ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 11| Issue: 1| January 2025|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

ACTINIC KERATOSIS, SCOPING REVIEW

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Article DOI: https://doi.org/10.36713/epra19917
DOI No: 10.36713/epra19917

SUMMARY

Introduction: *actinic keratoses, also called senile keratoses or solar keratoses, are benign intraepithelial neoplasms common in dermatologic consultation. Individuals with actinic keratoses may present with irregular, reddish, scaly papules or plaques on areas of the body exposed to solar radiation. These dysplastic proliferations of keratinocytes have the potential for malignant transformation and may progress to squamous cell carcinoma.*
Objective: *to detail the current information related to actinic keratosis, etiology, epidemiology, pathophysiology, histopathology, clinical presentation, evaluation, diagnosis, treatment and prognosis.*
Methodology*: a total of 32 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 21 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, Google Scholar and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: actinic keratosis, solar keratosis, dysplastic proliferations of keratinocytes, squamous cell carcinoma.*
Results: *actinic keratosis is a common condition associated with chronic sun exposure, especially in older people, with a prevalence up to 60 years of age. Exposure to ultraviolet radiation is the main risk factor, and individuals with fair skin, outdoor work or compromised immune systems. Diagnosis is made through clinical observation, dermoscopy and in some cases biopsy. Treatments include options such as cryotherapy, excision, light-based therapies and topical medications such as 5-fluorouracil, with a personalized approach depending on lesion characteristics and patient response.*
Conclusions: *actinic keratosis is a relevant dermatologic condition that requires constant vigilance due to its potential to progress to malignant forms. Preventive education on photoprotection and self-care, together with adequate and personalized treatment, are essential to control the disease and minimize the risk of serious complications, such as carcinoma.*
KEY WORDS: *Keratosis, Dysplasia, Keratinocytes, Carcinoma, Ultraviolet.*

INTRODUCTION

Actinic keratoses, also called senile keratoses or solar keratoses, are benign intraepithelial neoplasms frequently encountered in dermatologic consultation. Commonly linked to prolonged sun exposure, individuals with actinic keratoses may present with irregular, reddish, scaly papules or plaques on areas of the body exposed to solar radiation. Actinic keratoses are dysplastic proliferations of keratinocytes with the potential for malignant transformation. Early detection and implementation of an appropriate therapeutic plan are essential, as actinic keratoses have the potential to progress to invasive squamous cell carcinoma. Squamous cell carcinoma has shown a steady increase each year, representing a significant public health challenge. The mortality rates associated with dermal squamous cell carcinomas are comparable to those of melanoma, renal carcinoma and oropharyngeal carcinoma. In the following paper we will review the etiology, epidemiology, pathophysiology, histopathology, clinical presentation, evaluation, diagnosis, treatment and prognosis of actinic keratoses(1-3).

METHODOLOGY

A total of 32 articles were analyzed in this review, including review and original articles, as well as cases and clinical trials,

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of which 21 bibliographies were used because the information collected was not important enough to be included in this study. The sources of information were Cochrane, PubMed and Google Scholar; the terms used to search for information in Spanish, Portuguese and English were: actinic keratosis, solar keratosis, dysplastic proliferations of keratinocytes, squamous cell carcinoma.

The choice of bibliography exposes elements related to etiology, epidemiology, pathophysiology, histopathology, clinical presentation, evaluation, diagnosis, treatment and prognosis of actinic keratoses.

DEVELOPMENT

ETIOLOGY

Actinic keratoses arise primarily as a result of the cumulative effects of ultraviolet (UV) radiation on the skin, which occur over a person's lifetime of sun exposure(4).

EPIDEMIOLOGY

Actinic keratosis (AK) is a common cause of consultation in both primary and specialized care, representing the third or fourth most frequent reason in dermatology, to include up to 5-6% of patients seen. These lesions develop mainly on chronically sun-exposed areas of the body, especially in older people who have had sun exposure for many decades. The prevalence ranges from 11% to 60% in Caucasian individuals over 40 years of age. The most commonly affected areas include the face, scalp (especially in bald or sparsely hairy individuals), back of the arms and back of the hands. The risk of developing actinic keratosis is influenced by independent factors such as advanced age, due to accumulated sun exposure over the years and lack of sun protection, and male gender, as the prevalence is higher in men than in women.

People with fair skin (Fitzpatrick skin phototypes I and II) have less melanin, which makes them more vulnerable to sunburn and damage caused by ultraviolet radiation. These people usually have characteristics such as blond or red hair and light eyes, such as blue. In terms of geographic location, countries near the equator have higher rates of actinic keratosis. For example, in Australia, the prevalence is close to 60% due to its proximity to the equator and its high fair-skinned population. In contrast, in places outside the equatorial zone, such as the United States, the prevalence is around 20%. In addition, people with weakened immune systems, such as those receiving chemotherapy treatments, those infected with HIV/AIDS, those taking immunosuppressive drugs (used in combination after organ transplantation) or those with leukemia, are more likely to develop actinic keratosis.

A history of previous actinic keratosis or skin cancer may point to hereditary factors related to increased vulnerability to ultraviolet radiation and prolonged exposure to ultraviolet radiation. Those who have had excessive and continuous exposure to the sun during their lifetime are more prone to develop actinic keratosis. Ultraviolet radiation is the main factor in its development, although other individual factors also influence the predisposition to the formation of these lesions. The most exposed individuals include those who work outdoors (such as construction or agriculture) and those who practice outdoor sports (e.g., tennis, golf, baseball)(1,3,5-8).

PATHOPHYSIOLOGY

The pathophysiology of actinic keratosis is complex. Excessive and cumulative exposure to solar ultraviolet radiation can cause pathological alterations in the keratinocytes of the epidermis by modifying the regulatory pathways that control cell growth and differentiation. These alterations generate inflammation and immunosuppression, which favors the proliferation of dysplastic keratinocytes in the epidermis, which are the precursors of actinic keratosis(9,10).

HISTOPATHOLOGY

The main histopathologic feature of actinic keratosis is the presence of abnormal keratinocytes in sun-affected skin, which is limited to the lower third of the epidermis. In addition, disorganized and atypical keratinocytes are observed, predominantly in the basal layers of the epidermis (basal keratinocytic dysplasia). Pleomorphism is also identified, as well as large, hyperchromatic, dyskeratotic and apoptotic nuclei(1,8,11).

CLINICAL PRESENTATION, EVALUATION AND DIAGNOSIS

Clinically, actinic keratoses manifest as spots, bumps or thick plaques with a reddish background, which appear in sun-exposed areas. In their early stages, they are easier to detect by palpation than by visual observation. They may also present pigmentation and show different levels of infiltration; when multiple, they constitute the so-called field cancerization.
Some components of the affected individual's history are important when evaluating actinic keratosis:

- Initial symptoms: inquire about any symptoms related to the lesions, such as itching, pain, or bleeding after minor trauma. These symptoms may indicate an increased risk of cancer progression.
- Medical history and treatments: A complete review of the patient's health and medication history should be performed. Some medical conditions and medications, such as immunosuppressive treatments, may increase the risk of actinic keratosis.
- Previous treatments or interventions for skin cancer: it should be determined whether the patient has a history of previous therapies or surgeries for skin cancer. This information is crucial in assessing the patient's overall risk profile.
- Assessment of risk factors: A thorough assessment of all risk factors associated with actinic keratosis, as mentioned above, should be performed. This includes discussing the duration and history of sun exposure, previous sunburns, frequent use of sunscreen, sun protection habits, and the patient's occupation.

The physical examination consists of a detailed inspection of the skin over the entire body, with special attention to the number, size, distribution and characteristics of suspicious skin lesions or dermal pathologies. The focus is primarily on sun-exposed areas of the body, such as the head, face, scalp, neck, back of the forearms, and hands.

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Actinic keratosis can manifest itself in various forms, such as erythematous and scaly patches, papules, skin plaques. The surrounding skin may show sun damage, such as wrinkles, irregular pigmentation or telangiectasias. On palpation, actinic keratoses are usually appreciated by their rough texture due to varying degrees of hyperkeratosis(3,12).

Diagnosis of the lesions is based on clinical and dermatoscopic examination, however in some situations histopathological analysis may be required.

Dermoscopy may show characteristic features. Non-pigmented facial actinic keratoses may present with a "strawberry pattern", a pattern that includes a pseudo-network of erythematous vessels, prominent follicular openings and a surrounding white halo.

Occasionally, a biopsy may be necessary to confirm the diagnosis of actinic keratosis. Biopsy is usually reserved for individuals who do not respond to treatment or in situations where it is desired to determine whether an actinic keratosis has progressed to squamous cell carcinoma(3,13).

TREATMENT

The dermatologist provides treatment, long-term follow-up and preventive strategies to reduce symptomatic actinic keratosis and reduce the risk of progression to squamous cell carcinoma. The average risk of malignant transformation in immunocompetent individuals is 8%, however, this value varies between individuals, ranging from 0.025% to 16%.

Treatment alternatives for actinic keratosis can be classified into lesion-directed and field-directed therapies. It is usually said in the treatment of actinic keratosis that "no pain, no gain," meaning that effective treatment may involve some discomfort or side effects. Lesion-directed therapies focus on managing individual actinic keratoses. Standard alternatives are cryotherapy, curettage or surgical excision. These therapies are effective in treating specific visible lesions. In contrast, field-directed therapies have the advantage of treating multiple, widespread and subclinical actinic keratoses within a chronic sun-damaged surface. Treating the entire affected skin field rather than individual lesions. Field-directed therapies may include topical medications (chemotherapy creams or immunomodulators), light-based therapies such as photodynamic therapy (PDT) or laser resurfacing. These treatments effectively intervene visible actinic keratoses and subclinical lesions that may not be visible to the naked eye.

Treatment strategies should be individualized, taking into account multiple variables such as: lesion characteristics and symptoms, patient preferences and expectations, treatment availability, compliance of the affected individual with treatment regimens, tolerance of adverse effects and values. There are specific indications that warrant immediate attention and prompt intervention to prevent possible complications, including numerous lesions, bleeding, pain and rapid growth of lesions. It is important to clarify with patients the expected timeline of adverse effects of treatment, which may include blistering, erosion, crusting, burning, discomfort, pain, pruritus, erythema and edema, as well as the expected course of healing, regeneration and recovery after treatment, and instructions on how to care for the skin in the healing process.

It is crucial to know that no treatment for actinic keratosis is completely risk-free. Some of the most common potential adverse effects are pain, inflammation, healing problems, pigmentation changes and scar formation. Recurrence of actinic keratosis and the need for multiple treatments are common. The healing process can take from days to weeks, depending on the location and number of lesions treated. Possible reasons for treatment failure include noncompliance with the prescribed treatment regimen, misdiagnosis or, in rare cases, the possibility of malignant transformation to squamous cell carcinoma.

Actinic keratoses are a cutaneous manifestation of repeated sun exposure. Those diagnosed with actinic keratoses should undergo gradual skin cancer screening, and they should be educated about photoprotection strategies and skin cancer self-monitoring. Vitamin B3 (niacinamide) has shown promising findings in decreasing the number of actinic keratoses. A daily dose of 500 mg of vitamin B3 taken twice daily can reduce actinic keratoses after a few months of use(14-16).

Treatments Directed to The Lesions

They are directed individually, among them we have some examples, such as those mentioned below.

Cryotherapy: frequently used in the treatment of actinic keratoses. It consists of freezing the skin lesions by topical application of liquid nitrogen through a spray or cotton tip applicator, has excellent response rates. It is ideal in individuals with only a few actinic keratoses or isolated lesions. Healing will depend on the duration of liquid nitrogen application and the number of freeze-thaw cycles.

Curettage or shaving: removal of the lesion with a curette or blade is performed on hyperkeratotic actinic keratoses that may not respond to alternative treatments. It allows the collection of specimens for histopathological evaluation. Electrodesiccation may be applied post-curettage to help with hemostasis.

Surgery: is considered when the diagnosis is unclear or if there is a high suspicion of squamous cell carcinoma. Surgical excision provides tissue for histopathologic diagnosis and will aid in subsequent management(1,17).

Field-Directed Treatments

They treat multiple, generalized and subclinical actinic keratoses.

Dermabrasion: involves the mechanical removal of surface layers of skin on surfaces affected by actinic damage. During dermabrasion, a motorized hand-held device with attached abrasive material removes the surface layers of skin in areas of actinic damage.

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Laser: Ablative resurfacing lasers such as CO2 and erbium-YAG lasers can manage actinic keratosis by ablating the epidermis and superficial dermis.

Chemical peels: used to treat individuals with multiple or generalized facial actinic keratosis. A chemical peel involves the topical application of a caustic agent, such as trichloroacetic acid (TCA), to remove the outer layers of the skin to varying depths. The efficacy of chemical peels for facial actinic keratoses is about 75%.

Photodynamic therapy (PDT): is the topical application of a photosensitizer on a site to be treated, with subsequent exposure to a light source of a specific wavelength, according to the desired depth of penetration into the skin. This light activates the photosensitizer, which generates reactive oxygen species that selectively destroy the atypical keratinocytes. Conventional PDT therapy has some disadvantages such as pain during treatment, prolonged period in the office during treatment sessions. Daylight PDT is reported to have a similar lesion response rate to conventional PDT, but with the advantages of less discomfort and the convenience of out-of-office treatment.

Topical medications: There are multiple approved topical medications. Patient education is important for positive results. 5-Fluorouracil (5-FU) is a topical medication that is applied 1 or 2 times daily for several weeks, inhibits DNA synthesis and disrupts cell division. Imiquimod (IMQ) works to increase the immune response of the affected person at the site of application of the drug, it is indicated on limited areas of the face and scalp for several weeks. Diclofenac sodium (DFS) gel is a topical non-steroidal anti-inflammatory drug applied twice daily for 2 to 3 months. It is better tolerated than 5-FU. Ingenol mebutate (IM) derived from the plant Euphorbia peplus which induces the death of keratinocyte cells within a few hours after application, then triggers an inflammatory response for a few days, it also has immunostimulant effects(15,18,19).

DIFFERENTIAL DIAGNOSIS AND PROGNOSIS

Clinical variants of actinic keratosis include hyperkeratotic actinic keratosis, atrophic actinic keratosis, actinic cheilitis, pigmented actinic keratosis, lichenoid actinic keratosis and cutaneous horn. The diagnosis of actinic keratosis is made primarily through clinical assessment, based on the characteristic appearance and location of the lesions. Other skin lesions in the differential diagnosis include solar lentigo, seborrheic keratosis, verruca vulgaris, verruca plana, discoid lupus erythematosus and squamous cell carcinoma.

Actinic keratosis may exhibit erratic behavior over time. Several actinic keratoses may show spontaneous regression, although the mechanisms underlying this regression are not completely understood. On the other hand, other actinic keratoses may remain stable, showing minimal changes in size or appearance over time. It is important to know that actinic keratoses have the potential to progress and evolve into invasive squamous cell carcinoma (SCC), a type of skin cancer. Most squamous cell carcinomas form from pre-existing actinic keratoses or with areas containing actinic keratoses(20,21).

CONCLUSIONS

Actinic keratosis is a relevant dermatologic condition that requires constant surveillance because of its potential to progress to malignant forms, such as squamous cell carcinoma. Its management includes appropriate early detection, which involves regular follow-up and evaluation of new lesions or changes in existing ones. Preventive education on photoprotection and self-care, together with adequate and personalized treatment, are essential to control the disease, avoid the appearance of new lesions and minimize the risk of serious complications, such as carcinoma, thus contributing to a better quality of life and better prognosis.

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EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 11| Issue: 1| January 2025|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

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The Authors report no conflicts of interest.
The Authors report no funding from any organization or company.