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Effect of adjuvant tranexamic acid on melasma – A Pilot Study

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Objectives: To assess the additional effect of topical tranexamic acid on melasma
Methods: Ten melasma participants were included for an interventional split face trial for 8 weeks duration. Participants will receive 2 sessions of 1064 nm QS Nd: YAG laser plus topical tranexamic acid (group A) on one side of the face in one-month interval and 1064 nm QS Nd: YAG laser alone (group B) on the another side. Clinical responses were assessed by mexameter at baseline, 2nd, 4th and 8th week.
Results: Mean age of the participants were 44.6 years. All of them were female. The most common type of melasma was epidermal type, following by mixed type. At 8 weeks, melanin indices (combination group: 342.13 ± 24.17 – 334.13 ± 21.7; laser group: 345.06 ± 22.93 339.5 ± 22.32, p=0.452) and erythema indices (combination group: 365 ± 15.56 – 369.66 ± 18.87; laser group: 366.06 ± 13.8 348.26 ± 13.77, p=0.587) were not statistic significantly reduced from baseline. There was no difference reduction of melanin indices, erythema indices between the two groups.
Conclusion: Both topical tranexamic acid combining with low fluence QS Nd: YAG laser and laser treatment alone can reduce the pigmentation in melasma. According to the reduction of melanin indicies, in the combination treatment reveals the tendency in less pigmentation.

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Introduction

Melasma is a skin disease which associated with melanin disorders. The appearances of clinical symptoms are symmetrical hyperpigmented macules and patches. Melasma lesions occur mostly on forehead, nose, chin, cheeks and sunlight areas including the upper lip. It is much more common in constitutionally darker skin types (skin types IV to VI) than in Caucasians(1). The incidence of melasma is approximatedly from 1.5 to 33 percent based on population. Those with contraceptive pills, hormonal therapy, excessive sun light exposure, pregnancy and thyroid diseases are at risk. Moreover, some cosmetics and medications such as anticonvulsants and antithyroid drugs can induce melasma. Nevertheless, the pathogenesis of melasma is not yet fully understood.

Since melasma is one of the frequent cosmetic concerns, numerous treatments had been studied in order to evaluate the outcomes with less adverse effects. In term of laser treatment, ablative, non-ablative and semi-ablative laser had been used. However, a 1064-nm Q-switched neodymium-doped yttrium aluminium garnet (Nd:YAG), pigment specific laser was one of the most common laser treatments for melasma. For topical medications, though hydroquinone is the standard regimen for treatment(2). However, hydroquinone can cause several adverse effects such as irritation and undesirable ochronosis. Then, several alternative drugs had been demonstrated their efficacy in pigmentary reduction both in vivo and in vitro studies. Established effective substances for melasma are such as arbutin, vitamin C, kojic acid, licorice and tranexamic acid. Nevertheless, due to the limitation of an individual treatment, there is no standard guideline in melasma therapies.

A 1064-nm Q-switched neodymium-doped yttrium aluminium garnet laser (QS Nd: YAG) is widely used for the melasma treatment.Many sessions of treatment are required in order to demonstrate the effective results. However, hyperpigmentation is one of the frequent adverse effects from this therapy (3-5).

Tranexamic acid, a plasmin inhibitor, has recently obtained in popularity in melasma treatment. Moreover, it has been reported to show a decrease in hyperpigmentation effect (6, 7).

Therefore, this study aims to evaluate the additional effect of topical tranexamic acid (TA) combined with 1064 nm QS Nd: YAG laser for melasma.

Methods

Informed consent was provided to each participant. They were well informed about the aim of study, the potential risk, benefit and possible complications. The study was performed under the guideline of the Declaration of Helsinki. The study was approved by the institutional review board of Thammasat University (MTU-EC-OO-5-182/58).

Study design and subjects

It was an interventional, split-face trial on the treatment of 1064 nm QS Nd: YAG laser plus topical tranexamic acid drug (combination treatment) on one side of the face and with 1064 nm QS Nd:YAG laser alone on the other side of the face of the participants.

Participants aged 20 or more were recruited by dermatologist. The study included all types of the melasma. Diagnosis of melasma and its type were confirmed by wood's lamp examination. Exclusion criteria included pregnant or breast feeding women; on hormonal therapy or contraception; known allergy to tranexamic acid; history of any other depigmenting treatment in the past 1 month.

Table 1 Demographics data of the enrolled participants

number	sex	age	Type of melasma	Fitzpatrick skin type
1	female	49	Epidermal	IV
2	female	33	Mixed	IV
3	female	47	Mixed	IV
4	female	53	Epidermal	IV
5	female	41	Epidermal	V
6	female	47	Epidermal	III
7	female	39	Epidermal	IV
8	female	42	Mixed	V
9	female	43	Epidermal	IV
10	female	52	Epidermal	IV

All of the participants could follow up every visit as in the study protocol. There was no drop out subjects.

Treatment outcomes

At baseline, melanin indices on the side of combination was 342.13 ± 24.17 while the laser treatment alone was around 345.06 ± 22.93. Erythema indices was 365 ± 15.56 on the combination side and was approximately 366.06 ± 13.8 on the laser alone side. There was no difference on both melanin index and erythema index of both sides of the face.

At the end of the study, melanin indices on the side of combination was 334.13 ± 21.7 while the laser treatment alone was around 339.5 ± 22.32. Erythema indices was 369.66 ± 18.87 on the combination side and was approximately 348.26 ± 13.77 on the laser alone side. There was no difference on both melanin index and erythema index of both sides of the face.

At 8th week of the study, melanin index were decreased on both treatment groups. The reduction of melanin index was demonstrated since the second week after the first session of laser treatment and much more reduction at the 4 weeks after the laser treatment. However, 4 weeks after the second sessions of laser, melanin index was slightly increased. Nevertheless, there was no significant difference between the melanin index at baseline and at the end of study of both treatment groups ($p=0.452$).

For erythema index, both treatment regimens can reduce the score since the first session of laser. However, at the end of the study, erythema index was increased in the combination group while it was decreased in the laser treatment alone. Nonetheless, there was no statistical difference between both regimens ($p=0.587$).

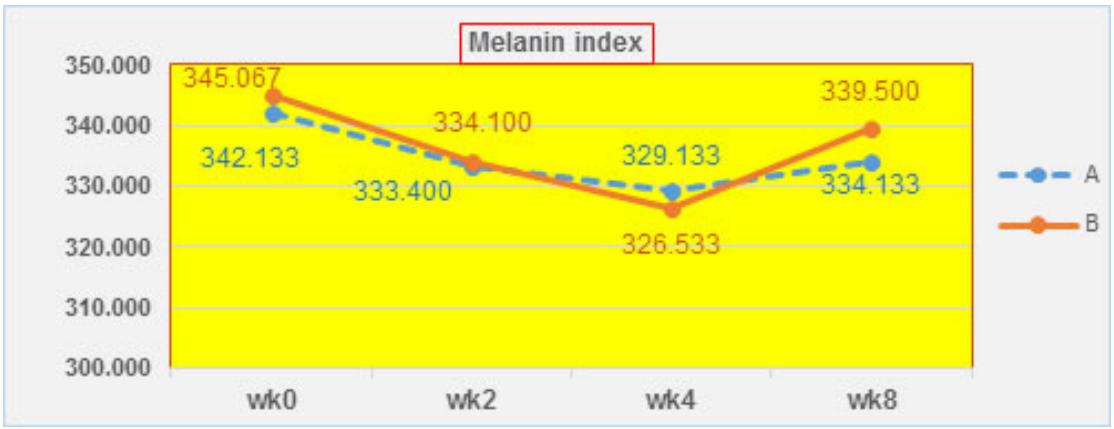

Figure 1. Melanin index of the combination treatment and the laser alone
A=combination treatment (1064 nm QS-Nd:YAG plus topical tranexamic acid)
B=laser alone (1064 nm QS-Nd:YAG alone)

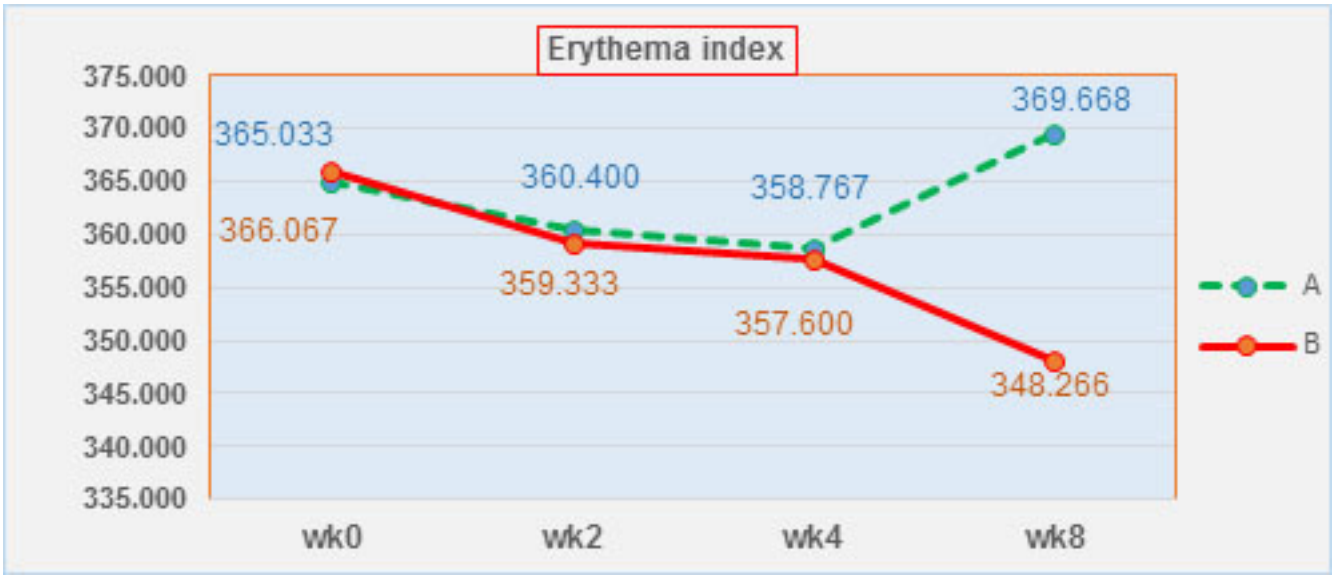

Figure 2. Erythema index of the combination treatment and the laser alone
A=combination treatment (1064 nm QS-Nd:YAG plus topical tranexamic acid)
B=laser alone (1064 nm QS-Nd:YAG alone)

Discussion

In spite of a variety of treatment options, melasma is a challenging hyperpigmented condition that still need a new effective treatment modality.

A 1064 nm Q-switch Nd: YAG laser is the most widely used in the treatment of melasma. There was a study using 1064nm Q-switch Nd: YAG laser in patients with melasma showed 50-74% improvement in skin lesions(5). Of note that, a common side effect is hyperpigmentation. In 2010, a study using 1064 nm Q-switch Nd: YAG laser in the treatment of melasma showed 92.5 percent improvement in skin lesion but 4 from 22 patients developed hyperpigmentation(8).

Tranexamic acid (TA) is a lysine analog that can prevent abnormal bleeding in several conditions(9). Research suggested that tranexamic acid inhibits the formation of melanin by the communication of the melanocytes and keratinocytes via the plasmin/plasminogen complex(10).A plasmin is a precursor for arachidonic acid and ultimately produces prostaglandins. Moreover, there was a study demonstrated that reduction of pigment after applied topical tranexamic acid on guinea pig owing to decreasing in arachidonic acid and prostaglandins. Additionally, tranexamic acid can also reduce vascular proliferation. This might provide a good result in treatment of telangiectasia melasma(7).

In this study, topical TA was used as an additional effect on melasma treatment. Both treatment regimens did not show difference improvement from baseline in term of both melanin index and erythema index. However, a combination group have a trend toward lower melanin index than laser alone group. Nc

Limitation of this study includes the number of the enrolled participants which may not be able to demonstrate the real effect of additional tranexamic acid. Also, in order to reveal the true outcomes of the melasma treatment, longer follow up may be needed.

Conclusion

Both topical tranexamic acid plus QS Nd: YAG laser and QS Nd: YAG laser alone can demonstrate the improvement of melasma. Though, both regimens did not reveal significant difference results, there are some trends in reducing pigmentation from laser by additional use of topical tranexamic acid.

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