

## Original Article

### The Role of Combination of 20% Azelaic Acid with 0.05% Tretinoin Cream in the Treatment of Melasma - A study in FMCH.

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#### Abstract:

Melasma is characterized by melanosis with sharply demarcated blotchy, brown macules usually in a symmetric distribution over the cheeks and forehead and sometimes on the upper lip and neck. It is most often seen in women during pregnancy, at menopause and while taking oral contraceptives; it occasionally occurs in women who are not pregnant or taking oral contraceptives, as well as men. So it is a great problem in our country. A clinical trial was conducted to find out the effect of the combination of 20% azelaic acid with 0.05% tretinoin cream in the treatment of melasma. Twenty clinically diagnosed cases of melasma attending the outpatient department of Dermatology and Venereology, Faridpur Medical College Hospital, Faridpur were enrolled. Majority of the study subjects (40%) were between 26 to 30 years of age and most of them (60%) were females. Regarding occupation, 60% were housewife. Out of the study subjects 75% were married and 60% were middle class. Around 60% cases had positive family history of melasma and maximum (90%) patient had no history of systemic drug and the maximum (80%) patients had no history of use of cosmetics. It was observed that highest (90%) number of patients had malar area involvement and 10% had centro-facial area involvement. The study showed moderate reduction of the severity of melasma after the treatment. Out of the study subjects, 40% and 20% developed burning sensation and erythema respectively. It could be concluded that combination of 20% azelaic acid and 0.05% tretinoin cream, has a moderate lightening effect in the treatment of melasma.

**Key words:** 20% Azelaic Acid, 0.05% Tretinoin, Melasma.

#### Introduction:

Melasma is a common disorder, with two predisposing factors:- sun exposure and sex hormones.

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It tends to affect darker-complexioned individuals, especially East, West and South-east Asians. Melasma is characterized by brown patches, typically on the malar prominences and forehead. The forearms may also be affected. There are three clinical patterns of facial melasma:- (i) centrofacial- most common pattern involving cheek, forehead, upper lip, nose, (ii) malar-involving cheek and nose, and (iii) mandibular-involving the ramus of mandible. The type of hyperpigmentation may be epidermal (brown), dermal (blue-gray) or mixed (brown-gray)<sup>1</sup>.

Melasma has been considered to arise from pregnancy, oral contraceptives, endocrine dysfunction, genetic factors, medications, nutritional deficiency, hepatic dysfunction, HIV infection and other factors. Sun exposure would appear to be an exacerbating factor in otherwise predisposed individuals<sup>2</sup>.

Melasma like hyperpigmentation has been observed in patients taking phenytoin. Melasma appears to be chronic process that is exacerbated by sunlight and artificial UVA and UVB. Up to a third of the cases in women and most in men are idiopathic<sup>3</sup>.

A recent study suggests that a high expression of MSH (Melanocyte Stimulating Hormone) in the lesional keratinocytes of melasma plays a key role in the pathogenesis of the hyperpigmentation of melasma skin<sup>4</sup>. Histologic studies of melasma developed skin, reveal increased melanin in the epidermis (epidermal type), dermis (dermal type) or both (mixed type)<sup>5</sup>. Studies suggest an increase in the number and activity of melanocytes: there is an increase in the formation, melanization and transfer of melanosomes to the epidermis as well as the dermis<sup>6</sup>. The diagnosis is usually readily established by clinical features. Post inflammatory hyperpigmentation can usually be excluded by history<sup>7</sup>.

Azelaic acid is a dicarboxylic acid found in food (Whole-grain cereals and animal products)<sup>8</sup>. The mechanism of action is thought to be normalization of the keratinization process (decreased thickness of the stratum corneum, decreased number and size of keratohyaline granules and decreased amount of filaggrin)<sup>9</sup>. There is no risk of exogenous ochronosis which can be associated with higher concentration of hydroquinone<sup>10</sup>. Local irritation with azelaic acid is more common than with hydroquinone<sup>8</sup>. Tretinoin is a yellow to light orange crystalline powder having characteristic floral odor<sup>11,12</sup>.

Tretinoin is an endogenous retinoid of vitamin A that binds with intracellular receptor in the cytosol and nucleus. Cutaneous level of tretinoin in excess of physiologic concentration occurs following application of a tretinoin containing topical product<sup>13</sup>. The local adverse effect observed include erythema, scaling, pruritus, stinging, dryness, irritation and patients also noted a decreased tolerance to ultraviolet radiation leading to phototoxicity reaction<sup>14</sup>.

**Materials and Methods :**

A clinical trial was conducted to find out the effect of the combination of 20% azelaic acid with 0.05% tretinoin cream in the treatment of melasma. Twenty clinically diagnosed cases of melasma attending the outpatient department of Dermatology and Venereology, Faridpur Medical College Hospital (FMCH), Faridpur, fulfilling the inclusion criteria were enrolled. The study was carried out from March 2014 to February 2015. An informed consent was taken from the patients to take part in the study. Data were recorded on pre-designed case record form. At the baseline visit, history of melasma regarding length of time present, relationship to pregnancy, hormonal therapy, sun exposure and cosmetic use etc. were taken. Patients were asked about previous use of azelaic acid and tretinoin and hypersensitivity to these agents. Family history of melasma was also taken.

MASI (Melasma Area and Severity Index) was calculated and recorded. The patients were advised to apply this preparation over the melasma once at every night and the patients were asked to report on 4<sup>th</sup>, 8<sup>th</sup> and 12<sup>th</sup> week for evaluation. The effect was evaluated clinically using Melasma Area and Severity Index (MASI) score as proposed by Kimbrough-Green et al<sup>15</sup>. At each visit, side effects were recorded and assessed on four point scale as absent, mild, moderate or severe. Female patients who were on oral contraceptives pill, pregnant and lactating females, persons having hypersensitivity to azelaic acid or tretinoin and patients suffering from any concomitant systemic illness were excluded from the study.

**Results:**

**Table I:** Distribution of the patients by age (n=20)

Age (in years)	Frequency (%)
20-25	1 (5)
26-30	8 (40)
31-35	6 (30)
36-40	3 (15)
>40	2 (10)
<b>Total</b>	<b>20 (100)</b>

Table-I showed the age of the patients of melasma, where majority (40%) cases were between 26 to 30 years, 5% were between 20-25 years, 30% were between 31-25 years old, 15% were between 36 to 40 years old and 10% were more than 40 years of old.

**Table II:** Distribution of the patient by epidemiological profile (n=20)

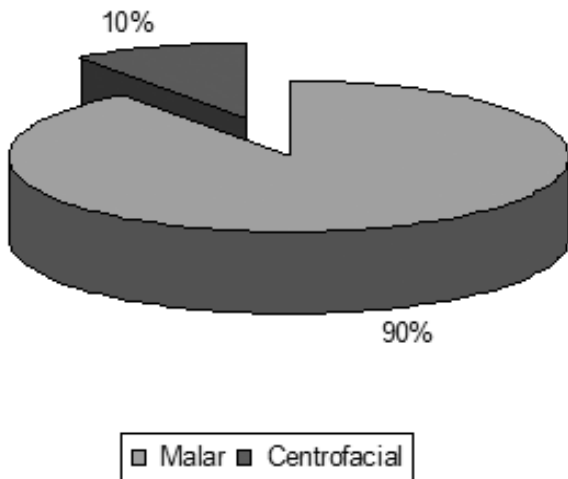
Epidemiological profile	Frequency (%)
<b>Sex</b>	
Male	8(40%)
Female	12(60%)
<b>Occupation</b>	
Housewife	12(60%)
Students	6(30%)
Business	2(10%)
<b>Marital Status</b>	
Married	15(75%)
Unmarried	5(25%)
<b>Socio-economic condition</b>	
Middle class	12(60%)
Lower class	8(40%)

Table II showed that majority (60%) of patients were females and 40% were males and Male to Female ratio was 2:3. Among the patients, 60% patients were housewives, 30% were students and 10% were involved in business. Regarding the marital status of the patient, maximum (75%) was married. On the basis of socio-economic condition, patients can be divided into 60% as middle class and 40% as lower class.

**Table III:** Distribution of the patient by personal profile (n=20)

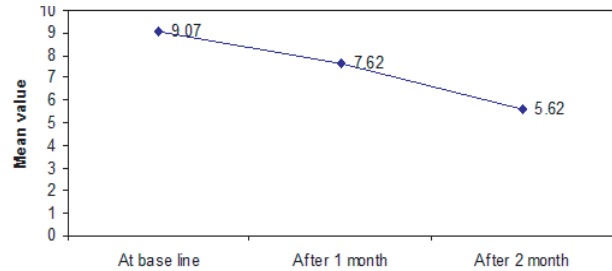
Personal profile	Frequency (%)
<b>Family history of melasma</b>	
Positive	12(60%)
Negative	8(40%)
<b>History of use of cosmetics</b>	
Positive	4(20%)
Negative	16(80%)
<b>History of systemic drug</b>	
Positive	2(10%)
Negative	18(90%)

Table III showed that regarding family history of melasma, positive history was present in 60% cases. Maximum (90%) patients had no systemic drug history and 80% patients had no history of use of cosmetics.



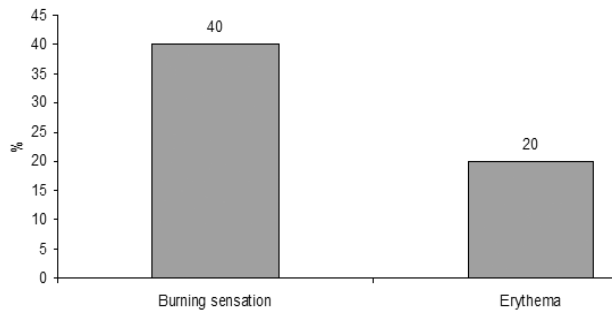
**Fig. I:-** Distribution of the patients by the site of involvement.

Figure I showed that the highest (90%) number of patients had malar area involvement and 10% had centrofacial area involvement.



**Fig. II:-** Changes of MASI score after treatment. (Mean ± SD of MASI score)

Figure II Showed the change of MASI score after treatment with combination therapy. About 12 weeks of treatment the average MASI score was decreased indicating moderate reduction of the severity of melasma (0=No reduction, up to 25% = mild, 26-50% = moderate, above 50% = remarkable reduction).



**Fig. III:-** Distribution of the patients by side effects.

Figure III showed that 40% and 20% patients developed burning sensation and erythema respectively.

**Discussion:**

A total of 20 clinically diagnosed cases of melasma fulfilling the inclusion criteria were included in this study. MASI was calculated and recorded. The patients were advised to apply this preparation over the melasma once at every night and the patients were asked to report on 4<sup>th</sup>, 8<sup>th</sup> and 12<sup>th</sup> week for evaluation. The effect was evaluated clinically using Melasma Area and Severity Index (MASI) score as proposed by Kimbrough-Green et al<sup>15</sup>. The evaluations were recorded at base line, at 4<sup>th</sup> week and 8<sup>th</sup> week. At each visit, side effects or tolerability were determined by burning and erythma etc.

The study showed that the age of the patients of melasma, in majority (40%) cases were between 26 to 30 years, 5% were between 20 to 25 years, 30% were between 31 to 35 years, 15% were between 36 to 40 years, and 10% were more than 40 years. Majority (60%) patients were females and male-female ratio 2:3. These findings are similar to the research work, done by Garcia A<sup>14</sup>.

Among the patients, 60% patients were housewives, 30% were students and 10% were involved in business. Regarding the marital status of the patients, maximum (75%) were married. On the basis of socio-economic condition, patients can be divided into 60% as middle class and 40% as lower class. Regarding family history of melasma, 60% cases had a positive history. A strong family history of melasma suggests an important genetic factor in the pathogenesis of this condition. It showed that highest (90%) number of patients had malar area involvement and 10% had centro-facial area involvement, which is similar to the research work of Garcia A, where 91% of the patients had malar distribution and 9% of the patients had centro-facial distribution<sup>14</sup>.

The study showed the change in MASI score after treatment with combination therapy. At 12 weeks of treatment the average MASI score was decreased indicating moderate reduction of the severity of melasma (0 = no reduction, up to 25% = mild, 26-50% = moderate, above 50% = remarkable reduction). It showed that 40% and 20% patient developed burning sensation and erythema respectively. The side effects disappeared after 4 weeks of therapy. These findings are mostly in accordance with the observations of Sarkar R, Bhulla M et al<sup>16</sup>.

Cutaneous side effects were limited to the burning sensation and erythema. The study was done in a small scale with shorter duration, it can not reflect the proper effect and possible side effects of combination of 20% azelaic acid and 0.05% tretinoin cream in the treatment of melasma.

### Conclusions:

An attempt was made to see the role of combination of 20% azelaic acid and 0.05% tretinoin cream in the treatment of melasma. It needs further elaborative study on a larger number of patients over a longer period of time. It could be concluded that of 20% azelaic acid and 0.05% tretinoin cream has a moderate lightening effect in the treatment of melasma.

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