverse effect and faster achievement of desired depigmentation. It serves as

an innocuous depigmenting combination. This case highlights the importance of timely initiation of depigmentation therapy considering the patient's quality of life. Animal studies on the use of retinoic acid-monobenzyl ether of hydroquinone combination are available, but we were unable to find any previous report or study in humans. This is the first case of clinical use of retinoic acid-monobenzyl ether of hydroquinone combination in humans. Further studies are needed to know its efficacy and side effects.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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#### Conflicts of interest

There are no conflicts of interest.

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