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BRIEF COMMUNICATION

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Treatment of Sebaceous Hyperplasia by Laser Modalities: A Review of the Literature and Presentation of Our Experience With Erbium-doped Yttrium Aluminium Garnet (Er:YAG)

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ABSTRACT

Introduction: Sebaceous hyperplasia (SH) is a common skin presentation in adults. Due to their unwanted yellow papular appearance, patients may desire their removal. Although several treatment modalities have been reported, the full range and efficacy of options are unclear.

Objective: To determine the efficacy of laser modalities in the treatment of SH. The authors will also specifically assess the efficacy, recurrence rate and side effect profile of SH treatment with Er:YAG wavelength using a variable long pulsed (VLP) Er:YAG laser (SP Dynamis Fotona laser, Ljubljana, Slovenia)

Methods & Materials: A comprehensive literature search was performed through PubMed, EMBASE, and Web of Science, using the search terms [(sebaceous hyperplasia)] and [(laser[s], Er:Yag, Er:Glass, Fraxel, CO2, PDL, Pulse dye laser, Diode, Xe-Cl, Excimer, Argon, KTP, Ruby, Alexandrite or Nd:YAG)]. The search yielded a total of 119 results and 8 were identified as relevant to this review

Results: Pulse dye laser (PDL) provides a wide range of treatment results from complete reduction to flattening of the SH without significant adverse events; recurrence rates were unreported. Short PDL showed faster treatment response than long PDL. CO2 laser can produce considerable positive cosmetic outcomes with marked clinical improvement without any recurrence, but significant adverse effects have been reported. The 1450-nm diode laser has been described to produce good (75%) clinical improvement and lesion shrinkage ranging from 50% to greater than 75% without lasting adverse effects. In our clinic, Er:YAG has provided very significant cosmetic outcomes with a low recurrence rate and minimal adverse effects.

Conclusions: Laser modalities can provide satisfactory results for removing SH. It is crucial that the laser is being used by an expert who is familiar with the device as well as understand the laser tissue interaction to minimize patient adverse effects while providing the best cosmetic outcome. In our experience, Er:YAG laser can provide a safe and highly effective solution for SH.

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INTRODUCTION

Sebaceous Hyperplasia (SH) is a common skin lesion that can develop after age 40, with a prevalence as high as 26% in older adults.[1] The classic senile variant presents as skin colored to yellow papules on the face with central umbilication. Other variants of SHs include transient SH in neonates from exposure to maternal hormones, presentation in rows within the juxta clavicular area, appearing in the context of familial disease, or as an adverse effect of cyclosporine.[2] Although a majority of SH may not be associated with an underlying disease, such as Muir-Torre syndrome, patients may desire their removal, particularly when there are multiple larger lesions on the face. There have been several described treatments for SH including isotretinoin,[3] electrodessication,[4] cryotherapy,[5] pulsed dye laser,[6] CO2 laser,[7] and photodynamic therapy.[8]

With the ongoing rapid advancement of energy-based devices, we explored the current literature on laser modalities to treat SH. To our knowledge, there has been no published literature review focusing on the treatment of SH by laser modalities. Additionally, there has been no published literature on the treatment of SH with the erbium-doped yttrium aluminum garnet (Er:YAG) laser.

OBJECTIVE

The objective of this study was to determine the efficacy of laser modalities in the treatment of SH. In particular, the authors assessed the efficacy, recurrence rate and side effect profiles associated with Er:YAG laser.

METHODS

A comprehensive literature search was performed through PubMed, EMBASE, and Web of Science on April 2, 2019, using the search terms [(sebaceous hyperplasia)] and [(laser[s], Er:Yag, Er:Glass, Fraxel, CO2, PDL, Pulse dye laser, Diode, Xe-Cl, Excimer, Argon, KTP, Ruby, Alexandrite, or Nd:YAG)]. The

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relevant records that met the following criteria were selected for inclusion: case reports, case series, and clinical trials using laser modalities for treatment of sebaceous hyperplasia. Exclusion criteria included non-English articles and review articles. Additional sources from the original source bibliographies were used to further supplement this review. The search yielded a total of 119 results: 41 from PubMed, 16 from EMBASE, 62 from Web of Science. 24 were duplicates, 73 had no information relevant to laser treatment of sebaceous hyperplasia, and 4 were non-English articles, and 8 were excluded due to incompatible article type, and 2 were unattainable due to resource limitations. Of the remaining 8, 1 was a randomized controlled trial (RCT), 1 was an observational study, 3 were case series, and 3 were case reports.

RESULTS

Results of all studies are summarized in Table 1.

Randomized Control Trials

Wang et al report a prospective split-face randomized trial comparing long pulse PDL (LPDL) and short pulse PDL (SPDL) in the treatment of sebaceous hyperplasia.[9] They identified 8 patients with a total of 75 sebaceous hyperplasia lesions. 42 lesions were randomized to receive SPDL, and the remaining 33 lesions received LPDL.

LPDL consisted of two sessions of 595-nm LPDL with 20-millisecond pulse duration, 5-mm spot size, 3-5 stacking pulses and 13-21 J/cm^2 fluence. SPDL consisted of two sessions of 595-nm SPDL with 0.45-millisecond (ms) pulse duration, 5-mm spot size, 3-5 stacking pulses, and 9-11 J/cm^2 fluence. Response rates were categorized into complete reduction, partial reduction and non-reduction.

SPDL showed faster treatment response rate than LPDL. Although all SH lesions responded to two sessions of SPDL or LPDL treatments at 8 weeks after the second session, complete reduction was noted in 20 of 42 lesions (47.6%) treated by SPDL, and in 11 of 33 lesions (33.3%) treated by LPDL. No statistically significant difference in the efficacy in reduction lesion diameter or thickness was noted between SPDL and LPDL. No significant difference was noted between the intensity of pain caused by each therapy. No significant difference was noted in post-treatment purpura resulting from SPDL or LPDL at 8 weeks after the second session.

Non-randomized Interventional Study

Kavoussi et al present a prospective, non-randomized trial on CO^2 laser therapy and curettage for the treatment of sebaceous hyperplasia.[7] They identified 46 patients over an 18-month period. All patients received CO2 laser therapy based on the thickness of their SH lesion, with 2 to 4 passes of pulsed CO2 laser at 5 to 8 watts and 400 ms pulse duration. The lesions were then removed using a disposable curette. Cosmetic outcomes were fair, moderate, and poor in 35 (76.1%), nine (19.6%), and two (4.3%) cases, respectively. The mean recovery time was 11.5 days. No recurrence was seen in patients during the 12-month follow-up period.

CASE SERIES

The authors identified three case series and their results are summarized in Table 1.

Kim et al report on a series of four patients with SH treated with 5-aminolevulinic acid and photodynamic therapy (ALA-PDT) combined with CO2 laser.[10] All patients received CO2 laser ablation in a focused mode at 1.0 W in a series of brief 0.05 second pulses until the papillary dermis was exposed, after which ALA was applied to the lesion only. Additional treatments were applied every four weeks (total number of treatments ranged from one to four), and final evaluation was performed four months after the last PDT. Clinical responses were evaluated by two dermatologists at four weeks after PDT and classified as no response (<30%), mild (30%-60%), moderate (60%-90%), marked improvement (90%) according to the decrease of lesion counts. Three of four patients showed marked improvement, and all tolerated the therapy. During follow-up at four months after the last PDT, none of the lesions recurred.

Aghassi et al describe their cohort of 10 patients with a total of 29 lesions of sebaceous hyperplasia treated with PDL.[11] Preoperative photographs were taken with a 35-mm camera, and confocal imaging was also performed on an accessible lesion with a near infrared, reflectance confocal laser scanning microscope. Each patient received treatment with a 585-nm PDL with 3 consecutive 5-mm pulses of 7 or 7.5 J/cm2 to each lesion. Follow up exams were conducted at 2, 4, and 8 weeks after treatment for repeated photography, clinical evaluation of the size and elevation of each treated lesion by at least two observers, and confocal imaging of the lesion previously imaged. At the final eight-week follow-up, disappearance was noted in 8 of 29 (28%) lesions, a decrease in diameter in 19 of 29 (66%), and flattening in 27 of 29 (93%). 28% recrudesced after initial involution, and 7% recurred completely. No scarring or pigmentary side effects were noted. Confocal imaging revealed a prominent "crown" of blood vessels surrounding the sebaceous duct and coagulation of these vessels with pulsed-dye laser treatment. However, despite the clinical responses, the vessels reappeared during follow-up, and no noticeable morphologic changes in the sebaceous duct were noted.

Finally, a study by No et al used the 1450-nm diode laser on their series of 10 patients with over 330 sebaceous hyperplasia lesions.[12] All patients received a 1450-nm diode laser delivered with a 4-mm spot size and a fluence of 16 to 17 J/cm2. Cryogen cooling was set at 40 to 50 ms. Most lesions were treated with a single pulse, except for thicker lesions, which were treated

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TABLE 1.

A Synopsis of Included Studies

Study	Type of Study	# pts enrolled	Treatment modality	Number of sessions performed	Beam Specifications	Follow up time	Clearance and other results
Noh, S., Shin, J. U., Jung, J.Y. and Lee, J. H. A case of sebaceous hyperplasia maintained on low-dose isotretinoin after carbon dioxide laser treatment *Int J Dermatol.* 2014 53 2 e151-3	Case Report	1	CO2 laser 2 years of low dose isotretinoin	3	Not specified	3 years after CO2 treatment, 1 year after isotretinoin treatment	Clearance of all lesions and no recurrence
Gonzalez, S., White, W. M., Rajadhyaksha, M., Anderson, R. R. and Gonzalez, E. Confocal imaging of sebaceous gland hyperplasia in vivo to assess efficacy and mechanism of pulsed dye laser treatment *Lasers Surg Med.* 1999 25 1 8-12	Case Report	1	585-nm PDL	1	Two overlapping pulses of 585-nm PDL at 7.0 J/cm2 with a 5 mm delivery point.	2 weeks, 2 months, 6 months	Progressive involution with no evidence of pigmentary changes or scars
Schonermark, M. P., Schmidt, C. and Raulin, C. Treatment of sebaceous gland hyperplasia with the pulsed dye laser *Lasers Surg Med.* 1997 21 4 313-6	Case Report	2	585-nm PDL	3 for patient #1, 2 for patient #2	Patient #1: 5mm laser probe, 7-8 J/cm2 and 300–450/msec. Patient #2: 5mm laser probe, 6.5 and 6.8 J/cm2, no pulse duration specified.	9 months for patient #1, 13 months for patient #2	Disappearance after 2–3 treatment sessions. No recurrence or scarring at each respective follow up
Kim, S. K., Do, J. E., Kang, H.Y., Lee, E. S. and Kim, Y. C. Combination of topical 5-aminolevulinic acid-photodynamic therapy with carbon dioxide laser for sebaceous hyperplasia *J Am Acad Dermatol.* 2007 56 3 523-4	Case Series	4	CO2 laser ALA-PDT	1 - 4	CO2 laser ablation in a focused mode at 1.0 W in a series of 0.05s pulses until the papillary dermis was exposed. Then ALA was applied to the lesion only.	4 months after last PDT	Three of four patients showed marked improvement, and all tolerated the therapy. During follow-up at four months, none of the lesions recurred.
Aghassi, D., Gonzalez, E., Anderson, R. R., Rajadhyaksha, M. and Gonzalez, S. Elucidating the pulsed-dye laser treatment of sebaceous hyperplasia in vivo with real-time confocal scanning laser microscopy *J Am Acad Dermatol.* 2000 43 1 Pt 1 49-53	Case Series	10	585-nm PDL	1	3 stacked 5-mm pulses at fluences of 7 or 7.5 J/cm2.	2, 4, 8 weeks	Complete disappearance in 28%, decrease in diameter in 66%, and flattening in 93%. 28% recrudesced after initial involution, and 7% recurred completely. No scarring or pigmentary side effects were noted.
No, D., McClaren, M., Chotzen, V. and Kilmer, S. L. Sebaceous hyperplasia treated with a 1450-nm diode laser *Dermatol Surg.* 2004 30 3 382-4	Case Series	10	1450- nm diode	1 - 5 (average of 2.2)	4-mm spot size and a fluence of 16 to 17 J/cm2. Cryogen cooling was set at 40 to 50 ms.	Not specified	The average patient and physician improvement scores were 3.1 ("very good") and 3.5 ("very good"), respectively. After 2-3 treatments, 84% of lesions shrunk greater than 50%, and 70% shrunk greater than 75%. Adverse effects included one atrophic scar which improved months later and one case of transient hyperpigmentation.

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TABLE 1. (CONTINUED)

A Synopsis of Included Studies							
Study	**Type of Study**	**# pts enrolled**	**Treatment modality**	**Number of sessions performed**	**Beam Specifications**	**Follow up time**	**Clearance and other results**
Kavoussi, H., Rezaei, M., Azimi, M., Kavoussi, R., Simmons, B. J., Griffith, R. D., Falto-Aizpurua, L. A., Bray, F. N., Nouri, K., International League of Dermatological, Societies and European Dermatology, Forum Combination of CO2 laser therapy and curettage for sebaceous gland hyperplasia	Non Randomized Interventional study	46	CO2 laser	1	2 to 4 passes of pulsed CO2 laser at 5 to 8 watts and 400 ms pulse duration. The lesions were then removed using a disposable curette.	12 months	A fair cosmetic outcome was seen in 76.1% of cases
Wang, S. P., Chang, Y. J., Chi, C. C., Wang, S. H. and Tsai, T. H. Using pulsed dye laser to treat sebaceous hyperplasia: comparison of short and long pulse-duration pulsed dye laser *Dermatologica Sinica.* 2017 2017 35 3 119-123	Randomized Controlled Trial	8	595-nm short PDL (SPDL) with 0.45-millisecond pulse duration or 595-nm long PDL (LPDL) with 20-millisecond pulse duration	2	LPDL: two sessions of 595-nm LPDL with 20-ms pulse duration, 5-mm spot size, 3-5 stacking pulses and 13-21 J/cm2 fluence. SPDL: two sessions of 595-nm SPDL with 0.45-ms pulse duration, 5-mm spot size, 3-5 stacking pulses, and 9-11 J/cm2 fluence.	1 and 4 weeks after first session; 1, 4, 8 weeks after second session	At 8 weeks after the second session, complete reduction was noted in 20 of 42 lesions (47.6%) treated by SPDL, and in 11 of 33 lesions (33.3%) treated by LPDL. SPDL showed faster treatment response rate than LPDL. No significant difference was noted between the intensity of pain caused by each therapy. No significant difference was noted in post-treatment purpura at 8 weeks after the second session.

with two pulses. Lesions larger than 5mm in diameter required additional single pulses to the entire lesional area. Patients received a total of one to five treatments (average of 2.2), spaced four to six weeks apart. Patients and investigators rated overall improvement of treated lesions on a 0 to 4 scale: 0=0% (none), 1=1% to 25% (moderate), 2=26% to 50% (good), 3=51% to 75% (very good), and 4=76% to 100% (excellent). The average patient and physician improvement scores were 3.1 ("very good") and 3.5 ("very good"), respectively. After two to three treatments, 84% of lesions shrunk greater than 50%, and 70% shrunk greater than 75%. Adverse effects included one atrophic scar which improved months later and one case of transient hyperpigmentation.

CASE REPORTS

Noh et al describe a 55-year-old man with multiple SHs to the face treated with two session of CO2 laser.[13] After recurrence within six months, he was treated with an additional session of CO2 laser, which cleared the remaining lesions. He was subsequently maintained on isotretinoin reaching a cumulative dose of 150mg/kg within two years and has not experienced recurrence for one year since discontinuing isotretinoin.

Gonzalez et al report a 51-year old woman with two sebaceous hyperplasia to her face treated with two overlapping pulses of 585-nm PDL at 7.0 J/cm^2 with a 5 mm delivery point.[14] Photographs and optical images by confocal microscopy (CM) were taken before and after treatment. Follow-up evaluation at two weeks, two months, and six months revealed progressive involution with no evidence of pigmentary changes or scars. Additionally, confocal images obtained immediately after treatment showed the selective photothermal damage confined to the blood vessels. Two-week and two-month follow-up showed a non-hyperplastic epithelial duct with smoother contours, and deeper penetrating images showed dense collagen bundles without dilated dermal blood vessels. Similarly, Schonermark et al also describe a treatment of sebaceous hyperplasia lesions with the 585-nm PDL on their two patients.[6] One 62-year-old woman was treated with three sessions of 300-450 ms pulse duration using the 5 mm laser probe with an energy dose of 7 J/cm^2 in the first session and 8 J/cm^2 in the following two sessions. A second 58-year-old man was treated in two consecutive sessions using a 5 mm laser probe, with 6.5 J/cm2 and 6.8 J/cm^2 energy dose, respectively (no pulse duration was specified). Both patients showed complete disappearance of their lesions after their final treatments, with no recurrence or scarring at nine and 13 months after their last sessions, respectively.

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ER:YAG LASER TREATMENT

Erbium-doped yttrium aluminium garnet (Er:YAG) has a 2940 nm wavelength which is well absorbed by water. It is also absorbed by hydroxyapatite which makes it an ideal laser for tissue vaporization. In our clinic, we treated 398 patients with SH for the past 5 years with the variable long pulsed (VLP) Er:YAG (Fotona SP Dynamis, Ljubljana, Slovenia) setting, using 0.2 mm spot size, 5 J/cm^2, VLP (1000 microsecond), 12 Hz. Patients had as few as 10 to as many as 40 SH that were treated in one session. The patient population consisted of 73% female to 27% male, with an age range of 35–77 years old. The patients received topical anesthetics preoperatively: a combination of benzocaine 20%, lidocaine 6%, tetracaine 4% for 30 minutes. Following that, a 0.2mm, very focused/defocused beam created a small crater consistent with the size of the sebaceous hyperplasia. The lesion was vaporized to the proper depth (~1mm), after which no remaining white-yellowish tissue was appreciated in the center of SH. It is very important to create a zone of vaporization of the exact same size as the SH lesion, since a larger crater may not completely heal and result in a pitted scar. Patients applied topical antibiotics daily for seven days and were advised to avoid sun exposure during the healing period. Patients were followed up between 1-36 months. Most lesions healed completely within 1-2 months and some had transient post-treatment erythema, which gradually completely improved (Figures 1 and 2). It is crucial to advise patients to minimize sun-exposure and encourage regular sunscreen use accompanied with usage of a wide bream hat to avoid post-inflammatory hyperpigmentation. We did not encounter any post-operative infection or persistent erythema. Patients should be advised with regards to potential adverse effects of treatment and proper consent should be obtained. If the white-yellow remnants within SH lesions are not completely vaporized, the SH can recur and may require an additional treatment.

DISCUSSION

PDL is a vascular-specific laser which will only non-specifically treat SH lesions through tissue destruction. Dermoscopic analysis of SH identify its fine vascular presentation which has been labeled as "crown vessels". Considering the vascular specificity of SPDL, it can be deduced that, through using sub-millisecond pulses, the fine vessels will absorb the incoming laser energy and transmit the heat to the surrounding tissue, resulting in partial destruction of lesions. However, LPDL can cause deeper penetration into the tissue while less specifically heating the surrounding tissue, resulting in a less-than-ideal tissue destruction. The LPDL 5mm spot size is much larger than the average 1-3 mm SH lesions and can, consequently, treat the surrounding normal skin. It is also important to note that the aforementioned article on SPDL and LPDL followed patients only for a short time interval (8 weeks).

FIGURE 1. One-month post treatment of sebaceous hyperplasia over forehead in a Fitzpatrick type II patient.

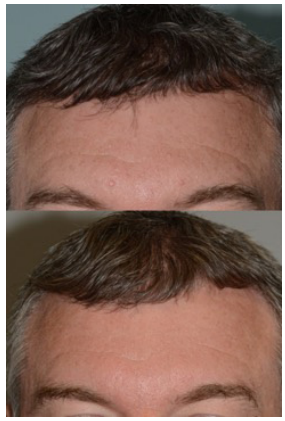
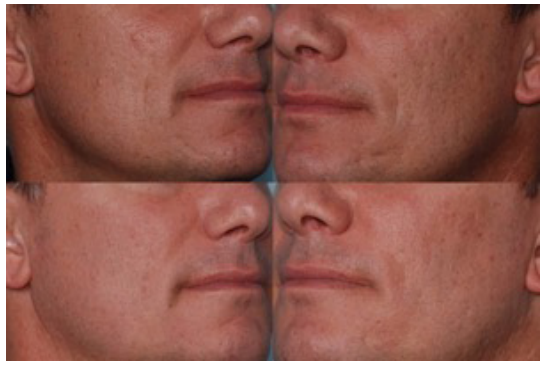
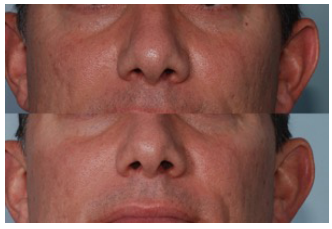


FIGURE 2. Four months post treatment of sebaceous hyperplasia over cheek in a Fitzpatrick type IV patient, side view (2A) and frontal view (2B).

(2A)



(2B)



CO2 laser in a tightly focused manner with proper settings can provide significant benefit in the treatment of SH. While CO2 laser can accurately destroy the lesions, it is associated with potential complications including scarring and pigment alterations. As most SHs are located on the face, some patients may prefer to keep their SH rather than face the more severe potential adverse effects of CO2 laser treatments. The use of ALA-PDT or curettage in combination with CO2 may be unnecessary, as the CO2 laser is an independently powerful method to completely treat SH lesions. Due to the aforementioned potential scarring and pigmentary abnormalities of the CO2 laser, the authors prefer the use of Er:YAG.

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We used a 1450 laser in our clinic for improvement of under eye laxity and can report the significant amount of pain associated with this wavelength based on our experience. The 4 mm spot size that was used with the reported1450 laser is also much larger than average 1-3 mm size of SH and would unnecessarily treat the normal surrounding tissue.

CONCLUSION

There are several different laser modalities that can be utilized to address the SH. Depending on the physician's expertise with lasers, satisfactory results can be achieved. However, Er:YAG provides the best cosmetic outcome for the patients. The laser non-specifically vaporizes the entire SH tissue and hence the lesion would be completely removed in one session which can significantly reduce the cost to the patient. The experienced physician should inform the patient with regards to potential adverse effects of the treatment and obtain proper consent form.

DISCLOSURES

Dr. Liu and Dr. Sotoodian have no conflicts of interest or funding sources to declare. Dr. Taylor is a spokesman for Fotona Lasers and has received discounted equipment from Fotona.

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