20%左旋維他命C與2%麴酸凝膠配方於黑斑病人之超聲波導入治療

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Sonophoresis with 20% L-Ascorbic Acid and 2% Kojic Acid Gel for the Melasma Patients

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We treated 17 female patients of melasma by using ultra-sonic equipment with 20% L-ascorbic acid, which contain 2% kojic acid gel. Each patient received a treatment of 15-minute sonophoresis twice weekly for 5 weeks. Regular photographs and UV photographs were taken before and after the course of treatment. The dermatologist read the result finally. All patients completed a questionnaire to evaluate the improvement of pigmented lesions, skin color, skin texture, wrinkles at the end of the treatment course. Photographs noted no significant improvement of pigmented lesions but improvement of skin texture and skin color.

No patient complained of adverse reactions during or after the treatment. Through our patients' evaluation, the satisfaction of treatment for the skin texture is better than that for pigmented lesions, skin color, and wrinkles. The method provides an alternative for people seeking better skin texture. Patients may feel facial skin color lightening if skin texture improved. Thus, it may be also an adjunctive therapy for melasma. (Dermatol Sinica 19 : 275-281, 2001)

Key words: Melasma, L-Ascorbic acid, Kojic acid, Sonophoresis

我們以超聲波導入20%左旋維他命C與2%麴酸凝膠配方，治療17位有黑斑的女性。治療前後照彩色照片及UV照片，最後由皮膚科醫師判讀結果。每位病人接受爲期5週，每週2次，每次15分鐘之超聲波導入治療。所有病人以問卷評估術後之色素斑病灶、膚色、膚質及皺紋的改善程度。照片顯示色素斑病灶無明顯改善，但膚色、膚質有改善。治療中或治療後無人出現不良反應。病人對膚質改善的滿意度優於對色素斑病灶、膚色及皺紋改善的滿意度。此法可作爲改善膚質的一種方法。膚質改善後，病人可能感覺臉部膚色較爲明亮。因此，此法或許亦可作爲黑斑治療的輔助療法。(中華皮誌19 : 275-281, 2001)

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Accepted for publication: August 22, 2001
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INTRODUCTION

Melasma continues to be a difficult problem. Although the cause is genetic, the condition is aggravated with sunlight, birth control pills and pregnancy.[1] The existence of multiple treatment modalities reflects the fact that none is uniformly effective or directly effective. The combination of blanching agents, glycolic acid peeling and broad-spectrum sunscreen are popular therapies, but the result may be disappointing or less than idea for both patients and physicians.

An inhibitory effect of ascorbic acid and kojic acid on melanogenesis has been described. Both are administrated to treat melasma patients.[2, 3]

Many methods including sonophoresis are developed to enhance the treatment effect of drugs by increasing transdermal absorption.[4, 5] L-Ascorbic acid is also used by sonophoresis recently. However, no published reports are available to review. The purpose of this study was to evaluate the improvement of the treatment of 20% L-ascorbic acid with 2% kojic acid gel by using sonophoresis on melasma patients.

MATERIALS AND METHODS

A total of 17 non-pregnant women between the ages 28 to 53 years old, Fitzpatrick skin type II to IV, with melasma were treated with 20% L-ascorbic acid with 2% kojic acid gel (formulated by liposome as the delivery system) by sonophoresis between June 2000 and August 2000. The patients discontinued other blanching agents, avoided sun exposure and used broad-spectrum sunscreen (SPF>15). After topical application of 20% L-ascorbic acid with 2% kojic acid gel, each patient received sonophoresis with an ultrasound frequency of 1.5 to 2.2MHz at an intensity of 1.5 W/cm^2 using ultra-sonic equipment. The technician conducted the sound head around the periorbital area with pulsed mode for 5 minutes and the rest of facial area with continuous mode for 10 minutes. The 15-minute sonophoresis treatment was performed twice weekly, for 5 weeks. Regular photographs and UV photographs were taken before and after the course of treatment. The dermatologist read the result finally.

All patients completed a questionnaire (Sheet-1) to evaluate the improvement of the pigmented lesions, skin color, skin texture, wrinkles at the end of the treatment course. The categories were classified as: very satisfied, satisfied, fair and not satisfied. They also were asked to grade the improvement percentage as a percentage, with intervals of 0%, 0~25%, 25~50%, 50~75%, or 75~100%. Clinical characteristics of patients including age, Fitzpatrick skin type, aggravating factors, solitary lesional size and severity, were also recorded before treatment.

RESULTS

Table-1 showed clinical characteristics of patients. Aggravation factors were sun exposure, pregnancy, insomnia, and hormone replacement therapy.

Table-2 showed improvement of pigmented lesions, skin color, skin texture, and wrinkles by dermatologist's assessment. UV Photographs noted no significant improvement of pigmented lesions (Fig. 1, Fig. 2), but regular photographs noted improved skin texture of 4 patients (Fig. 3, Fig. 4).

Table-3 showed satisfaction of treatment for the pigmented lesions, skin color, skin texture, and wrinkles according to subject's self-assessment. 3 patients (17.6%) were satisfied with the improvement of the pigmented lesions. 1 patient (5.9%) was very satisfied, 2 patients (11.8%) were satisfied with the result of the skin color improvement, and 13 patients (76.5%) had fair satisfaction. 7 patients (41.2%) were satisfied with the skin texture improvement and 8 patients (47.1%) had fair satisfaction. 5 patients (29.4%) felt fair improvement of wrinkles and 2 (11.8 %) patients were satisfied with the wrinkles improvement. The satisfaction of treatment for the skin texture is better than that for pigmented lesions, skin color, and wrinkles.

Table-4 showed improvement percentage of

melasma by the subject's self-assessment. 8 patients (47%) reported 0~25% improvement and 7 patients (41.2%) reported 25~50% improvement. 1 patient (5.9%) reported 50~75% improvement, but 1 patient (5.9%) reported no improvement.

No patient complained of adverse reactions during or after the treatment.

DISCUSSION

Ultrasound is a longitudinal sound wave with variable amplitude and a frequency above audible sound (greater than 20,000 Hz).[6] As ultrasound passes, particles will have periodic oscillations to their resting positions, with the displacement of a particle proportional to the intensity of the beam and the number of oscillations proportional to the frequency of the ultrasound waves. Since the waves are mechanical, there is also localized shear stress of the wave, which may cause structural alterations that could increase the permeability of the tissue.[7]

Sonophoresis (or phonophoresis) is defined as the transdermal application of a drug with ultrasound. It has been proposed that: 1) the radiation pressure from the ultrasound beam forces the medication away from the transducer into the target tissues;[8] 2) the heat created by the ultrasound enhances the diffusion potential of the tissue and dilates the blood vessels;[6] 3) the streaming created by the ultrasound changes cell permeability and enhances tissue diffusion;[9] 4) the sound waves increase the kinetic energy of the molecules, enabling a drug to diffuse more easily into the underlying tissue.[9] Therefore, sonophoresis is used to enhance transepidermal absorption of drugs.

Sonophoresis is commonly used by physical therapists to treat musculoskeletal injuries, wounds, and chronic inflammatory conditions.[10] It is also recently used to enhance

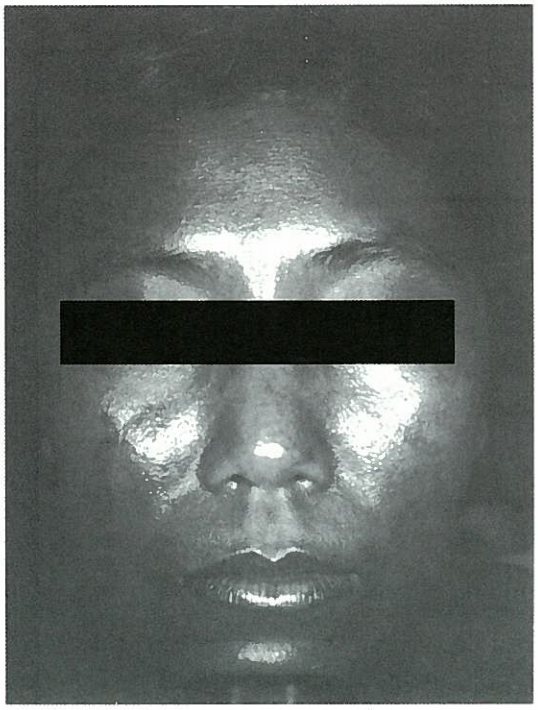

Fig. 1
UV photograph before the course of sonophoresis.

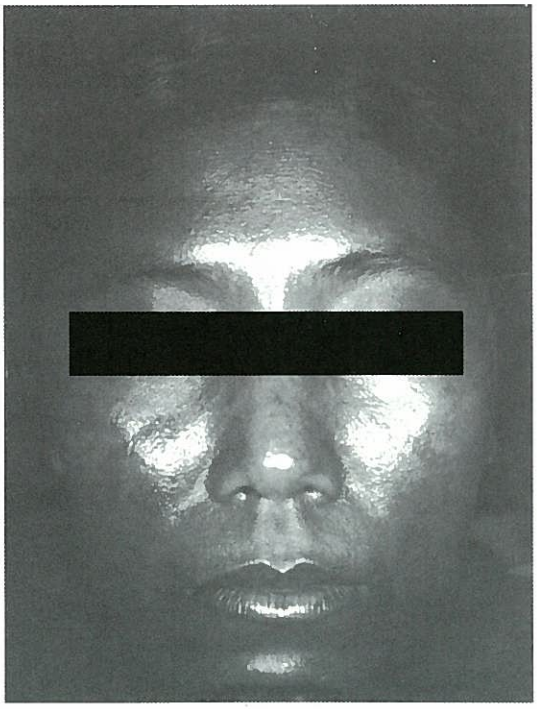

Fig. 2
UV Photograph noted no significant improvement of pigmented lesion after the course of sonophoresis.

transdermal absorption of L-ascorbic acid. However, no published reports are available to review.

The most common frequency used by physical therapists for therapeutic ultrasound is 1-3MHz.[11] The majority of sonophoresis studies used continuous mode ultrasound with an average intensity between 0 and 2 W/cm^2, high enough to produce heat.[6] Thus, we choose an ultrasound with frequency of 1.5 to 2.2MHz, and intensity of 1.5 W/cm^2. In order to avoid eyeball injury that may be caused by cavitation induced by continuous mode ultrasound, we choose pulsed mode ultrasound for periorbital area, and the rest of facial area with continuous mode ultrasound.

Application of therapeutic ultrasound (frequency: 1-3MHz, and intensity 0-2W/cm^2) enhances transdermal drug transport, but typical enhancement induced by therapeutic ultrasound is less than 10 fold.[12] Mitragotri et al. has concluded that application of low-frequency ultrasound (20 KHz, 125m W/cm^2, 100 msec pulses applied every second) enhances transdermal transport of drugs more effectively than that induced by therapeutic ultrasound.[4] So, a better selection of ultrasound parameters, such as a lower frequency, may be needed to induce a higher enhancement of transdermal drug transport by sonophoresis.

Mitragotri *et al.* has concluded that application of low-frequency ultrasound does not appear to cause any long-term damage to the barrier properties of the epidermis.[4] In addition, preliminary histological studies indicate no damage to the skin or underlying tissues of

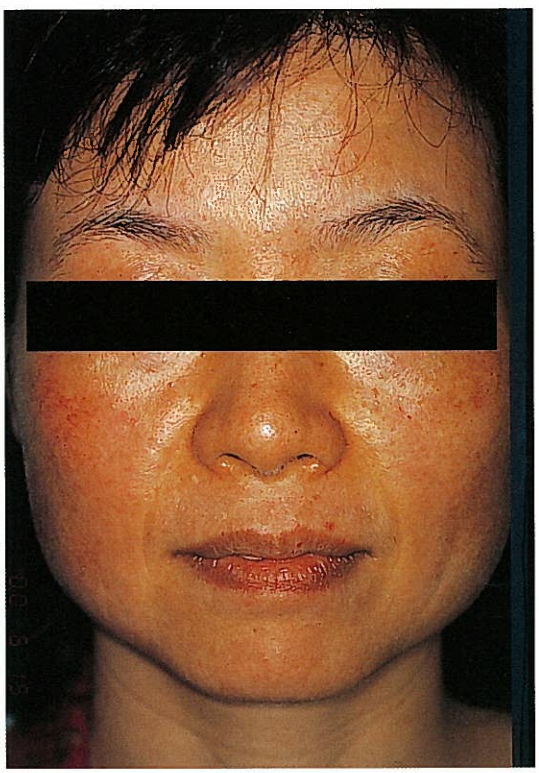

Fig. 3
Regular photograph before the course of sonophoresis.

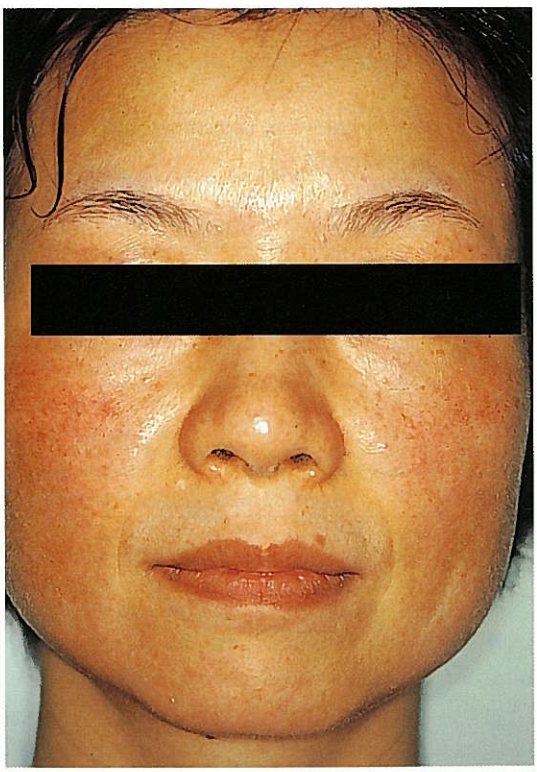

Fig. 4
After the course of sonophoresis, this patient satisfied with improvement of skin texture, but not satisfied with improvement of pigmented lesion. Better skin texture and facial color lightening were noted.

Table-1. The clinical characteristics of patients

P't	Age y/o	Skin type	Aggravating factors	Solitary lesional size	Severity
1	53	III	Insomnia	<5cm	Brown
2	48	IV	Sun exposure, insomnia	<5cm	Brown
3	40	III	Sun exposure	5~10cm	Brown
4	45	III	None	5~10cm	Dark brown
5	43	IV	Pregnancy, insomnia	<5cm	Black brown
6	33	III	Pregnancy	<5cm	Light brown
7	39	III	Sun exposure, pregnancy	<5cm	Dark brown
8	35	IV	Sun exposure, insomnia	<5cm	Brown
9	45	III	Pregnancy	<5cm	Dark brown
10	51	III	Sun exposure	5~10cm	Dark brown
11	41	III	Sun exposure, pregnancy, HRT, insomnia	5~10cm	Dark brown
12	41	III	Sun exposure	5~10cm	Dark brown
13	45	II	Sun exposure, pregnancy	<5cm	Dark brown
14	48	III	Sun exposure	<5cm	Light brown
15	48	III	Sun exposure	<5cm	Brown
16	28	III	Pregnancy	>10cm	Light brown
17	52	III	Sun exposure	5~10cm	Dark brown

HRT: hormone replacement therapy

Table 2. Improvement of pigmented lesions, skin color, skin texture, and wrinkles by dermatologist's assessment.

		Patients	
		0	(0%)
Pigmented lesions	Improved	(0%)	(100%)
	Not improved	17	(100%)
Skin color	Improved	4	(23.5%)
	Not improved	13	(76.5%)
Skin texture	Improved	4	(23.5%)
	Not improved	13	(76.5%)
Wrinkles	Improved	0	(0%)
	Not improved	17	(100%)

hairless rat exposed to low-frequency ultrasound.[4] Although no adverse reactions were found during and after our treatment by using therapeutic ultrasound, a lower frequency of ultrasound may be considered in further studies.

Our study shows a portion of the melasma patients satisfied with improvement of pigmented lesions. However, UV photographs noted no significant improvement. It may be due to improvement of dermal pigmentation, which UV camera cannot detect. Beside, regular photographs noted facial skin color lightening associated with skin texture improvement. Patients also felt facial skin color lightening if skin texture improved.

The satisfaction of treatment for the skin texture by our patients' evaluation is better than that for pigmented lesions, skin color, and

Table 3. The satisfaction of treatment for the pigmented lesions, skin color, skin texture and wrinkles according to subject's self-assessment.

		Patients	
Pigmented lesions	Not satisfied	7	(41.2%)
	Fair	7	(41.2%)
	Satisfied	3	(17.6%)
	Very satisfied	0	(0.0%)
Skin color	Not satisfied	1	(5.9%)
	Fair	13	(76.5%)
	Satisfied	2	(11.8%)
	Very satisfied	1	(5.9%)
Skin texture	Not satisfied	2	(11.8%)
	Fair	8	(47.1%)
	Satisfied	7	(41.2%)
	Very satisfied	0	(0.0%)
Wrinkles	Not satisfied	10	(58.8%)
	Fair	5	(29.4%)
	Satisfied	2	(11.8%)
	Very satisfied	0	(0.0%)

Table 4. Improvement percentage of melasma by the subject's self-assessment.

Improvement percentage	Patients	
0%	1	(5.9%)
0~25%	8	(47.1%)
25~50%	7	(41.2%)
50~75%	1	(5.9%)
75~100%	0	(0%)

wrinkles. The percentage of improvement of the subject's self-assessment varies from 0% to 75% in our study. The variation of the results indicates the different response among patients. Patient's assessment for the treatment results may also vary due to personal bias and should be taken into consideration.

The method provides an alternative for people seeking better skin texture. Patients may feel facial color lightening if skin texture improved. Thus, it may be also an adjunctive therapy for melasma.

A quantitative model should be done to predict the transdermal effect of this method in a further study.

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