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## Original Article

# The Role of Triple Combination Topical Agents in the Treatment of Facial Melasma

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**Abstract:**

Melasma is an acquired, symmetrical hypermelanosis of the face and is particularly seen in women with skin types IV to VI living in areas with intense UVR. So it is a great problem in our country. Treatment of melasma remains a challenge. Topical therapy with a triple combination topical agents appears to be the most clinically effective initial therapy for patients with melasma. A clinical trial was conducted to find out the efficacy of the triple combination of 4% hydroquinone, 0.05% tretinoin and 0.01% fluocinolone acetonide cream in the treatment of facial melasma. Fifty clinically diagnosed cases of melasma attending the Skin and VD outpatient department of General Hospital, Faridpur were selected randomly. Majority (54%) were between 21 to 25 years of age and most of them (86%) were female. After 20 weeks of treatment with triple combination agents, the average MASI score decreased significantly (P<.001). Reduction of the severity of melasma by 20 weeks is 82% and by 8 weeks is 71%. Regarding the distribution of melasma, 50% were found centrofacial, 45% malar and 5% mandibular. As side effects of the treatment, 36% developed erythema, 16% developed burning sensation, 6% developed pruritus and 4% developed desquamation. This study demonstrates that every night application of triple combination topical agent has significant effect on melasma.

**Key words:** Triple combination, Topical agent, Facial melasma.

## Introduction:

Melasma (from the Greek word, 'melas' meaning black) is a common, acquired, circumscribed hypermelanosis of sun-exposed skin. It is particularly seen in women with skin types IV to VI living in areas with intense UVR. It is rare before puberty, occurring most commonly in women of reproductive age[1]. Cutaneous melasma occurs most commonly in Asian and Hispanic women of childbearing years[2]. The exact etiology of melasma is unclear. Exposure to solar UV radiation is the most important environmental factor in the pathogenesis of melasma[3-4]. It is also associated with pregnancy and oral contraceptives, but the hormonal link to melasma is still not clearly elucidated[5]. Melasma-like hyperpigmentation has been reported from use of phenytoin. Upregulation of many melanin biosynthesis-related genes as well as melanocyte markers such as TYR, MITF, SILV, and TYRP1 has been noted in melasma skin[6]. Recently the iNOS (inducible nitric oxide synthetase) and NF-κB pathway have also been implicated in melasma pathogenesis[7].

It presents as hyperpigmented macules affecting the upper lip, cheeks, forehead, and chin. It is usually bilateral and is frequently symmetrical. It is classified as per the location of melanin as epidermal type, dermal type and mixed type. On the face it presents as centrofacial (63%), malar (21%) and mandibular (16%)[8].

The management of melasma is challenging and requires a long term treatment plan. In addition to avoidance of aggravating factors like oral pills and ultraviolet exposure, topical therapy has remained the mainstay of treatment[9-10]. Hydroquinone, azelaic acid, tretinoin, and topical corticosteroids have been used as monotherapy[10-14] or in various combinations[15-18]. Topical medications modify various stages of melanogenesis, the most common mode of action being inhibition of the

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enzyme, tyrosinase. Combination therapy is the preferred mode of treatment for the synergism and reduction of untoward effects. The most popular combination consists of hydroquinone, a topical steroid, and retinoic acid[19]. This study was done to see the role of triple combination of hydroquinone, tretinoin, and the fluorinated topical corticosteroid fluocinolone acetonide, in the treatment of facial melasma.

**Materials and Methods:**

Randomly selected fifty clinically diagnosed cases of melasma attending the Skin and VD outpatient department of General Hospital, Faridpur were studied. The study was carried out from March 2015 to February 2016. Those who were between 15 to 50 years of age, female not on oral contraceptive and taking no other drugs were included in the study. Informed consent was taken from the patients to take part in the study. Patient's data were recorded on predesigned case record forms. At the baseline visit, history of melasma regarding length of time present, relationship to pregnancy, oral contraceptives, and drug history were taken. Patients were asked about previous use of triple combination agents and any hypersensitivity to this agent. Patients were advised to apply triple combination agents (4% hydroquinone, 0.05% tretinoin and 0.01% fluocinolone acetonide cream) over the melasma once daily in the night and were asked to report on 2nd, 4th, 8th, 12th, 16th and 20th weeks for evaluation. The efficacy was evaluated using Melasma Area and Severity Index (MASI), as proposed by Kimbrough-Green et al. and at each visit, side effects were determined. Female patients who were pregnant, lactating and on oral contraceptives, persons having hypersensitivity to triple combination agents and patients suffering from any concomitant systemic illness, were excluded from the study.

**Results:**

**Table I:** Distribution of the patients by age.

| Age (in years) | Frequency | Percentage |
|---|---|---|
| 15-20 | 1 | 2 |
| 21-25 | 27 | 54 |
| 26-30 | 10 | 20 |
| 31-35 | 6 | 12 |
| 36-40 | 4 | 8 |
| >40 | 2 | 4 |
| **Total** | **50** | **100** |

Table-I shows the age of the patients of melasma, where majority (54%) cases were between 21 to 25 years and only 2% patients were in the 15-20 years age group.

**Table-II.** Distribution of patients by sex.

| Sex | Number | Percentage |
|---|---|---|
| Male | 7 | 14 |
| Female | 43 | 86 |
| **Total** | **50** | **100** |

Table-II shows that majority (86%) of the patients were female and 14% patients were male.

**Table-III.** Average MASI Score after treatment with triple combination agents.

| Baseline | 2nd week | 4th week | 8th week | 12th week | 16th week | 20th week |
|---|---|---|---|---|---|---|
| 10.96 | 7.98 | 6.56 | 3.17 | 2.65 | 2.3 | 1.97 |

Table-III shows baseline MASI score 10.96, 3.17 at the 8th week and 1.97 after 20 weeks of treatment with triple combination agents.

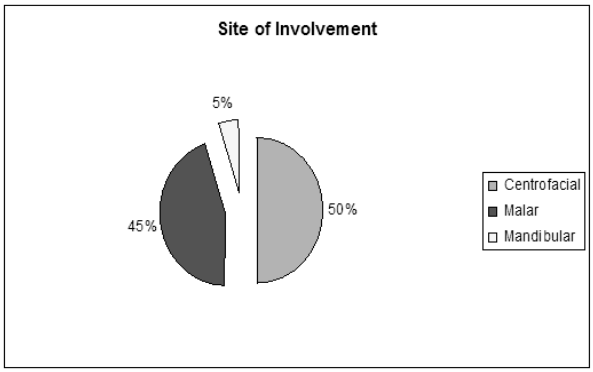


**Figure I:-** Distribution of the patients by the site of involvement.

Fig- I shows that 50% of patients had centrofacial, 45% had malar and only 5% had mandibular area involvement.

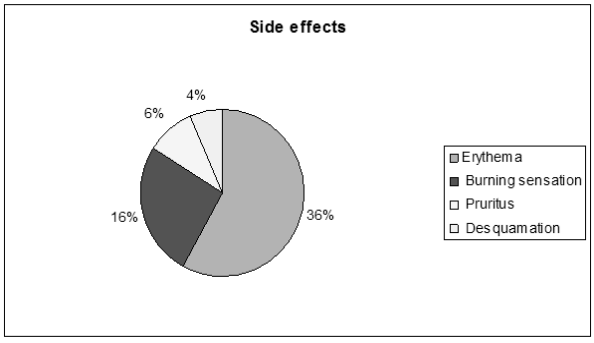


**Figure II:-** Distribution of the patients by side effects.

Fig-II shows that 36% patients developed erythema, 16% developed burning sensation, 6% developed pruritus and 4% developed desquamation.

**Discussion:**

A total of 50 clinically diagnosed cases of melasma fulfilling the inclusion criteria were included in the study. Patients were advised to apply triple combination agents over the melasma once daily in the night and the patients were asked to report on 2nd, 4th, 8th, 12th, 16th and 20th week for evaluation. At each visit, the effect was evaluated clinically using Melasma Area and Severity Index (MASI) score and side effects were determined by erythema, burning sensation, pruritus and desquamation.

The study showed that the age of the patients of melasma, in majority (54%) cases was between 21 to 25 years (Table-I), which correlates with the study done by Begum R et al[20] where it was found as 56%. Majority (86%) patients were females (Table-II) in our study whereas it was 90% in the study done by Begum R et al[20] which is very much similar.

The study showed the change in MASI score after treatment with triple combination agents. After 20 weeks of treatment with triple combination agents, the average MASI score decreased significantly (P<.001). Reduction of the severity of melasma by 20 weeks was 82% and by 8 weeks was 71% (Table-III) which is consistent with the findings of the study done by Sarkar R et al[21] and by Begum R et al[20].

It showed that highest (50%) number of patients had centrofacial, 45% had malar and 5% had mandibular area involvement (Fig-I), which is similar to the study done by Begum R et al[20] where 50% had centrofacial, 40% had malar and 10% had mandibular area involvement.

Cutaneous side effects noted throughout the study were erythema in 36% , burning sensation in 16%, pruritus in 6% and desquamation in 4% (Fig-II) which is accordance with the findings of Torok HM et al[22] and Cestari F at el[23].

**Conclusion:**

An attempt was made to see the role of triple combination agents (4% hydroquinone, 0.05% tretinoin and 0.01% fluocinolone acetonide) in the treatment of melasma. This study demonstrates that, every night application of triple combination agents has significant lightening effect on melasma. It needs further elaborative study on a larger number of patients over a longer period of time. Side effects of triple combination agents need further evaluation. Still it could be concluded that triple combination topical agent is safe and effective in the treatment of melasma.

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