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RANDOMIZATION CHALLENGES AND SUGGESTED STUDY DESIGN IN AESTHETIC, PHARMACEUTICAL AND REGENERATIVE MEDICINE

It is ideal in medical research to perform experimental (interventional) clinical studies, such as RCTs, in all clinical investigations, nonetheless, quasi-experimental and observational research can be appropriate with careful consideration of study design and potential biases in aesthetic, pharmacological, and regenerative medicine clinical setups. Selection bias, protopathic bias, attrition bias, and performance bias are examples of sources of bias that can occur in RCTs, but there is a chance that their effects could be more pronounced in quasi-experimental and observational studies because these types of studies are frequently conducted without protocols defining standardised interventions, outcomes assessments, and data recording procedures.

The most popular design for evaluating the efficacy of healthcare therapies is the randomised controlled trial, or RCT. The adoption of a randomization technique, which, when carried out correctly, assures that no participant's allocation to one treatment or another can be predicted, is the primary advantage of the RCT. In the absence of randomised controlled trials (RCTs), healthcare practitioners and policy-makers rely on non-randomised studies to provide evidence of the effectiveness of healthcare interventions. However, there is controversy over the validity of non-randomised evidence, related to the existence and magnitude of selection bias. Nevertheless, several scenarios remain under which an RCT may be unnecessary, inappropriate, impossible or inadequate. Furthermore, there must be hundreds of examples of interventions for which RCTs would be possible but have not yet been carried out, leaving the medical community to rely on non-randomised evidence. Some experts even feel that the majority of aesthetic medicine treatments cannot be subjected to RCTs under “real-world” conditions. Aesthetic techniques are rarely standardised and an inherent variation in performance exists between aesthetic practitioners. This variation is further exacerbated by the frequent need for procedural modification in response to individual circumstances. The exclusion of cases secondary to these variations introduces serious biases and may ultimately result in underpowered studies. In addition, the learning curve associated with many complex procedures may place newer techniques at a disadvantage when compared to well-established interventions. Patients also often reject the randomization process because they do not wish their treatment to be decided by chance.

Based on extensive research, there is inconsistent use of nomenclature when describing non-randomised studies, especially in the aesthetic, pharmaceuticals and regenerative medicine fields. Some taxonomies may apply different definitions to the same study designs. A proper taxonomy of study designs is needed for aesthetic clinical trial intervention for better understanding in creating the study structure. It is perturbing for beginners to comprehend the research trial design without proper taxonomy as a guide for them to conduct aesthetic medicine clinical trials.

Some of the research designs suggested for aesthetic, pharmaceuticals and regenerative medicine fields are:

Non-randomised trial/quasi-experimental study: The investigator has control over the allocation of participants to groups, but does not attempt randomisation (e.g. patient or physician preference). Differs from a 'cohort study' in that the intention is experimental rather than observational.

Historical cohort study: A variation on the traditional cohort study where the outcome from a new intervention is established for participants studied in one period and compared with those who did not receive the intervention in a previous period, i.e. participants are not studied concurrently.

Concurrent cohort study: A follow-up study that compares outcomes between participants who have received an intervention and those who have not. Participants are studied during the same (concurrent) period either prospectively or, more commonly, retrospectively.

Case-control study: Participants with and without a given outcome are identified (cases and controls respectively) and exposure to a given intervention(s) between the two groups is compared.

Before-and-after study: A comparison of outcomes from study participants before and after an intervention is introduced. The before and after measurements may be made in the same participants or different samples.

Controlled before-and-after study: A follow-up study of participants who have received an intervention and those who have not, measuring the outcome variable both at baseline and after the intervention period, comparing either final values if the groups are comparable at baseline, or change scores.

Cross-sectional study: Examination of the relationship between disease and other variables of interest as they exist in a defined population at one particular time point.

Case series: Description of several cases of intervention and outcome (no comparison with a control group).

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An Early Experience with Novuma®, A Calcium Hydroxylapatite Filler for Hand Rejuvenation

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Abstract

The aging hand is characterized by cutaneous and dermal atrophy, grooves between intermetacarpal spaces, prominent bones, tendons, and engorgement of reticular veins. Dermal fillers are a viable option available for physicians to restore the lost volume in aging hands. In this article, the use of the new calcium hydroxylapatite (CaHA; Novuma), for hand rejuvenation is reported. One-year follow-up results, dilution, and injection techniques have been described. Five female subjects with volume loss in the dorsum of their hands were enrolled in this study. A solution of 1.5 mL of Novuma mixed with 1.5 mL 2% lidocaine and a total amount of 3 mL was injected into the areolar plane between the subcutaneous layer and superficial fascia of the hand with a 25-G and ultra-thin cannula through one entry site. The injected dorsum was massaged to achieve an even hand dorsum surface without irregularities. Subjects were reviewed in controls at 1, 6 and 12 months. With a single injection, all patients were satisfied without requiring any touch-up injections afterwards. Patients and the physician were all satisfied according to the questionnaire scores in the follow-up period. Nodule or granuloma was not noted. A few adverse events such as transient oedema and ecchymoses were observed. Novuma, a % 35 CaHA-containing, filler is effective, safe, easily injectable, longlasting, and versatile option for creating youthful appearance in the aging hands.

Keywords: Calcium hydroxylapatite, hand rejuvenation, Novuma filler, aging hand

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Aging hand is another popular problem as well as facial aging. Changes in skin pigmentation, thinning of skin and loss of elasticity, soft tissue atrophy due to reduced collagen, elastin, and fat, and alterations in skin hydration are general features of hand aging. As a result of decrease in collagen content and loss of hydration, skin becomes loose, and wrinkles appear (1). Consequently, further thinning and atrophy of the hand skin results in visibility of extensor tendons and veins, and grooves between them (2). Usually, these changes result in hands to be perceived as “old”. These signs of aging are difficult to conceal, and concomitant changes in the face bothers the patients to seek treatments to reverse the signs of hand aging.

Current hand rejuvenation procedures involve topical agents, resurfacing laser and peeling procedures, sclerotherapy, fillers, and fat injections to reverse the volume loss related to fat atrophy (3). Fat injection is the best autogenous option for creating youthful hands; however, this is an invasive, donor site and anesthesia-dependent, time-consuming, and inconsistent procedure with frequent post-operative additional requirements for touch-ups (4). Dermal fillers are a viable option available for physicians to restore lost volume in aging hands. Hand rejuvenation by injectable fillers, and combinations of mesotherapy has been quite popular in the last two decades (5). CaHA filler-containing fillers have been more frequently used for the treatment of hand aging since the approval of Food and Drug Administration (FDA) for calcium hydroxylapatite treatment for this anatomical region (5,6). Hyaluronic acid, poly-L-lactic acid, polycaprolactone have all been used for hand rejuvenation with varying success and shortcomings (7,7,9). Objective of this study was to assess the safety and effectiveness of the new CaHA-containing filler, Novuma (Burgeon Biyoteknoloji ve Sanayi Tic. AŞ, Ankara, Turkey) for the correction of volume loss in the hands until twelve months after treatment. The CaHA concentration in Novuma is 35%. A 1:1

dilution of Novuma with lidocaine was used for volume restoration in the hand dorsum.

Methods

Patient population

Five female patients (aged 42 to 68, mean= 54.6) were enrolled in this study. All patients had soft tissue atrophy of the dorsum of their hands and decrease in skin texture due to hand aging. Exclusion parameters included prior soft tissue filler injections at the same sites, acute or chronic local infections, current or history of systemic collagen diseases, bleeding disorders or patients who are unable to pause stop the use of anti-coagulant drugs, Raynaud’s syndrome and other circulation disorders. Informed consent was obtained from all subjects after detailed explanation of the procedure and the follow-up protocol. The explanation involved the selection of Novuma CaHA for hand rejuvenation. Photographs were taken before (baseline), immediately after the treatment and after one year that involved both hands and each hand separately.

Treatment Protocol

Each Novuma syringe (1.5 mL) was mixed with 5-cc injector containing 1.5 mL of 2% Lidocaine (Jetokain Simplex 2-mL ampul, Adeka İlaç San. ve Tic., İstanbul, Turkey). To prepare a homogenous solution, the lidocaine was first withdrawn into the 5-mL syringe. The lidocaine-containing syringe was then connected to the CaHA syringe using the special Luer-lock connector (Novuma, Burgeon Biyoteknoloji ve San. Tic. AŞ, Ankara, Turkey). After attachment, pressing the CaHA in the syringe forced the material into the 5-mL syringe and by back-and-forth movements at least 15-20 times mixed the lidocaine with CaHA. We think that at least 15 passes are good enough to create an adequate mixture without compromising the rheology of the product. The CaHA was then withdrawn back into the 5-mL syringe and injected into the areolar plane between the subcutaneous layer and superficial

fascia of the hand using a 25-gauge and 5-cm TECH Co. Ltd., South Korea).

Before each procedure, the skin was prepped with a chlorhexidine-containing antiseptic and one central- dorsal hole was used to inject CaHA with a fanning technique. In every subject, 1.5 mL Novuma: 1.5 Lidocaine mixed solution was injected per hand. An entry hole for cannula insertion was opened with an 18-G needle in the middle of dorsal wrist crease. A special attention was paid to the dorsal vein anatomy to avoid unnecessary bleeding. The distant border for injection was the horizontal line connecting the metacarpophalangeal joints. The skin was lifted a little to pass underneath the vessels and the grooves between the tendons and engorged veins were retrogradely injected with CaHA. After completing the soft tissue augmentation, skin was gently massaged to spread the material evenly in all the treated areas. The massaging was done several times until optimal distribution is visible in the hand dorsum. Patients are advised to wear non-tight cloth gloves in the following three days and keep

long nano (ultra-thin) cannula (JBP, FEEL

their hands elevated, if possible. Table 1 gives a step-by-step and brief explanation of hand injection procedure.

Digital photographs were taken pre-injection and immediately after injection, using standard photographic setup. The patients were followed up in the post-operative period for ecchymosis, swelling, erythema, filler leak, infection, keloid formation, hypertrophic scarring, pigmentation problems, nodules and other side effects. All the treated patients were seen in the follow-up period in the office after six and twelve months. Photographs were taken at twelve months.

At each follow-up time-points, the injecting physician evaluated the degree of improvement and standardized photographs were taken (Figure 1 and 2). A questionnaire was also filled at each visit concerning the possible adverse effect. Both physician and patient were asked to evaluate the hand ((appearance) contour and/or volume replacement) by Novuma® filler using Patient

Table 1: Steps of CaHA injection for treatment of the aging hand in the office

- 1 Identifying the areas of treatment at the dorsum of the hand. The space that is injected is delineated laterally by the fifth metacarpal bone, medially by the second metacarpal bone, proximally by the dorsal wrist crease, and distally by the metacarpophalangeal joints.
- 2 Marking the outlines of injection area by the skin marker
- 3 Mixing 1,5-mL of CaHA with lidocaine, using a Luer-Lock connector for the CaHA syringe and a 5-mL syringe containing 1.5 mL of 2% plain lidocaine
- 4 Insertion of an 18-G needle to create an entry hole for the cannula at the middle of the dorsal wrist crease
- 5 Pinching and lifting the skin over the hand dorsum with the non-injecting hand to facilitate separation of the skin from vascular and tendinous structures at the entry hole
- 6 Linear injection of CaHA-lidocaine mixture into areolar plane between the subcutaneous layer and superficial fascia of the hand using a 25-gauge, 1.5-inch cannula.
- 7 Gently massaging the injection site until the filler is evenly spread
- 8 Advising patients to wear non-tight cloth gloves in the following 3 days and keep their hands elevated, if possible
- 9 Scheduling follow-up with patient in the office at six and twelve months



Figure 1: A 48-year-old patient, before treatment (1A) and one year after treatment (1B). Hand augmentation with 3 cc of 1:1 diluted CaHA filler with lidocaine, using a 25-gauge and 5-cm long nano cannula



Figure 2: A 58-year-old patient, before treatment (2A) and one year after treatment (2B). Hand augmentation with 3 cc of 1:1 diluted CaHA filler with lidocaine, using a 25-gauge and 5-cm long nano cannula

Satisfaction Scale a sixth and twelfth months. Satisfaction was self-reported using the following scale: 1=unsatisfactory, 2= poor, 3= satisfactory, 4= very good, and 5= excellent.

Results

Cosmetic results

Five patients were all followed up in the study until twelve months. One injection session was done in all the patients and no touch-up injections of CaHA were deemed as necessary. One syringe of 1.5-mL Novuma was mixed with 1.5 mL of lidocaine in 1:1 dilution to inject a total of 3 mL per hand was very pleasing for the youthful appearance after one year.

Adverse events

Relevant data about the adverse events just after the treatment and at each follow-up visit was collected. The staff nurse also proceeded with the follow-up of the patients through telephone calls about any adverse events. No serious complications were observed, and the post-injection period was uneventful. None of the patients had any discomfort after the procedure; however, a painkiller, usually of paracetamol type was prescribed after the hand rejuvenation procedures. A mild swelling can be considered as standard after soft tissue augmentations in the hand dorsum. The swelling lasted for three to seven days and resolved without any further medication and intervention, apart from Arnica montana cream massaging twice a day. Ecchymosis in small patches were observed,

beginning from the completion of injection was one in one patient. These ecchymosis islands resolved after one week with hand elevation, intermittent application of ice packs and application of Arnica montana cream to ecchymotic patches twice a day on the hand dorsum. There were no any other adverse events. No papules, nodules or granulomas were noted or reported.

Efficacy Rating by Treating Surgeon and by patient

Efficacy ratings were performed for all (n=5) patients. All patients were evaluated during the six-month follow-up visit. The patients' mean ratings of the appearance of the hands was 4.8. The physician's mean rating for the appearance of the hands at six-months was also 4.8. The scoring at twelve months after hand rejuvenation was also evaluated with the same scale. The patients' mean ratings of the appearance of the hands was 4.4. The physician's mean rating for the appearance of the hands at six months was still 4.6.

Discussion

Results of this study showed that Novuma, %35 CaHA-containing filler, results in significant improvement in the appearance of hands. Patient and physician scores were assessed using the Patient Satisfaction Scale. Novuma was delivered as a single injection, and 1:1 diluted with lidocaine. Overall appearance of the hand dorsum was satisfactory for the patients and the physician immediately and through the follow-up period. Several previous authors have reported marginal decrease in satisfaction scores both by the subjects and the physician near the end of the follow-up (6). We also observed a similar but minor decline in the evaluation scores at one year after the initial treatment, though scores were still high. The safety profile was good, and no serious adverse events were encountered. Novuma was an effective therapy for hand rejuvenation with

comparable success. The treatment was well tolerated by patients.

Since 2015, calcium hydroxyapatite is currently the only dermal filler approved by the FDA for hand rejuvenation. However, several other new fillers such as hyaluronic acid (HA), and poly-L-lactic acid (PLLA) for volume restoration of the hands has been reported in several articles (9,10). The treatment of hands with PLLA has been shown to result in marked aesthetic improvements lasting more than one year (2). However, multiple treatment sessions with varying dilution ratios may be required. Furthermore, PLLA is reported to have a higher potential for complications, such as nodule formation (2). Studies reporting the use of HA fillers for hands also show improved results within one year after the treatment (2,9). Use of HA fillers for the hands usually do not display the same longevity as CaHA-containing fillers. Aesthetic improvement in hands usually decline after six months with HA fillers (1). Thus, among available fillers for improving hand volume and texture, only PLLA can be compared with CaHA for the maintenance of the improvement over one year.

Since the first report by Busso et al in 2007 (11), there have been at least eight articles, demonstrating the efficacy of CaHA for aesthetic improvement of the hands in many patients. However, there is still no consensus on the number of entry sites, selection of injection techniques, use of cannula or needle, and dilution ratios (1). We have been using 25-G cannula through one entry site at the dorsal wrist crease without any adverse events. This technique can be performed with reproducible good results in the treatment of hand aging. Our technique has been given in detail in this article. We have one-year follow-up results of a limited number of patients, but several authors have reported the durability of results with CaHA, ranging from one to two years (3,12,13).

Safety profile in this study was favorable in all control time-points, with no serious adverse events. However, the number of patients enrolled in this study is limited and further studies with larger number of patients will be more meaningful to reach solutions. Most adverse events were related to the injection technique and were mild in severity. Mild oedema and erythema can be considered as routine in the first few days. Injection volume and dilution ratios can also be an important determinant in the incidence of adverse events. None of the patients in this study complained of any functional limitation for three days after the 1:1 diluted injection of CaHA. In the first few days, patients were given gloves to wear for decreasing the procedure-related oedema and possible ecchymosis. Thereby, an even distribution of diluted filler was achieved in the hand.

Several factors limit to draw generalizable inferences from the current study. The number of patients was small, making it unlikely that probability of adverse events is very low; one-year follow-up period might also be insufficient to observe any late-appearing safety concerns. The study was open-label and not active- or sham-controlled; thus, the potential for assessment bias cannot be ruled out. The study population lacked men, young patients, and people from different Fitzpatrick types. Furthermore, choice of techniques, dilution ratio, and methods of delivery, either through cannula or needle, may affect the outcomes as well as the experience level of the injector.

Conclusion

Novuma, CaHA filler, was safe and well-tolerated in all the subjects. Mixing lidocaine with CaHA was an easy and suitable anesthetic modality that enabled pain-free hand injections. The product was found to be safe, easily injectable, and devoid of any serious adverse events. Clinical improvement was still visible after twelve months after single injection. In

addition, enhancement of hand volume was immediate secondary to the rheological composition of the filler with sustaining results because of collagen stimulation. Patient satisfaction was high after initial injection and remained so until one-year time point, despite a minor decrease.

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The Efficacy of Combination Topical Hydroquinone with Oral Tranexamic Acid, Q-Switched Laser Monotherapy and the Combination of Such in the treatment of Melasma Among Malaysian Males and Females with Fitzpatrick Skin Type III-IV

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Abstract

Melasma is a skin condition typically occurring in the Asian population amongst the middle-aged group. Hence, this study aimed to evaluate the efficacy of oral tranexamic acid and topical hydroquinone combination therapy, monotherapy with the 1064nm Q-switched Nd: YAG laser, and the combination of both therapies in treating melasma among Malaysian males and females with Fitzpatrick skin types III-IV. A quasi-experimental, unblinded study was done among 30 participants. Participants were divided into three groups and treated over three months. Group 1 received oral Tranexamic acid with 4% topical hydroquinone; Group 2 was treated with laser only, and Group 3 was treated with a combination of those three modalities. The researcher collected the modified Melasma Area and Severity Index (mMASI) score and image pigmentation score using the JANUS-III machine at each follow-up. The mean mMASI score was 4.80 ± 3.17 for Group 1, 4.96 ± 2.10 for Group 2, and 7.43 ± 4.15 for Group 3. Meanwhile, the mean UV spot for Group 1 was -1.22 ± 16.75 , 2.09 ± 11.03 for Group 2 and -11.27 ± 5.83 for Group 3 respectively. The mean PL spots were 12.00 ± 12.073 for Group 1, 21.82 ± 10.19 for Group 2 and 9.36 ± 7.88 for Group 3. Both mean mMASI score and mean UV spot showed significant improvement after three months of treatment with a p-value < 0.05 . However, the mean PL spot showed the most significant improvement with a p-value < 0.05 . The study found that 1064nm Q-switched Nd: YAG laser monotherapy is a better treatment in treating melasma among Malaysian with Fitzpatrick skin types III-IV.

Keywords: Melasma, oral tranexamic acid, topical Hydroquinone, Q-switched Nd: YAG laser

Melasma is a common hyperpigmentation condition that mainly affects women of reproductive age, commonly occurring on the face [1]. This chronic condition often relapses, causes great emotional suffering, and negatively impacts the quality of life [2]. It is a condition that can only be managed but not cured completely [1]. Melasma affects people of all ethnicities. However, it occurs most commonly in Asian and Hispanic females [3]. The incidence of melasma in Southeast Asia was 0.25% to 4% of patients seen in dermatology institutes, peak incidence at age 30 to 44 years. A survey conducted at a dermatology clinic in Thailand found that the prevalence of melasma was as high as 40% in women and 20% in men. Melasma was estimated to affect 0.98 percent of the population in Indonesia and 4 percent of the people in Malaysia [4]. The prevalence of melasma in Southeast Asia is high due to the tropical climate with high sun exposure. Furthermore, Asians' lack of understanding about applying sunscreen leads to the development of melasma in the population [5].

There are various treatment options available for melasma, such as a combination of topical agents such as hydroquinone and chemical peeling agents where it stops the transfer of melanin pigment produced onto the surface of the dermal layer by a specific transporter. Besides that, antioxidants such as tranexamic acid play a vital role in combating melasma and stopping tyrosine conversion [6]. In clinic settings, the Q-switched Nd: YAG laser 1064 nm with specific fluence is widely used as the primary treatment for melasma [7]. Furthermore, combining this laser with topical agents and antioxidants is suggestive of good outcomes; however, possibly minimal to moderate side effects might happen [8].

Many studies have been done to evaluate the treatment of melasma using various approaches [9,10,11]. A survey by Nahla S. et al. showed that oral tranexamic acid and topical hydroquinone are more effective than

hydroquinone alone in treating melasma [12]. Nevertheless, there is a scarcity of studies on the efficacy of dual Therapy of topical 4% hydroquinone and oral tranexamic acid versus Q-switched Nd: YAG laser monotherapy versus a combination of them for melasma. Moreover, study findings on these treatment options were even scarce among Asian populations with Fitzpatrick skin type III-IV, such as in Malaysia. Hence, this study aims to determine the efficacy of these treatment options: topical 4% hydroquinone and oral tranexamic acid, Q-switched Nd: YAG laser monotherapy, and the combination of such for the treatment of melasma among Malaysian males and females with Fitzpatrick skin type III-IV. This study's findings may help establish the best treatment option for melasma among Malaysian males and females with Fitzpatrick skin type III-IV.

Methodology

This study was conducted as a quasi-experimental, unblinded study. The participants were assigned systematically into three groups. Group 1 received oral antioxidant tranexamic acid 250 mg twice daily and topical hydroquinone at a 4 percent concentration. Group 2 received Q-switched Nd: YAG (1064 nm) laser monotherapy, and Group 3 received combination therapy using all available modalities. Participants were enrolled in the study from July till December 2021. Adult Malaysians between the ages of 40 and 55 who had hyperpigmented lesions according to the modified melasma area and severity index (mMASI) score on their faces and had Fitzpatrick skin types III-IV were eligible to participate in this study. An mMASI score was determined by two researchers who were the clinician treating the patients in this study. Patients were excluded from the study if they were pregnant or lactating, taking oral contraception, had an active skin infection, had used laser treatment or similar treatments with depigmentation properties within the last four weeks before the study, had used oral retinoid or

other photosensitizing drugs such as nonsteroidal anti-inflammatory drugs, tetracycline, phenytoin, and carbamazepine, had contraindications or known allergies or adverse event, venous or arterial thromboembolic diseases or active thromboembolic diseases or chronic kidney disease patients.

The required minimum sample size for the study was 35, as calculated based on the resource equation approach for the independent t-test²². The patients were briefed about the study. Upon agreement, they were asked to sign the informed consent form to allow their demographic, lifestyle, clinical data, imaging results, and face photos to be used for research and publication purposes. Patients were informed that their participation was voluntary and that they could withdraw from the study at any time without risk to their other treatment or penalty. Patients did not receive any additional incentive besides the treatments they provided at free-of-charge.

Follow-ups were done at 0, 30, 60, and 90 days. For the second treatment arm, laser treatments were provided once a month. Demographic and lifestyle data such as age, gender, ethnicity, smoking status, the average duration of sun exposure, and clinical data, for example, Fitzpatrick skin type, health condition, medical, medication, and allergy history, modified Melasma Area, and Severity Index (mMASI) score that had been validated [8], image pigmentation score using JANUS-III and patient's satisfaction score were collected at baseline and every follow-up accordingly. The modified MASI (mMASI) score, as the subjective assessment of the total area of involvement and darkness of melasma, is recognized as a reliable tool in the analysis of melasma [16]. The mean mMASI scores from all three treatment groups were assessed by comparing baseline reading (visit 1) and post-treatment (visit four). In the Janus-III system, three separate light sources are used with a high-resolution digital camera (normal, polarized

(PL), and ultraviolet (UV) lights. It helps to evaluate the overall skin characteristic, including skin color, pores, sebum, porphyrin, and skin pigmentation. Various skin measurement devices have different measurement principles and algorithms for skin features. A previous study proved that the measured value of facial characteristics using the Janus-III system was highly associated with those made by a dermatologist [13]. They acquired the most accurate and similar data for pigmented areas since the measurement of the machine was based on high-resolution photographs, even with limited sample size [13].

Topical 4% hydroquinone of Melashine® and oral tranexamic acid 250mg bd (Transamine®) were used in treatment arm groups (1) and (3). The patients were instructed to use the topical agent every night on the melasma skin. Q-switched Nd: YAG (1064 nm) using Cosjet ATR® was utilized for laser therapy. Data were analyzed descriptively and inferentially using Excel and SPSS (Version 27, IBM Corp, New York, NY). Demographic data and patient satisfaction scores were presented as frequency, percentage, mean and standard deviation (SD). Inferential analysis was done using ANOVA to compare the pigmentation mMASI score and imaging analysis from JANUS-III, which is the UV spot and PL spot between the three groups. The before and after intervention score was compared using paired t-test. A *p*-value of <0.05 was considered a statistically significant level. The ethical approval of this study was obtained from MAHSA University Ethic Committee (RMC/EC56/2021). The researchers adhered to the principle of the Declaration of Helsinki and Malaysia Good Clinical Practice Guidelines. Only the principal investigator and research team members have access to the data. Data management was kept confidential on a protected computer for up to 2 years. Patients' personal information was kept confidential and anonymous and presented collectively so that

nobody would be able to identify them individually.

Results

A total of 30 participants were included in the study with nine participants in Group 1, 11 participants in Group 2, and 10 in Group 3. The mean age and standard deviation (SD) of patients in Groups 1, 2, and 3 were 50.44 ± 9.07 , 49.82 ± 7.48 and 47.91 ± 7.30 , respectively. In the study, female and Malay patients predominate in all three groups. The average sun exposure was reported to be higher in Group 2 with a mean of 4.36 ± 3.17 , followed by Group 3 with 3.09 ± 2.63 and Group 1 with 2.78 ± 3.38 to be the lowest. Amongst all groups, Group 2 has the highest frequency of sunscreen usage with a mean of 2.18 ± 1.54 . The mMASI baseline score was highest in Group 3 with the mean of 7.43 ± 4.15 , followed by 4.96 ± 2.10 in Group 2 and 4.80 ± 3.17 in Group 1. The mean for the UV Spot baseline shows the highest score referring to improvement in Group 3 which was -11.27 ± 5.83 followed by Group 1 which was -1.22 ± 6.75 and Group 2 which was 2.09 ± 11.03 . One way ANOVA test revealed that there were significant differences in PL spot baseline, $F(2,28) = 4.64$, p -value = 0.02, and UV spot baseline, $F(2,28) = 3.88$, p -value = 0.03, across the three groups. The post hoc test revealed a significant difference in PL spot baseline between group 2 (21.82 ± 10.19) and group 3 (9.36 ± 7.88). Similarly, for the UV spot baseline, there was a significant difference between group 2 (2.09 ± 11.03) and group 3 (-11.27 ± 5.83).

The pre and post treatments effectiveness were compared and analyzed for all three groups. All the treatment plan groups showed significant improvement in mMASI score with a p -value of < 0.05 . The largest mean difference (Standard Error, SE) in mMASI score pre- and post-intervention was seen in Group 3 with the value of -6.72 (SE = 3.36), followed by Group 1 with a mean difference of -5.23 (SE = 2.61) and Group 2 with a mean difference of -

3.55 and SE of 1.78. Regarding the UV spot outcomes, only Group 2 significantly improved melasma condition pre-post intervention with a mean difference of 16.63 and SE of 8.31 ($p = 0.005$). When mean PL spot outcomes were evaluated, a similar pattern was found. Only Group 2 had significant improvement pre- and post-intervention ($p = 0.001$) with a mean difference of 19.13 and SE of 9.56. Groups 1 and 3 did not report a significant improvement in mean UV spot and mean PL spot outcomes pre- and post-intervention. Table 2 summarizes pre-post melasma treatment efficacy for the different treatment types.

When treatment outcomes in each visit were evaluated, all measured outcomes reported a significant difference within groups ($p < 0.05$). However, only the mMASI score showed a significant difference between the groups ($p < 0.005$). In Group 1, the mean difference of mMASI score during the second visit was -2.22 (SE = 1.1), and this was further reduced in visit 3 with a mean of -0.47 (SE = 0.24). However, the score was increased in visit 4 with a mean of 1.24 (SE = 0.62). In Group 2, where patients received laser treatment as monotherapy, there was a continuous reduction in the mean difference mMASI scores from visits 2 to 4, which were -2.43 (SE = 1.22), -1.1 (SE = 0.55), and -0.02 (SE = 0.01). Among patients receiving combination treatment for Group 3, the mean difference of mMASI score at visit two was -3.12 (SE = 1.56), followed by -1.02 (SE = 0.51) in visit 3 to -2.58 (SE = 1.29) in visit 4.

For the PL spot outcomes, the mean difference in Group 1 between visit 2 and 1 was -2.6 (SE = 1.3), visit 3 and 2 of -0.8 (SE = 0.4), and a marked increase in score in the final visit with a mean difference of 3.4 (SE=1.7). for the laser treatment group, Group 2, the mean difference of PL spot during visits 2 to 1 was -2.75 (SE = 1.38). The result was further improved in visits 3 and 4 with mean differences of -1.13 (SE = 0.57) and -15.5 (SE = 7.63), respectively. In Group 3, the mean difference in

Table 1: Sociodemographic Comparisons for monotherapy, dual therapy and triple Therapy of participants (n=30)

Variables	Topical Hydroquinone + Oral Tranexamic Acid Dual Therapy (n=9) (n (%), Mean \pm SD)	Q-switched Nd: YAG Laser Monotherapy (n 11) (n (%), Mean \pm SD)	Topical Hydroquinone + Oral Tranexamic Acid + Q-switched Nd: YAG Laser Triple Therapy (n=10) (n %, Mean \pm SD)	p-value
Age	50.44 \pm 9.07	47.91 \pm 7.30	49.82 \pm 7.48	0.75
Gender				0.39
Male	0 (0)	0 (0)	1 (9.1)	
Female	9 (100)	11 (100)	10 (90.9)	
Ethnicity				0.39
Malay	6 (66.7)	10 (90.9)	8 (72.7)	
Chinese	0 (0)	0 (0)	0 (0)	
Indian	3 (33.3)	1 (9.1)	3 (37.3)	
Others	0 (0)	0 (0)	0 (0)	
Average sun exposure (hours)	2.78 \pm 3.38	4.36 \pm 3.17	3.09 \pm 2.63	0.47
Frequency of sunscreen usage	1.00 \pm 0.87	2.18 \pm 1.54	1.64 \pm 1.12	0.12
mMASI baseline	4.80 \pm 3.17	4.96 \pm 2.10	7.43 \pm 4.15	0.13
PL Spot Baseline	12.00 \pm 12.073	21.82 \pm 10.19*	9.36 \pm 7.88*	0.02*
UV Spot Baseline	-1.22 \pm 16.75	2.09 \pm 11.03*	-11.27 \pm 5.83*	0.03*

*Significant at 0.05

PL spot outcomes in visits 2 to 1 was 3.33 (SE = 1.67), -2.33 (SE = 1.17) for visits 3 to 2, and a slight increment in score in visits 4 to 3 with a mean difference of -3.67 (SE = 1.84).

As for the UV spot outcomes, the mean difference of score for Group 1 between visits 2 to 1 was -3.6 (SE = 1.8), 3.2 (SE = 1.8) for visits 3 to 2, and subsequently reduced slightly in the visit 4 to 3 with a mean of 0.6 (SE = 0.3). In Group 2, during visits 3 to 2 with a mean of 0.88

(SE=0.44) and the markedly increased during visit 4 to 3 with a mean of 17.13 (SE=9.07). In Group 3, mean difference of the UV spot score between visits 2 to 1 was -13.93 (SE = 3.67), with a marked reduction in visits 3 to 2 with a mean difference score of -0.5 (SE = 0.44). The score was further increased in visit 4 with a mean difference of 2.17 (SE = 1.09).

Table 3 summarizes the mean differences of mMASI, UV PL spots and UV spot outcomes for each intervention visit for the three treatment

Table 2: The mean difference of participants' mMASI, PL spots, and UV spots among three treatment regimens

Treatment Regimen	Topical Hydroquinone + Oral Tranexamic Acid Dual Therapy (n=9)		p-value	Q-switched Nd:YAG Laser Monotherapy (n=11)		p-value	Topical hydroquinone + Oral Tranexamic Acid + Q-switched Nd:YAG Laser Triple Therapy (n=10)		p-value
	Pre	Post		Pre	Post		Pre	Post	
Mean mMASI	4.57 ± 3.60	-0.66 ± 0.49	0.02*	4.61 ± 0.72	1.06 ± 0.72	0.01*	8.47 ± 4.65	1.75 ± 0.74	0.01*
Mean UV Spot	3.20 ± 14.36	2.20 ± 17.33	0.88	1.00 ± 10.80	17.63 ± 16.71	0.01*	-13.33 ± 6.65	-4.33 ± 21.23	0.24
Mean PL Spot	14.20 ± 7.19	14.20 ± 10.31	1.00	22.13 ± 10.80	3.00 ± 12.31	0.00*	9.17 ± 8.18	6.50 ± 8.67	0.27

modalities.

Discussion

Melasma is a chronic skin problem commonly happening among Asian women. Although there are numerous melasma treatment options, there is no "gold standard", which presents a dilemma for aestheticians and dermatologists. In this study, a total of 30 patients were recruited to the three treatment arms, with the majority of the patients included being female. This could be because the melasma problem was reported to be more common among females than males [14]. Malays and Indians have a higher number seeking treatment related to melasma in this study because they tend to have darker skin color, which has a higher risk of developing skin pigmentation problems than Chinese and others [24]. Since the patients were assigned to follow their specific treatment modalities, blinding was impossible to be done in this study.

Hydroquinone, tranexamic acid and Q-switched Nd: YAG laser were three treatment modalities used in this study. Hydroquinone

(used in treatment arms 1 and 3) is the most popular depigmenting agent used worldwide in treating melasma, especially of the epidermal [23]. Tranexamic acid (used in treatment arms 1 and 3) is the first systemic Therapy that has demonstrated efficacy for melasma in Asian skin over a short duration of treatment (8–12 weeks) besides its other advantages, such as being easy to administer and safe with few, reversible, mild side effects [12]. While Q-switched Nd: YAG laser (used in treatment arms 2 and 3) has been the most effective among Qs lasers, especially with the use of sub photo thermolytic fluencies to reduce side effects for the treatment of melasma [15]. A randomized, controlled, double-blind study has suggested that oral tranexamic acid in combination with topical hydroquinone significantly improves melasma [16].

Table 3: The mean difference of mMASI, PL, and UV spot for each visit (n=30)

	Topical Hydroquinone + Oral Tranexamic Acid Dual Therapy		Q-switched Nd: YAG Laser Monotherapy		Topical hydroquinone + Oral Tranexamic Acid + Q-switched Nd: YAG Laser Triple Therapy		Between Group F (p)	Within Group F (p)	Interaction (p)
	Mean difference	SE	Mean difference	SE	Mean difference	SE			
mMASI							4.65 (0.02)	32.27 (<0.001) *	1.55 (0.023) *
Visit 2-1	-2.22	1.10	-2.43	1.22	-3.12	1.56			
Visit 3-2	-0.47	0.24	-1.11	0.55	-1.02	0.51			
Visit 4-3	-1.24	0.62	-0.02	0.01	-2.58	1.29			
PL Spot							0.77 (0.48)	9.71 (0.001) *	8.20 (<0.001) *
Visit 2-1	-2.6	1.3	-2.75	1.38	3.33	1.67			
Visit 3-2	-0.8	0.4	-1.13	0.57	-2.33	1.17			
Visit 4-3	3.4	1.7	-15.5	7.63	-3.67	1.84			
UV Spot							1.63 (0.23)	5.11 (0.01) *	3.45 (0.02) *
Visit 2-1	-3.6	1.8	-0.62	0.31	-13.93	3.67			
Visit 3-2	3.2	1.6	-0.88	0.44	-0.5	0.44			
Visit 4-3	-0.6	0.3	17.13	9.07	2.17	1.09			

This study noted that the mean mMASI, mean UV spot, and mean PL spot showed the most significant improvement with a p-value of <0.005, <0.005, and <0.001, respectively. After three months of total study duration, there was a significant difference within groups ($p < 0.05$); however, only the mMASI score shows a significant difference between the groups ($p < 0.005$). Noted in the oral treatment group, there was an increase in the mean PL spot during the 4th visit, which was due to non-adherence to the sunscreen, as stated by the respondents after further questioning. Otherwise, the mean for the mMASI and UV spot showed a better outcome. This study showed that Q-switched Nd: YAG laser significantly reduced the mean mMASI score among melasma patients ($p=0.005$). Other therapies did not improve mean mMASI scores among melasma patients. This finding was similar to a previous study that showed a significant reduction in mean mMASI score after treatment with a Q-switched Nd: YAG laser [17].

The resulting data showed that only Q-switched Nd:YAG laser monotherapy significantly reduced the mean UV spot score ($p=0.005$) and the PL spot score ($p=0.005$).

From our data, the Q-switched Nd: YAG laser monotherapy had shown a greater efficacy for treating melasma than the combination of topical 4% hydroquinone and oral antioxidant tranexamic acid dual therapy and the combination therapy with all triple treatment modalities. This contradicted a previous study suggesting that combining topical hydroquinone and oral tranexamic acid dual therapy was associated with more significant improvement than oral tranexamic acid combined with Q-switched Nd: YAG laser dual therapy [18]. However, the study did not evaluate the effect of triple Therapy. Our finding was also contradicted by a systematic review by Neagu et al. that showed that combination treatments (combining oral treatment, micro needling, chemical peelings,

topical creams, or lasers) had been proved to be the best solution, either in double or triple combinations [19]. A reason to explain this contradiction was due to our study location. Malaysia is located near the equator line since sunlight strikes the Earth most directly at the equator, UV strength, at its highest intensity level. When combined with the possibility that the patients in Group 3 who received the triple Therapy developed dehydrated skin compared to the rest, this location factor explained the slower progress of melasma treatment in Group 3 patients.

Our finding was similar to a previous study by Vachimaron et al. that studied the efficacy of laser alone compared to a combination of laser and glycolic acid peels. They reported temporary improvement on both sides, but the side effects, such as post-inflammatory hyperpigmentation, were more common on the side treated with a combination protocol [20]. The strength of our study was its quasi-experimental design that mimicked an experiment, provided a high level of evidence, and was less expensive. Our study evaluated the real-world efficacy of an intervention implemented by clinicians rather than the effectiveness of an intervention implemented by research staff under research conditions. Another strength of this study was that we used two types of melasma assessment tools: subjective-based, referring to the mMASI score, and objective-based, referring to the Janus-III system. By having these two assessment tools, the results were more reliable as another captured the skin conditions that were not captured by one assessment tool.

While conducting this study, we encountered various limitations. Because the study was conducted during the pandemic of covid-19, we could not acquire a significant sample size. As a result, we could not gather all the participants in one location and had to locate some of them in separate locations. For various reasons, some of our patients failed to follow up during subsequent sessions. Conflict arose in

the first group when the patients opted not to come because there was concern about taking the oral drug for three months after reading about the misconception risks on the internet. The patients' compliance with everyday skincare routines, such as sunscreen usage at home, was one element we could not avoid. Aside from that, we also had no control over the patient's working environment; due to the difference in the working environment, some of them may be exposed to the sunlight for more than 5 hours a day which potentially disturbed the progress of existing pigment disruption. Further research needs to be done to study the rate of recurrence and rebound of melasma after all three treatments. There is also a need for another study using larger sample size.

Conclusion

The Q-switched Nd: YAG laser monotherapy is superior to the combination of topical 4% hydroquinone and oral antioxidant tranexamic acid dual therapy and the combination therapy with all triple treatment modalities in the treatment of melasma in patients with Fitzpatrick skin type III-IV. Thus, we suggest that the Q-switched Nd: YAG laser monotherapy should be considered the first treatment option in treating melasma in this population.

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Conflict Of Interest

There is no conflict of interest reported in this study.

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Therapeutic Efficacy of RuVY Touch (Ruby-like Versatile YAG) Q-Switched 660nm Wavelength Treatment on Ephelides (Freckles): A Case Report

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Abstract

Ephelides is a common pigmentation characteristic observed in both Asians and Caucasians which has become a concerning cosmetic problem. We herein present a case of 24 years old Fitzpatrick type III gentleman with more than 10 years of ephelides receiving 8 sessions of Q-switched RuVY Touch 660nm wavelength without additional topical or oral medicine.

RuVY Touch treatment has a relatively weaker absorption rate by hemoglobin, lower the risk of vascular damage and associated post-inflammatory dyspigmentation. However, the absorption in melanin is still high, although slightly lower absorption compared with the 532nm beam. Hence, the safety level for treatment of discrete epidermal lesions is increased, which means faster healing and less unsightly erythema and crusting, which is an advantage for the patient.

In conclusion, our data suggest that RuVY Touch treatment, utilizing a converted wavelength of 660 nm, can be effectively used for the treatment for ephelides- freckles.

Keywords: Ephelides, freckles, Q-switched RuVY, laser

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Freckles, the lay term for ephelides, is a common pigmentation characteristic which is known as superficial benign pigment spots observed both in Asians and Caucasians. Superficial pigmentation includes freckles, solar lentigines and brown birthmarks are becoming a concerning cosmetic problem.

Ephelides often appear as small, pigmented spots (~1–2 mm, but can be larger), red to light brown in color, in fair-skinned and/or red-haired individuals and usually first appear at the age of 2–3 yr, then increase during adolescence and often partially disappear with age (10). This suggests ephelides are generally genetically determined, also induced or aggravated by ultraviolet (UV) light (2) in a chronically sun-exposed skin.

Mentioned in Zhang et al., 2004³, freckles are considered cosmetic disfigurements in Asia population, whereas in Western culture, freckles are considered fashionable. Many techniques and modalities have been described and used for the treatment of ephelides. For example, laser surgery/ light therapy, cryotherapy, topical or chemical peeling preparations.

In the 90's, popular methods of treatment or removal was superficial ablation, especially by light electrodesiccation, cautery or application of solid carbon dioxide or liquid nitrogen (4). However, these methods cause scarring and damage to the normal tissue. As the advancement in the dermatology field, melanin specific selective photothermolysis using Q-switched Ruby laser was introduced in 90's. Fast forward 30 years later, RUVY Touch (Ruby like Versatile YAG) Q-Switched 660nm wavelength has been widely practised in the treatment of superficial pigmentation.

In this case report, we will be focusing on light therapy treatment on ephelides, reporting the efficacy of RUVY Touch (Ruby like Versatile YAG) Q-Switched 660nm wavelength treatment on ephelides.

Case Presentation

A 24-year-old Chinese gentleman, Fitzpatrick type III with no known medical illness was presented to our clinic with pigmentations over bilateral cheeks and nose for 10 years prior to his visit to our clinic. He claimed that the pigmentations got worse after he started working as a salesman. He is actively involved in outdoor activities and basketball sports during his leisure time. Both his father and sister also have had similar pigmentation problems since young. Previously he has never undergone any depigmentation treatment before this. He felt insecure and low self-esteem with the noticeable pigmentations, as he received many comments at work who pointed out the appearance. He felt the customers will focus on his pigmentations rather than his work performance which affects his confidence. On physical examination, there are multiple light brown, small spots, round in shapes, covering bilateral cheeks, nose and forehead. He was diagnosed with ephelides or better known as freckles.

Management And Outcome

This patient was started on depigmentation treatment in our clinic using Lutronic RuVY Touch Q-switched 660nm wavelength without any additional topical or oral medicine. He was treated with 1-2 passes and adjusted depending on the skin reaction. The end point of RuVY Touch Q-switched 660nm wavelength is whitening, hence the fluency is thus adjusted depending on the reaction. Patient also received Nd: YAG Q-Switched low-fluenced 1064nm laser treatment while undergoing RuVY treatment.

Customer is very satisfied with the overall results of his pigmentations with the global aesthetic improvement scale (GAIS) score of 1 (very much improved, optimal cosmetic results) and continues the treatment to obtain further improvement.



Figure 1: Front, right face (45 degree) and left face (45 degree) view photos of patient during the first presentation. Noted that there are multiple freckles over bilateral cheeks, nose and forehead.

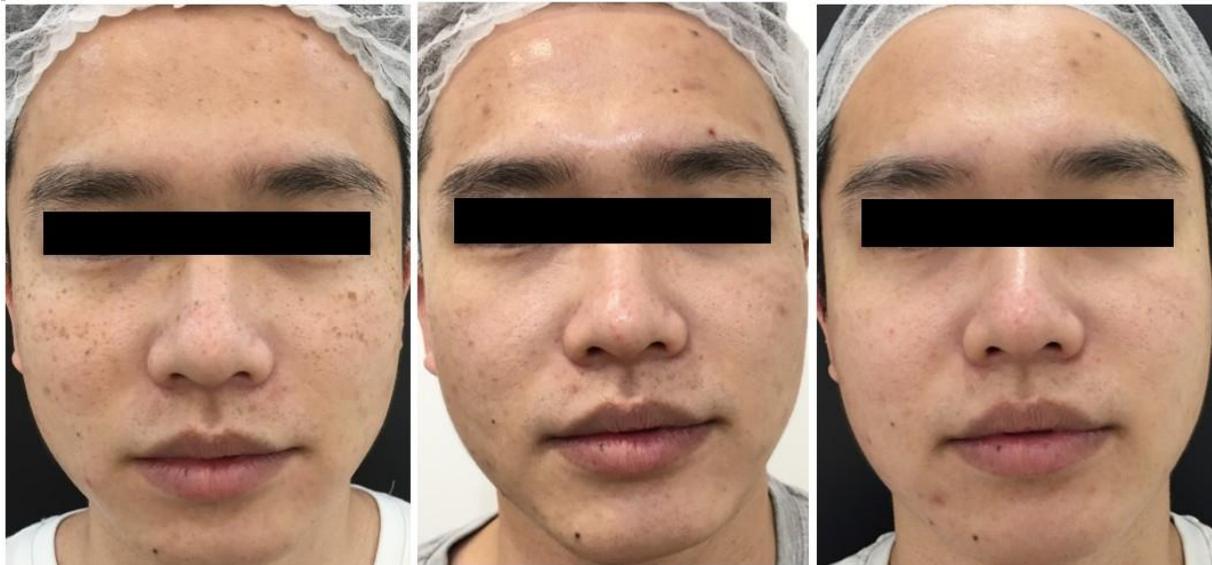


Figure 2: Front view photos of first (left), fourth (center) and eighth (right) treatment. Noted that there is significant improvement of the freckles on whole face.

Discussion

Q-switched (QS) lasers are widely used to effectively treat a variety of cutaneous pigmentation lesions by targeting pigments via non-ablative selective photo-thermolysis. Melanin absorption is higher in QS 532-nm neodymium-doped yttrium aluminum garnet (Nd:YAG) laser treatment than other QS laser treatments; however, better absorption rates to target tissues are not always associated with

better clinical outcomes. For example, higher absorption by hemoglobin of QS Nd:YAG laser energy at 532 nm significantly increases the risk of unexpected side effects, in particular damage to superficial vessels. Additionally, Asian patients of darker skin type with higher amounts of melanin are at higher risk of post-laser therapy hyperpigmentation and erythema.



Figure 3: Right face (45 degree) view photos of first (left), fourth (center) and eighth (right) treatment. Noted that there is significant improvement of the freckles on right side of face.



Figure 4: Left face (45 degree) view photos of first (left), fourth (center) and eighth (right) treatment. Noted that there is significant improvement of the freckles on left side of face.

Although QS 532- and 1,064-nm Nd:YAG lasers are still the most widely used devices for treating various pigmentation disorders, QS ruby lasers with a wavelength of 694 nm have been shown to facilitate better absorption by melanin than QS 1,064-nm Nd:YAG lasers and weaker absorption by hemoglobin than 532-nm lasers. Reportedly, QS ruby lasers have proven successful in tattoo removal and in treating cutaneous pigmentations lesions, including melasma,

freckles, lentigines, café-au-lait macules, Becker's nevus, and nevus of Ota. Using a handpiece equipped with solid dye, 532-nm QS Nd:YAG laser energy can be converted to 660-nm laser energy for use in ruby-like versatile YAG (RuVY) laser treatment.

In this study, we attempted to demonstrate the clinical efficacy of RuVY treatment on ephelides-freckles. RuVY treatment was performed by converting 532-nm QS Nd:YAG laser energy to 660nm laser

Table 1: Parameters used during each session of treatment.

Session	Date	Mode	Fluence (J/cm ²)	Frequency (Hz)
1	6/10/20	RuVY Q-switched 660nm	0.75	1
2	4/11/20	RuVY Q-switched 660nm	0.80	1
3	2/12/20	RuVY Q-switched 660nm	0.75	1
4	16/3/21	RuVY Q-switched 660nm	0.80	1
5	13/4/21	RuVY Q-switched 660nm	0.80	1
6	23/6/21	RuVY Q-switched 660nm	0.85	1
7	14/7/21	RuVY Q-switched 660nm	0.85	1
8	11/5/22	RuVY Q-switched 660nm	0.85	1

energy. Although QS lasers are preferred and widely used for the treatment of epidermal and dermal pigmented disorders, a shorter pulse duration can result in post-therapy hyper- or hypopigmentation due to higher risk of unwanted photomechanical effects on adjacent tissue components, especially blood vessels. As with QS ruby lasers with a wavelength of 694-nm, the wavelength-converted 660-nm laser, which is a quite similar but not identical to 694-nm lasers, was theoretically expected to offer better absorption by melanin and weaker absorption by hemoglobin.

This patient was treated with 8 sessions of RuVY treatment using a QS Nd:YAG laser device (SPECTRA XTMM, Lutronic Corporation, Goyang, Korea). A handpiece equipped with solid dye was used to convert 532-nm wavelength laser energy to 660-nm wavelength laser energy. At each RuVY treatment session, a single or two passes were made with the device using the settings of a 660-nm wavelength, a pulse energy of 0.75-0.85 J/cm², a frequency 1Hz, and a 3-mm spot size. As RuVY treatment involves delivery of laser energy over a small spot size of 2-3 mm and has

a wavelength of 660 nm for relatively weaker absorption rate by hemoglobin, the risk of vascular damage and associated post-inflammatory dyspigmentation is potentially low. The absorption in melanin is still high, but with slightly lower absorption compared with the 532nm beam, the safety level for treatment of discrete epidermal lesions is increased. The 660nm RuVY Touch can deliver intense energy onto the same spot size compared with 532nm and can precisely treat only the lesion; unnecessary heat damage to the surrounding areas is therefore contained as the undesired laser energy is not delivered. Accordingly, the skin reaction is comparatively milder after RuVY Touch treatment, which means faster healing and less unsightly erythema and crusting, which is an advantage for the patient.

In conclusion, our data suggest that RuVY treatment, utilizing a converted wavelength of 660 nm, can be effectively used for the treatment for ephelides- freckles.

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Complication and Approach to Safe Laser Hair Removal in Skin Type Fitzpatrick VI: A Case Report

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Abstract

Laser hair removal is one of the most popular aesthetic treatments that is considered safe and effective. Comparatively, it is more effective than shaving, waxing, plucking, and epilation in terms of pain, speed and accuracy. Nevertheless, the complication of laser hair treatment for darker skin can be of concern. Treatment parameters must be adjusted to patient skin type and chromophore. Longer wavelengths and cooling are safer for patients with darker skin types. Hair removal with intense pulse light (IPL) sources is not recommended for hair removal in skin type Fitzpatrick 5 and 6 due to the high risk of hyperpigmentation. This paper addresses the complications and approach to safe laser hair removal in skin type Fitzpatrick 5 and 6.

Keywords: Laser, Hair, Removal, Fitzpatrick, Complications

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Unwanted facial and body hair is a common presentation among patients, for instance, females with hirsutism (1). This issue could be tackled using the latest developing technology in laser and light. The hair is successfully reduced by selective photo-thermolysis. Thermal damage to adjacent stem cells responsible for hair regrowth done by targeting melanin in the hair follicle. The damage will occur when adequate fluence at a wavelength, preferentially absorbed by that target, delivered during a time (pulse duration) equal to or less than the thermal relaxation time of the target (2). Based on this principle, some types of hair removal systems available in the market including ruby laser(694nm), alexandrite laser (755nm), diode laser (800nm), intense pulsed light source (590 to 1200nm) and the neodymium: yttrium aluminium-garnet (Nd:YAG) laser (1064nm), with or without the application of carbon suspension (2).

Looking into the subset of skin type, predominantly in dark skin (Fitzpatrick skin types (FST) IV VI), there will be epidermal melanin interference whereby light is absorbed in the epidermis and converted to heat rather than reaching the target melanin in the hair shaft. This could lead to higher rates of thermally induced side effects such as hypo- or hyperpigmentation, blisters and crust appearance leading to poorer outcome (1). Longer wavelengths, longer pulse durations, conservative fluences and more efficient cooling systems could reduce these complications (3). Nd-YAG is an example of longer wavelength lasers which are absorbed less efficiently by epidermal melanin which causes lesser damage. Nd-YAG has shown lowest incidence of adverse events, therefore preferred in darker skin populations (4).

Case Presentation

A 41-year-old female presented to our clinic with a keen desire for facial hair removal. Written consent was provided, by which the

patient agreed to the use and analysis of her data. She has underlying polycystic kidney disease diagnosed in our center and has expressed desire for removal of facial hair. She has gone to multiple centers however was denied therapy as risk of complication was higher in view of her skin type. With patient fully understanding the risks, she has given written and verbal consent for laser hair removal in our center.

The patient has only experienced facial hair removal using wax in beauty centers. She has never undergone any non-invasive or invasive procedures such as fillers, injectables or laser therapy on her facial area.

Patient's overall facial skin was normal with no significantly enlarged pores or acne. Her concern was mainly coarse facial hair around her upper lip and chin.

She had undergone facial laser hair removal using a high range Nd:YAG multimodal laser. She required no local analgesia for the procedure. The laser hair removal was done in about 15 minutes. Immediate post procedure, all of the facial hair at the concerned areas was not visible. She had some erythema however overall had no obvious visible burns (Figure 1).

On follow up at Day 1, she experienced some burning sensation hence reported to our center. However, on follow-up Day 2, she experienced burns on her chin with hyper-pigmented spots around her chin (Figure 2), and noticeable erythema on her forehead with hyperpigmented spots has appeared on her forehead at Day 3 (Figure 3).

Local steroid application has been prescribed to reduce inflammation and after Day 7, the obvious burns have recovered well. Patient was generally satisfied with her hairless face however she had to face some unwanted burns and hyperpigmentation which subsequently improved overtime.

Upon further history, patient admitted



Figure 1: Immediate post procedure

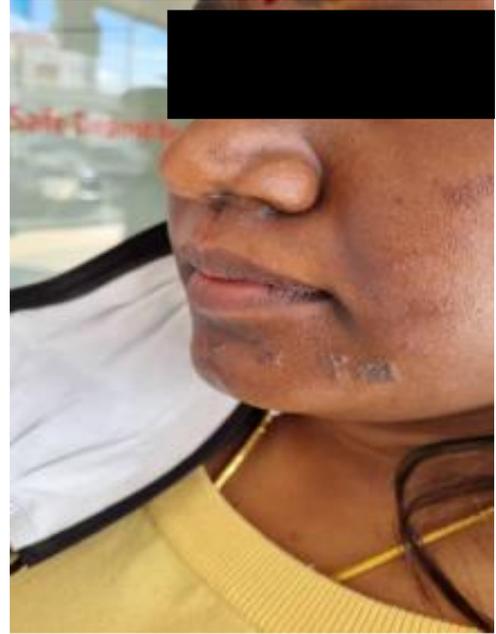


Figure 2: Day 2 Post procedure



Figure 3: Day 3 Post Procedure

to performing face hair bleaching a week prior to laser hair removal. Post procedure, she was compliant with sunscreen application, however,

sun exposure was not limited in view of work commitments, thus increased her risk for developing hyperpigmentation especially considering Malaysia has a tropical climate.

Management And Outcome

Treatment considerations for skin types Fitzpatrick V and VI:

1. Wavelength - consider chromophore (especially risk of absorption by epidermal melanin); longer wavelengths associated with less epidermal absorption and therefore greater safety in patients with higher skin type.
2. Treatment parameters – employ settings that minimize extent of epidermal and dermal injury (typically more conservative than in skin type

- Fitzpatrick I–III, often requiring a greater number of sessions), e.g., lower fluences and longer pulse durations for laser hair removal; lower treatment densities (microthermal zones cm^{-2}) for fractional laser resurfacing
3. Pre-and post-treatment sun protection (sun-protective behaviours, broad-spectrum sunscreen $\text{SPF} \geq 30$)
 4. Consider pre- (≥ 2 weeks prior) and post-treatment bleaching agents (e.g., hydroquinone 4% cream)
 5. Judicious epidermal cooling, e.g., slower treatment speeds when using lasers with contact cooling; pausing between passes of resurfacing lasers to reduce bulk heating; icepacks post-procedure
 6. Consider topical corticosteroids post-treatment (to reduce inflammation), especially when significant post-procedure erythema or oedema noted.

In addition to the removal of unwanted hair for cosmetic reasons, laser-assisted hair removal is also employed as a primary or adjunctive treatment of several hair disorders that are disproportionately prevalent in individuals of African ancestry -pseudo-folliculitis barbae, acne keloidalis nuchae, dissecting cellulitis of the scalp, and folliculitis decalvans. When performing laser hair removal in individuals with richly pigmented skin, epidermal melanin acts as a competing chromophore and, therefore, the risk of adverse events from epidermal injury is greater than in lighter skin types. Key strategies to minimize the risk of epidermal injury in skin of colour include employing longer wavelength lasers, longer pulse durations and judicious epidermal cooling techniques.

Longer wavelength lasers are associated with deeper penetration and therefore, the ratio of the temperature of the hair bulb to the temperature of the epidermis is

increased, allowing for follicular destruction with relative sparing of the epidermis. The safest wavelengths for skin type Fitzpatrick IV–VI are those in the near infrared range: the 800–810-nm diode and the 1064-nm neodymium-doped yttrium aluminium garnet (Nd:YAG) lasers. The lowest incidence of adverse events associated with laser hair removal in darker skin types has been shown with the long pulsed 1064-nm Nd:YAG and therefore, this is the preferred wavelength for patients with skin type Fitzpatrick VI (among whom the risk of complications from laser hair removal is highest). Thermal injuries resulting in hypopigmentation can occur when the 800–810-nm diode laser is used in skin type Fitzpatrick V and VI, and, therefore, test spots are strongly advised.

Higher fluences are associated with an increased risk for epidermal injury in darker skin types. A study by Ross et al. found the highest tolerated fluences in darkly pigmented skin to be 100 J cm^{-2} for skin type Fitzpatrick IV and V, and 50 J cm^{-2} for skin type Fitzpatrick VI. Therefore, lower fluences are recommended for higher skin type to minimize excessive thermal injury to the epidermis, which can be associated with disfiguring pigmentary alterations.

Long pulse durations facilitate efficient epidermal cooling and are therefore associated with fewer adverse events in dark skin types (5). Examples of long pulse durations that are considered safe for laser hair removal in skin type Fitzpatrick IV–VI include, 400 ms for the 810-nm diode and 30 ms for the 1064-nm Nd:YAG with contact cooling.

Cooling of the epidermis pre- and postoperatively is paramount when performing laser hair removal in darkly pigmented skin (6) as thermal injuries can cause pigmentary abnormalities that may last for several months. Epidermal cooling during laser hair removal is achieved by one of two mechanisms – contact or cryogen spray cooling. In the former type, a

chilled copper plate or sapphire window is used to cool the epidermis on contact before the laser pulse is delivered. In the latter, a cryogen is applied for 20–100 ms prior to the pulse of laser energy. For post-cooling, the chilled surface of the laser hand piece can be reapplied to the treated area, or the cryogen spray can be administered up to 100 ms after the laser pulse. Other epidermal cooling strategies include application of refrigerated gels prior to treatment (for contact cooling devices) and ice packs for 5–10 min post-procedure. While either contact or cryogen spray cooling laser hand pieces can safely be used in darker skin types, dyspigmentation has been reported when suboptimal cryogen settings and/or poor operator technique have been employed.

Intense pulsed light (IPL) is not recommended for hair removal in skin type Fitzpatrick V and VI due to the high risk of hyperpigmentation (5).

Discussion

Removing unwanted hair procedure has been practiced regularly in our community. The purpose usually due to personal hygiene and desire to be cosmetically improved. Prior to laser hair removal, multiple conventional procedures have been used; ranging from abrasion, threading, plucking, waxing, chemical depilators and shaving. These procedures have non-permanent result and only delay hair growth. Laser hair removal had been introduced as permanent hair removal, but it was originally contraindicated in patients with ethnically dark or sun-tanned skin. As years goes by, the laser hair removal technology had advanced and now it is available to all patients including patients with darker skin type Fitzpatrick V and VI.

For laser hair removal, laser light must pass through the pigmented epidermis to treat the dermal hair target. There will be difficulty in patient with skin type Fitzpatrick V and VI as the melanin in the epidermis compete as chromophore for laser light. The melanin will

absorb the laser light and converts it to heat and when heat accumulate, it will create thermal damage and cause epidermal blistering, dyspigmentation and scarring (7). Besides that, it will reduce its efficacy as less laser light will be directed towards dermal hair target (8). For our patient above, she had mild thermal damage at epidermis causing cutaneous side effect which are hyper-pigmentation and mild skin burn, after her laser treatment, as seen in Figure 2 and Figure 3.

Nowadays, new generation laser hair removal devices can provide safe & effective hair removal treatment in patients with skin type Fitzpatrick V and VI (8). Longer wavelengths laser is safer in treating darker skin patient as there is greater depth penetration and less superficial chromophore absorption, hence decrease the melanin absorption and less thermal damage. Longer pulse durations also allow for more efficient cooling of the epidermis. The slower the light energy deposited into the skin; slower pigmented epidermis absorbed lights & heats up. It is more efficient to remove heat from slow-heating object (7).

We had used Nd:YAG laser for our patient's laser hair removal treatment as mentioned above. Nd:YAG (1064nm) laser & Diode(800nm) laser are among the laser frequently used for laser hair removal in patient with darker skin (9). Nd:YAG laser has got the longest wavelength, but the melanin absorption is less. It can be used safely with high energy and the penetration is comparatively less, hence lower incidence of adverse effects in darker skin type Fitzpatrick V and VI (10). Diode laser penetration is not as much as Nd:YAG laser but its penetration is still safe and effective for darker skin (5).

In addition, cooling devices is also important to ensure safe laser hair removal in dark skin patient. It selectively cools the most superficial layers of the skin & ensure the maintenance of a lower temperature at the

epidermal level yet reaching the required higher temperature at the target level. The basic principle is to protect the superficial layers of the skin from collateral thermal damage. It can be achieved by cold air convection, contact cooling or cryogen spray cooling (6).

Furthermore, proper patient selection also needs to be done before treatment. Patient selection and tailoring of the fluence used to the patient's skin type remain the most important factors in efficacious and well tolerated laser treatment (2). Patient selection can be done by thorough history taking, which include medication history, history of herpetic infections, history of keloid or hypertrophic scars and pregnancy status (8).

Test spots are also necessary to be done before the treatment, to determine the appropriate laser parameters later. Test spots should be performed at the similar treatment area to match closely with the skin color, sun exposure and hair density level. The test should start with safest parameters (longer fluence & longer pulse duration). Patient with darker skin will have one to two days delay to show the cutaneous side effects. Thus, we need to wait and monitor more than 48 hours for the cutaneous reaction to be present (8). The cutaneous side effects in our patient were also observed about one to two days after her laser treatment, as seen in Figure 2 and Figure 3.

Besides that, the treatment area needs to be closely shaven prior to laser treatment because superficial hair heating will cause skin blistering and discoloration. In the event of any thermal damage-related cutaneous side effects, a topical antibiotic or corticosteroids should be applied and prescribed, as what we had prescribed to our patient above. Subsequently, the cutaneous side effects had resolved with time. Most of cutaneous side effects are generally temporary and reversible (3). If the previous treatment had caused any cutaneous side effects, a thorough history has to be taken,

recent sun exposure, new medications, new skin products, and post treatment regimen. More conservative parameters also should be applied on next laser treatment. This is to ensure patient safety.

Conclusions

Laser hair removal is the most efficient method of long-term hair removal. It can be done safely with the new generation laser, regardless of skin type & ethnicity. It is done safely by combining longer wavelengths, longer pulse duration, efficient cooling devices, thorough history (good patient selection), test spots (to determine laser parameters), good pre and post treatment care. Both Nd: YAG laser and Diode laser are safe to be use for laser hair removal for skin type Fitzpatrick V and VI, however, one should select a system that minimizes side-effects (4).

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Clinical, Dermoscopy and Histopathological features of Nevus Lipomatosus Cutaneous Superficialis: A Multi-Center Case Series of 10 Patients

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Abstract

Nevus lipomatosus cutaneous superficialis (NLCS) is a rare benign hamartomatous skin condition of unknown etiology. Clinically, NLCS can be classified into two clinical types: 1) Classical Hoffman-Zurhelle or the multiple type and 2) solitary pedunculated type. Histopathologically, hematoxylin-eosin would reveal ectopic mature adipose tissues interspersed with thickened collagen bundles in the dermis separate from the subcutaneous fat which is pathognomonic of NLCS. Although the clinical diagnosis of such condition is straightforward, sometimes it can be mistaken for other skin-colored pedunculated skin lesions. The authors hope that the result of the case series will guide dermatologists in differentiating NLCS from other skin-colored pedunculated skin lesions. A good clinical eye together with histopathology remains to be the gold standard for the diagnosis of this skin condition. Excision remains to be one of the most effective treatments of choice with minimal recurrence. Other treatment modalities such as carbon dioxide laser excision and cryotherapy may also be offered.

Keywords: amartoma, nevus lipomatosus cutaneous superficialis, excision

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Nevus lipomatosus cutaneous superficialis (NLCS) is a rare benign hamartomatous skin condition of unknown etiology characterized by the appearance of ectopic mature adipocytes in the papillary or reticular dermis separate from the subcutaneous fat (1). Clinically, NLCS can be classified into two clinical types. Classical Hoffman-Zurhelle or the multiple type are characterized by multiple soft, skin-colored to yellowish papules or nodules coalescing to form plaques with smooth, wrinkled or peau d'orange appearance of surface. Classical lesions are usually present at birth or in the first two to three decades of life (2), distributed in linear, zonal or segmental fashion over the buttocks, lower back or upper thighs (3). However, lesions can also be found in areas such as the upper trunk, abdomen, axillae, genitalia or face (4). The solitary pedunculated type is characterized by papule, nodule or tumor with either "smooth" or "cerebriform" surface in a study by Baraldi et. Al (5). This type usually appears during the third to sixth decades of life and can appear in different locations of the body but has a predilection for the trunk (6). The exact pathogenesis of this rare skin condition is yet to be determined. In a study by Buch, fat deposition in NLCS may have been secondary to the degenerative changes in connective tissue. In 1937, Robinson and Ellis hypothesized that NLCS may be a true connective tissue nevus which resulted from the focal heterotopic development of adipose tissue (7). In 1975, Light microscopy studies by Jones et. Al. suggest dermal adipocytes of this condition originated from the pericytes of blood vessels during fetal lipogenesis (8). Further cytogenetic study looked into the genetic factor in the development of these lesions which revealed mosaicism for a 2p24 deletion (9).

NLCS is asymptomatic but cosmetically disfiguring. This condition has not been associated with tendency towards malignant changes but are associated with multiple cutaneous disorders such as the following:

follicular papules, hypertrophic pilosebaceous units, angiokeratoma of Fordyce, café-au-lait macules, scattered leukoderma, and hemangioma (6).

Case Presentation

A total of 10 patients were included in this case series. All of them are females with Fitzpatrick skin phototype IV, with mean age of 42.4 ± 13.5 years old. All patients reported appearance of solitary pedunculated tumors of varying size and duration (Table 1). No other associated skin abnormalities were present at the time of consultation. All patients voluntary requested removal of lesions for cosmetic reasons. Informed consents on excision biopsy, photography and publications were secured.

In all cases, the authors performed dermoscopy using a manual polarized light device (Dermlite DL2x10; 3Gen, San Juan Capistrano, CA). Dermoscopic findings for cerebriform pattern with sulci and gyri, yellow structureless areas, white structureless areas, irregularly distributed linear loop-like or linear-coiled vessels (8/8; 100%). (Figure 2a). Dermoscopic findings for smooth surfaced revealed yellow structureless areas, white structureless areas, irregularly distributed linear loop-like or linear-coiled vessels. (2/2; 100%). (Figure 2b).

Shave excision prior to electrocautery or carbon dioxide laser were performed on all cases. Histopathologic findings of the cases revealed acanthosis, papillomatosis and absence of spongiosis in the epidermis. (Figure 3a). The dermis contained varying amounts of mature adipose interspersed with fibrous connective tissue septae and blood vessels. Thick and fibrillary brightly eosinophilic collagen in



Figure 1: Solitary brown-colored pedunculated tumor with cerebriform surface on 8 patients (8/10, 80%) and solitary skin-colored nodule with smooth surface measuring on 2 patients (2/10, 20%)

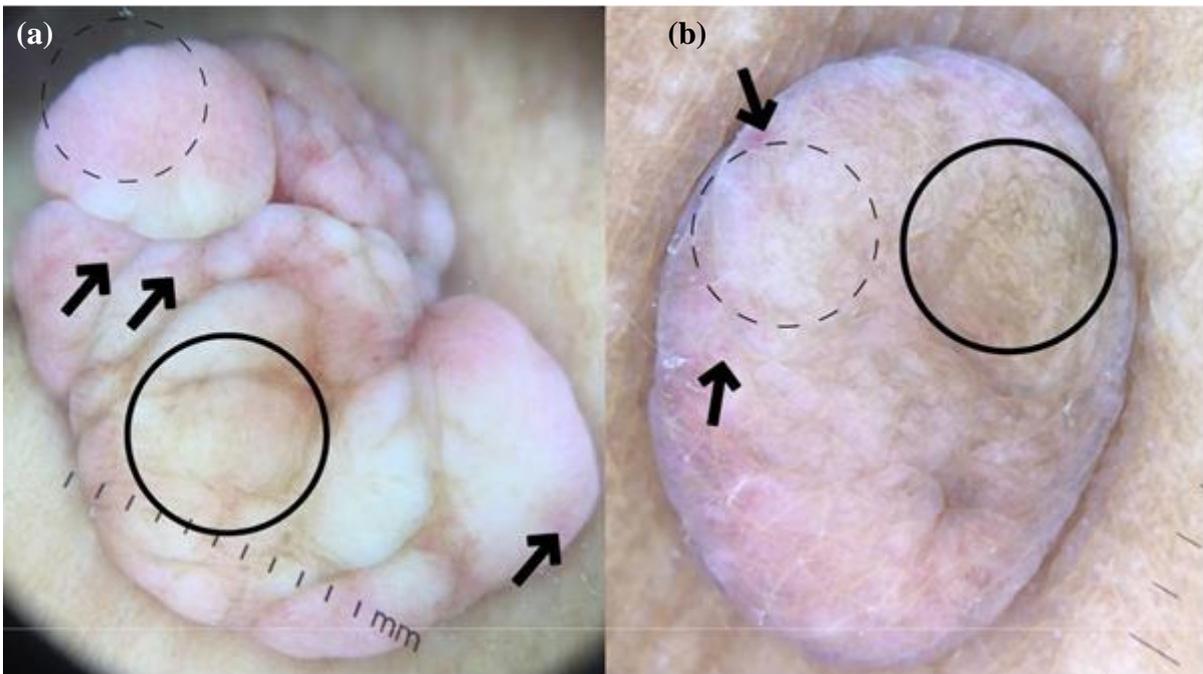


Figure 2: Representative photos of the dermoscopy of nevus lipomatosus cutaneous superficialis. Yellow structureless areas (black circle), white structureless areas (dotted circle) and irregularly distributed linear loop-like or linear-coiled vessels (black arrow). (a. Dermlite DL2x10 ; b. Dermlite DL2x10)

haphazard array with mild diffuse inflammatory infiltrate of lymphocytes were also noted. (Figure 3b). In the cases of nevus cutaneous lipomatosus cutaneous superficialis with a smooth surface, acanthosis and papillomatosis were absent as compared with the variability in the cerebriform type. There was also noted

absence of mature adipose tissue in the superficial dermis fat in the case of NLCS with smooth surface as compared with the presence in all superficial, mid-dermis and deep fat in the cerebriform type. The group also noticed that the ectopic fatty tissue present in the superficial, mid and deep dermis is not connected with the fat of

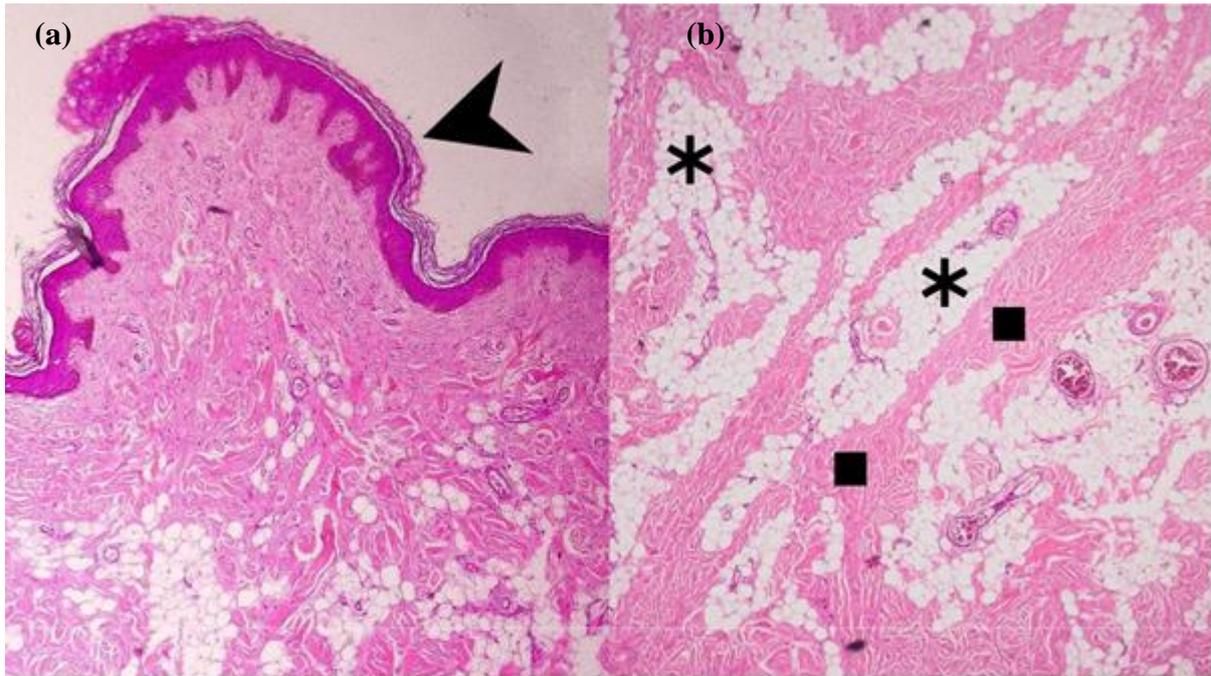


Figure 3: H&E shows acanthosis and papillomatosis (arrowhead), varying amounts of mature adipose interspersed with fibrous connective tissue septae and thick and fibrillary brightly eosinophilic collagen in haphazard array (black square) with mild diffuse inflammatory infiltrate of lymphocytes (a&b. H&E, 100x)

the underlying subcutaneous tissue. Summary of all the histopathological findings observed in our patients can be seen in Table 2.

Management And Outcome

In approaching patients with nevus lipomatosus cutaneous superficialis, reassurance that the condition is benign is very essential. In our patients, electrocautery or carbon dioxide laser excision was done in all cases and no recurrence were noted.

Discussion

NLCS appears clinically as a multiple or solitary skin-colored to yellowish papule, nodule or tumor with smooth or cerebriform surface. Dermatologists and other practitioners should be guided with the possibility of an NLCS diagnosis when evaluating a patient with an isolated, pedunculated skin-colored papule, nodule or tumor. In this case series, the group investigated the dermoscopic and histopathological

correlation of NLCS in order to differentiate it from other skin-colored pedunculated lesions.

For the dermoscopic findings of the solitary type with cerebriform surface, our group found the appearance of sulci and gyri, yellowish structureless areas, white structureless areas, irregularly distributed linear loop-like or linear-coiled vessels on all eight cases. This is in contrast with the dermoscopic findings of the solitary type with smooth surface which revealed yellow structureless areas, white structureless areas, irregularly distributed linear loop-like or linear-coiled vessels on the two cases. The findings of the yellow and white structureless areas in our study were similar to the findings of Kinnera et.al. The yellowish structures correspond to the dermal adipocyte while the white structures correspond to the thickened collagen in the dermis. (10). Our findings were consistent with the dermoscopic features previously described by Vinay et al who

Table 1: Summary of Patients

Case No.	Sex	Age	Duration	Location	Clinical features	Treatment
1	M	40	5 years	Right gluteal area	solitary brown-colored pedunculated tumor with cerebriform surface measuring 2.5cm x 1.0cm	Excision
2	M	40	3 years	Right gluteal area	solitary flesh-colored pedunculated tumor with cerebriform surface measuring 0.5cm x 0.5cm	Excision
3	F	38	10 years	Left chest	solitary skin-colored pedunculated tumor with cerebriform surface measuring 1.0cm x 1.0cm	Excision
4	M	34	4 years	Right pelvic area	solitary skin-colored to brownish pedunculated tumor with cerebriform surface measuring 2.0cm x 2.0cm	Excision
5	M	28	5 years	Right gluteal area	solitary flesh-colored pedunculated tumor with cerebriform surface measuring 1.0cm x 1.0cm	Excision
6	M	56	35 years	Right shoulder	solitary skin-colored pedunculated tumor with cerebriform surface measuring 3.0cm x 2.0cm	Excision
7	F	54	10 years	Right medial thigh	solitary skin-colored pedunculated tumor with cerebriform surface measuring 1.0cm x 1.0cm	Excision
8	M	64	2 years	Trunk	solitary skin-colored pedunculated tumor with cerebriform surface measuring 0.5cm x 0.5cm	Excision
9	F	20	4 years	Back	solitary skin-colored nodule with smooth surface measuring 0.5cm x 0.5cm	Excision
10	M	50	4 years	Left posterior thigh	solitary skin-colored nodule with smooth surface measuring 0.5cm x 0.5cm	Excision

Table 2: Histopathological findings of nevus lipomatosus cutaneus superficialis

	Acanthosis	Papillomatosis	Spongiosis	Superficial Dermis fat	Mid-dermis fat	Deep dermis fat	Blood vessels	Infiltrate
Case 1	mild	present	absent	Present	present	present	present	mild
Case 2	moderate	present	absent	present	present	present	present	sparse
Case 3	absent	present	absent	present	present	present	few	sparse
Case 4	absent	present	absent	present	present	present	few	sparse
Case 5	mild	present	absent	present	present	present	few	sparse
Case 6	absent	present	absent	present	present	present	few	sparse
Case 7	absent	present	absent	present	present	present	few	sparse
Case 8	absent	present	absent	present	present	present	few	sparse
Case 9	absent	absent	absent	absent	present	present	present	sparse
Case 10	absent	absent	absent	absent	present	present	few	sparse

was able to describe five features of NLCS: cerebriform appearance, web-like regular pigment network, rim showing a white veil, yellowish structureless areas, and comedo-like openings. In addition to the yellowish and whitish structureless area seen in the dermoscopy, irregularly distributed linear loop-like or linear-coiled vessels were also observed in both the “cerebriform” and “smooth” type of solitary pedunculated NLCS. The presence of irregularly distributed linear loop-like or linear-coiled vessels correspond to the vascularity histopathologically. Our study was similar with the findings of Buch et al showing increased vascularity in the subpapillary and papillary dermis with perivascular with mononuclear cell (11).

In a study by Triki et al, they found out that the epidermis may show mild to moderate acanthosis, basket weave hyperkeratosis and focal elongation of rete ridges (12). The group were able to observe similar findings of

acanthosis, papillomatosis and absence of spongiosis in the epidermis of our specimens. In all cases, the groups observed aggregates of mature adipose tissue embedded among the collagen bundles of the dermis were separated from the subcutaneous fat. This is similar in with the study of Ionnidou et al who stated that the most characteristic feature of NLCS is that there is usually no connection with the subcutaneous fat tissue (13). Our findings were also in line with the findings of Kinnera et al, that the adipose tissues typically form small aggregates around blood vessels or eccrine sweat glands and separate collagen bundles. (10) The adipocytes may extend to the papillary dermis (14). Avhad and Jerajani observed that the proportion of adipose tissues in the papillary and reticular dermis varies greatly and ranges from from 10% to 50% of the lesion. (15). In a study by Baraldi et al on the clinical, dermoscopic and histopathological features of solitary NLCS, they concluded that the histopathological features of

the solitary type nevus lipomatosus cutaneous superficialis are similar. They were able to conclude that the adipocytes are present both in reticular and papillary dermis in the cerebriform type and adipocytes are present only in the reticular dermis in the smooth-surfaced type. (5). This is quite similar with our findings, as the group noted absence of mature adipose tissue in the superficial dermis fat in the case of NLCS with smooth surface as compared with the presence in all superficial, mid-dermis and deep fat in the cerebriform type.

Due to the similarities between acrochordon, neurofibroma and nevus sebaceous clinically, histopathology still remains to be the gold standard of diagnosis. Acrochordon are usually less than 1 cm in size and with variable adipose tissue in the dermis of its larger variants. Neurofibroma would reveal proliferation of spindle shaped cells with wavy nuclei embedded in a myxoid matrix. Nevus sebaceous would reveal presence of adnexal structures (immature sebaceous gland, immature hair structures) and/or ectopic apocrine gland.

Treatment options for NLCS are mainly limited to excision with either electrosurgery, carbon dioxide laser or cryotherapy. Excision is curative as report of recurrence is rare post-excision (16). As any hamartomas, NLCS can gradually increase in size, causing apprehension among patients. The authors hope that the result of the case series will guide dermatologists and surgeons in differentiating NLCS from other skin-colored pedunculated skin lesions. Previously, cases of NLCS were misdiagnosed as acrochordons. In contrast with acrochordons however, NLCS is not associated with insulin resistance or metabolic disorders. Patient reassurance that this condition is benign and not a known marker for any other underlying conditions is essential. (17). A good clinical eye together with histopathology remains to be the gold standard for the diagnosis of this skin condition. Excision remains to be one of the

most effective treatments of choice with minimal recurrence.

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Combination Treatment of Antibiotic, Retinoids and Chemical Peeling in Young Adult with Acne Scars: A Case Report

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Abstract

Acne vulgaris is a disorder of the pilosebaceous unit, which runs a chronic course and it is self-limiting. It is characterized by the presence of open and closed comedones, papules, pustules, and dermal tissue damage that eventually would cause hypertrophic scar formation. In the vast majority of cases, it is not until puberty that acne becomes a more significant problem. Acne often heralds the onset of puberty. In these young patients, the predominant lesions are comedones. Acne prevalence hits its peak during the middle-to-late teenage period, with more than 85% of adolescents affected, and then steadily decreases. However, acne may persist through the third decade or even later. The prevalence of high school students with moderate-to-severe acne was 19.9% in those students with a family history of acne and 9.8% in those students without a family history of acne. Acne in young adult male patient may start during adolescence and persist or have an onset in adulthood. Acne has various psychosocial effects that impact patients' quality of life. Treatments vary widely and treatment should be tailored specifically for each individual. In this paper, we will focus on the management and treatment options for young adult male patient with acne vulgaris.

Keywords: Acne Vulgaris, pilosebaceous unit, hypertrophic scar

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Acne vulgaris (AV) is a disease of the pilosebaceous unit that causes non-inflammatory lesions (open and closed comedones), inflammatory lesions (papules, pustules, and nodules), and varying degrees of scarring (1). While the course of acne may be self-limiting, the sequelae can be lifelong, with pitted or hypertrophic scar formation (2).

The four major pathogenic processes that lead to the formation of acne lesions are alteration of follicular keratinization that leads to comedones; increased and altered sebum production under androgen control; follicular colonization by *Cutibacterium acnes*; and complex inflammatory mechanisms that involve both innate and acquired immunity (3,4).

Treatment regime of patient's acne should be initiated early and be sufficiently aggressive to prevent permanent sequelae (2). Management of acne vulgaris in primary and specialist care includes advice on topical and oral treatments (including antibiotics and retinoids), treatment using physical modalities, and the impact of acne vulgaris on mental health and wellbeing (5).

Erythromycin and clindamycin are commonly used topical antibiotics for the treatment of acne. The development of *C. Acne* resistance towards antibiotics is less likely in patients who are treated with a combination of benzoyl peroxide/erythromycin or clindamycin. Therefore, the combination of these two products is preferable over monotherapy with topical antibiotics (2).

The tetracycline derivatives, doxycycline and minocycline, are commonly used in the treatment of acne. Although the oral administration of tetracyclines does not alter sebum production, it does decrease the concentration of free fatty acids and may take several weeks to become evident. Tetracycline may also act through direct suppression of the

number of *C. acnes*, but part of its action may be due to its anti-inflammatory activity (2).

The use of oral retinoid, isotretinoin, counteracts all the four pathophysiological factors. Although the mechanisms of isotretinoin that prolonged remission are not completely understood, it has been found that there is marked reduction in sebaceous gland activity and size other than altered follicular microclimate. Furthermore, there is also a reduction in toll-like receptor-2 (TLR2) expression on circulating mononuclear cells that is persistent for several months post-therapy of said mechanism. (2,6).

Chemical peeling is a skin resurfacing procedure commonly used for facial rejuvenation and aesthetics. It causes a manageable injury to the skin, thus resulting in subsequent regeneration of a new epidermal layer of the dermal tissues. The injury depth (superficial, moderate or deep) is determined by the concentration of acid used, and by the type of vehicle, buffering and duration of skin contact. Chemical peels have antibacterial, anti-inflammatory, keratolytic and comedolytic effects, and they can reduce sebum production. (7).

Case Presentation

22-year-old Chinese gentlemen, with no history of medical illnesses, presented to us with the complaint of recurrent acne lesions over his face, cheeks, chin and forehead for a more than a year. The patient has a habit of mechanically extracting pustular acne lesions and mechanically extracting comedonal lesions with his own fingers. Acne lesions have caused him psychological stress in his social life, as well as a decrease in his self-esteem. He is a graphic designer.

The patient has been experiencing work stress in recent weeks and will need to put in extra hours at night to meet his project deadlines and had previously sought numerous medical opinions for his acne lesions but stopped

receiving treatment after switching jobs a year ago. Upon performing an acne examination, numerous papular lesions, nodulocystic lesions, and white and black comedonal lesions were found over his forehead, cheeks, and U zone.

Clinically, he has acne vulgaris of moderate severity with grading of CASS 3 acne with predominantly papules and pustules lesion. Before the treatment begun, his blood investigation has taken as baseline prior to treatment. His result has showed normal liver enzymes of transaminases AST of 11 U/L, ALT of 23U/L and GGT 16 IU/L.

A variety of treatment regimens were suggested to him, including the use of oral and topical antibiotics, topical retinoids, chemical peeling, and oral retinoids. He has shown good response in the first two months of the 8-month treatment period following the oral and topical antibiotic combination. Following the start of low dose oral isotretinoid, a month of oral isotretinoin treatment revealed a significant improvement in his nodulocystic acne lesions.

Once his active lesions had lessened, chemical peeling was introduced to the patient. Trichloroacetic acid (TCA) 40% was applied with a moderate peeling depth until a light frosting was evident. Patient received a cooling and hydrating mask after each chemical peel to stop further skin erythema and inflammation.

In the following months, we used a combination of oral isotretinoid, chemical peeling, and sufficient skin hydration to control and prevent the recurrence of new acne lesions. After the duration of total 8 months of active treatment, he was advised to maintained on good healthy lifestyle, proper diet and regular follow up of his skin conditions.

Management an outcome

The patient was treated for 8 months using a combination of treatments. He was initially started on T.Minocycline 100mg daily for 8 weeks together with topical Zindaclin 1% twice

daily to treat nodular and papular lesions on his cheeks, U zone, and T zone area. On top of that, he was advised to a proper skincare regime consisting of salicylic acid/benzoic acid cleanser and moisturizer.

After 8 weeks of oral minocycline 100mg OD treatment, there was a slight improvement where a reduction in papular lesions is seen. Subsequently, the patient was started on oral Isotretinoin 10 mg daily. He was advised to continue the application of the topical antibiotic treatment on the papular lesion.

On the 4 months of acne treatment, he underwent his first chemical peel session with Trichloroacetic acid (TCA) 40% to to reduce comedonal lesions, post-inflammatory hyperpigmentation and scarring due to acne. The results of TCA chemical peeling showed significant reduction in comedones and post-inflammatory hyperpigmentation.

For the upcoming subsequent months, the patient underwent another 3 sessions of a chemical peel with TCA 40% with 6 weeks interval of each chemical peelings. Overall, the patient noticed an improvement in his skin texture with no acne flare-ups and a reduced appearance of post-inflammatory hyperpigmentation.

He continued using topical retinoin once at night and topical zindaclin twice daily. Oral Isotretinoin was discontinued with total of 6 months durations and he was advised to continue topical retinoin 0.125% as maintenance.

Discussion

In this case study, a combination of topical antimicrobial and retinoid therapy as first-time therapy for acne vulgaris has come up with good outcome. Retinoids are comedolytic and have anti-inflammatory effects, whereas topical antibiotics have antimicrobial effects. Chemical peeling with Trichloroacetic acid (TCA) reduces



Figure 1. 22 years old gentleman with active skin lesions (A) Before treatment; (B) Slight reduction of papules and pustules after 8 weeks of oral antibiotics



Figure 2. Marked reduction in active acne lesions after 1 months of oral isotretinoin



Figure 3. (A) Slight improvement of hyperpigmentation after 1 session of chemical peeling (B) Significant whitening of the skin after 4-5 sessions of chemical peeling

sebum production, less comedone and improves acne scar with increased collagenesis.

Topical antibiotics are mainly used for their role against *C. acnes*. They may also have anti-inflammatory properties. Topical antibiotics are not comedolytic, and bacterial resistance may develop to any of these agents. Commonly prescribed topical antibiotics for acne vulgaris include clindamycin, erythromycin, dapsone and minocycline.

Topical retinoids are comedolytic and anti-inflammatory. They normalize follicular hyperproliferation and hyperkeratinization. Topical retinoids can continue as maintenance therapy to inhibit further microcomedone formation.

In this case, isotretinoin (systemic retinoid) also appears to be highly effective in the treatment of severe, recalcitrant acne vulgaris. Isotretinoin causes normalization of epidermal differentiation, depresses sebum excretion by 70%, is anti-inflammatory, and even reduces the presence of *Cutibacterium acnes*.

Trichloroacetic acid (TCA) 40% was used and the result was very satisfactory for patient in inducing long term remission of acne lesions and reducing scarring. TCA causes denaturation of epidermal and dermal proteins, destruction of dermal collagen, and coagulative necrosis of epidermal cells. The clinical effects are the result of dermal structure reorganization and increased collagen, glycosaminoglycans, and elastin in the dermis. TCA peels (15–50% concentrations) are available for the treatment of active acne. This peel self-neutralizes and has very low systemic absorption. Trichloroacetic acid (TCA) 40% peels are one of the low-cost modes of therapy for active acne vulgaris and associated scarring with no complications.

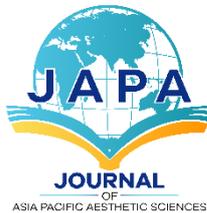
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Treatment of Melasma by Low-fluence 1064nm Q-Switched Nd:YAG Laser: A Case Report

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Abstract

This severity of melasma, a common aesthetic issue, can range from a mild pigmentation during pregnancy that goes away on its own to a persistent, problematic, disfiguring condition. Melasma has a complex pathogenesis which is still unexplained. However, exposure to uv radiation and genetic or hormonal factors are important contributors. Since ultraviolet exposure has a well-known ability to stimulate proliferation of melanocytes, their migration and melanogenesis, its exposure is a major triggering and exacerbating factor in the development of melasma. In melasma cases reported with usage of estrogen-progesterone oral contraceptives by mechanism of induction of melasma by estrogen may be related to the presence of estrogen receptors on the melanocytes that stimulate cells to produce more melanin. Clinical features of melasma are symmetry of hyperpigmentation and distribution related to trigeminal nerves, which suggest that neural involvement may play a role in pathogenesis of pigmentation. Clinically, melasma presents as a symmetrically distributed macular pigmentation with irregular borders, which can vary in color ranging from a light to dark, brown or brown, gray. The Melasma Area and Severity Index (MASI) used to assess melasma patients. There are numerous melasma treatment options available today, each with a varied success rate. Today, there are plenty of melasma treatments available, each with a different success rate. This article will discuss current advancements in low fluence 1064nm Q switched Nd:YAG laser melasma treatment and its implications for new therapeutic strategies.

Keywords: melasma, UV radiation, MASI, Nd:YAG laser therapy

This severity of melasma, a common aesthetic issue, can range from a mild pigmentation during pregnancy that goes away on its own to a persistent, problematic, disfiguring condition. It is an acquired increase in skin pigmentation that is characterised by symmetrical gray-brown patches, particularly on exposed skin [1].

Melasma has a complex pathogenesis which is still unexplained. However, exposure to uv radiation and genetic or hormonal factors are important contributors. Other potential causes of melasma include cosmetic ingredients, phototoxic and anti-seizure medications, endocrine diseases such as thyroid or ovarian malfunction, hepatic dysfunction, and nutritional deficiencies. It is significant to highlight that up to one-third of cases of melasma in women and the number of cases in men are idiopathic [1].

Since ultraviolet exposure has a well-known ability to stimulate proliferation of melanocytes, their migration and melanogenesis, its exposure is a major triggering and exacerbating factor in the development of melasma [2]. Unlike melasma, UV-induced hyperpigmentation typically returns on its own, whereas melasma does not. Recently, Kim et al. discovered down regulation of the H19 gene on microarray analysis of hyperpigmented and normally pigmented skin in patients with melasma [3].

In melasma cases reported with usage of estrogen-progesterone oral contraceptives by mechanism of induction of melasma by estrogen may be related to the presence of estrogen receptors on the melanocytes that stimulate cells to produce more melanin [4]. Mild ovarian dysfunction may cause an idiopathic condition of melasma as Sawney and Anand found high prevalence of chronic inflammatory disease in women with melasma [5]. There are cases reported in men using estrogen derivatives for treatment of prostate cancer. However, many observations strongly suggest the role of genetic factors. familial occurrence of melasma has been

reported to vary from 20-70% in different studies [6].

Clinical features of melasma are symmetry of hyperpigmentation and distribution related to trigeminal nerves, which suggest that neural involvement may play a role in pathogenesis of pigmentation [1]. Bak et al. (2009)⁷ found higher level of neural endopeptidase in melasma lesion and suggest that neuroactive molecules, including nerve growth factor, are critical factors for pathogenesis of melasma [7]. Human melanocytes may respond to angiogenic factors because normal human melanocytes express functional receptors for vascular endothelial growth factor (VEGF) [8]. In some type of melasma, a pronounced telangiectatic erythema confined to melasma-lesional skin has been observed. Besides neural factors and hormone receptors, blood vessels may play a role as major histologic findings in melasma showed increased vascularity.

Clinically, melasma presents as a symmetrically distributed macular pigmentation with irregular borders, which can vary in color ranging from a light to dark, brown or brown, gray [1]. Pigmentation may be guttate or confetti-like, linear, or confluent that evolved slowly over weeks or years and may fade in winter and get worse in summer. According to the distribution of lesions, there are three clinical patterns of melasma: centrofacial, malar and mandibular. There are 3 types of melasma: epidermal, dermal, and mixed types, depending on the level of increased melanin in the skin [1].

The Melasma Area and Severity Index (MASI) used to assess melasma patients with severity of melasma in each of the four regions; forehead, right and left malar region, chin, that based on three variables; percentage of the area involved (A), darkness (D), homogeneity (H) [1].

Today, there are plenty of melasma treatments available, each with a different success rate. A laser's efficiency is based on the

theory of selective, which states that heating and injury are restricted to the target with less damage to the surrounding tissue when a specific wavelength of energy is delivered in a period of time shorter than the thermal relaxation time of the targeted chromophore. Thermal relaxation of melanosomes, time required for the target to cool to one-half of its peak temperature after laser light absorption, range from 50 nsec to 500nsec and the absorption spectrum of melanin is broad, therefore a variety of laser are accesible for removal of hyperpigmented spot. Short-pulsed high energy laser are the most commonly employed, including; the 510 nm pigmented lesion dye laser (PLDL), the Q- switched neodymium-yag (QS Nd: YAG) laser at 532nm and at 1064nm, the 694 nm Q-switched ruby laser (QSRL), and the 755 nm Q-switched alexandrite laser [9].

There is a growing need for an efficient melasma treatment due to modern lifestyles that include increased UV exposure, widespread use of hormones for contraception and hormone replacement therapy, as well as rising demands for aesthetics. The cornerstones of treatment are consistent use of sunscreen and topical medications that decrease melanogenesis.

This study covers recent advancement in understanding melasma pathophysiology and their implications for potential therapeutic approaches.

Case Presentation

A 28-year-old Malaysian woman of Malay ethnicity presented to our clinic with a 1-year history of hyperpigmentation on her face. Written consent was signed, provided that patient agreed to the use and analysis of her data. She came with complaint of discoloration of her face area. Physical examinations revealed multiple light to dark brown colored, irregularly shaped patches and macules with ill-defined margins on both malar areas, forehead and chin (Figure 1). There is history of using local products containing mercury for a year and patient claimed the hyperpigmentation started

appearing soon after she stopped using the products. Patient work as a hawker and is always exposed to the sun and heat at work. Sunscreen application is not routinely done. There is no history of using any hormonal contraception and no significant family history of melasma. Based on the distribution of lesions, a clinical diagnosis of centrofacial melasma was made.

Management and Outcome

Patient was treated with 3 sessions of low-fluence 1064-nm Q-Switched Nd:YAG laser, using a 1064-nm wavelength setting, with a fluence of 1.5 to 2.0 J/cm², pulse duration of 8 nanoseconds, and a 6-mm spot size. Treatments were repeated at 4-week intervals. The clinical endpoint for all three lasers was defined as mild erythema. Immediately after the procedures, the lesions were cooled with ice packs, and antibiotic ointment was applied to the irradiated area. Patient was advised to avoid sun exposure and apply a broad-spectrum sunscreen daily. There were no reported serious side effects during the course of the treatment. Digital photographs of the patient's face were taken at three different angles (frontal, right lateral, and left lateral) before initiating treatment and after completion of 3 sessions.

Follow-up assessment was done 1 month after the last treatment. As can be seen in [Figure 2], the hyperpigmented patches and macules have decreased significantly in size and intensity. To compare, pre- and post-treatment changes were analyzed using the Melasma Area and Severity Index score (MASI) in (Table 1) by reviewing patient's digital photographs before initiating the treatment and after completion of 3 treatments.

Patient is really satisfied with the outcome and rendered it successful in reducing her melasma.

Discussion

Our skin is made up of three layers. The outer layer is epidermis, the middle layer is dermis and the deepest layer is the subcutis. The epidermis

layer contains cells called melanocytes that store and produce a dark colour (pigment) known as melanin. In response to light, heat or ultraviolet radiation or hormonal stimulation, the melanocyte produces more melanin.

Melasma (previously called chloasma) is a common acquired skin disorder that presents as a bilateral, asymptomatic, light-to-dark brown macules or patches with irregular borders. Melasma is more common in women than in men and onset is typically between the ages of 20 and 40 years old.

Melasma is more common in people who tan easily or have naturally brown skin. Common areas of melasma are on the cheeks, nose, chin, above the upper lip and the forehead. Occasionally it affects the arms, neck and back. In fact, melasma can affect any part of the skin that is exposed to sunlight.

Distinct patterns include:

- Centrifacial — forehead, cheeks, nose, upper lip (sparing the philtrum); 50-80% of presentations
- Malar — cheeks, nose
- Mandibular — jawline, chin
- Erythrosis pigmentosa faciei — reddened or inflamed
- Extrafacial — forearms, upper arms, shoulders in a sun-exposed distribution.

The cause of melasma is complex. It has been proposed to be a photoageing disorder in genetically predisposed individuals. The pigmentation results from the overproduction of melanin by melanocytes (pigment cells) which is either taken up by the keratinocytes (epidermal melanosis) and or deposited in the dermis (dermal melanosis, melanophages). Factors implicated in the development of melasma include family history, sun exposure, pregnancy, use of oral contraceptives, thyroid disorder, medications and scented products.

There are 3 types of melasma. The three types are epidermal, dermal, and mixed types,

depending on the level of increased melanin in the skin.

1. Epidermal melasma is defined by dark brown, well-defined border, and appears more obvious under wood lamp. Dermoscopy will show scattered islands of brown reticular network with dark fine granules. Epidermal melasma usually has a good response.
2. Dermal melasma is defined by light brown to blue-grey, ill-defined border, no accentuation arciform structures. Dermal melasma usually has poor response.
3. Mixed melasma is the most common type, and is defined by combination of blue-grey, light and dark brown colour. Mixed patterns seen with Wood lamp and dermatoscope. Treatment usually shows partial improvement.

Melasma is usually a clinical diagnosis based on the clinical appearance, and examination with a Wood lamp and dermatoscope. Serial photography and severity indices such as the Melasma Area and Severity Index (MASI) or modified MASI was used to monitor response to treatment. The MASI value was calculated according to the following equation:

$$\text{MASI} = 0.3(\text{DF}+\text{HF}) \text{ AF} + 0.3 (\text{DMR}+\text{HMR}) \text{ AMR} + 0.3 (\text{DML}+\text{HML}) \text{ AML} + 0.1 (\text{DC}+\text{HC}) \text{ AC}$$

Where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar, and C is chin. The MASI score for the patient was evaluated before and after treatment was taken. [9].

In this study, the patient showed improvement in MASI value after 3 sessions of low-fluence 1064-nm Q Switched Nd:YAG laser treatment. Melanocytes in melasma lesions are

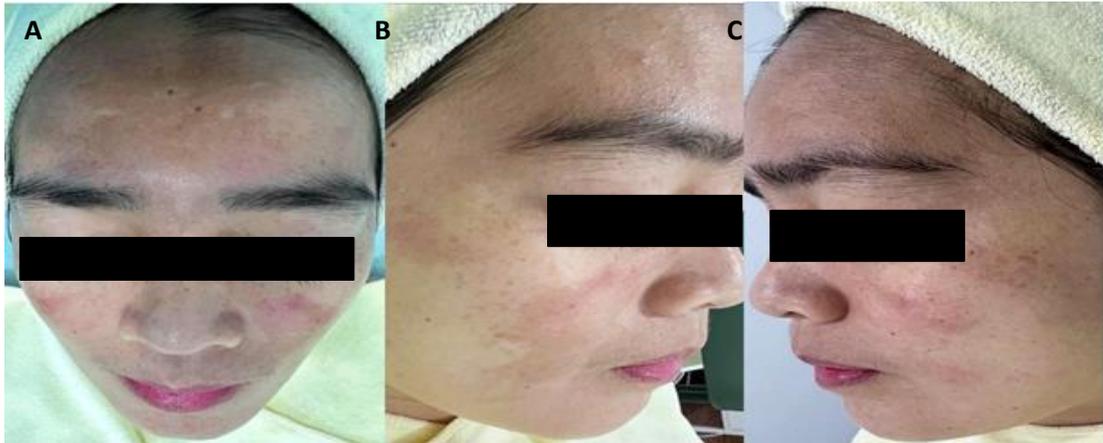


Figure 1: A 28-year-old female with centrofacial melasma. Pre-treatment photographs (A: frontal view, B: right lateral view, C: left lateral view)

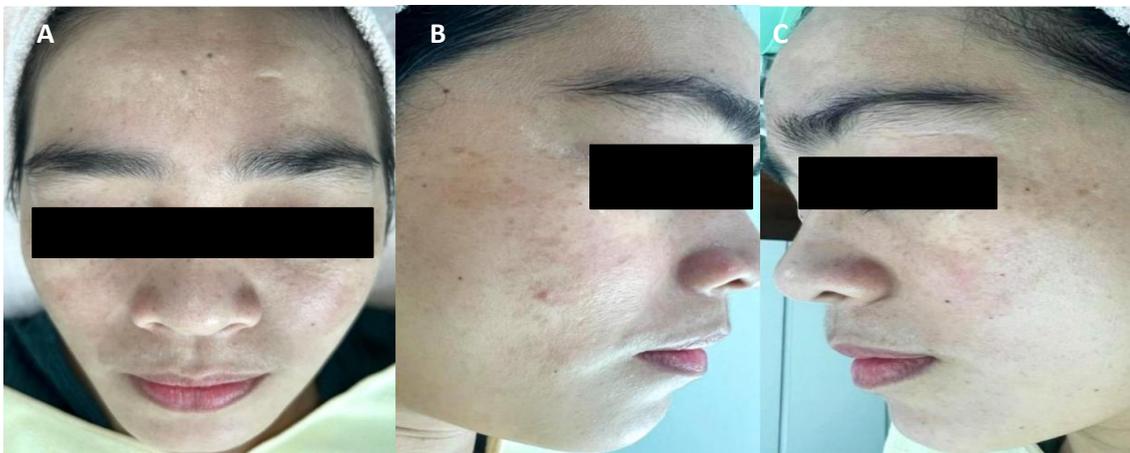


Figure 2: Post-treatment photographs (A: frontal view, B: right lateral view, C: left lateral view)

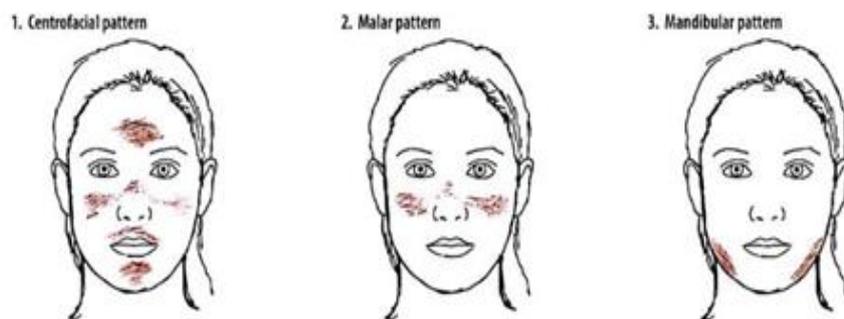


Figure 3: Pattern of Melasma

Table 1: shows the total MASI score of 34 before initiating treatment and down to 11 after 3 sessions of laser. The MASI score has decreased by 67%, on average.

Area (A) of involvement	MASI score	Before Treatment	After Treatment
Forehead	$0.3 \times A(D+H)+$	10.5	4.8
Left Malar	$0.3 \times A(D+H)+$	6.3	1.8
Right Malar	$0.3 \times A(D+H)+$	6.3	1.8
Chin	$0.1 \times (A (D+H)+$	10.8	2.4
Total score (roundup)		34	11

Table 2: Melasma Area and Severity Index score

	0	1	2	3	4	5	6
Darkness of pigment (D): Severity scale (scale 0-4)	None	Slight	Moderate	Marked	Very marked		
Homogeneity of pigment (H): (scale 0-4)	No pigment	Specks	<2 cm patches	>2cm patches	Homogenous		
Surface area involved (A)		<10%	10%-29%	30%-49%	50%-69%	70-89%	90%-100%
Site involved	Forehead	Rt. malar	Lt. malar	chin			
MELASMA AREA (scale 1-6) MA							
Multiplication factor (MF)	0.3	0.3	0.3	0.1			
MA x MF							Total area (A)

believed to be overactive in function and easily stimulated. The efficacy of Q-switched laser treatment for pigmentary lesions is based on the theory of selective photo-thermolysis. Evidence showed that low-fluence 1064-nm Q Switched Nd:YAG laser was an effective therapy treating melasma through subcellular-selective photothermolysis. The low fluence-mode application of the 1064-nm QS Nd:YAG laser is now a widely used therapy for melasma without serious side effects, especially in Asians.

As per recent studies by Niwat Polnikorn (1998)¹⁰ regarding the efficacy and safety of the Erbium (ER): YAG laser used in the treatment of Asian skin. It was concluded that significant improvement was noted in all individuals in the study. Shorter periods for re-epithelization and erythemaduration were noted when compared to previously reported results following carbon dioxide laser resurfacing and hence strengthening the use of YAG lasers as a safe and effective in the treatment of Asian skin.

Regardless, it is important to understand that while the use of the 1064-nm QS Nd:YAG laser is widely used in the treatment of melasma, side effects and complications of treatment are common.

However, the most documented complications were not serious. As investigated by Wattanakrai (2010)¹¹, in his study regarding the effectiveness and safety of the (QS-Nd:YAG) laser treatment. He postulated that among the 22 patients in his study who underwent five sessions at 1-week intervals. He noted a significant improvement of melasma from baseline with an improvement of 75.9% of mMASI score. However, during follow-up, four of 22 patients developed rebound hyperpigmentation, and all patients had recurrence of melasma. It was then concluded that the QS-Nd:YAG laser only provided temporary improvement with common complications such as hypopigmentation, melasma recurrence, and rebound hyperpigmentation.

Hence it is important to note that most treatments of Melasma range from cases to case. It is then valuable to identify those high-risk individuals during history taking in determining the severity and likelihood of these side-effects and complications during treatment. Pre-treatment care has proven to be very effective in reducing the risk of side effects and complications.

In a recent study by Jeong et al (2010)¹², who compared the clinical efficacy and adverse effects of low fluence Q switched Nd:YAG (1064 nm) laser when performed before and after treatment with topical triple combination creams (TCCs). The author concluded that pre-treatment with TCCs was more effective as this decreases melanin production before laser injury, hence chances of post inflammatory hyperpigmentations are reduced and the melasma is improved. If TCC is used after laser treatment, melanin is being produced at full capacity, hence increasing chances of PIH and slowing improvement of melasma. It was recommended that medical treatment for hyperpigmentation for at least 8 weeks before laser treatment to achieve optimal results.

In conclusion, the overall use of the 1064-nm QS Nd:YAG laser proved effective in the treatment of Melasma amongst Asians. However, it is important to get proper history taking prior treatment in predicting the risk and complications of the procedure. Pre-treatment and post treatment care has proven to be valuable in increasing the effectiveness of this treatment followed with compliance in subsequent visits to the clinic for review.

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Combination of Glycolic Acid Peel and Microneedling for Treatment of Acne Scar in An Asian Male Skin: A Case Report

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Abstract

Acne scars are a common and long-term complication of acne vulgaris which is caused by the severity of the condition and delay in treatment. Nowadays, there is various treatment option for acne scar but treating it remains to be a challenge. Microneedling is among the method that have been used to improve acne scarring. Furthermore, several studies have shown that combination of microneedling with glycolic acid peel may increase the efficacy of treatment compared to microneedling alone. In this case report, we describe a case of a 42-year-old Indonesian gentleman with moderate acne vulgaris condition and severe acne scar. The patient has suffered from acne since adolescence and has a strong family history of acne. Dermapen treatment in combination with glycolic acid peel was given to him and a near total acne scar recovery was successfully achieved after 20 weeks of treatment. Combination of dermapen and glycolic acid peel for acne scar treatment is effective, safe and well tolerated by the patient without severe side effects and complications.

Keywords: scar recovery, acne vulgaris, glycolic acid peel, dermapen

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Acne refers to a chronic inflammatory disease of the pilosebaceous unit.[1] It involves alteration of keratinization within the pilosebaceous unit, increased in sebum production, proliferation of *Propionibacterium acnes* (*P. acnes*), and production of perifollicular inflammation [2]. Acne is characterised by the formation of erythematous papules, comedones, pustules, and/or nodules (i.e., pseudocysts) and these can be accompanied by scarring. Acne is most seen in individuals aged 15 to 24 years and affects the face more compared to the trunk. A study conducted in Muar, Malaysia shows that the prevalence of facial acne among adolescents is about 67.5% [1].

Scarring is the primary long-term physical complication of acne due to an altered wound healing response to cutaneous inflammation, with an inflammatory cell infiltrate [1]. These have been found in 77% of atrophic scars condition. Furthermore, aberrant production and degradation of collagen during the healing process will produce different type acne of scar [2]. An effective early treatment might reduce the long-term complications of acne vulgaris. There are various treatment options available for treating the condition and these includes diets, topical agents, systemic agents or antibiotics and adjunctive procedural therapy. A multimodal approach for acne treatment has been recommended and it should be individualised depending on the severity, types of acne and how it affects the patient's quality of life [3].

The management of acne scars should focus on each component of scarring process. Erythema should be targeted early if present and the treatment should then focus on addressing the scarring. Besides that, the treatment approach should also depend on the types of scars present and whether generalised or individual scars predominate. Combination of treatment can offer high probability of significant improvement for post-acne scar. Furthermore, providing an early treatment for an active acne is the best way to prevent or limit

acne-related scarring [2].

Case Presentation

We present a 42-year-old man from Indonesia with complained of worsening facial acne and scar for the past 8 months. He has oily facial skin with multiple scars from previous acne lesions and had been experienced acne since adolescence. The patient had never sought any medical treatment for his skin condition prior to this visit. Besides that, he does not use any skincare products other than 3-in-1 shower cream for hair, face and body for his skin management. The patient has a strong family history of acne vulgaris as his mother and younger brother suffered from a similar condition. This patient is a non-smoker and there is no evidence of psychological stress and other medical illness present.

Dermatological examination showed greasy skin (Fitzpatrick skin type IV) with painful erythematous papules, pustules, and mixture of close and open comedones affecting the forehead, cheeks, nose, chin, and anterior part of the neck (Figure 1). Based on Global Acne Grading System (GAGS), the global score was 20 which is a presentation for moderate acne. There were also combination of boxcar and rolling scars on the cheek, nose and chin. Severe grading was recorded based on Goodman and Baron qualitative grading system.

Management And Outcome

Combination therapy was used to treat this patient. The treatment started with antimicrobial therapy such as Adapalene cream and oral Doxycycline, 100mg daily. Doxycycline was administered for a duration of 3 months. He was also advised to use a gentle gel cleanser and sun protection product with minimum SPF 30 daily. Skin improvement was observed within six weeks after starting the treatment. The frequency of breakouts on the face and neck has decreased.

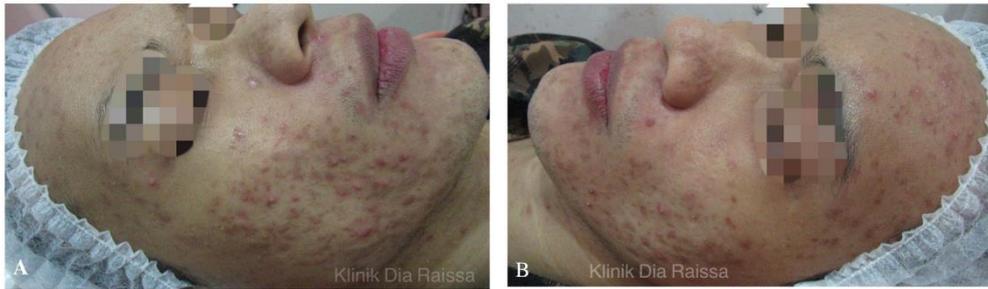


Figure 1: Patients' face on the first visit (A: Right), (B: Left)



Figure 2: Patients' face after 20 weeks of treatment (A: Right), (B: Left)

After three months, the treatment focus changed to acne scar improvement. The patient had 3 sessions of chemical peeling with 20% glycolic acid (GA) at pH 3.2 performed on full facial area, alternated by microneedling using Dermapen in 3-4 weeks intervals. A total of 3 sessions of GA chemical peel and microneedling treatment were performed on the patient.

In this case, a significant improvement in atrophic acne scars was observed within 20 weeks of treatment. According to the Goodman and Baron qualitative grading system, the grade changes from severe (Figure 1) to mild (Figure 2). The patient experience mild and transient adverse reactions such as mild erythema and skin flaking post-therapy which lasted to 48 to 72 hours and resolved spontaneously. The patient's utmost satisfaction was achieved.

Discussion

Adult-onset acne (AOA) is defined as a chronic inflammatory disease of the pilosebaceous units occurring beyond the age of 25 years. Acne that persists from adolescence into adulthood is called persistent acne, while acne that appears after the age of 25 is late-onset acne [2]. A study conducted by Goulden et al (1997)⁸ reported that

AOA is persistent in the majority of cases, generally ranging from mild to moderate in severity and presents with more inflammatory lesions and fewer comedones compared to adolescent acne. In the same study, a family history of AOA was detected in 50% of the patients [7]. Furthermore, a twin study of acne found that genetic factors account for 81% of the variance in acne [8]. In this case report, a 42-year-old male patient suffered from persistent acne condition from adolescence with atrophic post-acne scar and has a strong family history of acne. This might be the cause of persistent acne condition in this patient. Besides that, poor hygiene and the use of comedogenic products on acne-prone areas may also contribute to the persistence of acne in this patient.

The patient's initial treatment option given are adapalene and doxycycline for controlling acne breakouts as new breakouts can lead to a formation of new acne scars. During treatment, this patient was advised to avoid sun exposure and use sunscreen due to the photosensitivity reaction of doxycycline. Scar treatment approach was conducted after active acne was treated.

A combination of physical therapy and minimal invasive surgical therapy had been used for scar treatment, which is chemical peeling and dermabrasion, respectively. Chemical peeling with 20% glycolic acid at pH 3.2 was performed on full face, alternated with microneedling session using Dermapen in 2 weeks interval for six sessions. Microneedling or percutaneous collagen induction is a safe, minimally invasive, and effective esthetic treatment modality for atrophy acne scars remodelling, skin rejuvenation and tightening. It creates numerous microchannels in atrophic acne scars and physically breaks apart the compact collagen bundles in the superficial layer of the dermis while simultaneously inducing the production of new collagen and elastin underneath the scar.[3] With its fast post-treatment recovery, limited side effect profile, and impressive clinical results, microneedling is a valuable alternative to more invasive procedures such as laser skin resurfacing and deep chemical peeling. In addition, microneedling has demonstrated definitive histologic changes that are directly responsible for the clinical improvement observed. [4]

According to Clinical Practise Guideline management of Acne, 2012, chemical peeling was recommended as an adjuvant treatment for facial acne and scars. Chemical peeling creates controlled destruction of a part or entire epidermis, leading to exfoliation of superficial lesions followed by regeneration of epithelia. Chemical peeling with glycolic acid also inhibits post-inflammatory hyperpigmentation (PIH) by the action of glycolic acid, accelerates the turnover of the epidermis and inhibits melanin formation in melanocytes.

Saadawi et al. (2019)¹⁰ found a significant improvement of atrophic acne scarring in patient with different types of atrophic acne scars who received combination treatment of 35% GA and dermapen compared to the use of dermapen alone with mean improvement of 80% and 100% in microneedling and combination groups

respectively. This supports our case report finding where a combination of glycolic acid 20% and dermapen show a significant improvement in acne scars [9].

Pain, erythema and edema have been reported as adverse reaction of microneedling in several studies. For this case, a mild side effects of treatment such as erythema and skin dryness were reported for up to one week. Within 20 weeks of the treatment course, no severe side effects and complications were observed. In conclusion, the combination therapy of microneedling and GA peel were effective in treating patient with acne vulgaris and acne scars with minimal risks of side effects.

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Prominent Vagina Rejuvenation Treatment in ASEAN World Today

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Dear Editor,

"Vaginal rejuvenation" refers to any interventional procedure that improves vaginal laxity and/or restores vaginal contour. The procedures improve the woman's vaginal functionality, elasticity, sexual pleasure, and overall well-being (1).

A growing number of women strive to overcome issues related to vaginal laxity to enhance sexual function to achieve more satisfaction during coital activity. Vaginal laxity caused by physiologic changes such as vaginal childbirth, ageing, and menopause is well-known to lead to sexual dissatisfaction among women. In most cases, vaginal rejuvenation methods have improved vaginal tone and friction.

Over the years, the advancement of technology has provided a platform for surgical and non-surgical vaginal treatments with the sole aim of improving vaginal rejuvenation. The primary objective of vaginal rejuvenation is to tighten the vagina by reducing the vaginal canal dimension and restoring the strength of the posterior vaginal wall along with the perineal body. Women usually seek vagina rejuvenation for sexual reasons, among others, due to the standardized representation of female genitalia in a culture or community or the "perfect vagina" or trying to "fulfill" their partner's expectations. The ease of pornography material available at the click of a button has also fuelled requests to "beautify" and "restore" one's intimate area.

Common procedures for vagina rejuvenation include surgical such as vaginal tightening, labia minoraplasty, labia majoraplasty, clitoral hood reduction or unhooding, lipofilling, and hymen reconstruction) or non-surgical approaches (e.g., energy-based treatments, platelet-rich plasma /PRP, and fillers, among others (2,3).

It has a wide range of therapeutic effects, such as "tightening" the vagina, treating vaginal atrophy, relieving dryness or itching, helping with incontinence issues, treating discomfort during sexual activity, and enhancing sexual experience (4), especially among women troubled by Genitourinary Syndrome of Menopause (GSM).

Despite the lack of evidence to show clear medical benefits, vaginal rejuvenation procedures have increased in popularity over the recent decade, with about a 30% increase in patient demand in western countries, due to aesthetic concerns or the desire to improve sexual function (5). A quasi-experimental study by Abedi et al. in 2014 found that low vaginal lubrication and dyspareunia are among patients seeking vaginal rejuvenation therapies.

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Although the demand for vaginal rejuvenation treatment is increasing, there is still a lack of evidence-based support. Surgical procedures are provided by surgeons frequently driven by a large demand from patients seeking cosmetic vaginal transformation or management of sexual dysfunction experienced by them and/or their partners (4). Digesu further states that the outcomes of any interventions on vaginal rejuvenation, female sexual dysfunction, and vaginal laxity are inconclusive and difficult to comprehend. Federal agencies like The Food and Drug Administration (FDA) also pointed out that even though equipment like lasers is utilized for numerous surgical procedures, the agency has not authorized their use for any particularly gynaecological indication (6).

Many women have undergone non-invasive and minimally invasive procedures such as employing energy-based devices, PRP, or other therapies for vaginal rejuvenation. It is under-reported in Malaysia. It is a time to do further studies to explore our patient's awareness, preferences, and the safety and efficacy of the various procedures available.

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