

Cosmetic Outcomes of Treatments for Actinic Keratoses: An Emerging Endpoint of Therapy

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Multiple treatment modalities have been developed for the treatment of actinic keratoses (AKs). No systematic review has been undertaken to compare the cosmetic outcomes of these various modalities. We reviewed all available publications on PubMed on the treatment of AKs. We concluded that photodynamic therapy and imiquimod have the greatest amount of evidence indicating superior cosmetic outcomes. In general there is a lack of reported cosmetic outcomes in publications on the treatment of AKs. Further research is needed in this area.

Actinic keratoses (AKs) are in situ keratinocyte-derived dysplasias which arise as a result of chronic sun damage. While the actual rates of transformation to squamous cell carcinoma are a subject of active debate, it is generally agreed that the rate is substantial enough to warrant medical intervention, particularly in the case of multiple, long-standing, or thicker lesions.

While a large body of research has been done regarding a number of treatment modalities for AKs, the focus has primarily been on the efficacy of these treatments. Recently the *British Journal of Dermatology* published

guidelines for the management of AKs. They took into account efficacy, ease of use, morbidity and cost benefit in their recommendation of treatment, but not cosmetic outcome.¹ While these recommendations are certainly of benefit in the management of AKs, this is simply one example of how the actual cosmetic outcome of the treatment of AKs is often overlooked when researching and considering treatment modalities.

As some of the younger population has increased their overall sun exposure, dermatologists occasionally have to treat AKs in this age demographic who are particularly concerned about long-term cosmetic outcomes of treatment. Even in older adults, particularly in the professional population, long-term appearance of treated lesions has taken on an increased importance. Additionally, if the patient's overall appearance can be improved, patients are likely to be more compliant with further management of precancerous and cancerous lesions. As compliance can already be an issue given the substantial erythema and erosions that occur with all treatments for AKs, reassuring long-term cosmetic data has an important place in convincing patients to follow through with treatment.

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COSMETIC OUTCOMES

Our goal herein is to review the literature and report all available cosmetic data regarding treatment modalities for AKs.

METHODOLOGY

We reviewed PubMed using keywords “cryotherapy,” “photodynamic therapy” (PDT), “actinic keratosis” with “imiquimod” (IMQ), “5-fluorouracil” (5-FU), “diclofenac,” “tretinoin,” “dermabrasion,” “trichloroacetic acid” (TCA), “laser,” “Erbium:YAG (Er:YAG),” “pulsed dye laser (PDL),” and “carbon dioxide (CO₂).” Additionally, multiple review articles on the treatment of AKs were reviewed for any additional primary sources referenced by those articles. Search yielded 866 results, 92 of these articles were selected by the authors for further review, and 60 of those were primary sources, which included relevant information regarding cosmetic outcome and have been included here.

CRYOTHERAPY

Cryotherapy currently is the most frequently used treatment for AKs.² However, as this has been such a longstanding and established treatment modality, there are very few publications looking at cryotherapy alone. The majority of research done with cryotherapy for AKs is in comparing it with other treatment modalities to establish the efficacy and cosmetic results of these newer modalities.

The best single study of cryotherapy for AKs with cosmetic data reported was performed by Thai et al³ in 2004. Eighty-nine patients with 421 eligible AKs were enrolled; the clearance rate for individual lesions was 67.2%.³ At the 3-month follow-up, both investigators and patients graded their cosmetic outcome, and came to similar conclusions. Patients and investigators graded the appearance of treated areas to be excellent in 56% and 51% of patients, good in 38% and 43%, and fair in 6% and 6%, respectively. Hypopigmentation was found in 29% of treated lesions, and reached 50% in lesions treated for 15 to 20 seconds. The authors hypothesized that freeze times of greater than 10 seconds but less than 15 seconds achieved the optimum balance of efficacy with decreasing risk of hypopigmentation. Additionally, hyperpigmentation was found in 6% of lesions, scar formation in 2%, and tissue defect in 5%.³ An example of the hypopigmentation associated with cryotherapy can be seen in the Figure.

It is interesting to note that in this study,³ freeze times of greater than 20 seconds resulted in hypopigmentation 25% of the time, as opposed to 50% of the time in the 15- to 20-second group. This is in opposition to prior publications which hypothesized that freeze times of greater than 30 seconds to be most strongly associated with hypopigmentation.⁴



This 59-year-old man has had 6 rounds of cryotherapy to his scalp over the prior 2 years. While relatively free of actinic keratoses (AKs) at the time of evaluation, multiple areas of hypopigmentation can be appreciated.

In one of the best studies available comparing treatment modalities for AKs, 75 patients were randomized to either cryotherapy (20–40 seconds per lesion, with second treatment performed 2 weeks later if not cleared, n=25), 5-FU cream 5% (twice daily for 4 weeks, n=24), or IMQ cream 5% (applied 3 times weekly for 1 month followed by a 1-month rest period, and followed by 1 month retreatment if any lesions persisted, n=26).⁵ Cosmetic outcomes in this trial were judged by both investigators and patients between 1 and 2 months after completion of therapy and at 12 months after completion. While there were no differences between treatments shortly after treatment, when evaluated after 1 year, 81% of patients in the IMQ group had an excellent cosmetic outcome compared with only 4% in both the cryotherapy and 5-FU groups ($P=.0001$). Between cryotherapy and 5-FU, approximately 40% of investigators and patients found 5-FU to have a good cosmetic outcome compared with none in the cryotherapy group. In evaluation for overall skin quality, 83% of the IMQ group was judged to have a normal skin surface, compared with 58% of the 5-FU group, and only 16% of the cryotherapy group.⁵

The majority of cosmetic data available on cryotherapy comes from recent studies comparing PDT to cryotherapy.⁶⁻¹⁰ A summary of these publications can be seen in Table 1. In general, while the efficacy is comparable between the 2 modalities, the cosmetic outcome is invariably in favor of PDT, by investigator as well as patient judgment. Additionally, hypopigmentation tended to be notably lower in PDT-treated patients. All of these studies were funded at least partially by the manufacturers of the PDT products.^{6,9}

TABLE 1

Photodynamic Therapy vs Cryotherapy

Study	Patients/ AKs, n	Study Design	Methods of Adminis- tration	Participants in Each Arm, n	Efficacy	Cosmetic Outcome	Participant Preference
Hauschild et al ⁶	449/NA	2 separate parallel group studies; participants randomized to either 5-ALA-PDT or placebo PDT in study 1; 5-ALA-PDT, placebo PDT, or cryo in study 2	5-ALA-PDT or placebo patches applied 4 h prior to narrowband red light (630 nm) (length of treatment not specified); cryo was treated with a single cycle, average freeze time 7.3 s	Cryo 149; 5-ALA- PDT 217; placebo PDT 83	At week 12, study 1: 5-ALA- PDT clearance 82%, placebo PDT 19%; study 2: 5-ALA-PDT clearance 89%, placebo PDT 29%, cryo 77%	In study 2, patients rated excellent cosmetic result 5-ALA-PDT 68% vs 42% cryo; hyperpigmentation occurred in 33% of cryo-treated lesions, compared with 12% in 5-ALA-PDT	NA
Morton et al ⁷	119/1501	Split-face, each participant received PDT on half, cryo on half	MAL applied for 3 h prior to narrowband red light (630 nm) for 9 min, 2 cycle cryo spray (average time 16 s)	113 (6 dis- continued)	At week 24, efficacy comparable (lesion reduction of 89.1% PDT, 86.1% cryo)	Investigator rated "excellent cosmetic outcome" 70.8% PDT and 57.4% cryo at week 12; 77.2% PDT and 49.7% cryo at week 24	If offered retreatment with either, 64.8% preferred PDT, 31.5% preferred cryo
Kaufmann et al ⁸	121/1343	Split-face, each participant received PDT on half, cryo on half	MAL applied for 3 h prior to narrowband red light (630 nm) for 8.5 min, 2-cycle cryo spray (average time 20 s)	106 patients completed the study per protocol	At week 24, cryo was more efficacious (lesion reduction 78% PDT, 88% cryo, P=.002)	Investigator rated "excellent cosmetic outcome" 79% PDT, 56% cryo; 50% of patients favored PDT for somatic outcome, 22% preferred cryo	If offered retreatment with either, 59% preferred PDT, 25% preferred cryo (P<.001)

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TABLE 1 (CONTINUED)

Photodynamic Therapy vs Cryotherapy

Study	Patients/ AKs, n	Study Design	Methods of Administration	Participants in Each Arm, n	Efficacy	Cosmetic Outcome	Participant Preference
Freeman et al ⁹	204/855	Randomized to cryo, MAL-PDT, or placebo PDT	MAL applied 3 h 10 min prior to red light (570–670 nm), average time 10 min for MAL-PDT, 11 min for placebo-PDT; 2 cycles of PDT; cryo consisted of single cycle of therapy, average treatment time varied by size	Cryo 89; MAL-PDT 88; placebo PDT 23	At 3 mo, lesion response in MAL-PDT 91%, cryo 68%, placebo PDT 30%	Cosmetic outcome rated as excellent in 83% of MAL-PDT vs 56% of cryo; hypopigmentation present in 5% of PDT vs 29% of cryo	MAL-PDT rated better than previous treatments for AKs in 61% of assessments; placebo-PDT rated better than previous treatments in 21%; cryo was not mentioned
Szeimies et al ¹⁰	202/732	Randomized to MAL-PDT or cryo	MAL applied for 3 h 10 min prior to red light (570–670 nm) for 11 min, 2-cycle cryo spray, single session (average time 24 s)	Cryo 100, PDT 102	At 3 mo, complete response rate 69% for PDT, 75% for cryo	Investigator rated cosmetic outcome excellent or good 96% PDT, 81% cryo (P=.035); patients rated excellent or good 98% PDT, 91% cryo	Of previously treated patients, 32 of 43 (74.4%) rated PDT as better than previous treatments

Abbreviations: AKs, actinic keratoses; NA, not available; 5-ALA, 5-aminolevulinic acid; PDT, photodynamic therapy; cryo, cryotherapy; MAL, methyl aminolevulinic acid.

In addition to lesion-focused cryotherapy, there is the alternative of “cryopeeling” or extensive cryotherapy to an entire field. Chiarello¹¹ reviews 373 patients treated with this modality and reports a 4% recurrence rate at 6 months. He reports favorable cosmetic results, but no specific data.¹¹

A study was performed using diclofenac gel 3% twice daily for 12 weeks followed by cryotherapy for any unresolved lesions.¹² The authors offered a number of possible advantages of this combined modality, including “a lower risk of cryotherapy related scarring.” While this hypothesis may be valid, no cosmetic outcomes are reported.¹²

One final note on cryotherapy for AKs: alopecia is common with long freezes, but also may occur after short freezes, and the associated hair loss is usually permanent, and should be considered when using this modality in hair-bearing areas.¹³

PDT

Photodynamic therapy is a relatively newer therapy in the treatment of AKs, with the first clinical trials being done in 1996.¹⁴ Studies performed on older modalities of treatment tended to focus on efficacy and safety data in their clinical trials; however, the majority of studies on PDT have included data on cosmetic outcome even in special circumstances such as in organ transplant patients. The data for available trials on PDT is summarized in Table 2. The data described here shows PDT to have very good cosmetic results, though this was not always statistically different from the compared treatment modalities.¹⁵ The definition of what represented a good cosmetic outcome was not usually explicitly defined; however, good concordance between patient and evaluator data indicate there was good agreement about what represented good cosmetic outcome.¹⁸ Additionally, cosmetic outcome can be defined by more concrete criteria, such as hyper- or hypopigmentation, as in the study by Tschen et al.¹⁹ In the case of this study, PDT performed favorably with regard to this criteria.

Other publications reviewed on PDT for the treatment of AKs did not include specific quantification of cosmetic outcome.^{20,21} Another publication on the treatment of AKs in organ transplant recipients asserted that PDT yielded excellent cosmetic results with “absence of scar formation or alteration of pigmentation” but without specific numeric or standardized data.²²

Of note, an interesting study was done by Tierney et al²³ regarding patient perceptions of various treatments for AKs, specifically targeting patients who had had PDT in the prior 2 years. Thirty-nine patients responded to the survey. Regarding cosmetic outcome, 89.7% (34/39) believed their appearance was much improved after PDT; this number was not statistically varied from other

treatment modalities, with the exception that surgical excision was nearly statistically significant ($P=.06$). This outcome is significantly different from the prior presented data which found a difference in outcome for PDT versus cryotherapy. This discrepancy may be due to the significant delay in questioning after treatment. Patients in this study significantly preferred PDT over 5-FU ($P<.001$) or IMQ ($P=.03$).

Regarding the variations in photosensitizers and light sources, the use of aminolevulinic acid (ALA) versus methyl aminolevulinic acid (MAL) did not appear to make a difference in overall cosmetic outcome, nor did the spectrum of light used.

IMQ

Topical IMQ is another relatively new treatment available for the treatment of AKs, with some of the first trials for the treatment of AKs becoming available in 2002.^{24,25} We have already discussed what likely represents the most thorough research on long-term cosmetic outcome of IMQ, in which 81% of patients treated with IMQ had an excellent cosmetic result at 12 months compared with 4% for both 5-FU and cryotherapy.⁵ Only one other publication reported specific cosmetic outcomes data on IMQ, which was against PDT and is listed in Table 2. In 30 patients, investigator-reported cosmetic outcome was good or excellent in 95% of those treated with IMQ cream 5% at month 6, versus 99% in those treated with PDT ($P>.05$).¹⁵ Another study following the long-term outcome of IMQ used 2 to 3 times per week for 16 weeks commented that “there were no long-term adverse changes in skin quality” among treated patients, though there was one patient with moderate hair loss in one eyebrow after treatment in that area.²⁶

The remainder of data available on the treatment of AKs with IMQ is only regarding the acute reactions associated with treatment, including erythema, erosion, scabbing, etc. One study is available, which compares IMQ to 5-FU, with patients being treated with 5-FU twice daily for 2 to 4 weeks or IMQ twice weekly for 16 weeks.²⁷ Erythema was recorded to be higher in patients treated with 5-FU at 4 weeks, with patient averages showing “moderate” erythema. As expected given the longer treatment regimen, IMQ had longer duration of erythema given the longer treatment regimen, but the greatest degree of erythema never reached the moderate average level of erythema shown with 5-FU; IMQ remained in the mild to moderate range. Other studies available on IMQ include data only on acute cutaneous reactions.^{20,28-33} Overall rates of severe erythema, scabbing, and flaking are 27% (401/1480), 25% (374/1480), and 13% (189/1458), respectively.^{24,28-31,33} Other studies on IMQ lacked specific numbers regarding inflammatory reactions.

More recently, trials on IMQ cream 3.75% have been performed. None of these trials include any specific data regarding cosmetic outcomes. The trials do include data regarding the same inflammatory reactions as other IMQ trials; the cumulative rates of severe erythema, scabbing, and flaking are 34% (117/341), 23% (78/341) and 10% (34/341), respectively.³⁴⁻³⁶ The higher rates of severe erythema observed in the trials of IMQ cream 3.75% compared with IMQ cream 5% are somewhat surprising, but are likely due to the increased frequency of application (daily for 2 weeks) compared with 3 times weekly with IMQ cream 5%. While erythema is certainly not an effect desired by patients cosmetically, there is evidence that increased rates of erythema correlate with the rates of clearance of actinic lesions.²⁹

5-FU

Topical 5-FU has long been in use for the treatment of AKs. Unfortunately, little has been published regarding the cosmetic outcomes of its use for the treatment of this condition. The most useful article in evaluating cosmetic outcomes is the prior discussed article by Krawtchenko et al⁵ comparing cryotherapy, IMQ, and 5-FU. It has been discussed that 5-FU and cryotherapy were comparable in that 4% of both groups achieved an excellent cosmetic result. It is important to note that approximately 40% of investigator-rated patients achieved a good result with 5-FU compared with none of the liquid nitrogen group.

In a different comparative study, a trial of 5-FU cream 5% applied twice daily versus 5-FU cream 0.5% applied once daily was conducted as a split-face trial.³⁷ In this study, while signs of acute inflammation (erythema, erosion) were statistically comparable, 8 of 21 patients thought their skin looked better after treatment with 5-FU cream 0.5%, as opposed to 1 of 21 with 5-FU cream 5%. Additionally, 17 of 21 patients found the 0.5% preferable and more tolerable compared with 3 of 21 who preferred the 5%.

A study by Witheller et al³⁸ compared a medium-depth chemical peel with Jessner solution and TCA cream 35% with 5-FU cream 5% twice daily for 3 weeks. Fifteen patients completed the split-face trial. Of these, 13 patients completed a 6-month follow-up questionnaire; 12 believed they showed considerable cosmetic improvement overall. Five patients saw no difference between treatments, 4 believed the peel gave superior results, and 4 believed 5-FU gave superior results. Nine of 12 patients preferred the peel, which was thought to be due to convenience of application and shorter morbidity.

The only other trial to evaluate cosmetic outcomes with 5-FU was previously discussed in Table 2 and evaluated

5-FU versus PDT.¹⁶ In short, 8 of the 5-FU-treated patients had moderate to good outcomes, whereas all 9 patients in the PDT-treated group had excellent cosmetic results.¹⁶

The remainder of available data is regarding irritation around the time of treatment. Ranges of significant clinical erythema (moderate to severe) were 50% to 83%.^{39,40} This erythema tends to peak at week 3 when used twice daily for 4 weeks, and then declines after discontinuation.^{27,21} As with IMQ, there is evidence that increasing erythema correlate positively with greater clearance of actinic lesions.⁴¹ The remainder of available studies on topical 5-FU lack data on cosmetic outcomes as well as immediate reaction data.^{42,43-46}

DICLOFENAC

Topical diclofenac is often used for the treatment of AKs when the amount of erythema produced by IMQ or 5-FU would be considered intolerable to a patient. It is therefore surprising that there is no available long-term cosmetic data available on this treatment modality. One publication has made the claim that diclofenac “results in a lower risk of cryotherapy-related scarring of exposed sites,” but themselves collected no data on scarring or cosmetic outcome.¹²

Overall, rates of erythema at the time of treatment appear to be lower with diclofenac than other topical treatment modalities. In a head-to-head study with 5-FU 27% (n=28) of patients experienced moderate to severe erythema at any point versus 83% treated with 5-FU cream 5% twice daily.⁴⁰ In a trial comparing diclofenac (once daily for 3 months) to IMQ (3 times weekly for 12 weeks) results were more comparable, with 40% of IMQ patients developing substantial erythema versus 46% of diclofenac patients.³² Overall, rates of what are judged to be clinically relevant erythema are between 26% and 46%.^{32,40,47}

Other studies of diclofenac report local adverse reactions with less standardized methodology. Skin irritation was reported in 72% of patients using diclofenac in one smaller study.⁴⁸ In a larger study done by the same author as the previous, incidence of “rash” not otherwise specified was not statistically different from vehicle.⁴⁹

TRETINOIN, DERMABRASION, CHEMICAL PEELS

Other lesser used treatment modalities for AKs have no significant cosmetic data available. Data available for tretinoin in the treatment of AKs is limited. Rates of severe erythema have been reported at 50% in patients using tretinoin cream 0.05% twice daily for 16 weeks,⁵⁰ and 35% in patients using tretinoin cream 0.1% twice daily for 24 weeks.⁵¹

TABLE 2
Studies Evaluating Photodynamic Therapy With Cosmetic Outcomes Reported

Study	Participants/ AKs, n	Study Design	Methods of Administration	Efficacy	Cosmetic Outcome	Participant Preference
Sotiriou et al ¹⁵	30/256	Each patient received 2 treat- ments of 5-ALA-PDT to 1 arm and 1 or 2 rounds of IMQ 5% 3 times weekly for 4 wk	20% 5-ALA-PDT applied 4 h prior to red light (570– 670 nm, 75 J/cm ²). IMQ applied for 8 h, 500 mg (2 sachets); second round of IMQ if not cleared after 1 round	At 6 mo, complete response was 65% for PDT, 55% for IMQ	Investigator reported cosmetic outcome excellent 80% PDT, 75% IMQ (<i>P</i> > .05)	70% prefer PDT vs 30% prefer IMQ
Perrett et al ¹⁶	8/9 lesional areas, patients with organ transplantation	Each patient received 2 treat- ments of MAL-PDT to 1 area and 3 wk of twice daily 5-FU cream 5% to a comparable area	MAL applied for 3 h prior to Nb red light (633 nm, 75 J/cm ²), 2 treat- ments 1 wk apart; 3 wk of twice daily 5-FU cream 5% to a compar- able area	Complete resolution at 6 mo was 8/9 treated areas for PDT, 1/9 for 5-FU	PDT judged to have excellent cosmetic result in all patients, 5-FU excellent cosmetic results in 1/9	100% prefer PDT to 5-FU
Tarstedt et al ¹⁷	211/413	Participants randomized to receiving either 1 treatment of MAL-PDT, repeated 3 mo later if not completely clear or 2 treatments 1 wk apart	MAL applied for 3 h prior to Nb red light (634 nm) for 8 min	At 3 mo after last treatment, complete clearance in regimen 1, 89% vs 80% in regi- men 2	Excellent cosmetic outcome of hyperpigmentation in 75% of regimen 1 and 90% of regimen 2; hypopigmentation, scar, and tissue defect were all judged excellent >90%	PDT rated as better than cryo in 66% of regimen 1 and 58% of regimen 2

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TABLE 2 (CONTINUED)
Studies Evaluating Photodynamic Therapy With Cosmetic Outcomes Reported

Study	Participants/ AKs, n	Study Design	Methods of Administration	Efficacy	Cosmetic Outcome	Participant Preference
Pariser et al ¹⁸	80/502 Treatment group: 42/260 Placebo group: 38/242	Participants randomized to either MAL-PDT for 2 treatments 1 wk apart, or placebo PDT 2 treatments 1 wk apart	MAL applied for 3 h and 14 min prior to treatment with red light (570–670 nm) for an average of 8 min 40 s	At 3 mo after the last treatment, efficacy was 82% for MAL-PDT treated lesions vs 21% for placebo PDT	By investigator assessed outcome, excellent cosmetic result was achieved in 97% of MAL-PDT treated lesions, and 91% by participant-assessed outcome; placebo PDT was not reported	Participants preferred MAL- PDT to any other previous therapy for their AKs 73% of the time
Tschen et al ¹⁹	110/968	Participants treated with ALA- PDT at baseline, and treatment was repeated at month 2 if required; participants followed for 1 y	ALA solution 20% applied for 14 to 18 h prior to blue light (417 nm)	At 4 mo, 86% of lesions were judged clear, which decreased to 78% at month 12	Hypopigmentation was 8% at baseline, decreased to 3% at months 1 and 2, and increased to baseline (8%) at month 12; hyperpigmenta- tion was found in 27% at baseline, and the number of these lesions had decreased by 69% at 12 mo	NA

Abbreviations: AKs, actinic keratoses; ALA, aminolevulinic acid; PDT, photodynamic therapy; IMQ, imiquimod; MAL, methyl aminolevulinic acid; NB, narrowband; cryo, cryotherapy; NA, not available.

Only one notable study has been done on the treatment of AKs with dermabrasion, and while the study showed the modality to be efficacious with a mean time to recurrence of 4 years, there were no data on cosmetics or morbidity associated with the procedure.⁵² It has been reported that pigmentary change after dermabrasion, particularly hypopigmentation may be as prevalent as 10% to 20%.⁵³

Cosmetic data available on medium-depth peels for AKs have been discussed previously in a publication comparing 5-FU to a Jessner solution and TCA peel.³⁸ The 2 modalities were comparable cosmetically, with 4 of 13 patients preferring the peel aesthetically, and 4 of 13 preferring 5-FU. A survey of 17 patients who received Jessner and TCA peels found that all of the patients who had received cryotherapy in the past (n=8) preferred the peel in terms of discomfort and healing.⁵⁴

LASER THERAPY

Erbium:YAG, CO₂, and PDL used in conjunction with ALA have all been used in the treatment of AKs in a few studies. There exists significant discordance between studies regarding cosmetic outcomes. In a retrospective case control study of 25 patients who underwent resurfacing with CO₂ or Er:YAG for widespread AKs with long-term follow-up (mean 39 months), 44% of patients experienced hypopigmentation, 20% experienced atrophy/easy bruising, and 4% each experienced milia and scarring.⁵⁵ While one other study by the same author also found high rates of hypopigmentation,⁵⁶ other studies have found contrary results. Two studies of Er:YAG note there was no evidence of pigmentary change or scarring, though neither reported data or how this was evaluated.^{57,58} Likewise, other studies of CO₂ and PDL report excellent cosmetic result, but are not specific as to how these conclusions were reached.⁵⁹⁻⁶¹ One publication on CO₂ for AK did not note cosmetic results.⁶⁰

COMMENT

While a number of treatment modalities have become available for the treatment of AKs, there remains a decided paucity of data regarding cosmetic outcomes both in short-term and particularly in long-term follow-up. With newer treatment modalities, particularly PDT, there has been an increase in available cosmetic data as the manufacturers of these products will attempt to provide practitioners evidence that their newer products provide an advantage over existing treatment modalities. Indeed, it is noteworthy that nearly all of the articles on PDT and IMQ were sponsored by the manufacturers of these products.

Of the various treatment modalities discussed, PDT by far has the greatest amount and most convincing evidence of good cosmetic outcome. Most of these trials compared PDT to cryotherapy, which, while the most common treatment modality employed for the treatment of AKs, is probably not a fair comparison from a cosmetic perspective given the risk of hypopigmentation associated with cryotherapy. A larger head-to-head comparison between PDT and a more targeted therapy such as IMQ or 5-FU would be helpful in clinical decision making.

Even in studies where cosmetic outcome was evaluated, how the outcome was determined was often left as a relatively undefined concept. Studies wherein both the patient and investigator judged outcomes were reported are reassuring when the reported evaluations are relatively congruous. The article by Krawtchenko et al⁵ did an exemplary job defining specific cosmetic outcomes, saying cosmesis is “based on the amount of scarring, atrophy, or indurations and in pigment change within the treatment area by comparison to adjacent, untreated skin.”

Also of note, some cosmetic data that is accumulated is likely not reported. The publication by Szeimies et al²⁸ on IMQ reported that “because of inconsistencies in the investigators’ interpretation of hyperpigmentation, hypopigmentation, and mottled skin, these data are not presented.” Ideally, all cosmetic outcomes available would be reported.

One final area of research that would be of interest is if cosmetic outcome could be correlated with the inflammatory response seen as a result of treatment. Rates of erythema and other acute reactions are often reported in clinical trials, but these have not been directly correlated with the long-term cosmetic outcomes.

CONCLUSION

While cosmetic outcomes are increasingly being reported with new treatment modalities, there remains a relative shortage of evidence-based medicine available on this topic. Photodynamic therapy decidedly has the most established base of evidence to support excellent cosmetic outcome, though a small amount of evidence supports that IMQ and 5-FU also have relatively low incidence of scarring and good long-term cosmetic outcome. More head-to-head trials of available modalities would be of the greatest benefit in decision making regarding the most appropriate treatment for patients given varying clinical circumstances.

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