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Evaluation Safty And Efficacy Of Fractional Ablative Erbium: Yag Laser Andglycolic Acid 70% In Treatment Of Melasma

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ABSTRACT

Introduction: Melasma is a common dyschromia that often motivates the search for dermatological care. The treatment options of melasma, including topically applied agents as chemical peelings and the use of various laser systems.

The aim: This study aims to compare the clinical efficacy and safety offractional ablative erbium:YAG Laser versus giycolic acid 70% in the treatment of melasma.

Patients, materials and methods: The present study included 30 patients with melasma on their face aged 21-51 years. The patients were divided into two groups. Group I, 15 patients were treated by fractional erbium YAG laser at 4 weeks interval. Group II, 15 patients were treated by glycolic acid 70%.

Results: The percentage of improvement in patients treated by fractional erbium YAG laser was 25 – 80% and the percentage of improvement in patients treated by chemical peeling was 30 – 85 %. So, the percentage of improvement in both groupswas not significant (P- value = 0.811).
Conclusion: It was observed that both fractional erbium YAG and 70% glycolic acid peel are effective in treatment of melasma.

Keywords: Melasma, peeling, Erbium YAG laser

INTRODUCTION

The word melasma has been originated from a greek word 'melas' which means black. It is known as 'chloasma' when it occurs during pregnancy **(Kaur et al. 2018).** Melasma is an acquired chronic hypermelanosis which mainly affects women during fertile age in more pigmented phenotypes (Fitzpatrick skin types III-V). Melasma is characterized by irregular brown macules symmetrically distributed on sun-exposed areas of the body, especially on the face **[Handel et al. (2014)**, **Ogbechie-Godec and Elbuluk. (2017)].** The exact causes of melasma are unkown, although some triggering factors are described, such as sun exposure, pregnancy, use of oral contraceptives and use of cosmetics

and photosensitizing drugs **(Tamega et al. 2013)**.By Wood's lamp examination and dermoscopy, the following types of melasma are described, Epidermal type, Dermal type and Mixed type **(Dharni et al. 2018).**

Dermatoscope helps in diagnosis and prognosis of melasma. Therapeutic efficacy of various modalities can be monitored using dermatoscope. **(Kaur et al. 2018).** Dermoscopic findings are the mirror of underlying histopathological features. So it forms a link between macroscopic clinical dermatology and microscopic dermatopathology **(Ramadan et al. 2014).**

The treatment options of melasma include topically applied agents, chemical peels and the use of various laser systems as Qswitched Nd: YAG, Q-switched alexandrite and different fractional lasers **(Ogbechie-Godec and Elbuluk. 2017).**The ablative fractional lasers as fractional Erbium:YAG lasers (2940 nm) target the water. These lasers canindirectly reduce melanin deposits from both theepidermis and dermis by vaporization of tissue includingnumber of abnormal epidermal melanocytes and melanincontent **(Wanitphakdeedech et al. 2009).**

The most frequently used peeling agents for melasma are glycolic acid (GA), trichloracetic acid (TCA), and Jessner's solution (JS) **(Sharad. 2013).**

AIM OF THE STUDY

To compare the clinical efficacy and safety of both fraction alablative erbium: YAG Laser andglycolic acid 70% in treatment of melasma.

PATIENTS, MATERIALS AND METHODS

Thirty patients with melasma on their face aged 21-51 years, divided into two groups. Group (I), 15 patients were treated by fractional erbium YAG laser. Group (II), 15 patients were treated by Glycolic acid 70%.

The patients who had previously been treated within the past 6 months, pregnant patients or lactating women were excluded in this study.

The study protocol was approved by the ethical committee of National Institute of Laser Enhanced Sciences (NILES), Cairo University. In addition, the study followed the ethical guidelines of the National Institute of Laser Enhanced Sciences (NILES), Cairo University. Informed consent was obtained from all patients.

The melasma was done by both Wood's lamp and Dermoscopy, its distribution on the face, and its severity index by MASI score, and its vascular and pigmentary component by dermoscopy.

Treatment was every 4 weeks for four sessions with fractional ablative erbium:YAG (2940 nm) laser and glycolic acid 70%.

Pre-operative measures were application of topical anesthesia for one hour before laser.Post-operative measures were application of local cooling, antibiotic ointment, sunscreen and mild topical steroid was used if erythema and edema persist more than 3 days. Avoidance of rubbing and scratching was advised.

Assessments of the results were depended on clinical patient satisfaction, histopathology examination and dermoscopic evaluation.

Dermoscope was used to evaluate degree of pigmentation and vascular component of melasma.

Followed up for six months after the end of thetreatment to observe any recurrence or any side effects.

Safety assessment to detect any complications as burning pain erythema, edema, infection, any allergic manifestations, post inflammatoryhypo or hyperpigmentation etc…

Statistical analysis for the data was done.

RESULTS

This study included thirty patients with melasma on their face, with average age of 36 years and with skin types II – IV. There were two groups of 15 patients each. In group I, patients were subjected to four sessions of 2940 nm Erbium YAGfractional laser. In group IIpatients, four sessions ofchemical peeling with 70% glycolic acid were done.

The type of melasma was classified by woods light and dermoscope in to 3types (epidermal, dermal, and mixed). In group (I), therewere 9 patients with epidermal melasma, 4 patients with dermal melasma, and 2 patients with mixed melasma. Ingroup (II), there were 10 patients with epidermal 2patients with dermal melasma, and 3 patients with mixed melasma.

According to MSI score, severity index of melasma inlaser group, there were 2 patients with mildmelasma, 9 patients with moderate melasma and 4patients with severe melasma. But glycolic acid 70% group, there were 3 patients with mildmelasma, 9 patients with moderate melasma and 3patients with severe melasma**.**

The percentage of improvement by laser therapy was50 – 80 % in epidermal melasma, 25 - 55 % in dermalmelasma, and 20 – 40 % in mixed type. There was significant improvement in epidermal type by lasertreatment (P- value = 0.001*)**Table (1).**

The percentage of improvement by peeling therapy was55 – 85 % in epidermal melasma, 35 - 55 % in dermalmelasma and 35 – 45 % in mixed type. There wa ssignificant improvement in epidermal type by chemicalpeeling treatment (P- value = 0.002*)**Table (2).**

The percentage of improvement in patients treated byfractional erbium YAG laser was 25 – 80 % and the percentage of improvement inpatients treated by chemical peeling was 30 – 85 %. So, there was no significantdifference in bothgroups (P- value = 0.811). Clinical, histopathological and dermoscopic images of some patients are shown in**Figs. 1, 2**.

In group (I), patients withmild melasma improved by 55%, patients with moderatemelasma improved by 20-80% and patients with severe melasma improved by 30-75% with non-significant value (p. value =0.69)**.**

In group (II), the improvement was 30-60% in patientswith mild melasma, 30-85% in patients with moderatemelasma and 40-80% in patients with severe melasmawith non-significant value (p. value =0.45)**.**

By dermoscopy, The percentage vascular component decline in group (I) was 25-65% and ingroup (II) was 15-35% with significant decrease invascular component in patients treated by fractional Erbium YAG laser (P. value= 0.001*)**Table (3)**.

In present study, all patients were followed up after 3 months and after 6 months. The recurrence occurred insome cases after 6 months in both groups. The total percentage of recurrence in all patients in both groupswas 33.3 %.

Burning pain and erythema occurred in all patients of both groups, but this erythema was improved bythe topical steroid.. No post inflammatoryhypo or hyperpigmentation was occurred.

Table (1): The percentage of improvement in different types of melasma in group (I)

Improvement %	**Epidermal**	**Dermal**	**Mixed**
Range	50 – 80%	25 – 55%	20 – 40%
Mean ± SD	68.13± 7.53	38.0± 13.04	40.0 ± 14.14
F. test	**15.349**		

p. value	**0.001***

Table (2): The percentage of improvement in different types of melasma in group (II)

Improvement %	Epidermal	Dermal	Mixed
Range	55- 85	35 - 55	35 – 45
Mean ± SD	66.25 ± 13.30	43.33 ± 11.55	35.0 ± 5.77
F. test	**11.143**		
p. value	**0.002***		

Table (3): The percentage of decrease of vascular component in both groups by dermos copy

Decrease of Vascular component% by dermoscopy	Group (I) Erbium YAG Laser	Group (II) Chemical Peeling
Range	25 – 65	15 – 35
Mean ± SD	45.23 ± 12.46	24.33 ± 7.24
T. test	34.968	
P. value	0.001*	

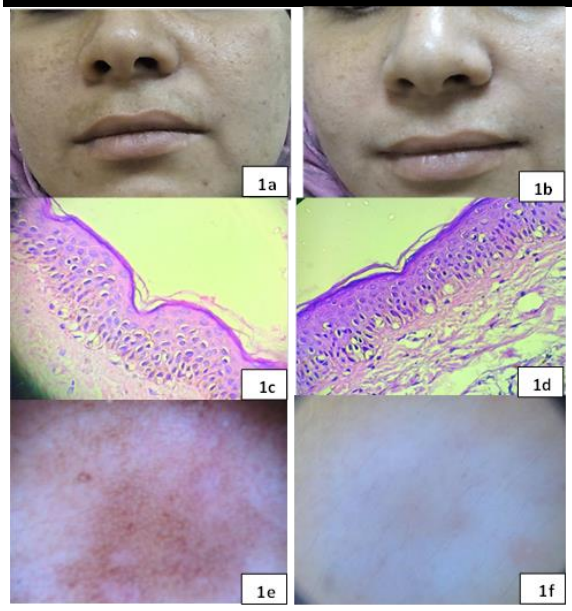

Fig. (1): 1a: Female patient aged 32 years with epidermal melasma (before treatment), 1b: The same patient after 4 sessions of fractional Erbium YAG laser with very good improvement, 1c: Histopathological examination of the same patient before treatment stained with hematoxylin and eosin, 1d: Histopathological examination of the same patient after 4 sessions of fractional Erbium YAG laser with very good decrease in the melanin content, 1e: dermoscopic examination of the same patient before the treatment showing (dark brown color + blue gray color areas), 1f: Dermoscopy of melasma lesion after treatment showing (no brown coloration).

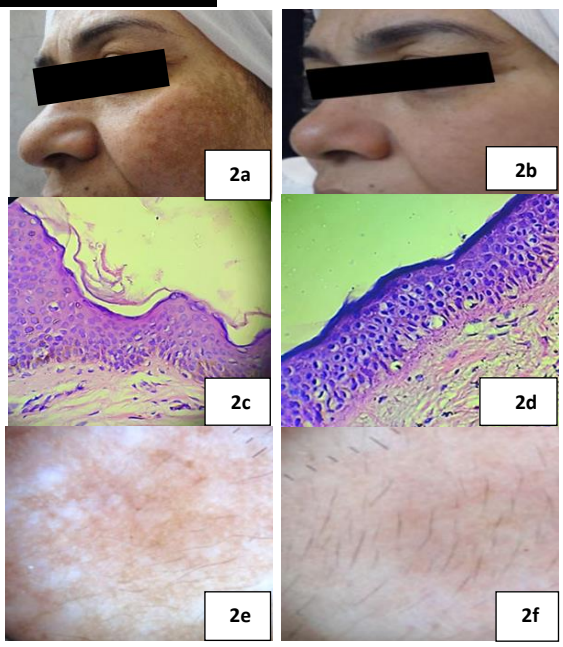

Fig. (2): 2a: Female patient aged 31 years with epidermal melasma (before treatment), 2b: The same patient after 4 sessions of chemical peeling with glycolic acid 70% with very good improvement, 2c: Histopathological examination of the same patient before treatment stained with hematoxylin and eosin, 2d: Histopathological examination of the same patient after 4 sessions of chemical peeling with glycolic acid 70% with very good decrease in the melanin content, 2e: dermoscopic examination of the same patient before the treatment showing (dark brown color + blue gray color areas), 2f: Dermoscopy of melasma lesion after treatment showing (very light brown coloration)

DISCUSSION

In this study, the type of melasma was divided by woods light and dermoscopy in to 3 types (epidermal, dermal, and mixed). In group (I), there were 8 patients with epidermal melasma, 5 patients with dermal melasma, and 2 patients with mixed melasma. In group (II), there were 8 patients with epidermal melasma, 3 patients with dermal melasma, and 4 patients with mixed melasma according to **Tamler et al in (2009), Hammerschmidt et al in (2012)**, **Lee et al in (2017) and Dharni et al in (2018**).

AsMSI is illustrated as a useful measure in the clinical classification of melasma **(Majid et al. 2016)**. The severity index of melasma in the current study, in group (I), there were 2 patients with mild melasma, 9 patients with moderate melasma and 4 patients with severe melasma. While in group (II), there were 3 patients with mild melasma, 9 patients with moderate melasma and 3 patients with severe melasma.

Concerning the percentage of melasma improvement in the present study, in group (I), it was 60 – 80 % in epidermal melasma, 20 - 50 % in dermal melasma, and 30 – 50 % in mixed type. There was significant improvement in epidermal type by laser treatment (P- value = 0.001*). This can be explained by the statement of **Wanitphakdeedech et al in (2009) and Sarkar and Ailawadi in (2017)**who reported that the fractional ablative lasers, by targeting water, can indirectly reduce melanin deposits from both the epidermis and dermis. Due to tissue vaporization, the number of abnormal epidermal melanocytes and melanin content are decreased, as probably occurs with the amount of melanin deposited into dermal melanophages occasionally reached by laser beams. It could be also explained by the fact that during healing process, the epidermis is regenerated from the appendiceal units; therefore, it is believed that the inward migration of new melanocytes to the epidermis is unable to produce localized areas of hyperpigmentation **[Wanitphakdeedech et al. (2009)&Sarkar and Ailawadi. (2017)]**.

Manaloto and Alster in 1999 treated 10 female patients with refractory melasma using erbium:YAG laser at energy levels of 5.1 J/cm to 7.6 J/cm. There was a marked improvement of melasma immediately post treatment **(Manaloto and Alster. 1999).**

Ablative fractionated resurfacing lasers (AFL) such as CO2 lasers and erbium:YAG lasers have been reported for the treatment of patients with melasma **(Morais et al. 2013).** The cutaneous absorption of the Er:YAG laser energy by water (2940 nm) is 10-fold more efficient than that of the carbon dioxide laser and allows for more superficial tissue ablation but with minimal thermal damage.

Attwa et al in 2015 conducted an uncontrolled study on the effectiveness of Er-YAG laser and reported significant improvement in MASI score. However, PIH was a statistically significant side effect **(Attwa et al. 2015)**

On the other side, Sarma et al in 2017 stated that fractional and ablative lasers as single therapies are no longer used due to higher incidence of post inflammatory hyperpigmentation. These have been used with lower fluences **(Sarma et al. 2017).**

Also Abdel Raouf et al in 2019 reported that By calculating the mean MASI score on the right side of the face at baseline and 3 months after treatment, melasma was found to be highly significantly decreased after treatment by fractional Er:YAG laser with a percentage of reduction 43% **(Abdel-Raouf et al. 2019).**

In group (II), the percentage of improvement was 50 – 85 % in epidermal melasma, 30 - 50 % in dermal melasma, and 30 – 40 % in mixed type. There was significant improvement in epidermal type by chemical peeling treatment (P- value = 0.002*). It was in agreement with**Morais et al in (2013)** and **Trivedi et al in (2017)** who stated that melasma can be treated by chemical peels such as glycolic acid. Chemical peels are used to create an injury of a specific skin depth to stimulate skin growth and

improve surface, texture and appearance. The exfoliating effect of chemical peel stimulates new epidermal growth and collagen with more evenly distributed melanin **[Morais et al. (2013) and Trivedi et al. (2017)].**

Also **Kalla et al in (2001), Khunger et al in (2004), Faghihi et al in (2011) and Mahajan et al in (2015)** reported that GA peelsignificantly improved MASI of melasma.

Concerning the effect of erbium YAG laser and glycolic acid 70% chemical peel for melasma treatment in the present study, the percentage of improvement in patients treated by fractional erbium YAG laser was 20 – 80 % with a mean 54.33 ± 18.01 and the percentage of improvement in patients treated by chemical peeling was 30 – 85 % with a mean 53.33 ± 18.09. So fractional erbium YAG laser and glycolic acid 70% chemical peel are effective treatments for melasma.

This is in agreement with**Manaloto and Alster T in (1999)**, **Sarkar et al in (2012)**, **Lee et al in (2017)**, **Alavi et al in (2017) and Raka et al. (2019)** as they reported that the Erbium YAG laser improves melasma and also different types of chemical peels as glycolic acid are effective in treatment of melasma**[Manaloto et al. (1999), Sarkar et al. (2012),Sharad. (2013), Lee et al. (2017) and Raka et al. (2019)].**

Regarding the comparison between erbium YAG laser and glycolic acid 70% chemical peel for melasma treatment in the present study, there was no significant difference in the percentage of improvement in both groups (P- value = 0.881). This shows that the effect of both procedures is comparable.

Trivedi et al in 2017stated that Laser and light therapy represent an alternative third-line approach to treat melasma and may be particularly beneficial for patients with melasma that is refractory to topical therapy or chemical peel regimens, or when a patient wishes for an accelerated pace of improvement. Analogous to chemical peels, these modalities accelerate the removal of pathways for melanin but do not target the melanin production itself **(Trivedi et al. 2017).**

Manstein et al in (2004) and Garg et al in (2019) explained that fractional laser therapy is more accurate method of treatment. As fractional lasers create selective columns of microthermal damage (MTZ) with intervening areas of normal skin. Lesser inflammation means a better recovery with less risk of scarring or PIH. In melasma, they act via a shuttle mechanism that eliminates melanocytes and keratinocytes containing melanin granules via the MTZ **[Manstein et al. (2004) and Garg et al. (2019)].**

Diosti et al in 2012 stated that fractional Erbium:YAG laser can clinically and histologically improve the degree of hyperpigmentation of the skin**.**

According to histopathological evaluation in the present study, Skin biopsies were taken before and after the treatment using hematoxylin and eosin (H&E) stain. The amount of melanin significantly decreased in most of the patients of both groups. There was thinning of stratum corneum and the malpighian layer and neocollagenosis more in laser therapy than in peeling treatment.

This goes with**Diosti et al in (2012) and Abdel-Raouf et al in (2019)**, who reported that there were a decreased total number of melanocytes and the percent of the decreased melanocytes from pre- to post-treatmentof both laser and peeling **[Diosti et al. (2012) and Abdel-Raouf et al. (2019)].**

Histopathological changes after fractional Er:YAG laser could be explained as follows: A dermally focused laser beam is absorbed by water, creating columns of thermal damage (MTZs). The surrounding tissue is relatively unaffected by the laser and serves as a source of cells and inflammatory mediators involved in the wound repair process **(Abdel-Raouf et al. 2019)**.

According to dermoscopic assessment of patients in the present study, by dermoscopy, melasma has pigmented component in all patients and vascular component in 63.3% of patients of both groups. In group (I), the percentage of improvement of pigment component was 20 – 80 % with a mean 54.33 ±

18.01 and there were 10 patients (66.6%) with vascular component and the percentage of vascular improvement 20-60%. In group (II), the percentage of improvement of pigment component was 30 – 85 % with a mean 53.33 ± 18.09 and there were 9 patients (60%) with vascular component and the percentage of vascular improvement 10-30% with significant vascular improvement in patients treated by laser (P. value= 0.001*)**.** This goes with**Errichetti in 2020** whostated that dermoscopy of melasma shows very characteristic changes. It is possible to observe the vascular component, which is present in a large number of patients**(Errichetti. 2020)**. Also **Katz et al in 2010** stated that the vascular improvement by the laser might be due to thermal effect of laser on blood vessels causing thermal necrosis (**Katz et al. 2010)**. This explained why laser therapy more effective in vascular component of melasma.

Also there was improvement in pigment component of melasma with chemical peel GA 70%. This goes with**Ibrahim et al in 2014**who compared the dermoscopic color changes before and after treatment of melasma by chemical peels and found decreasing in color density after the treatment **(Ibrahim et al. 2014)**.

Regarding recurrence rateduring the follow up of patients, showed recurrence in 6 patients of 15 patients in group I (40 %) and 4 patients of 15 patients in group II (26.7 %). So there was no significant difference between both groups (P – value = 0.439). The total percentage of recurrence in all patients in both groups was 33.3 %. This goes well with**Sheth et al in 2011** and**Sardesai et al in 2013** who stated that due to the incomplete understanding of pathogenesis of melasma, treatments of melasma aim, essentially, at blocking solar radiation (through strategies that reduce the biosynthesis, transport and transfer of melanin), and reducing the amount of epidermal melanin, instead of aiming at the causal dysfunction of the disease. This supports the statement that long-term therapies are necessary, since recurrence rates are high **[Sheth et al. (2011)andSardesai et al. (2013)]**.

The recurrence of hyperpigmentation after treatment of melasma by fractional erbium YAG laser may have resulted from several factors, including the tendency for the condition to recur in the absence of treatment, or the lack of treatment associated with the use of sunscreen **(Diosti et al. 2012)**.

As regards side effects of melasma treatment, all patients (100%) suffered from burning pain during and immediately after session with variable degree in both groups. All patients (100%) suffered from erythema after laser sessions but this erythema was improved by the topical steroid. Only 5 patients (30%) suffered from erythema after peeling sessions. No post inflammatory hypo or hyperpigmentation was occurred. This agrees with**Sheth and Pandya in (2011),Sharad in (2013) and Puri et al in (2013)** who reported that the minor side effects of glycolic acid reported are: erythema, stinging sensation, sensation of pulling of facial skin, mild burning. **Sheth and Pandya in 2011** stated that GA can also cause transient post-inflammatory hyperpigmentation, erosive blisters and scarring. In rare cases, hypopigmentation, persistent erythema, and flare-up of pimples have been reported**[Sheth and Pandya. (2011), Sharad. (2013) and Puri et al. (2013)].**

Finally, fractional erbium YAG laser as well as glycolic acid 70% chemical peel are effective and safe tools in melasma treatment.

CONCLUSION

From the present study, it can be concluded that Fractional ablative Erbium YAG lasers as well as glycolic acid 70% chemical peeling were effective clinically in the improvement of melasma and their effect was comparable without significant difference.**However**Dermoscopic examination showed significant decrease of vascular component in patients treated by fractional ablative Erbium YAG laser and Histopathological examination showed thinning of stratum corneum and the malpighian layer and

neocollagenosis more in laser therapy than in peeling treatment. There was recurrence in both groups after 6 months with non-significant difference between the two groups.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

FINDING

There are not any financial ties to include.

ETHICAL APPROVAL

"All procedures performed in studies involving humanparticipants were in accordance with the ethicalstandards of National Institute of Laser EnhancedSciences (NILES), Cairo University. In addition, the studyfollowed the ethical guidelines of the National Institute ofLaser Enhanced Sciences (NILES), Cairo University."

INFORMED CONSENT

Informed consent was obtained from all individualparticipants included in the study.

REFERENCES

- **Abdel-Raouf Mohamed H, Ali Nasif G, Saad Abdel-Azim E, Abd El-Fatah Ahmed M. Comparative study of fractional Erbium: YAG laser vs combined therapy with topical steroid as an adjuvant treatment in melasma. J Cosmet Dermatol. 2019;18:517–523.**
- **Alavi S, Abolhasani E, Asadi S, Nilforoushzadeh M. Combination of Q-switched Nd:YAG and fractional Erbium:YAG lasers in treatment of melasma: a randomized controlled clinical trial. J Lasers Med Sci. 2017;8(1):1-6.**
- **Attwa E, Khater M, Assaf M, Haleem MA. Melasma treatment using an erbium:YAG laser: A clinical, immunohistochemical, and ultrastructural study. Int J Dermatol. 2015;54:235–44.**
- **Dharni R, Madke B, Singh AL. Correlation of clinicodermatoscopic and Wood's lamp findings in patients having melasma. Pigment Int 2018;5:91-5.**
- **Diosti GM, Mulinari-Brenner F, Filus Neto J, Nascimento A, Piva FM. Clinical and histological evaluation of patients with refractory melasma treated with fractional Erbium:YAG laser. Surg Cosmet Dermatol 2012;4(2):114-20.**
- **Errichetti E. Dermoscopy in Monitoring and Predicting Therapeutic Response in General Dermatology (Non- Tumoral Dermatoses): An Up-To-Date Overview. Dermatol Ther (Heidelb) (2020) 10:1199–1214.**
- **Faghihi G, Shahingohar A, Siadat AH. Comparison between 1% tretinoin peeling versus 70% glycolic acid peeling in the treatment of female patients with melasma. J Drugs Dermatol. 2011;10:1439–42.**
- **Garg S, Vashisht KR, and Makadia S. A prospective randomized comparative study on 60 Indian patients of melasma, comparing pixel Q-switched NdYAG (1064 nm), super skin rejuvenation (540 nm) and ablative pixel erbium YAG (2940 nm) lasers, with a review of the literature. JOURNAL OF COSMETIC AND LASER THERAPY 2019, VOL. 21, NO. 5, 297–307.**

- **Hammerschmidt M, Mattos SM, Freitas CF, and Mukal MM. Evaluation of melasma classification methods based on response to treatment. SurgCosmetDermatol 2012;4(2):155-8.**
- **Handel AC, Miot LD, Miot HA. Melasma: a clinical and epidemiological review. An Bras Dermatol. 2014;89(5):771–82.**
- **Ibrahim ZA, Gheida SF, El Maghraby GM & Farag ZE. Evaluation of the efficacy and safety of combinations of hydroquinone, glycolic acid, and hyaluronic acid in the treatment of melasma. Journal of Cosmetic Dermatology. 2014, 113—123.**
- **Kalla G, Garg A, Kachhawa D. Chemical peeling—glycolic acid versus trichloroacetic acid in melasma. Indian J Dermatol VenereolLeprol. 2001;67:82–4.**
- **Katz TM, Glaich AS, Goldberg LH, Firoz BF, Dai T, Friedman PM. Treatment of melasma using fractional photothermolysis: A report of eight cases with long-term follow-up. Dermatol Surg. 2010;36:1273–80.**
- **Kaur S, Kaur J, Sharma S, Sharma M, Mahajan A, Singh A. A clinico-dermatoscopic study of 100 cases of melasma in a tertiary care hospital. Int J Res Dermatol 2018;4:41-5.**
- **Khunger N, Sarkar R, Jain RK. Tretinoin peels versus glycolic acid peels in the treatment of melasma in dark-skinned patients. Dermatol Surg. 2004;30:756–60.**
- **Lee BW, Schwartz RA,Janniger CK. Melasma. G ItalDermatolVenereol. 2017;152(1):36-45.**
- **Mahajan R, Kanwar AJ, Parsad D, Kumaran MS, Sharma R. Glycolic acid peels/azelaic acid 20% cream combination and low potency triple combination lead to similar reduction in melasma severity in ethnic skin: Results of a randomized controlled study. Indian J Dermatol. 2015;60:147–52.**
- **Majid I, Haq I, Imran S, Keen A, Aziz K, Arif T. Proposing melasma severity index: A new, more practical, office-based scoring system for assessing the severity of melasma. Indian J Dermatol 2016; 61:39-44.**
- **Manaloto RMP andAlster T. Erbium:YAG laser resurfacing for refractory melasma. Dermatol Surg 1999;25:121–3.**
- **Manstein D, Herron GS, Sink RK, Tanner H, Anderson RR. Fractional photothermolysis: A new concept of cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med. 2004;34:426–38.**
- **Morais OO, Lemos EF, Sousa MC et al. The use of ablative lasers in the treatment of facial melasma. An. Bras. Dermatol. 2013; 88:590 – 596.**
- **Ogbechie-Godec O. A. and Elbuluk N. Melasma: an Up-to-Date Comprehensive ReviewDermatolTher (Heidelb). 2017; 7:305–318.**
- **Puri N and Puri A. A study on fractional erbium glass laser therapy versus chemical peeling for treatment of melasma in female patients. J CutanAesthet Surg. 2013; 6(3):148 – 151.**
- **Raka A and Brahmbhatt VU. Comparative study of efficacy of glycolic acid (50%) peel and lactic acid (92%) peel in the treatment of melasma. Int J Res Dermatol. 2019;5(2):370-375.**
- **Ramadan W.M, El Desouky K.I, Hassan A., El Tokhy A.M, Abd El Halim M.A. Correlation between dermoscopic features of melasma with the histolopathology. Msc Thesis Tanta University. Chapter (1). 2014; pp 34 – 37.**
- **Sardesai VR, Kolte JN, Srinivas BN. A clinical study of melasma and a comparison of the therapeutic effect of certain currently available topical modalities for its treatment. Indian J Dermatol. 2013;58:239.**

- **Sarkar R and AilawadiP. Treatment of Melasma: The Journey Ahead.Indian J Dermatol. 2017; 62(6): 555–557.**
- **Sarma N., Chakraborty S., Poojary S.A., Rathi S, Kumaran S, Nirmal B, et al. Evidence-based Review, Grade of Recommendation, and Suggested Treatment Recommendations for Melasma. Indian Dermatol Online J. 2017; 8(6): 406–442.**
- **Sharad J. Glycolic acid peel therapy – a current review. Clinical, Cosmetic and Investigational Dermatology 2013:6 281–288.**
- **Sheth VM, Pandya AG. Melasma: a comprehensive update: part II. J Am AcadDermatol. 2011;65:699-714.**
- **Tamega A A, Miot LD, Bonfietti C, Gige TC, Marques ME, Miot HA. Clinical patternsand epidemiological characteristics of facial melasma in Brazilian women. JEurAcadDermatolVenereol. 2013;27:151-6.**
- **Tamler C, Fonseca RM, Pereina FB and BarcaniCB.Classification of melasma by dermoscopy: comparative study with Wood's lamp.Surgical& Cosmetic Dermatology 2009;1(3):115-119.**
- **Trivedi M.K., Yang F.C., Cho B.K. A review of laser and light therapy in melasma. International Journal ofWomen's Dermatology 3. 2017;11–20.**
- **Wanitphakdeedech R, Manuskiatti W, Siriphukpong S et al. Treatnent of melasma using variable square pulse Er:YAG laser resurfacing. Dermatol Surg. 2009; 35:475-481.**

- **Jalil, A. T., Al-Khafaji, A. H. D., Karevskiy, A., Dilfy, S. H., & Hanan, Z. K. (2021). Polymerase chain reaction technique for molecular detection of HPV16 infections among women with cervical cancer in Dhi-Qar Province. Materials Today: Proceedings.https://doi.org/10.1016/j.matpr.2021.05.211**
- **Hanan, Z. K., Saleh, M. B., Mezal, E. H., & Jalil, A. T. (2021). Detection of human genetic variation in VAC14 gene by ARMA-PCR technique and relation with typhoid fever infection in patients with gallbladder diseases in Thi-Qar province/Iraq. Materials Today: Proceedings.https://doi.org/10.1016/j.matpr.2021.05.236**
- **Jalil, A. T., &Karevskiy, A. (2020). The Cervical Cancer (CC) Epidemiology and Human Papillomavirus (HPV) in the Middle East. International Journal of Environment, Engineering & Education, 2(2), 7-12.https://doi.org/10.5281/zenodo.3972634**
- **Turki Jalil, A., Hussain Dilfy, S., Oudah Meza, S., Aravindhan, S., M Kadhim, M., & M Aljeboree, A. (2021). CuO/ZrO2 nanocomposites: facile synthesis, characterization and photocatalytic degradation of tetracycline antibiotic. Journal of Nanostructures.**
- **Jalil, A. T. (2020). COVID-19 most affected age groups and lethality in Europe, Glob. J. Public Health Med, 2, 179-184.https://doi.org/10.37557/gjphm.v2iSP1.51**
- **Mezal, E. H., Yousif, A. F., Hanan, Z. K., Hanan, A. K., & Jalil, A. (2020). Isolation, Assessment of Antimicrobial Sensitivity of Bacterial Pathogens from Post-Cesarean section Infection of patients in Thi-Qar Province. European Journal of Molecular & Clinical Medicine, 7(3), 958-964.**
- **Mubark, N. N., Jalil, A. T., &Dilfi, S. H. (2020). DESCRIPTIVE STUDY OF HYDATIDIFORM MOLE ACCORDING TO TYPE AND AGE AMONG PATIENTS IN WASIT PROVINCE, IRAQ. Global Journal of Public Health Medicine, 2(1), 118-124.https://doi.org/10.37557/gjphm.v2i1.30**
- **Turki Jalil, A. ., Dilfi, S. H. ., &Karevskiy, A. . (2019). SURVEY OF BREAST CANCER IN WASIT PROVINCE , IRAQ. Global Journal of Public Health Medicine, 1(2), 33–38. https://doi.org/10.37557/gjphm.v1i2.7**

- **Jaleel, A. T. (2018). SURVEY THE PREVALENCE OF VIRAL HEPATITIS A, B, C INFECTION IN DHI-QAR PROVINCE (IRAQ). ББК 20.1 А43 Редакционнаяколлегия: ИБ Заводник (отв. ред.), АЕ Каревский, ОВ Янчуревич, ОВ Павлова, 95.**
- **Jalil, A. A. T. EPIDEMIOLOGY OF CERVICAL CANCER AND HIGH RISK OF HUMAN PAPILLOMA VIRUS IN PATIENT. ББК 28.6 3, 85(7).**
- **Roomi, A. B., Widjaja, G., Savitri, D., Turki Jalil, A., Fakri Mustafa, Y., Thangavelu, L., ... &Aravindhan, S. (2021). SnO2: Au/Carbon Quantum Dots Nanocomposites: Synthesis, Characterization, and Antibacterial Activity. Journal of Nanostructures.**
- **Raya, I., Chupradit, S., Mustafa, Y., H. Oudaha, K., M. Kadhim, M., Turki Jalil, A., J. Kadhim, A., Mahmudiono, T., Thangavelu, L. (2021). Carboxymethyl Chitosan Nano-Fibers for Controlled Releasing 5-Fluorouracil Anticancer Drug. Journal of Nanostructures**