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Review Article

Lasers and Energy-based devices for treating Pre-cancerous and Non-Melanoma Skin Cancers: A Review of literature

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Abstract

Skin cancer has been the most common type of malignancies overall with an increasing incidence. The standard of treatment is surgical excision or Mohs Microscopic surgery for high-risk cancer or sensitive areas. Lasers have been used with promising results for treating non-melanoma skin cancers. This paper provides an overall review of the available lasers and energy-based devices utilized for treating NMSK; Squamous Cell Carcinoma In Situ, Invasive Squamous Cell Carcinoma, Basal Cell Carcinoma, Keratoacanthoma, Verrucous carcinoma, and the pre-cancerous Actinic keratosis, and Porokeratosis.

Keywords: Skin cancer; Laser therapy; Actinic keratosis; Porokeratosis

1. Introduction

Non-melanoma skin cancers (NMSK) are the most common cancers among the light-skin populations [1,2]. These include basal cell carcinoma (BCC), invasive squamous cell carcinoma (SCC), and the pre malignant actinic keratosis and squamous cell carcinoma in situ (Bowen's disease). The current treatment options for NMSK include surgery, chemotherapy, immunotherapy, photodynamic therapy with the relatively recent use of laser and energy-based devices therapy [3]. Although surgery is still the preferred method for treating NMSK over the other methods, the increasing incidence of these cancers and the occurrence on sensitive locations like the face, digits or genitals, made the use of laser therapy for treating cutaneous carcinomas which has the potentially postulated superior cosmetic outcome and organ functional preservation especially for less invasive and aggressive malignancies, a more preferred treatment option by both some of the patients and

clinicians [2]. The aim of this review is to focus on the use of different laser and energy-based devices for the treat-ments of NMSK; Squamous Cell Carcinoma In Situ, Invasive Squamous Cell Carcinoma, Basal Cell Car-cinoma, Keratoacanthoma (KA), Verrucous carcinoma and the pre-cancerous Actinic keratosis, and Porokeratosis as the primary treatment modality.

2. Method and Materials

This is a review of literature of the National Library of Medicine MEDLINE search of available English-language abstracts was performed using the terms "skin cancer", "laser therapy" ,"Actinic keratosis", "Porokeratosis" and "Energy-based device" in humans. All publications from the date of inception to March 2021 were considered. We excluded studies that did not specifically focus on the use of laser or energy-based devices for the treatment of premalignant and malignant skin cancers, such as basal cell carcinoma, squamous cell carcinoma, porokeratosis, actinic keratosis and keratoacanthoma.

2.1 Actinic Keratosis

Actinic keratosis (AK) is a prevalent skin lesion on sun-exposed areas of fair-skin individuals with a pro-gression rate into SCC ranging from 0- 0.075% and up to 20% per AK lesion per year [4]. Multiple stud-ies have demonstrated the safety and efficacy of lasers and energy-based devices in treating AK for single lesion or as a field therapy as a sole treatment or as an adjuvant delivery method for topical anti-tumorigenic medications [5]. Several lasers have been used to treat AK with various responses ranging from 46%-100% (Table 1). In one study done by IYER et al, a retrospective chart review of a total of 24 patient with widespread AKs (more than 30 AKs) treated with Carbon Dioxide laser (CO_2) with or without Er:YAG achieved a reduc-tion of 94% at two weeks follow up and with a total of 87.5% remained lesions free after one year of treatment [6]. In this study, there was no profound adverse effect in this study except for one patient who developed a periodical scar treated successfully with intralesional 5-fluorouracil. Two patients developed S.aureus infection treated with dicloxacillin, and one patient developed Postoperative hy-perpigmentation resolved spontaneously within three months without treatment. In another prospec-tive 6-months clinical trial, fractionated 1927-mm thallium laser was used in 24 patients with a total of 4 treatments. Laser settings ranged from 5 to 20-mJ fluences with treatment densities ranging from 40-70% coverage. Patients followed for a total of 6-months. Although at one month after the last treatment, the total reduction of AKs from baseline was 91.3%, the clearance rate was declined to 86.6% at a 6-months interval from the baseline [7]. No major side effects were reported during the study. On the other hand, both ablative and non-ablative lasers used as vehicles to facilitate the delivery of specific local topical treatments [8]. For instance, in a pilot study comparing the use of topical imiquimod alone as a standard treatment protocol for AKs or combining Erbium:YAG laser with imiquimod, patients treated with the latter method showed a clearance rate of 77% compared to 50% in the Imiquimod alone group with fewer treatment sessions. Patients in the laser group had faster clearance time with no severe side effects reported. The use of laser and energy-based devices is not limited to the treatment of AKs but also to prevent the future development of new AKs as several studies have shown that both ablative and non-ablative resurfacing lasers could help to prevent the future development of AKs [8-10]. A randomized prospective clinical trial with a total of 34 patients with a history of

facial or scalp AKs or BCC were randomized into three treatment groups. In this study, the authors used CO_2 laser resurfacing in one arm, 30% trichloroacetic acid peel in the second arm, or 5% fluorouracil cream applied twice daily for three weeks in the third arm. In all three arms, patients showed a lower rate for the new development of NMSK with no clinical significance between the three methods of the treatment [10]. The ability of laser to prevent new development of AKs was also demonstrated in a retrospective study of 24 patients with widespread AKs of the face treated either the $UPCO_2$ or Er:YAG laser, or a combination of both. In this study, patients had at least 30 AKs. Twenty-three of the 24 patients were treated with at least one pass with the $UPCO_2$ laser at 200-300 mJ/cm^2 on the entire face, followed by spot therapy with the 3 mm spot. Fourteen of these patients had two additional passes with the Er:YAG with the following laser settings; energy output 1.7 J, 2 mm spot following CO_2 resurfacing to remove the layer of thermal necrosis generated by the $UPCO_2$ laser-tissue interaction. Nine patients were treated with two passes with the CO_2 laser only, and one patient was treated with four passes of the Er:YAG only. Fourteen of the 24 patients (58.3%) showed no new lesions during a 2-year follow-up, with an overall 94% reduction in the total number of AK [6].

Author	N	Laser type	Laser settings	Note	Number of treatments	Outcome
Weiss et al [7]	24	fractionated 1927-nm non-ablative thulium laser	Fluence:5-20 mj Density: 40-70%		4	86.6% reduction in absolute num-ber of lesions at 6 months
Nourmo hammad Pour et al [49]	10	fractional laser 1540-nm	Spot size:10 mm. Pulse du-ration 15 ms. Fluence: 50 to 70 mJ. Passes: 2-3		3	79% reduction in severity at month 3
Katz et al [50]	14	fractionated 1550-nm erbi-um-doped fiber	Fluence: 20-70 mJ. Passes: 8-10	Biopsy proven at baseline	5	73.1% reduction by month 1
Lapidoth et al [51]	17	fractional 1540-nm erbium glass laser	Fluence:75 mJ Pulse Duration: 15 ms Spot size: 10 mm		2-3	50%-100% at month 3
Gans et al [9]	9	Ablative fractional CO2 laser (Ultrapluse)	Fluence: 70 mJ Power: 9 W. Density: 4	This is a split face study	1	71% reduction at month 1 but no sustained results at month 3 (49% untreated Vs 57% treated areas)

IYER et al [6]	24	Ultrapluse CO_2 +/- Er:YAG	CO_2 laser: Fluence: 500 mJ Spot size: 3 mm. Passes: 1-2 Er:Yag laser: Fluence:1.7 J Spot size: 2 mm.	14 patients treated with CO_2 plus Er:YAG. 9 patients treated with CO_2 laser only 1 patient treated with 4 passes or Er:YAG	1	94% reduction in number of Aks
S. P. Prens et al [52]	10	1550 nm fractional laser (Sel-las)	Coverage:256–532 MTZ/cm2 Fluence:12–18 mJ. Passes:1 pass for sun-dam-aged skin and a second pass focally on AK lesions.		5-10	46% reduction in AKs at 24 weeks after last treat-ment

N, Number of patients; nm, nanometer, mm, millimeter; ms, milliseconds; MTZ, Microthermal zone; J, Joules

Table 1: summary for laser treatment for Actinic Keratosis, laser type and outcome

2.2 Squamous Cell Carcinoma in Situ (Bowen disease)

Squamous cell carcinoma in situ or Bowen disease is defined by the proliferation of the neoplastic keratinocyte within the epidermis with no invasion into the underlying dermis. The rate of transfor-mation is estimated to be 4-5% [11]. The limited involvement of squamous cell carcinoma in situ (SCCIS) to the epidermis with no invasions to the underlying dermis make the use of laser and energy-based devices a feasible and effective method to treat SCCIS, especially with the tendency for these lesions to occur on vital locations [12]. Despite the lack of large randomized clinical studies in the literature, several case reports and case series have demonstrated the efficacy of CO_2 lasers for curing SCCIC, with response rates ranging from 80% to 100% [13]. In a large retrospective case series of 44 patients with primary solitary lesion ranging between 1-4 cm in size, several passes of CO_2 laser achieved clearance after 1 treatment in 86.3% (38 patients), with only 7.9% of these patients developed recurrence of the lesion on an average follow up of 18.8 months [14]. In this study, all patients had initial an pass with the focalized mode at 2 W/cm^2, and then several passes were completed depending on the depth of the lesion. Side effects were seen in 14 patients with only one patient developed a keloid scar at the treatment site, and the rest had minimal erythema and postinflammatory hypo/hyperpigmentation. Another small prospective case series of 6 patients with biopsy-proven Bowen disease on the digits with two patients had a history of chronic arsenic exposure. All patients were treated with CO_2 laser in the continuous mode with a spot size of 3 mm at 5 to 8 W. The visible lesion (size ranged from 0.5 to 4 cm) and 4 mm of the surrounding normal

skin were ablated. All patients showed complete clearance and no signs of recurrence after seven years from treatment [15]. Though CO_2 laser can be effective in SCCIS, a study was done by Humpherys et al, showed that Pulsed CO_2 failed to completely clear biopsy-proven SCCIS with three passes in thick or keratotic le-sions [16]. In this study, the average thickness for the SCCIS was 0.57 mm. The entire area and 3 mm of surrounding skin were first treated with either 2 or 3 passes of a PCO_2 laser using a 3-mm collimated handpiece at 500 mJ, 2 to 4 W. The authors of this study recommended against using Pulsed CO_2 alone, especially for SCCIS showing hyperplasia or hyperkeratosis or that have a significant follicular extension. Lasers have also been used as an adjuvant tool with (PDT) and methyl aminolevulinate (MAL) for add-ed efficacy for the treatment of Bowen disease. For instance, in a randomized clinical trial were 21 patients with multiple lesions randomized into either Er:YAG laser combined with PDT (AFL-PDT) or MAL-PD, D.Y. Ko et al found the one-session use of Er:YAG laser with AFL-PDT was more effective than the two sessions of MAL-PDT (93.8% Vs. 73.1%) with fewer chances for recurrence but almost similar cosmetic outcome [17]. Both techniques were used on the same patient but in different locations to avoid any potential for bias. The efficacy decreased at 12 months to 84.9% for Er:YAG AFL-PDT method and 48.2% for the MAL-PDT method. Finally, as SCCIS occur in the form of Erythroplasia of Queyrat (EOQ) on the penis when tissue preser-vation and sexual functionality play significant importance, a systematic review conducted in 2016 showed the use of lasers for the treatment of EOQ in a total of eight studies with three studies con-sisted of multiple patients and the rest of the studies being single case reports demonstrated com-plete remission on 33 out of 34 patients (97.1%) after follow up period ranged from 6 weeks to 40 months. In this review, a total of 27 patients were treated with CO_2 laser, and seven patients have treated with Nd:YAG lasers with total of 1 to 3 sessions [18]. It is worth mentioning that 96% (26/27) of patients treated with the CO_2 laser experienced CR. In contrast, 14 % experienced relapse when treated with the Nd:YAG laser.

2.3 Squamous Cell Carcinoma (SCC)

Cutaneous squamous cell carcinoma is the second most common skin cancer accounting for 20% of all skin cancer [19]. With the tendency to develop thicker tumors and deeper invasion into the underlying dermis, for this reason, lasers are a less reliable option to treat SCCs due to limited penetration to the deeper structures [3]. The evidence is very limited for the efficacy of laser and energy-based device for treating SCC in the literature [13]. Nevertheless, several case reports showed successful treatment for superficial SCCs with different laser modalities. In one 10-case report study were patients with stage T1 SCCs of the lower lip treated with CO_2 in continuous mode with the focus of 0.8 mm, power of 10 W, and the entire lesion with a 10-mm margin. Histopathological review of all surgical specimens showed that all margins were dis-ease-free. After 30 days, all patients had complete wound healing with full re-epithelization at the site of the surgery. All patients showed no evidence of recurrence after a follow-up period of up to 5-years [20]. All patients had minimal bleeding except for one were transectioning and suturing of the ar-tery were needed to control the bleeding. All patients reported only minimal discomfort during the first 24 h after surgery, and there were no reported bleeding episodes.

Another large retrospective series of 46 patients treated with Nd:YAG laser for histopathologically proven T1N0M0 SCC of the lip over a period of 10-years [21]. Most of the patients included had lesions on the lower lip with a size less than 2 cm and no lymph node involvement. The Author used power between 30-50 watts and the pulse duration at one second at pulsed mode. The lesions were fully coagulated with the laser, and the entire lesion was coagulated in a punctate manner at 8 mm of in-terval for 1-2 seconds each. Lesions were left to heal with secondary intention with 30 days follow-up period, and a repeat biopsy of the treated area was done at the end of one month (for residual lesion) and at one year to detect recurrence. 5 out of 46 patients demonstrated residual cancer by the end of 1-month follow-up. By a 5-year follow-up period, only 29 patients continued to follow to the end of the study, who demonstrated recurrence free-survival for five years of 85.1% with an overall success rate of 88.14% at a mean of 56 months. All patients in this case series had excellent cosmetic outcomes and no complications.

2.4 Basal cell carcinoma (BCC)

Basal cell carcinoma is the most common keratinocyte cancer in the world with an increasing inci-dence [1]. In the literature, more lasers and energy-based devices have been tried with varying success rates to treat BCCs when compared to other NMSK1. As shown in (Table 2), response rates showed significant variation based on the tumor characteristics, i.e., superficial vs. nodular BCC, the depth of invasion, and the type of lasers and energy-based devices. For instance, in a prospective study where CO_2 was utilized to tread a total of 51 BCCs included 28 nodular, 21 superficial, and two infiltrative BCCs with an average size of 13.6 mm. Only 3 of 21 superficial tumors were incompletely ablated. Compared to 28 nodular tumors, half of the tumors were incompletely ablated with tendencies for larger tumors to have less successful rates for ablation. The overall response from this study was a 67% complete ablation rate (34/51) [22]. After the laser treatment, all patients had normal excision as per standard practice for the ultimate treatment of the BCCs. The Nd:YAG 1064-nm laser has also been used for treating BCCs with excellent results. This was demonstrated in 2 small studies with a clearance rate approaching 100% with one treatment con-firmed with biopsies after treatment [23,24]. In the first study, a prospective open-label study with a total of 10 patients with 13 biopsy-proven BCCs mainly on the trunk or extremities with tumor size less than 1.5 cm and an average size of 6 mm. The authors of this study used a fluence ranging from 80 to 120 J/cm^2 and a pulse duration of 10 milliseconds with no use of epidermal cooling. The entire tumor and the adjacent 4 mm margin treated with three passes. In this study, superficial was the most common type of BCC (8 superficial, three nodular, and two mixed) [24]. After the first laser treatment, BCC tumors had a 92% clearance rate (12 of 13 BCC tumors). This was further increased to 100% after the fluence risen from 80 to 120 J/cm^2. All patients had an excisional biopsy after the treatment to demonstrate the histological clearance. No significant adverse effects were reported in this study ex-cept for mild erythema which sometimes persisted for one month after the treatment. These findings were further solidified with a multi-center retrospective study on 16 cases with super-ficial and nodular BCC with one subject had four BCC fulfilling criteria for Mohs Micrographic Surgery. The size of tumors ranged from 4 to 21 mm. The settings used in this study: 5 mm spot, fluence 140 J/cm^2, pulse duration of 8 ms, with 9-45 pulses. The entire tumor

and 5 mm margin was treated. All patients showed a complete clearance after one session of treatment after a mean follow-up of 9 months with no long-term adverse events reported and no recurrence [23]. Ablative lasers have also been tried with a great outcome for the treatment of BCCs. In a large pro-spective comparative study with a total of 286 patients with recurrent nodular BCCs. In this study, pa-tients were assigned to three groups, either to PDT with topical application of ALA methyl ester (Method A), solitary Er:YAG laser ablation (Method B), or combined Er:YAG laser ablation reducing tumor size below 2 mm with subsequent ALA methyl ester PDT (Method C). For Method B, patients were treated with a fluence of 600-1,000 mJ of energy at a frequency of 7 Hz. All patients had a total of 3 tumors and were followed up to 12 months after the treatment. By the end of the study, the complete remission rates were 96.4%, 94.3%, and 99.2% for Method A, B, and C, respectively. Alt-hough this study showed superior remission rates with the combined Er:YAG with subsequent ALA-PDT methods, most patients preferred the solitary Er:YAG 67% patients laser treatment over the PDT method (20%) and the combined treatment (13%) for the simplicity of the procedure [25]. As BCCs tend to develop a vascular network for their growth, vascular lasers such as pulsed dye lasers (PDL) which mainly target oxyhemoglobin, serve as a viable option with various success rates to treat BCCs. In one pilot study with a total of 20 biopsy-proven superficial and nodular BCCs treated with four 595-nm PDL sessions at 2-week intervals with the following parameters: one pass, 15 J/cm^2 energy, 3 ms pulse length, and 7mm spot size with 10% overlap. The entire tumor area and 4 mm margin were treated. By the end of the laser treatments, the clearance rate for BCCs less than 1.5 cm was 91.7% compared to 25% only for the BCC measuring >1.5 cm. All patients had an excisional biopsy at least two weeks after the last treatment to histologically evaluate the efficacy of the laser treatment. It is worth mentioning that the clearance rate correlated with tumor diameter. The average diameter of complete responders was 1.1 cm when compared to non-responders (2.2 cm) with an overall re-sponse rate of 65% [26]. In a similar study of fourteen patients with a total of 20 biopsy-proven BCCs on the trunk and extremi-ties with the same PDL laser parameters used as in the SHAH et al study [26]. The BCCs included in this study were superficial, nodular, infiltrative, and metatypical types with the exclusion of the high-risk locations. Complete clinical was seen with 19 out of 20 treated BCCs, regardless of size. Of the 19 BCCs, one patient had a recurrence after 17 months. Overall, 18 out of 19 (95%) BCCs less than or equal to 1.7 cm in diameter showed no evidence of residual tumor clinically or on histology 12-21 months after last PDL treatment [27]. At 12-21 months after PDL treatment, no scar, erythema, or textural changes were noted. The dual-wavelength copper vapor laser (CVL) with the emission of two wavelengths, 511 nm, and 578 nm that targets the melanin on the basal layer and ectatic vascular beds, respectively, was found to help the eradication of malignant cells. This has been demonstrated in a small 8-cases of nodular and ulcerative BCCs located mainly in the periorbital area. The authors of this study used the CVL with the power level of 3 W, and the exposure time was equal from 200 to 600 ms, pulse duration of 15 ns, and a fluence ranging from 30 to 300 J/cm^2. The entire tumor and the adjacent tissue of 5 mm and the total borderline of the surrounding intact skin area were irradiated. Tissue sampling for all patients showed no evidence of remaining basaloid or tumor cells six months after the

laser treatment with no signs of recurrence in the 2-years follow-up period [28]. Although this was a challenging location, no ocular or adverse effects were reported except for mild post-operative swelling, which resolved within few days after the laser treatment.

Author	Number of BCCs	Laser type	Laser settings	BCC type	Number of treatments	Outcome
Ahluwalia et al [23]	16	1064nm Nd:YAG laser	Fluence: 140 J/cm^2. pulse duration:8 ms spot size: 5mm 9-45 pulses.	3 Superfacial 8 Nodualr 5 Superficial and Nodular	1	100% clearance at 9 months.
Jalian et al [54]	13	Combined PDL and Nd:YAG laser	PDL: spot size:7 mm. Fluence:8 J/cm^2. Pulse duration: 2ms Nd:YAG: Fluence: 40J/cm^2 and Pulse Dura-tion:15 millisecond	4 Nodular 9 Superficial and Nodular	1	58% histological clearance
Konnikov et al [27]	20	PDL	Fluence:15 J/cm^2. pulse duration:3 ms Spot size:7 mm	7 superficial. 9 nodular. 2 superficial and nodular. 1 infiltrative, 1 metatypical.	1	90% clearance 12 months
Minars et al [55]	39	PDL	Fluence:15 J/cm^2 Pulsed Duration:3ms Spot size:7mm	1 Superficial 20 Nodular 14 mixed 1 ulcerative 2 keratinized 1 Micronodular	1-4	75% clearance (24/32) at 3 months.
Alonso-Castro L et al [56]	7	PDL	Fluence:15 J/cm^2. Pulse Duration:2 ms Sot size:7mm	6 Nodular 1 Infiltrative	3	Complete clinical response was achieved in 5/7 cases (71.4%) assessed by Mohs micrographic surgery

Shah et al [26]	20	PDL	Fluence:15 J/cm^2 Pulse duration: 3ms. Spot size: 7mm	9 Superficial, 2 Nodular, 10 Mixed types	4	Histological com-plete clearance of 91.7% for BCCs <1.5 cm with overall 65%
Klyucha reva et al [28]	8	Copper Vapor laser (CVL)	Power level:3 W. Fluence: 30-300 J/cm^2 Exposure time: 200-600 ms. Pulse Duration:15 ns. Repetition rate: 16.6 kHz	7 Nodular. 1 Ulcerative.	1	100% histological clearance in all patients at 6 months after laser treatment with no recurrence at 24 months period.
Ortiz et al [24]	13	1064nm Nd:YAG laser	Fluence: 80-120 J/cm^2. Spot size: 5mm. Pulse Duration:10 ms.	8 superficial 3 Nodular 2 mixed	1	Overall 92% (12 of 13 BCC tumors) histological clear-ance rate
Iyer et al [53]	61	UltraPulse CO2 laser	pulse energy: 300 mJ or 3-mm spot with a 500-mJ pulse set at 10Hz passes: 2-8	44 superficial 9 Nodular 8 Uclassified	1	97% cure rate at mean follow up of 41.7 months.
Horlock N et al [22]	51	1020 Carbon Dioxide laser	Power:10 W Passes: 2-4	21 Superficial 28 Nodular 2 Infiltrative	1	Histological com-plete ablation rate: 67% (34/51).

Table 2: laser treatments for BCC, laser types, parameters, and response rates

2.5 Keratoacanthoma (KA)

Keratoacanthoma is a common, rapidly growing skin tumor. Although there is no complete agreement whether KAs are benign tumors or a malignant variant of SCC, KA should be treated due to the ex-panding and the disfiguring nature of the tumor [29]. Lasers and energy-based devices have found to both induce the formation and treat KA. In many case reports, lasers were associated with the devel-opment of KAs which is believed to be secondary to thermal trauma. the reported cases involved the use of CO_2 laser for resurfacing, 532-nm picosecond laser for red tattoo removal, and the 1550 nm fractional laser [30-33]. On the other hand, the efficacy of laser has been utilized in treating KAs in a case series of seventeen patients presented with solitary confirmed histopathologically. KA treated with 488 and 514 nm Argon laser with a continuous exposure technique, a power setting of 4.5 watts W, and a beam diameter of 1 mm were selected; the irradiance was about 570 W/em. All patients had KAs less than 1 cm located on different areas on the face and auricles. All patients had complete clearance, with ten patients (65%) had no residual scars, and seven patients developed slight scar only. Patients

were followed up for two years with no sign of recurrence after the laser treatment [34]. No complaints during the post-operative period were reported in this study.

2.6 Verrucous Carcinoma

Verrucous carcinomas (VC) are rare well-differentiated squamous cell carcinoma with locally destruc-tive behavior associated with human papillomavirus (HPV) types 16 and 1835. With the tendency for these tumors to occur on the genital and perianal areas, clinicians should bear in mind the importance of functional and anatomical preservation while treating these areas. Although there are no large case series or controlled trials in the literature, multiple case reports have demonstrated the efficacy of CO_2 lasers for treating oral and genital VCs either alone or in combination with surgical excision [35-40]. In a case of a 16-week pregnant patient with oral VC treated with CO_2 laser with continuous mode at a power level of 7 W, patient showed complete clearance with great cosmetic outcome and no local recurrence at 21-month follow up after the laser treatment [38]. The authors have found the use of CO_2 laser was superior to conventional surgical removal to control bleeding, precise excision, and better visualization of operational field.

2.7 Porokeratosis

Porokeratosis is a rare disorder due to abnormal keratinization of the epidermis which presents with one or more keratotic plaques characterized by coronoid lamella. Multiple variants have been identi-fied, with a small number of cases progress into malignant lesions [41]. Higher risk for progression, especially into squamous cell carcinoma or basal cell carcinoma have been associated with the linear and disseminated superficial actinic porokeratosis (DSAP) types with some reports of risk for trans-formation into SCC as high as 10% [42,43]. Different laser modalities have been used to treat variant types of porokeratosis. In the literature, CO_2 lasers have been extensively employed to treat all kinds of porokeratosis successfully. A case report of a resistant linear porokeratosis in a 23-year-old man who failed cryosurgery, electrosurgery, and keratolytics, CO_2 laser with a beam point size of 0.17 mm in diameter and a resultant power density of 2,941 watts/era showed complete clearance after one treatment. The patient showed no recurrence at 6-months after the treatment with only minimal pain reported as a side effect postoperatively [44]. Another case report of a biopsy-proven Porokeratisis of Mibelli in a 14-year-old male treated initially with a test spot with CO_2 with a power of 10 W and 2-mm spot size. Three months after the test spot treatment, the patient had a full lesional treatment with complete clearance at 6-months from the initial treatment. The patient was treated monthly after that with the same laser parameters until two years from the 1st treatment. No sign of recurrence and a biopsy after two years from the initial treatment was unremarkable [45]. DSAP was extensively treated with various ablative and non-ablative lasers. In a split-face study, were a CO_2 laser was tried on one patient with DSAP. The patient in this study received a series of five treatment sessions at 1-2-month intervals with the 10 600-nm wavelength CO_2 laser on the right side of the face and high-dose (0.002%) application of tacalcitol ointment daily to the left side of the face for one year. The patient showed almost a complete clearance after five sessions, but no remarkable changes in the side treated with tacalcitol ointment. The patient sustained the results four years after the last laser treatment and showed no signs of recurrence [46]. In another case of one patient treated

with Q-switched Ruby laser for DSAP persistent for four years, mainly on the sun-exposed areas with energy density of 4.3 J/cm^2 using a spot size of 6.5 mm for a small test spot which subsequently treated in all the affected areas showed a significant improvement with no reported side effects and no clinical recurrence 8-months after the laser treatment. Erbi-um laser was also utilized for the treatment of resistant DSAP on a 62-year-old for seven years [47,48]. The patient received a total of 13 treatments at 2-4 weeks interval with an energy level of 0.3 J with total passes varying from 4 to 10 depending on the lesion thickness [49-52]. Treatments spaced from 2 to 4 weeks intervals with post-laser erythema lasting from 2 to 3 weeks was the only complaint. The patient showed no signs of recurrence at 1-year [53-56].

3. Discussion

Despite the fact lasers and energy-based devices are not intended to be used to treat skin cancers, the striking finding of this review is the wide range of applications of lasers for the treatment of all types of skin cancers. For one reason, lasers can be more cost-effective in treating larger surface areas af-fected with pre-cancerous conditions such as widespread actinic keratosis and DSAP, as it has been demonstrated in multiple cases and case series both ablative and non-ablative lasers used as a field treatment with cure rates competing for the conventional methods of treatment such topical 5% 5-fluorouracil. Though, specific laser types and parameters cannot be generalized for treating different skin cancers. This could be due to the fact different behavior of each type of skin cancer. As evident from this re-view, owing to the fact that SCCIS and BD are intradermal processes with no invasion to the dermis, lasers could serve a good alternative for treatment, especially for difficult locations such as the digits or genitalia when the surgical choice is limited due to scarcity of tissue for repair. On the contrary, lasers should only be used in very selected cases for treating invasive squamous cell carcinoma as the literature failed to demonstrate positive results. This might be as a result of SCCs tend to develop larger tumors with often thicker and more dysplastic lesions than SCCIS. Furthermore, not all laser devices, settings, or techniques will provide adequate depth of removal to achieve tumor clearance. It is important to recognize even when using the same laser with the same settings, the response can vary differently based even on one variant, such as tumor size. This was proven in the Shah et al. pilot study were all BCCs <1.5cm in diameter showed response rate of 91.7% to four PDL treatments. This response dropped dramatically to 25% for BCCs measuring 1.5cm or more using the same settings and number of passes regardless of the histological type of the tumor treated [26]. It is noteworthy to know as mentioned at several points in this review the extent of using lasers and energy-based devices is much greater when combined with other treatment modalities for achieving better outcomes. For example, this was demonstrated in the D.Y. Ko et al. study were the one-session use of Er:YAG laser with AFL-PDT was more effective than the two sessions of MAL-PDT for treating SCCIS [17]. Additionally, lasers showed they can be utilized either alone or as an adjuvant treatment to decrease the mutilating surgical effect especially for lower grade locally aggressive tumors such as verrucous carcinoma on sensitive areas like lips or the genitals [38,40]. As apparent from this review, many lasers and energy-based devices showed superior cosmetic out-comes and fewer complications than conventional treatment methods. Still, due to the variety of la-sers available at different wavelengths and different settings used to

treat skin cancers, it is fundamental for dermatologists to be aware of the evidence behind the use of their particular laser type in the cutaneous lesion of interest. Even when using a laser with proof of efficacy, the lack of certainty of completely removing the malignant tissues makes lasers equivalent to the other non-surgical methods for treating skin cancer in this aspect as the importance of completely removing the malignant tissue is the cornerstone when it comes for treating skin cancers.

4. Conclusion

Over the years, lasers and energy-based devices have been increasingly showing promising results in demonstrating the efficacy and safety in treating non-melanoma and precancerous skin lesions, with increasing evidence showing superior esthetic outcomes. They can serve as an alternative for treating low-risk, small and superficial skin cancer in low-risk locations, especially for poor surgical candidates. Nevertheless, lasers and energy-based devices still have limited use for treating skin cancers due to this limited penetration and the inability to confirm the clearance of malignant cells. Additional larger studies with randomized clinical trials are needed to optimize parameters, determine maximum efficacy, and provide long-term follow-up.

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