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RESEARCH ARTICLE

THE NEW TREATMENT OF CAFE AU LAIT SPOT USING DR. HOON HUR'S GOLDEN PARAMETER THERAPY WITH A HIGH FLUENCE 1064NM Q-SWITCHED ND: YAG LASER

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ABSTRACT

The Café-au-lait spot (CALS) is a benign hyperpigmentary skin disorder which may vary in color from light brown to dark brown. Generally, treating CALS with traditional laser therapies including 532nm Nd:YAG laser, 694nm ruby laser and 755nm alexandrite laser can provoke side effects such as purpurae, crusts, post-inflammatory hyperpigmentation (PIH), mottled hypopigmentation and scarring. Unfortunately, there is no golden standard for the laser treatment of CALS yet. Therefore, in order to investigate the efficacy and safety of Dr. Hoon Hur's Golden Parameter Therapy (GPT) using a high fluence 1064nm Q-switched Nd: YAG laser (QSNL) for treating CALS, this study was performed. Ninety-seven Korean patients with a solitary CALS were treated with a 1064nm QSNL at a one-week interval for 50 treatment sessions of Dr. Hoon Hur's GPT. The parameters were a spot size of 7 mm, a fluence of 2.4 J/cm² and a pulse rate of 10Hz with a slow single pass by a slidingstacking technique over the CALS. At the week of the final treatment, all of the 97 patient with a solitary CALS were achieved the complete clearance of pigmented lesions without any side effects such as purpurae, crusts, PIH, mottled hypopigmentation and scarring. No recurrences were observed in any of the patients after a follow- up of 6-12 months. We suggest that Dr. Hoon Hur's GPT using a high fluence 1064nm QSNL is a safe and effective method without side effects and recurrences for treating CALS.

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INTRODUCTION

Café au lait spot (CALS) is a benign cutaneous pigmentarydisorder with light or dark brown coloration which may occur on any parts of the body excluding palms and soles at birth or in infancy. The size may vary in the diameter of 0.5cm-30cm. It's histopathologic findings show no nevus cell in the basal layer of epidermis and CALS does not proceed into malignant lesion (Shah, 2010 and Landau, 1999). Treatment is not necessary for CALS except cosmetic concerns (Shah, 2010 and Hur, 2016). However, treatment for CALS without side effects such as purpurae, crusts, PIH, mottled hypopigmentation and scarring, and recurrences is very difficult (Michel, 1997 and Polder, 2011). Therefore, in order to investigate the efficacy and safety of Dr. Hoon Hur's Golden Parameter Therapy (GPT) using a high fluence 1064nm Qswitched Nd: YAG laser (QSNL) for treating CALS without any side effects and recurrences, this study was performed.

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MATERIALS AND METHODS

This study was performed on ninety-seven Korean patients (age range: 1-42 years old, mean age: 15.6 years old) who clinically diagnosed with a solitary (Fig.1,3,5,7,10). No significant medical or familial history was found in the patients. Written informed consents were obtained from all of the 97 patients before proceeding into treatment. Briefly, 9.6% lidocaine cream of topical anesthetics (Inistbio, Hawsung, South Korea) was used 30 minutes under occlusion before the laser treatment. And all of the 97 patients were received 50 treatment sessions of Dr. Hoon Hur's GPT using a high fluence 1064nm QSNL(Spectra Laser, Lutronic, South Korea) at a one-week interval with a spot size of 7mm, a fluence of 2.4J/cm² and a pulse rate of 10Hz using slowly one pass by a sliding-stacking technique over the CALS. After the laser treatment, the lesion of CALS was cooled with ice packs but the patients did not use a broad-spectrum sunscreen. Standardized digital photography using a Canon Camera G11 (Japan) was used for the evaluation by comparing photos taken

on the day of the treatment and those taken 4 weeks after the final treatment session. The physician's clinical assessment of the degree of improvement of the patients (mean score of two investigators who did not attend the treatment) was also carried out 4 weeks after the last treatment session and reported as percentage resolution as follows: poor (0-25% clearance), fair (26-50% clearance), good (51-75% clearance), excellent (76-95% clearance) and complete (96-100% clearance) by analyzing the clinical photographs of patients. The patients were asked to report any side effects, pain or discomfort during the treatment.

RESULTS

Ninety-seven Korean patients with a solitary CALS were enrolled in this study(Table 1).All of the 97 patients with a solitary CALS were achieved complete clearance of the pigmented lesions (Table 2). And there were no significant side effects including purpurae, crusts, PIH, mottled hypopigmentation and scarring except slight pain during the laser treatment (Fig.2,4,6,8,11). No recurrences have been detected after a follow-up of 6-12 months (Fig.9,12).

Table 1. The demographic data of 97 patients with CALS and the characteristics of CALS

Age	
Age range	1-42 year-old
Mean age	15.6 year-old
Gender	
Male	42
Female	55
Family history	(-)
Characteristics of color	
Light brown color	27/97 (27.8%)
Dark brown color	70/97 (72.2%)
Characteristic of shape	
Homogenous round shape	42/97 (43.3%)
Heterogenous irregular shape	55/97 (56.7%)

Table 2. The results of treatment with Dr. Hoon Hur's GPT

Treatment response	Number of patients
Poor (0-25 % clearance)	0
Fair (26-50% clearance)	0
Good (51-75 % clearance)	0
Excellent (76-95% clearance)	0
Complete (96-100% clearance)	97 (100%)



Fig. 1. A solitary brown rectangular-shaped patch on the left zygoma area (before treatment)



Fig.2. A complete clearance of café au lait spot (after Dr. Hoon Hur's GPT)



Fig. 3. A brown reticulate patch on the right infraoribal area, right zygoma and right cheek (before treatment)



Fig. 5. Multiple brown band-like patch on the right thigh (before treatment)



Fig. 6. A complete clearance of café au lait spot (after Dr. Hoon Hur's GPT)



Fig. 7. A brown irregular-shaped patch on the right cheek (before treatment)



Fig.8. A complete clearance of café au lait spot (after Dr. Hoon Hur's GPT: 2017/11/9)



Fig. 9. There is no recurrence at 6 months follow-up (2018/4/6)



Fig. 10. A brown irregular-shaped patch on the right infraoribal area, right zygoma and right cheek (before treatment: 2015/1/17)



Fig. 11. A complete clearance of café au lait spot (after Dr. Hoon Hur's GPT: 2016/3/5)



Fig. 12. There is no recurrence at 12 months follow-up (2017/3/11)

DISCUSSION

Café au lait spot (CALS) is a benign cutaneous pigmentary disorder, presenting as a hyperpigmentedpatch with a sharp border (Shah, 2010 and Landau, 1999). There are two types of CALS in general. The common one is the non-syndromic solitary CALS. The other one is more rare and associated with genetic syndrome including neurofibromatosis type 1, McCune-Albright syndrome and tuberous sclerosis, called the multiple café au lait spots (CALSs) (Shah, 2010 and De Schepper, 2006). In non-syndromic solitary CALS, NF1 somatic mutations do not occur in the melanocytes and keratinocytes, nor in the surrounding normal skin, and the epidermal melanocytes do not have macromelanosomes (Shah, 2010 and De Schepper, 2006). Meanwhile in multiple CALSs with neurofibromatosis type1, NF1 somatic mutations can be found in the melanocytes and keratinocytes in the epidermis and fibroblasts in the dermis. NF1 somatic mutations can also be found in the surrounding normal skin. The epidermal melanocytes have macromelanosomes (Shah, 2010 and De Schepper, 2006). In non-syndromic solitary CALS, the expression of endothelin-1 is increased in the keratinocytes and the expression of stem cell factor (SCF) and hepatocyte growth factor (HGF) are increased in the fibroblasts compared to those of normal skin. The increased expression of endothelin-1, SCF and HGF lead to the activation of the melanocytes and increases melanin synthesis in the melanosomes, which cause CALS(Hattori, 2004 and Okazaki 2003 & 2005). Especially, the increase of expression of the endothelin-1 in the keratinocytes, and the increase of expression of the SCF and HGF in the fibroblasts are more higher in both multiple CALSs with neurofibromatosis type1 and normal skin with neurofibromatosis type1 when compared to those in the nonsyndromic solitary CALS. This can lead to the activation of melanocytes thus increasing the synthesis of melanin in the melanosomes which may cause multiple CALS (Hattori, 2004 and Okazaki 2003 & 2005).

As we know, melasma or PIH can occur due to the increased secretion of basic fibroblast growth factor (bFGF) from the damaged keratinocyte. However, the expression of bFGF in the keratinocytes of CALS is not increased and bFGF may not provoke CALS (Hattori, 2004 and Okazaki 2003 & 2005). A case of a giant soltary CALS was followed for 20-30 years, NF1 somatic mutations have not been found in melanocytes and keratinocytes in the epidermis and fibroblasts in the dermis (Nguyen, 2004). The development of a giant solitary CALS into neurofibromatosis was never found either (Nguyen, 2004). But if more than 6 multiple CALSs, even without neurofibromatosis, occur then the occurrence of NF1 somatic mutations may either happen or not in the epidermal melanocytes. In the case of more than 6 multiple CALS, they may start without neurofibromatosis but then eventually develop into neurofibromatosis (Shah, 2010 and De Schepper, 2006). The his to pathological findings of CALS show moderate elongation of rete ridge with increased number of melanocytes and increased melanin deposition in the epidermis, and a few melanophages in the upper dermis. CALS does not transform into a malignant lesion because there is no nerve cell (Shah, 2010 and Landau, 1999). To date, traditional laser treatments such as ruby laser, alexandrite laser and 532nm QSNL have been widely used in the treatment of CALS. However, traditional laser treatments were unsatisfactory because they caused purpurae, crusts, PIH, mottled hypopigmentation and scarring (Michel, 1997 and Polder, 2011). In particular, it is

extremely difficult to treat CALS without PIH (Michel, 1997 and Polder, 2011). There are possible several reasons that treating CALS with traditional laser therapy may end up in failure. Generally, the 532 nm wavelength of the QSNL, the 694 nm wavelength of the ruby laser, the 515-755 nm wavelength of intense pulsed lights, and the 755 nm wavelength of the alexandrite are absorbed by melanin much more than the 1064 nm wavelength of OSNL (Hur, 2016 & 2017). This higher absorbance to melanin produces laser energy that destroys epidermal melanocytes and at the same time damages surrounding keratinocytes in the lesions (Hur, 2016 & 2017). When the damaged keratinocytes secrete interleukin-1(IL-1), which stimulates keratinocytes to secrete some keratinocytic injury-induced cytokines such endothelin-1, α-melanocyte stimulating hormone (MSH), adrenocorticotropic hormone (ACTH) and prostaglandin (PGE2, PGF2α). These melanogenic cytokines activate melanocytes, thereby increasing melanin synthesis in melanosomes. For this reason, PIH occurs and CALS becomes worse (Hattori, 2004 and Okazaki 2003 & 2005). The damaged keratinocytes secrete the single-chain urokinase type plasminogen activator (sc-uPA), which converts plasminogen into plasmin. The plasmin-stimulated keratinocytes secrete a basic fibroblast growth factor (bFGF). Then melanocytes are activated by this bFGF, resulting in an increase in melanin synthesis in melanosomes, leading to PIH (Hattori, 2004 and Okazaki 2003 & 2005). However, bFGF may not cause CALS if bFGF does not increase in the lesional keratinocytes of CALS (Hur, 2016).

In the traditional laser treatments, the laser energy which is strong enough to cause purpurae and crusts, and causes damage to fibroblasts, mast cells, lymphocytes, macrophages and vascular endotheliums simultaneously. Especially, stem cell growth factor (SCF) and hepatocyte growth factor (HGF) secreted from damaged fibroblasts activate melanocytes to increase melanin synthesis in melanosomes and eventually induce PIH and exacerbate CALS (Hattori, 2004 and Okazaki 2003 & 2005). Finally, the reactive oxygen species such as free radical oxygen and peroxide or nitric oxide generated by damaged keratinocytes activate melanocytes and increase melanin synthesis in melanosomes, eventually leading to PIH and exacerbating CALS (Hattori, 2004 and Okazaki 2003 & 2005). The authors devised a new treatment using a Dr. Hoon Hur's GPT with a high fluence1064nmQSNL (Spectra Laser, Lutronic, South Korea), a spot size of 7 mm, a fluence of 2.4 J/cm², a pulse of 10 Hz and a sliding stacking technique that slowly irradiated the laser to the lesion site of CALS at intervals of one week to minimize side effects such as purpurae, crusts, PIH, mottled hypopigmentation and scarring caused by the traditional laser therapy. We think that Dr. Hoon Hur's GPT using a high fluence 1064 nm QSNL is safer and more effective than traditional CALS treatments tried so far (Hur, 2016). In previous papers, the authors also reported that Dr. Hoon Hur's GPT using a high 1064 nm QSNL is effectively treated without side effects such as PIH, mottled hypo pigmentation or scarring in various skin lesions such as café au lait spot, partial unilateral lentiginosis, Becker's nevus, Ota's nevus, Hori's nevus, congenital melanocytic nevus and Riehl'smelanosis (Hur, 2016, 2017& 2018). We think that Dr. Hoon Hur's GPT, which is performed every week continuously with minimal damage to the epidermis, induces gradual destruction of melanocytes in the epidermis or dermis and promotes the apoptotic melanocytic cell death program(Hur, 2016 & 2017). Because of the poor absorption

by epidermal melanin, Dr. Hoon Hur's GPT has adopted a wavelength of 1064nm. This mechanism of Dr. Hoon Hur's GPT using a high fluence 1064-nm QSNL is to minimize epidermal damage and destroy the melanosomes in the epidermal melanocytes, causing epidermal melanocytes to lose functions and turn into ghost cells(Hur, 2016 & 2017). The more weekly Dr. Hoon Hur's GPT using a high fluence 1064 nm OSNL is performed, the more epidermal melanocytes are destroyed and the apoptosis of epidermal melanocytes is promoted. And the dispersed melanosomes and melanins, the end product of destroyed melanocytes, are either eliminated by transepidermal elimination or by dermal melanophages through the lymphatic system (Hur, 2016 & 2017). The lesional melanocytes are progressively replaced by normal melanocytes, which migrate from the outer root sheath of hair follicles by apoptotic melanocytic cell death program and homeostasis. Finally, CALS can be completely removed without any side effects or recurrences (Hur, 2016 & 2017).In this study, all 97 patients with a solitary CALS were received 50 treatment sessions of Dr. Hoon Hur's GPT with a high fluence 1064 nm QSNL at a one-week interval with a spot size of 7 mm, a fluence of 2.4 J/cm² and a pulse rate of 10 Hz with slowly one pass by a sliding-stacking technique.

A single pass of a fluence at 2.4 J/cm² by a sliding-stacking technique is critical to minimize epidermal damage (Hur, 2016). If double passes of a fluence of 2.4 J/cm² by a slidingstacking technique were performed, the epidermal damages can be occurred. The damaged keratinocytes might have secreted the melanogenic cytokines such as endothelin-1, α-MSH, ACTH, bFGF and prostaglandin (PGE2, PGF2α), and reactive oxygen species such as free radical oxygen and peroxide or nitric oxide that could induce PIH and exacerbate CALS(Hur, 2016). In short, the end point of Dr. Hoon Hur's GPT with a high fluence 1064 nm QSNL is not to cause petechiae or purpurae, but to induce erythema only. Because Dr. Hoon Hur's GPT is less absorbed by epidermal melanin, it transmits enough energy without destroying normal background tissue, destroys epidermal melanocytes, does not cause crusts and purpurae, and prevents PIH and scarring (Hur, 2016 & 2017). However, in order to completely remove CALS without recurrences, this treatment must be treated 50 consecutive times a year. In this study, we treated all 97 patients with a solitary CALS (Fig.1,3,5,7,10) using Dr. Hoon Hur's GPT with a high fluence 1064 nm QSNL. The complete removals of the pigmented lesions were achieved without PIH and scarring in all 97 patients with a solitary CALS (Fig.2,4,6,8,11). There is no recurrence after 6-12 months of follow-up (Fig.9, 12). All patients treated with Dr. Hoon Hur's GPT using a high fluence 1064 nm QSNL were satisfied with the results.

Conclusion

In this study, CALSs were treated by Dr. Hoon Hur's GPT using a high fluence 1064 nm QSNL and were completely eliminated without side effects and recurrences. We suggest that Dr. Hoon Hur's GPT using a high fluence 1064 nm Qswitched Nd:YAG laser is a new, safe and good treatment option to expect complete clearance of CALS.

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Figure legends (CALS-HoonHur)

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