Actinic Keratoses—Surgical and Physical Therapeutic Modalities

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Actinic keratoses (AKs) are the most common epithelial premalignant lesions seen by dermatologists today. The vast therapeutic armamentarium for treating AKs can be roughly divided into 2 categories: topical and surgical/physical modalities. It is important for clinicians to be familiarized with the various therapeutic options for treating AKs and to deliver individualized treatments. This article will review the surgical and physical modalities available for the treatment of AKs.

Actinic keratoses (AKs) are the most common epithelial premalignant lesions seen by dermatologists today. It is estimated that more than 60% of predisposed persons older than 40 years have at least one AK[1] and that 1 in 6 Americans will develop a skin cancer during his or her lifetime.[2] In addition, more than 26% of cutaneous squamous cell carcinomas (SCCs) were reported to begin as an AK, and more than 82% of the cutaneous SCCs were found to have concomitant AK giving rise to, and/or in close proximity to, the SCC.[3] Therefore, it is important to prevent AK, if possible, as well as to be proactive in treating these premalignant lesions when diagnosed.

There are many modalities that are highly effective treatments for AK. Although the options of therapy are numerous, not all treatments are appropriate for all patients or lesions. For these reasons, treatments must be individualized and appropriately selected by the physician. Thus, it is essential for the clinician to be familiar with both the topical, systemic, and surgical treatments available. For the purpose of this article, the surgical and physical modalities available for the treatment of AK will be discussed. These include cryosurgery, curettage with or without electrosurgery, dermabrasion, ablative lasers, chemexfoliation, and photodynamic therapy (PDT).

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Cryosurgery

In 1907, Pusey[4] treated skin lesions with carbon dioxide (CO_2) snow that was collected in a leather bag and compressed into sticks. These cryogenic agents were used until the 1940s, when liquid nitrogen became readily available. Liquid nitrogen (−195.8°C) is the most common cryogen used today.[5] By lowering the skin temperature to −50°C with the application of the cryogen, the atypical cells of the AK are destroyed.[5] Cryosurgery is the most frequently utilized treatment method for AK in the United States. Liquid nitrogen is applied with a cotton-tip applicator or through a spray apparatus. In 1990, the American Society for Dermatologic Surgery reported that more than 87% of its members performed cryosurgery for the treatment of AK.[6]

Cryosurgery represents a well-tolerated, safe, effective, and time-efficient treatment method that yields good cosmetic results. Lubritz and Smolewski[7] reported cure rates of 98.8% in the treatment of 70 patients with 1018 AKs. Complications are rare when experienced practitioners perform cryosurgery. Hypopigmentation, resulting from melanocyte sensitivity, can be a problem. Patients report some discomfort while the cryogen is being applied; therefore, its application is restricted to small areas with limited lesions. Chiarello[8] reported successful removal of many AKs during full-face cryosurgery, or so-called cryopeel. However, there has been a report of scarring after such treatment in a patient with cryofibrinogenemia.[9] A patient's history should be taken to exclude this condition, and, if indicated, laboratory studies should be performed before treating a large area of the face with cryosurgery.

Cryosurgery is often the treatment of choice for a limited number of well-delineated AKs. However, when the actinic damage is diffuse or the lesions are obscured by other dermatoses, a multistage cryosurgery treatment plan or alternative methods should be considered.

Curettage With or Without Electrosurgery

The use of a curette to mechanically remove atypical cells is a very useful and effective treatment for AK.[10] The major advantage of curettage is the ability to obtain a specimen for histologic analysis.[1] Electrosurgery may be used to stop bleeding or to apply more damage to the area of the atypical cells of AK. Currently, no study is available comparing the cure rates of AK with curettage alone verses with electrosurgery. Therefore, the physician must determine whether electrosurgery should be applied to burn the skin after the curettage procedure. The combination of cryosurgery and curettage make up about 80% of the treatments for AK in the United States.[11] A disadvantage to the curettage method is the need to apply a local anesthetic prior to the procedure. In addition, overly vigorous curettage and/or electrosurgery can result in a scar. Curettage is effective for almost all clinical types of AK but is particularly useful for lesions thought to be closer to invasive SCC or for lesions resistant to other treatments.[12]

Dermabrasion

In 1905, Kromayer[13] introduced a technique to treat a variety of skin diseases using rotational instruments. This procedure is now known as dermabrasion. Dermabrasion is an excellent treatment for severe widespread actinic damage and has well-documented long-term protective effects.[14] Coleman et al[15] evaluated recurrence rates after treatment, with the average dermabrasion results persisting 4 years before a single AK reoccurred in the treatment area. Benedetto et al[14] demonstrated microscopic normalization of actinically damaged epidermis and dermis with normal posttreatment epidermal thickness, rete pattern, and polarity, as well as the absence of dyskeratosis.

Although dermabrasion has been shown for many years to be an effective treatment for AK, it is not a widely used modality. The technique requires more training than do the alternative therapeutic approaches, and it carries the risk of blood splatter for the physician and assistants. In addition, prophylaxis against bacterial and viral infections is usually undertaken with the use of systemic antimicrobials. On the other hand, dermabrasion is usually well tolerated by most patients, and recovery times are similar to other treatments for AK.[16] For extensively thickened AK, especially on the scalp, dermabrasion has achieved dramatic improvement.[15,17] Although dermabrasion is a more complicated procedure, it is one of the few modalities that affords long-term prophylaxis, as well as treatment of AK.

Microdermabrasion, utilizing aluminum oxide crystal, was initially developed in Italy in 1985 and has recently become popular for facial rejuvenation.[18] A recent study investigated the use of microdermabrasion for actinic damage.[19] These patients were noted to have both mild clinical and histologic improvement. Microdermabrasion is a simple, rapid procedure that is painless and noninvasive. This procedure may have a place in the treatment of mild and/or localized actinic damage, although additional studies are required for its role in the treatment of AK.

Carbon Dioxide/Erbium Laser

The advent of lasers (light amplification by stimulated emission of radiation) in 1960 revolutionized the treatment of many dermatologic conditions. Precise skin depth control and targeting of specific chromophores conferred treatment advantages not achieved previously with other modalities.

Treatment of AK with lasers, similar to other modalities, has been primarily ablative/destructive. Most reports have been with CO_2 and Erbium: Yttrium-Aluminum-Garnet (Er:YAG) lasers.

The Er:YAG laser emits infrared light with a wavelength of 2940 nm, which is strongly absorbed by water. The high absorption coefficient, as compared with the CO_2 laser, allows for a depth of 0.01 to 0.05 mm for thermal damage.[20]

Drnovsek-Olup et al[20] reported 6 patients with AK treated with the Er:YAG laser at 300 mJ with a 4-mm spot size and 2.4 J/cm^2 with 2 to 4 passes. They achieved 100% clearance rate with a follow-up of 12 to 15 months. Mean reepithelization time was 7 to 10 days. There were no reports of scarring or infection.[20]

Wollina et al[21] reported 29 patients with AK who were treated with the Er:YAG laser. Of these patients, 89.7% (26) achieved complete response and 10.3% (3) achieved partial response. Healing time was reported to be 7 to 10 days. Patients received local anesthesia for the procedures.[21] Er:YAG laser is a valuable tool in the treatment of a few localized, as well as multiple, AKs.

The CO_2 laser emits infrared light at 10,600 nm with a skin penetration depth of 0.2 mm. Success in the treatment of AK using the CO_2 laser has been variable. Fulton et al[22] reported 35 patients with extreme sun damaged skin who underwent

laser resurfacing. Of these patients, 14.3% (5) developed AK or basal cell cancers following resurfacing. The authors concluded that short-pulse CO_2 laser resurfacing was inferior to dermabrasion, chemabrasion (a single procedure in which a deep, full-face chemical peel is followed immediately by dermabrasion), or deep chemical peel for prophylaxis of AK.[22] Side-effects such as pigmentary alteration, pain, and longer healing time also make the CO_2 laser an inferior choice to the Er:YAG laser in the treatment of AK. In addition, studies have shown a 95% to 99% success rate in the treatment of actinic cheilitis with the CO_2 laser by destruction of the entire epidermis.[23,24]

Chemexfoliation (Chemical Peels)

There are a variety of chemicals that have been used for the treatment of actinic damage. Superficial peels, such as 10% to 35% trichloroacetic acid (TCA), have been used for widespread AK, with inconsistent efficacy. Conversely, deeper peels with TCA or phenol are efficacious but are characterized by an increased frequency of scarring and hypopigmentation.[25,26] Phenol, though utilized in the past, has very limited use today because of its numerous toxicities. Therefore, intermediate-depth peels were developed to improve the results of superficial peels while reducing the risk of morbidity associated with deeper peels.

Intermediate-depth peels can be achieved in many different methods. A CO_2 freeze followed by application of 35% TCA was introduced by Brody and Hailey[27] in 1986. The combined use of Jessner's solution (resorcinol, lactic acid, and salicylic acid dissolved in ethanol) and 35% TCA was described by Monheit[28] in 1989. In a study comparing the combination of Jessner's solution with 35% TCA verses 5% fluorouracil, the efficacies and safety profiles were similar.[29] Other preoperative and postoperative combinations that have been reported include 70% glycolic acid followed by 30% TCA and 35% TCA with tretinoin.[30]

Chemexfoliation produces a stinging sensation at the onset of application that may progressively intensify, though most patients tolerate the procedure well. Hyperpigmentation and hypopigmentation are the most common side effects.[31] Again, prophylaxis against bacterial and viral infections may be undertaken with the use of systemic antimicrobials. Physicians should seriously consider this bloodless procedure in lieu of dermabrasion in patients with communicable infections. The intermediate-depth peels have the advantage of single-application convenience and usefulness, particularly among poorly compliant patients.

Photodynamic Therapy

In 1978, Dougherty et al[32] presented extensive data on the successful use of PDT for the treatment of cutaneous cancer, thereby expanding clinical application of this novel technique. In the basic sense, PDT is a treatment modality involving the administration of photosensitizing compounds and the accumulation of the sensitizer molecules in the target cells, followed by selective irradiation of the lesion with visible light. In recent years, PDT has undergone remarkable expansion of its dermatologic applications and is emerging as a promising treatment modality for AK.[11]

The advances of PDT in the treatment of AK were pioneered by the development that permitted the topical application of 5-aminolevulinic acid (ALA). ALA, not technically a photosensitizer, acts as a prodrug that is then converted endogenously to the efficient photosensitizer protoporphyrin IX within the cells.[33] Initially, photosensitizer protoporphyrin IX is taken up by most normal and malignant cells but is retained longer in tumors and rapidly proliferating cells,[34] though the mechanism of this selective prolonged retention is not well understood. Three to 6 hours after ALA application, the lesions are exposed to visible light at 630 to 635 nm,[35] thereby resulting in selective destruction of the atypical squamous cells in AK. PDT is similar to other treatment modalities with a 2-week healing phase.[36] Recently, a new topical photosensitizer, methyl aminolevulinate,[37] was developed and may offer advantages over ALA of improved skin penetration as a result of enhanced lipophilicity and greater selectivity for neoplastic cells.

PDT has the advantage of being more selective in directing the maximal injury to AK and relatively sparing the surrounding tissue. It is well tolerated and has high patient and physician satisfaction, as well as excellent cosmetic results. The long-term efficacy appears favorable, with sustained eradication of AK observed in several patients 4 years post-treatment.[38] PDT is a promising area of research with a bright future.

Conclusion

Surgical treatment of AK should be tailored to the individual patient. Particular attention should be paid to the number of lesions to be treated, potential side effects, pain control, and healing time. Cure rates for most surgical procedures make them optimal first line treatment options for certain patients.

REFERENCES

1. Drake LA, Ceilley RI, Cornelison RL, et al. Guidelines of care for actinic keratoses. *J Am Acad Dermatol.* 1995;32:95-98.

2. Gloster HM, Brodland DG. The epidemiology of skin cancer. *Dermatol Surg*. 1996;22:217-226.
3. Mittelbronn MA, Mullins DL, Ramos-Caro FA, et al. Frequency of preexisting actinic keratosis in cutaneous squamous cell carcinoma. *Int J Dermatol*. 1998;37:677-681.
4. Pusey W. The use of carbon dioxide in the treatment of nevi and other lesions of the skin. *JAMA*. 1907;49:1354-1356.
5. Kuflik EG. Cryosurgery updated. *J Am Acad Dermatol*. 1994;31:925-934.
6. Hanke CW, Bailin PL. Current trends in the practice of dermatologic surgery. *J Dermatol Surg Oncol*. 1990;16:130-131.
7. Lubritz RR, Smolewski SA. Cryosurgery cure rate of actinic keratoses. *J Am Acad Dermatol*. 1982;7:631-632.
8. Chiarello SE. Cryopeeling. *J Dermatol Surg Oncol*. 1992;18:329-332.
9. Stewart RS, Graham G. A complication of cryosurgery in a patient with cryofibrinogenemia. *J Dermatol Surg Oncol*. 1978;4:743-745.
10. Schwartz RA. Therapeutic perspectives in actinic and other keratoses. *Int J Dermatol*. 1996;35:533-538.
11. Feldman SR, Fliescher AB, Willford PM, et al. Destructive procedures are the standard of care for treatment of actinic keratoses. *J Am Acad Dermatol*. 1999;40:43-47.
12. Dinehart SM. The treatment of actinic keratoses. *J Am Acad Dermatol*. 2000;42:S25-S28.
13. Kromayer E. Rotation instruments: ein neues technisches verfahren in der dermatologischen Kleinchirurgie. *Dermat Ztschr Berl*. 1905;12:26.
14. Benedetto AV, Griffin TD, Benedetto EA, et al. Dermabrasion: therapy and prophylaxis of the photoaged face. *J Am Acad Dermatol*. 1992;27:439-447.
15. Coleman WP, Yarborough JM, Mandy SH. Dermabrasion for prophylaxis and treatment of actinic keratoses. *Dermatol Surg*. 1996;22:17-21.
16. Yarborough JM. Dermabrasive surgery state of the art. *Clin Dermatol*. 1987;5:75-80.
17. Winton GB, Salache SJ. Dermabrasion of the scalp as a treatment for actinic damage. *J Am Acad Dermatol*. 1986;14:661-668.
18. Tsai RY, Wang CN, Chan HL. Aluminum oxide crystal microdermabrasion: a new technique for treating facial scarring. *Dermatol Surg*. 1995;21:39-42.
19. Tan MH, Spencer JM, Pires LM, et al. The evaluation of aluminum oxide crystal microdermabrasion for photodamage. *Dermatol Surg*. 2001;27:943-949.
20. Drnovsek-Olup B, Vedlin B. Use of Er:YAG laser for benign skin disorders. *Lasers Surg Med*. 1997;21:13-19.
21. Wollina C, Konrad H, Karamfilov T. Treatment of common warts and actinic keratoses by Er:YAG laser. *J Cutan Laser Ther*. 2001;3:63-66.
22. Fulton JE, Rahimi AD, Helton P, et al. Disappointing results following resurfacing of facial skin with CO_2 lasers for prophylaxis of keratoses and cancers. *Dermatol Surg*. 1999;25:729-732.
23. Johnson TM, Sebastien TS, Lowe L, et al. Carbon dioxide laser treatment of actinic cheilitis. *J Am Acad Dermatol*. 1992;27:737-740.
24. Alamillos-Granados FJ, Naval-Gias L, Dean-Ferrer A, et al. Carbon dioxide laser vermillionectomy for actinic cheilitis. *J Oral Maxofac Surg*. 1993;51:118-121.
25. Collins PS. The chemical peel. *Clin Dermatol*. 1987;5:57-74.
26. Collins PS. Trichloroacetic acid peels revisited. *J Dermatol Surg Oncol*. 1989;15:933-940.
27. Brody HJ, Hailey CW. Medium-depth chemical peeling of the skin: a variation of superficial chemosurgery. *J Dermatol Surg Oncol*. 1986;12:1268-1275.
28. Monheit GD. The Jessner's + TCA peel: a medium-depth chemical peel. *J Dermatol Surg Oncol*. 1989;15:940-950.
29. Lawrence N, Cox SE, Cockerell CJ, et al. A comparison of the efficacy and safety of Jessner's solution and 35% trichloroacetic acid vs 5% fluorouracil in the treatment of widespread facial actinic keratoses. *Arch Dermatol*. 1995;131:176-181.
30. Brodland DG, Roenigk RK. Trichloroacetic acid chemexfoliation (chemical peel) for extensive premalignant actinic damage of the face and scalp. *Mayo Clin Proc*. 1988;63:887-896.
31. Lotter AM. Human pigment factors relative to chemical face peeling. *Ann Plast Surg*. 1979;3:231-240.
32. Dougherty TJ, Kaufman JE, Goldfarb A, et al. Photoradiation therapy for the treatment of malignant tumors. *Cancer Res*. 1978;38:2628-2635.
33. Peng Q, Warloe T, Berg K, et al. 5-Aminolevulinic acid-based photodynamic therapy clinical research and future challenges. *Cancer*. 1997;79:2282-2308.
34. Lui H, Anderson RR. Photodynamic therapy in dermatology: recent developments. *Dermatol Clin*. 1993;11:1-13.
35. Kalka K, Merk H, Mukhtar H. Photodynamic therapy in dermatology. *J Am Acad Dermatol*. 2000;42:398-413.
36. Jeffes EW, McCullough JL, Weinstein GD, et al. Photodynamic therapy of actinic keratosis with topical 5-aminolevulinic acid. *Arch Dermatol*. 1997;133:727-732.
37. Kloek J, Beijersbergen Van Henegouwen. Prodrugs of 5-aminolevulinic acid for photodynamic therapy. *Photochem Photobiol*. 1996;64:994-1000.
38. Jowler JF Jr, Zax RH. Aminolevulinic acid hydrochloride with photodynamic therapy: efficacy outcomes and recurrence 4 years after treatment. *Cutis*. 2002;69(suppl 6):2-7.