

Therapy of Melasma with Lentigo Solaris

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Abstract: Melasma and lentigo solaris are common, recurrent, and refractory acquired hyperpigmentation disorder. Azelaic acid (AA) is a depigmenting agent acts by inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects on melanocytes. Glycolic acid (GA) peels alone or in combination with topical hypopigmenting agents has shown encouraging results. However, there is paucity of controlled trial demonstrating the efficacy of GA peels in conjunction with topical AA. **Case:** A 42-years-old female, a street vendor, had dark brown spots on both cheeks, nose, chin and forehead that spreads to whole face since one year ago. She had a history of using contraceptives. There were multiple well-circumscribed, irregular hyperpigmented macules that asymmetrical, with size ranging from lenticular to plaque on the maxillary, left buccalis, mentalis and frontalis region. We also found a numular dark brown hyperpigmented macules on right zygoma. She was diagnosed with melasma and lentigo solaris. The Melasma Area Severity Index (MASI) score was 25.6, which classified as moderate melasma. She was treated with 20% azelaic acid cream twice a day, broadspectrum sunscreen with SPF 50 and GA 20% peeling. **Result:** After 6 weeks of treatment, there were significant improvement in both melasma and lentigo solaris.

Keyword: Azelaic Acid, Glycolic Acid, Melasma, Lentigo Solaris

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1 Introduction

Melasma and lentigo solaris are common, recurrent, and refractory acquired hyperpigmentary disorder [1,2]. Study of Jusuf conducted in Cosmetic Dermatology Clinic H. Adam Malik General Hospital Medan from 2012-2015, the largest proportion of pigmentation disorder was hypermelanosis, with melasma as the most common diagnosis [3]. In spite of variety of therapeutic options available for this cosmetically disfiguring condition, their treatment is really challenging. Currently available treatment modalities include topical agents such as hydroquinone, azelaic acid (AA), kojic acid, retinoic acids, and their various combinations; and chemical peels such as glycolic acid (GA), lactic acid, trichloroacetic acid, phenol, and Laser. Unfortunately, the results of monotherapies are usually disappointing, especially in dark-skinned individuals [1,2].

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Azelaic acid (AA) is a depigmenting agent which acts by inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects on melanocytes. Moreover, it acts selectively on hyperactive and abnormal melanocytes; thus, neither leukoderma nor exogenous ochronosis is associated with its use [4]. Glycolic acid (GA) peel act in hyperpigmentation due to the effect on epidermal remodeling, accelerated desquamation, and its additive inhibitory effect on melanin synthesis, resulting in quick pigment dispersion. GA peel is considered to be the most versatile peeling agent as it has good penetration because of its low molecular weight, increased bioavailability, easily neutralized, and being superficial, and it has very few postpeel complications [5,6].

Recently, some studies have combined GA peel with various topical hypopigmenting agents such as hydroquinone 4% [7], azelaic acid 20% plus adapalene gel 0.1%,2 and modified Kligman's formula to enhance the efficacy of treatment and have found to produce better results. As there is paucity of studies demonstrating the efficacy and safety of combining GA peel and 20% AA cream in treatment of epidermal melasma, this treatment was undertaken.

2 Case

A 42 years old female, married, work as a street vendor came to our clinic on 12 December 2017 with dark brown spots without pain and itching on both cheeks, nose, chin and forehead which started a years ago and spread to whole face within one year. Initially, light brown spots appeared on both cheeks then extended to the nose, chin and forehead with darker color. Patients had never use sunscreen or protective hats when they were outdoors. She also had never used drugs to get rid of this complaint. She had history of using injectable contraception for 10 years and replaced with oral contraceptives for 4 years, but within 3 months the patient had stopped using contraception. Family history of suffering from the same thing was denied by the patient. Dermatological examination showed multiple well-circumscribed, irregular hyperpigmented macules that asymmetrical, with size ranging from lenticular to plaque on the maxillary, left buccalis, mentalis and frontalis region. We also found a numular dark brown hyperpigmented macules on right zygoma. (Figure 1). The differential diagnosis of the patient were melasma + lentigo solaris, exogenous ochronosis + actinic keratosis, and efelid + seborrheic keratosis,. The patient was diagnosed with melasma + lentigo solaris.

The assessment based on the MASI score for these patients when she first arrived was:

$$\begin{aligned}
 \text{MASI} &= 0.3 (D_F + H_F)A_F + 0.3 (D_{MR} + H_{MR})A_{MR} + 0.3 (D_{ML} + H_{ML})A_{ML} + 0.1 (D_C + H_C)A_C \\
 &= 0.3 (1+1)2 + 0.3 (4+4)5 + 0.3 (4+4)5 + 0.1 (1+1)2 \\
 &= 25.6 \text{ (moderate melasma)}
 \end{aligned}$$



Figure 1 First visit: multiple well-circumscribed, irregular hyperpigmented macules that asymmetrical, with size ranging from lenticular to plaque maxillary region, frontal and nasal regions. There are also numular size hyperpigmented macules to multiple plaques, discrete in the right zygoma region.

Patient was treated with 20% azaleic acid cream which applied in the morning and night, also SPF 50 sunscreen cream which applied to 15 minutes before exposure to sunlight. In addition, patients are also recommended to avoid direct exposure to sunlight by wearing a protective umbrella such as an umbrella or hat when outdoors. Patients were also recommended for control 2 weeks later for chemical peels with 20% GA, with discontinuation of the azaleic acid cream 3 days before.

The patient came after 3 weeks of treatment, there was little significant improvement on multiple hyperpigmented macules on maxillary region, frontal and nasal regions also on numular sized hyperpigmentation macule on the zygoma region (Figure 2). Assessment of MASI score was $0 + 9.6 + 9.6 + 0.1 = 19.3$ which classified as mild melasma. Chemical peel with 20% AG solution was performed. The other treatment of patient was still continue as before. Patient was asked to control again 3 weeks later for repetition of chemical peels.

After 6 weeks of treatment, there were all improvement on hyperpigmented macules on maxillary region, frontal and nasal regions, also numular sized hyperpigmentation macule on the zygoma region (Figure 3). MASI score assessment was $0 + 2.4 + 2.4 + 0.1 = 4.9$ which classified no melasma. The therapy was still continue with azaleic acid cream as maintenance therapy.



Figure 2 After 3 weeks of treatment: A slightly faded, well-circumscribed multiple hyperpigmented macules with irregular, asymmetrical edges, numular size to plaque, on maxillary region, frontal and nasal regions. There was still no improvement on numular sized hyperpigmentation macule on the zygoma region.



Figure 3 After 6 weeks of treatment: There were overall improvement on multiple hyperpigmented macules on the maxillary region and frontal and buccal region. The numular sized hyperpigmentation macule on right zygoma is also faded.

3 Discussion

Therapeutic modalities for melasma and lentigo solaris are similar. Chemical peeling is the most innovative weapon in the therapeutic armamentarium for melasma and also lentigo solaris. The benefits of alpha hydroxy acids as peeling agents have long been recognized, of which glycolic acid is the commonest peeling agent. However, even with the higher concentration of GA peel, that is, 50%, an average improvement in terms of MASI score of only 46.7% has been observed in epidermal melasma [5]. Thus, with the aim of improving the degree of response to therapy, many workers have used GA peeling in conjunction with various topical hypopigmenting agents[2,7]. Azelaic acid is a safe and effective hypopigmenting agent in melasma especially in epidermal variety. So it would be interesting to combine GA peels with topical AA for enhancing the improvement in melasma, thereby improving the health related quality of life and patient's satisfaction [4,7].

The patient's job as a street vendor causes longer sun exposure and she had also a history of using oral and injected contraceptives which accordance with the risk factors for melasma are

environmental and endocrine factors [8-11]. Prolonged UV exposure-induced dermal inflammation and fibroblast activation may upregulate stem cell factors in the melasma dermis, causing increased melanogenesis [8-10]. Mahdalena et al found 20,5% melasma among hormonal contraceptive acceptors which is oral contraceptive pills is the highest proportion followed by injection and implant [11]. Various studies showed evidence of hormonal involvement in the genesis of the disease, since high levels of estrogen, progesterone and melanocortin are possible triggering factors of melasma during pregnancy. Estrogen increases vascularization of the skin, suppresses the activity of sebaceous glands and also increases pigment cell activities. Progesterone increase the spread of melanin in cells and the expression of PR proteins in skin hyperpigmentation due to melasma [9-11].

However, clinical experience of combination of GA peel with azelaic acid in melasma is very limited [12]. Azelaic acid is a depigmenting agent which acts by inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects on melanocytes. Moreover, it acts selectively on hyperactive and abnormal melanocytes; thus, neither leukoderma nor exogenous ochronosis is associated with its use [4]. GA peel act in melasma due to the effect on epidermal remodeling, accelerated desquamation, and its additive inhibitory effect on melanin synthesis, resulting in quick pigment dispersion. GA peel is considered to be the most versatile peeling agent as it has good penetration because of its low molecular weight, increased bioavailability, easily neutralized, and being superficial, and it has very few postpeel complications [5,6].

The improvement in MASI scoring were significant in 6 weeks of treatment without any side effect. This reflects higher efficacy of the combination therapy as compared to the topical AA cream alone. Based on the findings of Erbil et al who had also shown a statistically significant decrease in mean MASI and percentage decrease in MASI in the combination group as compared to control group at completion of the study. In the Erbil et al study, the percentage decrease in MASI after completion of treatment was higher (83.8%) as compared to study group (58.72%). This might be due to the reason that in our case, we used only AA cream with serial GA peel, while in Erbil et al.'s study, they have used AA cream with 0.1% adapalene gel in combination with serial GA peel [2]. Thus, the use of additional topical agent, that is, adapalene 0.1% gel which acts in lightening of melasma by accelerating skin turnover and enhancing the efficacy of bleaching agents, may be responsible not only for higher percentage decrease in MASI score but also in side effects like erythema, pruritus, and post inflammatory hyperpigmentation (PIH) [7,12].

4 Conclusion

The combination of topical AA cream and 20% GA peels are well-tolerated and highly effective strategy in melasma and lentigo solaris, thereby leading to improved patient's compliance.

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