RESEARCH ARTICLE

Melasma removal using Q-Switched Neodymium-doped Yttrium Aluminium Garnet laser toning and high-intensity focussed ultrasound

Shahad Abdulhadi, Mustafa Salih Al Mousawi, Wissam Majeed Kattoof

Abstract

Objective: To evaluate the effectiveness of combining high-intensity focussed ultrasound and a Q-switched neodymium-doped yttrium aluminium garnet 1064nm low-fluence toning laser in the treatment of melasma.

Method: The experimental study was conducted from November 2020 to August 2021 at the medical physics laboratory, College of Medicine, Mustansiriyah University, Baghdad, Iraq, and comprised individuals of either gender aged >25 years having mixed form melasma in malar and forehead areas. Each participant received high-intensity focussed ultrasound treatment on the right side. After 2 weeks, Q-switched neodymium-doped yttrium aluminium garnet 1064nm low-fluence toning laser was applied to the melasma patches 4 times at one-week intervals. Melasma area and severity index scores were noted at baseline and at each visit for each patient. Visual analogue scale was used for objective evaluation. After the 4 laser sessions, all the patients completed a 3-month follow-up. Data was analysed using SPSS 24.

Results: Of the 25 subjects, 15(60%) were females and 10(40%) were males. The overall mean age was 41.6±8.46 years (range: 22-60 years). There was a significant improvement with high-intensity focussed ultrasound ($p<0.05$). In the 3rd laser session, there was a significant difference in melasma area and severity index score of 2.48 for the right side and 3.12 for the left side ($p<0.05$). In the 4th session, there was a significant difference in melasma area and severity index score of 1.68 for the right side and 2 for the left side ($p<0.05$). No post-inflammatory hyperpigmentation or rebound was noted.

Conclusion: High-intensity focussed ultrasound combined with toning laser was more effective than Q-switched neodymium-doped yttrium aluminium garnet 1064nm low-fluence laser alone in removing difficult melasma from the malar area in the 2nd, 3rd and 4th sessions, and from the forehead in the 3d and 4th sessions.

Key Words: Aluminum, Neodymium, Melanosis, Yttrium

(JPMA 74: S326 (Supple-8); 2024) **DOI: https://doi.org/10.47391/JPMA-BAGH-16-75**

Introduction

Melasma is a dermatological condition, and not a systemic disease, with women more likely to have it than men[1]. People with darker skin tones are at particular risk[2]. It appears as black or brown spots on various areas of the face, including the forehead, chin, malar and the entire face[3,4]. Melasma is very difficult to treat definitively due to its recurrence even after treatment[5]. A novel method of melasma treatment is innovative and based on high-intensity focussed ultrasound (HIFU), which is a technology that uses high-frequency ultrasound to create precise thermal damage at a certain depth beneath the skin, which, in turn, causes dermal collagen renewal and superficial muscular aponeurotic system contraction without harming the epidermis or the surrounding tissue[6]. Recently, several clinical studies have favoured laser toning through the Q-switched neodymium-doped yttrium aluminium garnet (Nd-YAG) laser for its tangible effectiveness in treating all types of melasma[7]. Melasma has been successfully treated using a Q-switched Nd-YAG (QS-Nd: YAG) laser with 1064nm wavelength[1]. Non-ablative face treatments with the Nd:YAG laser at 1064nm have been shown to be safe and effective[3]. The QS-Nd: YAG laser 1064nm was first used in Asia for skin tone and facial pigmentation treatment many years ago. The wavelength of 1064nm reaches deeper into the dermis, while avoiding the epidermis[1]. However, sub thermolytic QS treatment is generally associated with some degree of damage, but this damage is described to be less than that caused by typical photo thermolytic therapy [3]. As a result, there is still a need to find a method that reduces the amount of skin damage, while also reducing pain severity. The theory behind using sub thermolytic low fluences to treat melasma patients is that pigment disruption occurs via a photoacoustic mechanism that only destroys the pigment while sparing the keratinocytes and melanocytes[6]. HIFU was designed to use a thermal effect on tissue heating and denaturation caused by ultrasound absorption. Because the heating rate is determined by the local acoustic intensity, the temperature rises to the point

Department of Physiology, Mustansiriyah University. Baghdad, Iraq.

Correspondence: Munawar Luie Esmaiel

Email: shahad.hadi1988@gmail.com

where the tissue is abated only in the focussed region. At lower HIFU focal intensities, thermal ablation is the primary interaction. The evolution of HIFU medical technology has reached a tipping point with this ultrasound-induced tissue disintegration. The procedure's name has its origins in the Greek language in which the prefix 'histo' means 'tissue'[8]. Lee MC et al.,[9] in 2014 conducted treatment of melasma with 1064nm QS-Nd: YAG laser toning and improved the impact of vitamin C request using ultrasonic technology. They suggested using this strategy to treat tough facial pigmentation issues, like melasma, as it can provide better results. When comparing laser monotherapy to ultrasonic vitamin C treatment, the results revealed a considerable improvement. During the 2nd, 3rd and 4th sessions, the improvement was more obvious. During the 3-month follow-up period, there was no rebound, or post-inflammatory hyperpigmentation. Melasma responded faster to a combination of 1064-nm QS-Nd:YAG laser therapy and ultrasonic application of topical vitamin C[1]. On the other hand, a 2020 study[4] having 21 Asians with Fitzpatrick (FPT) skin types III and IV reported that the HIFU-treated side had a larger reduction in relative lightness index and melasma area and severity index (MASI). However, between the two groups, there were no differences that were statistically significant. In 11 individuals, there was a 50% improvement on the treatment side (52.4%). There were very few side effects. No one's melasma had worsened.

The current study was planned to evaluate the effectiveness of combining HIFU and QS-Nd: YAG 1064nm low-fluence toning laser in the treatment of melasma.

Patients and Methods

The experimental study was conducted from November 2020 to August 2021 at the medical physics laboratory, College of Medicine, Mustansiriyah University, Baghdad, Iraq. Approval was obtained from the institutional ethics review committee, and informed consent was taken from all the patients.

The sample was raised using consecutive nonprobability sampling technique. Those included were individuals of either gender aged >25 years having mixed form melasma in malar and forehead areas. Those exposed to laser in the preceding 3 months, pregnant or lactating women, hormonal dysfunction, and those with any recent extreme inflammatory disorders on the face were excluded.

During the intervention, all patients were asked to refrain from using any whitening cream. Data was collected using a questionnaire. The diagnosis was clinically done with two dermatologists and by the aid of Wood's light. The face of all eligible participants was cleansed prior to the treatment by a gentle cleanser. On the right side, a water-based gel (ECG Gel, Camcare Gels, Ely, Cambridgeshire, United Kingdom) was applied to the skin surface and then exposed to HIFU with a 0.2J/cm^2 fluency, while the left side of the face was sealed and considered a control side in the first HIFU session to test the efficacy of the combination therapy. After 2 weeks, and after ensuring that no participant had experienced any side effects or discomfort, laser toning using a 1064nm QS-Nd: YAG laser with several passes (6mm spot size and 2.5J/cm^2 fluency at 9Hz) was applied to melasma spots on both sides repeated every week for 4 consecutive weeks. Before each treatment session, standard digital photographs (Canon camera focused 17MP, Japan) were taken in two views (front and both sides) of the face. MASI scores were recorded at the first visit and after the last session. The subjects were instructed to avoid direct sunlight exposure. They were given medicated sunscreen (Pharmace SPF 50+, China) and daily use was confirmed throughout the treatment. The subjects were also asked to avoid the use of any other topical medication. After treatment, the subjects were monitored for 3 months.

The severity of melasma was measured by two blinded dermatologists using MASI at baseline and at each visit for each patient. MASI score was calculated using the equation MASIm=(D+H)×A where A was the percentage of involvement ranging 0-6, D was pigment darkness ranging 0.0-4 (0 = absence or normal colour of the skin without hyperpigmentation, 1 = slight hyperpigmentation, 2 = mild hyperpigmentation, 3 = marked hyperpigmentation, 4 = severe hyperpigmentation), and H was hyperpigmentation homogeneity or density (per-unit facial surface, the number of pigmented lesions) ranging 0-4.

Visual analogue scale (VAS) score was used for objective evaluation of pain, ranging 0-10. The dermatologists evaluated any negative effects at each visit.

Data was analysed using SPSS 24. Data was expressed as frequencies and percentages, or as mean ± standard deviation, as appropriate. The significance of the difference between various quantitative means was assessed using the students' test for independent means or the paired t-test for dependent means. When there were more than 2 means to be compared, analysis of variance (ANOVA) was employed. $P<0.05$ was considered statistically significant.

Results

Of the 25 subjects, 15(60%) were females and 10(40%) were males. The overall mean age was 41.6±8.46 years (range: 22-60 years). In 14(56%) cases, melasma size ranged 5-10cm. Melasma was found in the malar area in 20(80%) cases, and in the forehead in 5(20%).

The baseline MASI score for both the left and right sides was 0.72. After the HIFU treatment, there was no significant difference in MASI score on both treated sides with laser at the 1st and 2nd sessions (p>0.05). In contrast, the third session resulted in a significant difference in MASI score of 0.16 for the right side and 0.28 for the left side (p<0.05). In the 4th session, there was a significant

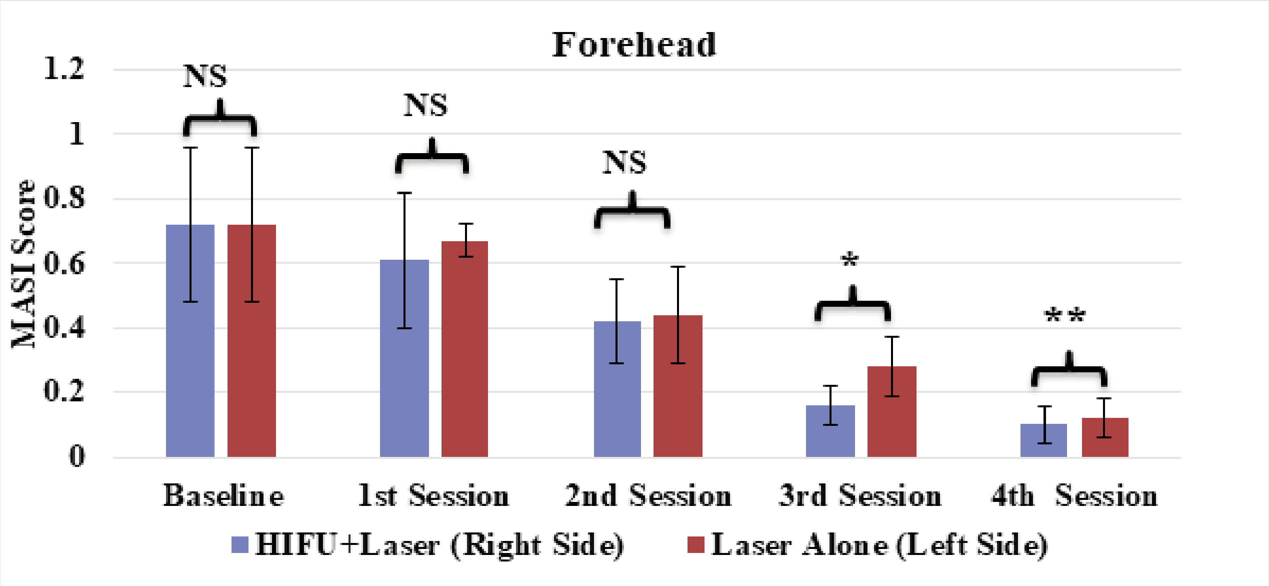

Figure-1: Comparison between the HIFU + laser and laser alone groups in all forehead treatment sessions.
*p<0.05, **p<0.001. NS: Non-significant, HIFU: High-intensity focussed ultrasound, MASI: Melasma area and severity index.

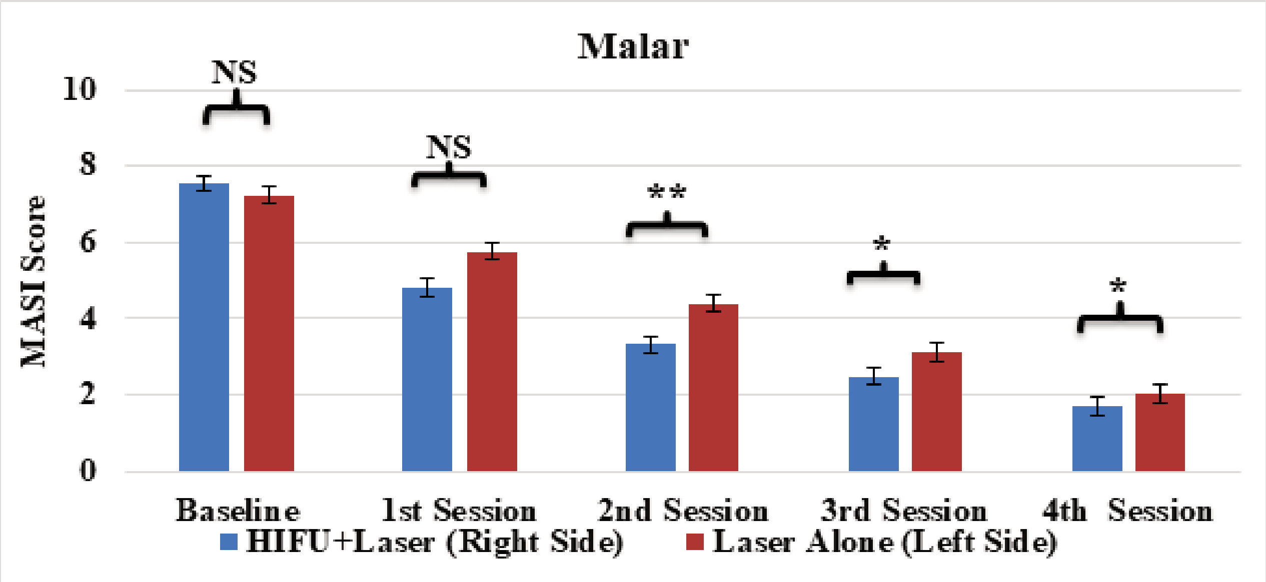

Figure-2: Comparison between HIFU+ laser and laser alone groups in all malar treatment sessions.
*p<0.05, **p<0.001. NS: Non-significant, HIFU: High-intensity focussed ultrasound, MASI: Melasma area and severity index.

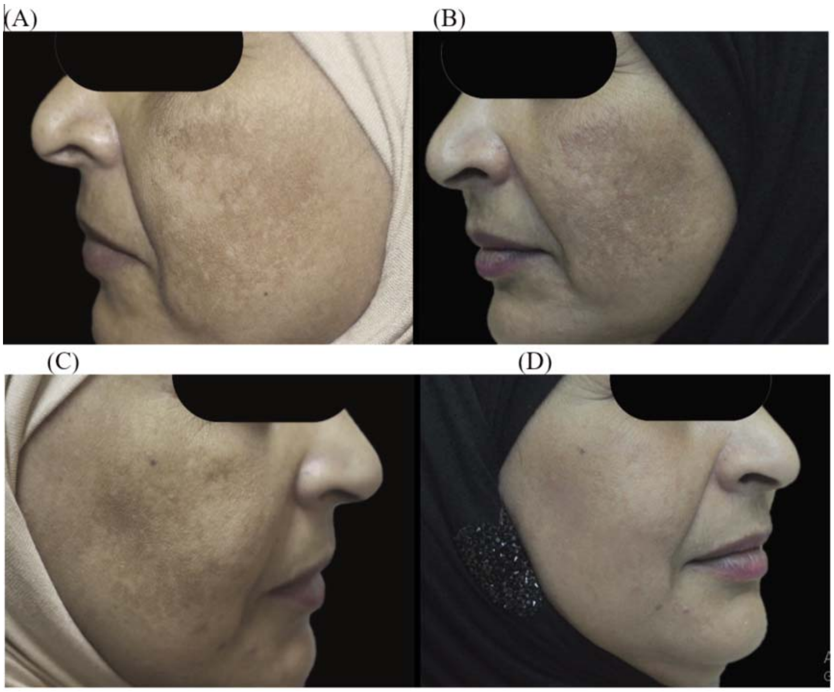

Figure-3: A subject with malar melasma. (A) Baseline side before treated. (B) Control side before treated. (C) HIFU+laser treated. (D) Treated with laser alone. HIFU: High-intensity focussed ultrasound.

difference in MASI score of 0.1 for the right side and 0.12 for the left side ($p<0.001$) (Figure 1).

MASI score was noted for malar in HIFU-laser combination site and the laser-alone side. The baseline MASI scores for the right and left sides were 7.56 and 7.24, respectively ($p>0.05$). After the HIFU treatment, there was no significant difference in MASI score on both treated sides with laser at the 1st session ($p>0.5$). The 2nd session resulted in a significant difference in MASI score of 3.32 for the right side and 4.4 for the left side ($p<0.001$). In the 3rd session, there was a significant difference in MASI score of 2.48 for the right side and 3.12 for the left side ($p<0.05$). In the 4th session, there was a significant difference in MASI score of 1.68 for the right side and 2 for the left side ($p<0.05$) (Figure 2). No post-inflammatory hyperpigmentation or rebound was noted. The visual effect of the treatment was noted (Figure 3).

Across all the sessions, the pain level which was assessed by grading from 0 to 10, in group of patients who exposed to combined Laser and HIFU was slightly higher[2-3] than in patients who were treated by laser alone[1-2].

Discussion

Melasma is a refractory disease of pigmentation disorders that has a major negative effect on one's quality of life. Several trials have shown that laser and light therapy are effective treatments for the disease [8-11]. Many procedures have been used in the past to treat melasma, but they all resulted in hyperpigmentation or hypopigmentation, and, in many cases, inflammation. Besides, in all cases, it was not completely removed, with a high probability of recurrence during or immediately following the treatment[11-15] . As a result, finding a new method was needed. The current study combined HIFU and QS-Nd: YAG toning laser for the purpose. Previous research has found that HIFU, with no specific depth below the skin, causes drastic pigmentation reductions in darker skin types, and can play a key function in eliminating myelinophagia with certain resistant dermal pigment disorders[2]. HIFU removes melanin from the epidermis and dermis by mechanical destruction, resulting in dermal collagen regeneration. In human participants with FPT skin types III and IV, the efficacy and reliability of HIFU for hyperpigmentation induced through ultraviolet B (UVB) have been examined[6]. In 2019, Bove et al.[16] examined the use of HIFU on 52 subjects with skin types III–VI, and found that it was effective and safe in people with darker skin. The vibration and friction of pigments that transcend HIFU-induced melanin degradation can be explained by the mechanical destruction of melanin collected above the thermal coagulation point (TCP) plane caused by HIFU in the treatment of hyperpigmentation[4]. Mechanical disruption is accomplished by repeatedly exposing tissue to high-intensity ultrasound pulses of a microsecond to millisecond length. This technique fractionates the tissue in a regulated manner, resulting in complete separation of the tissue into submicron fragments, resulting in a liquefied area that can be easily extracted by natural wound healing responses. This is the most important advantage of mechanical ablation[10].

The current study compared the efficacy and safety of HIFU with laser to laser-alone in the treatment of melasma in the forehead and malar. The melasma condition did not deteriorate in any of the patients. In terms of patient evaluations, roughly half of the participants regarded the improvement as >50% on the HIFU-treated side, while the majority assessed the improvement as >50% on the control side (26-50%). The results suggested that HIFU had beneficial effects in the treatment of melasma. This is backed by the postulated mechanism whereby HIFU causes vibration and friction in the epidermis and upper dermis, resulting in mechanical destructive effects that further remove melanin and pigmented debris[4]. Nautiyal et al.[2] found that 4 clinically favourable improvements in hyperpigmentation could be seen as early as 2 weeks after HIFU therapy. As a result, it is possible that a shorter therapy time and/or a greater number of HIFU sessions would result in more noticeable findings.

On the treated side in the 2nd session, the significance of HIFU increased, and it continued to increase steadily in the 3rd and 4th sessions. While lasers can target pigments at certain depths beneath the skin alone for the photoacoustic effect, they can lead to a more extreme pigmentation reduction in darker kinds, and play a major part in the eradication of monophagous in some resistant dermal pigment diseases. The laser disrupts the pigment via an optical mechanism that only breaks down the pigment while protecting the keratinocytes and melanocytes. Longer wavelengths are harmless to the skin, and do not absorb haemoglobin, whereas melanin absorbs 1064nm QS-Nd: YAG well[2,7]. Deep penetration of the skin also aids in the targetting of cutaneous melanin. The low-dose QS-Nd: YAG laser causes melanosomes to break down and rupture in the cytoplasm, resulting in near-fatal injury. The upper cutaneous vascular plexus, which is a pathogen in melasma, also has cellular damage. Collagen production is stimulated by injury to the underlying dermis[2,16]. Kim et al.[17] demonstrated that Fontana-Masson and Melan-A stains revealed a pronounced decrease in melanin and melanocytes in the basal layer, findings similar to those seen in punctate leukoderma, and hypothesised that the pigment decrease after Nd:YAG toning laser was a phototoxicity-induced injury to melanin. Despite the fact that melanocytes existed, Aleem et al.[18] discovered a decrease in pigment as a result of toning laser for melasma in 16 patients, and three-dimensional (3D) scanning electron microscopy revealed a significant decrease in the size and amount of melanocytic dendrites, which bring melanin to keratinocytes.

To our knowledge, the current is the first to use HIFU and laser in combination to treat melasma. All the participants were pleased with the outcomes. During the HIFU session, none of the participants experienced any adverse effects. The redness and pain, as with all sessions, faded after 2-3 hours, and lasted no longer than one day in the most severe of cases. During the 3rd and 4th laser sessions, some subjects experienced painless peeling. During the sessions, no hyperpigmentation or hypopigmentation was observed.

Limitation: The current study has limitations as the sample size was not calculated which could have affected the power of the study

Conclusion

HIFU combined with QS-Nd: YAG toning laser was more effective than laser alone in removing difficult melasma from the malar area in the 2nd, 3rd and 4th sessions, and from the forehead in the 3d and 4th sessions.

Acknowledgments: We are grateful to the supervisors and to the College of Medicine, Mustansiriya University, for facilitating the study.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Iranmanesh B, Khalili M, Mohammadi S, Amiri R, Aflatoonian M. The efficacy of energy-based devices combination therapy for melasma. Dermatol Ther 2021;34:e14927. doi: 10.1111/dth.14927.
2. Nautiyal A, Wairkar S. Management of hyperpigmentation: Current treatments and emerging therapies. Pigment Cell Melanoma Res 2021;34:1000-14. doi: 10.1111/pcmr.12986.
3. Micek I, Pawlaczyk M, Kroma A, Seraszek-Jaros A, Urbańska M, Gornowicz-Porowska J, et al. Treatment of melasma with a low-fluence 1064 nm Q-switched Nd:YAG laser: Laser toning in Caucasian women. Lasers Surg Med 2022;54:366-73. doi: 10.1002/lsm.23474.
4. Vachiramon V, Iamsumang W, Chanasumon N, Thadanipon K, Triyangkulsri K. A study of efficacy and safety of high-intensity focused ultrasound for the treatment of melasma in Asians: A single-blinded, randomized, split-face, pilot study. J Cosmet Dermatol 2020;19:375-81. doi: 10.1111/jocd.13044.
5. Yahia MJ, Hasan JA, Musawi MS. Biostimulation effect of DPSS laser irradiation with different power densities and radiation times on blood viscosity in vitro. AIP Conf Proc 2020;2213:020118. DOI:10.1063/5.0000438.
6. Trivedi MK, Yang FC, Cho BK. A review of laser and light therapy in melasma. Int J Womens Dermatol 2017;3:11-20. doi: 10.1016/j.ijwd.2017.01.004.
7. Feng J, Shen S, Song X, Xiang W. Efficacy and safety of laser-assisted delivery of tranexamic acid for the treatment of melasma: a systematic review and meta-analysis. J Cosmet Laser Ther 2022;24:73-9. doi: 10.1080/14764172.2022.2148186.
8. Maxwell A, Sapozhnikov OA, Bailey M, Crum L, Xu Z, Fowlkes JB, et al. Disintegration of Tissue Using High Intensity Focused Ultrasound: Two Approaches That Utilize Shock Waves. Acoust Today 2012;8:24. DOI:10.1121/1.4788649.
9. Lee MC, Chang CS, Huang YL, Chang SL, Chang CH, Lin Y, et al. Treatment of melasma with mixed parameters of 1,064-nm Q-switched Nd: YAG laser toning and an enhanced effect of ultrasonic application of vitamin C: a split-face study. Lasers Med Sci 2015;30:159-63. DOI:10.1007/s10103-014-1608-2.
10. Al Musawi MS, Jaafar MS, Al-Gailani B, Ahmed NM, Suhaimi FM, Suardi N, et al. Effects of low-level laser irradiation on human blood lymphocytes in vitro. Lasers Med Sci 2017;32:405-11. doi: 10.1007/s10103-016-2134-1.
11. McKesey J, Tovar-Garza A, Pandya AG. Melasma Treatment: An Evidence-Based Review. Am J Clin Dermatol 2020;21:173-225. doi: 10.1007/s40257-019-00488-w.

12. Nam JH, Choi YJ, Lim JY, Min JH, Kim WS. Synergistic effect of high-intensity focused ultrasound and low-fluence Q-switched Nd:YAG laser in the treatment of the aging neck and décolletage. Lasers Med Sci 2017;32:109-16. doi: 10.1007/s10103-016-2092-7.
13. Izadifar Z, Izadifar Z, Chapman D, Babyn P. An Introduction to High Intensity Focused Ultrasound: Systematic Review on Principles, Devices, and Clinical Applications. J Clin Med 2020;9:460. doi: 10.3390/jcm9020460.
14. Abbas KF, Al Musawi MS, Kattoof WM. Fast tattoo removal using Q-Switching ND-YAG laser technique with multi pass sessions. J Pak Med Assoc 2021;71(Suppl 8):s161-5.
15. Guo X, Cai X, Jin Y, Zhang T, Wang B, Li Q, et al. Q-PTP is an optimized technology of 1064-nm Q-switched neodymium-doped yttrium aluminum garnet laser in the laser therapy of melasma: A prospective split-face study. Oncol Lett 2019;18:4136-43. doi: 10.3892/ol.2019.10743.
16. Bove T, Zawada T, Serup J, Jessen A, Poli M. High-frequency (20-MHz) high-intensity focused ultrasound (HIFU) system for dermal intervention: Preclinical evaluation in skin equivalents. Skin Res Technol 2019;25:217-28. doi: 10.1111/srt.12661.
17. Kim HJ, Moon SH, Cho SH, Lee JD, Kim HS. Efficacy and Safety of Tranexamic Acid in Melasma: A Meta-analysis and Systematic Review. Acta Derm Venereol 2017;97:776-81. doi: 10.2340/00015555-2668.
18. Aleem S, Majid I. Unconventional Uses of Laser Hair Removal: A Review. J Cutan Aesthet Surg 2019;12:8-16. doi: 10.4103/JCAS.JCAS_97_18.