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BASAL CELL CARCINOMA: UPDATES AND PERSPECTIVES ON TREATMENT OPTIONS

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Abstract: INTRODUCTION: Basal cell carcinoma (BCC) is the most common skin cancer, originating in the basal cells of the epidermis. Its incidence has been increasing, with estimates of 2.7 to 4.3 million annual cases in the USA. The main cause is chronic exposure to ultraviolet (UV) radiation, especially UVB, which damages the DNA of the basal cells, causing genetic mutations. Factors such as immunosuppression, exposure to chemical substances and genetic predisposition also increase the risk. BCC can manifest itself in subtypes such as nodular, ulcerative, superficial and scleroderma, with distinct clinical characteristics. Understanding these factors is essential for prevention, early diagnosis and effective treatment. OBJECTIVES: This integrative review evaluates different therapeutic approaches for the treatment of Basal Cell Carcinoma (BCC), such as Mohs Surgery, Surgical Excision, Curettage, Cryotherapy, Topical Treatments, Photodynamic Therapy and Radiotherapy, considering efficacy, precision, aesthetic and functional preservation. The aim is also to highlight the importance of early diagnosis, prevention, self-examination, the use of sunscreen and regular dermatological follow-up, in order to reduce recurrences, complications and improve prognosis. ME-THODOLOGY: The search was carried out on the PUBMED, VHL and MEDLINE databases, covering articles from 2018 to 2023, in English, using keywords such as "Basal Cell Carcinoma" and "Surgical Treatment". Initially, 643 articles were identified, of which 192 were selected for full reading. After evaluation, 45 studies were included in the final analysis, after excluding duplicates, irrelevant articles and those with insufficient methodology. RE-SULTS AND DISCUSSION: Biopsy is essential to confirm the diagnosis of Basal Cell Carcinoma (BCC), distinguishing it from other dermatological conditions. Early diagnosis is crucial, as it allows for more effective treatments, reducing complications and increasing the chances of a cure. Prevention is equally important, and can be achieved through measures such as using sunscreen and carrying out regular self-examinations. Treatment for Basal Cell Carcinoma varies depending on the characteristics of the tumor, and options include. Mohs surgery: A highly precise technique indicated for high-risk tumors or those located in delicate anatomical areas, such as the face. It has a high cure rate and significant aesthetic preservation, being one of the most effective options. Surgical excision: Used for smaller, localized tumours, this is an effective and affordable treatment. However, it can leave more visible scars and is less precise than Mohs surgery. Curettage and electrodissection: A less invasive technique, indicated for superficial tumors. Although effective, it has a higher risk of recurrence and lower precision compared to other approaches. Cryotherapy: A minimally invasive procedure that uses cold to destroy tumor cells and is recommended for small superficial tumors. Its effectiveness is limited in deeper lesions. Topical treatments (Imiquimod, Fluorouracil): Used on superficial and low-risk lesions, these treatments are applied directly to the skin. Although effective, they can cause skin irritation and have a higher chance of recurrence in some cases. Photodynamic Therapy (PDT): This consists of using light combined with photosensitizing agents to treat superficial lesions. It is a non-invasive and well-tolerated option, but is more suitable for early and less aggressive tumors. Radiotherapy: Indicated in cases where surgery is not feasible, such as in patients with tumors located in areas that are difficult to operate on or in patients with conditions that would contraindicate surgery. Radiotherapy is also useful in treating recurrences and can be an effective alternative for hard-to--reach tumors, with good local control rates. However, it can cause side effects such as skin

changes and, in rare cases, the risk of developing another cancer in treated areas. Each approach should be chosen based on the characteristics of the tumor, location and general condition of the patient, always aiming for the best therapeutic and aesthetic result. CON-CLUSION: Basal cell carcinoma (BCC) is the most common skin cancer, with slow growth and low metastatic capacity, but it can cause local damage if left untreated. Early identification is essential to avoid complications. Therapeutic options, such as Mohs surgery, surgical excision, curettage, cryotherapy, topical treatments, PDT and radiotherapy, should be chosen based on the type, size and location of the tumor, as well as the patient's condition. Mohs surgery is highly precise, especially in sensitive areas. Prevention, such as the use of sunscreen, is also key to reducing the incidence and improving treatment results.

Keywords: Basal Cell Carcinoma, Epidemiology, Surgical Treatment, Skin Cancer Prevention, UV Exposure

INTRODUCTION

Basal cell carcinoma (BCC) is the most common type of skin cancer and originates in the basal cells of the epidermis, the deepest layer of the skin. This cancer results from a complex interaction between genetic and environmental factors, which drive the development of the tumor and favor the disordered proliferation of cells [1,2]. Basal cell carcinoma (BCC) is the most common type of cancer in the world, with an incidence that has been increasing consistently over the last few decades. In the United States, it is estimated that between 2.7 and 4.3 million new cases of BCC are diagnosed each year [1,2,3]. A person's lifetime risk of developing BCC is significant, with rates of over 20% in the general population and over 30% among white individuals. The pathophysiology of BCC involves specific mechanisms, such as mutations in cellular DNA and chronic exposure to ultraviolet (UV) radiation, with sunlight being the main trigger [1,2,3]. In addition, factors such as immunosuppression, exposure to chemical substances and genetic predisposition also contribute to the risk of developing this type of cancer. A detailed understanding of these aspects is crucial for prevention strategies, early diagnosis and appropriate treatments [3,4].

The main mechanism leading to the development of BCC is the occurrence of genetic mutations in the basal cells of the skin [3,4]. These mutations directly affect genes involved in cell cycle control, particularly those that regulate cell growth and division [3,4]. As a result, the affected cells lose the ability to control their proliferation, forming the tumor. This genetic alteration is often triggered by ultraviolet radiation, which is able to penetrate the superficial layers of the skin and cause damage to the DNA of the basal cells. This gradual process of mutations accumulates over a lifetime, with UVB radiation being the main mutagen involved [4].

UV radiation, especially UVB rays, is one of the most relevant risk factors for BCC, due to its ability to promote cellular alterations [4]. Prolonged and frequent exposure to the sun leads to cumulative DNA damage, especially in exposed regions of the skin [4,5]. People with greater genetic susceptibility, such as those with fair skin, light eyes and red or blond hair, are particularly vulnerable to these effects. Ionizing radiation is also associated with the risk of BCC, especially in individuals undergoing radiotherapy or other types of continuous exposure to radiation that reaches the deeper layers of the skin [5].

Other factors besides UV radiation contribute to the risk of developing BCC, including immunosuppression and exposure to chemical substances. Immunosuppressed patients, such as transplant patients or individuals with HIV, are at greater risk, as the reduction in cell repair capacity favors the growth of abnormal cells [5,6]. Exposure to arsenic and other chemical substances also increases the risk of BCC, since these agents can induce genetic mutations in epithelial cells [5,6]. Furthermore, the presence of a family history of skin cancer indicates a significant genetic component, suggesting that hereditary predispositions also influence the development of this cancer [6].

BCC has different subtypes with specific clinical characteristics, such as nodular, which is the most common, ulcerative, superficial and scleroderma. The nodular subtype manifests as a pearly nodule, usually with dilated blood vessels, while the ulcerative subtype presents a central ulcer with raised borders [6,7]. Superficial BCC is characterized by a reddish lesion that spreads horizontally, and scleroderma presents as a hardened area that resembles a scar. Identifying these subtypes helps with diagnosis and choosing the most appropriate treatment strategy, since each one has a different clinical and biological behavior [6,7].

Understanding the pathophysiology of BCC, including risk factors and subtypes, allows for a more precise approach to the prevention and management of the disease [6,7]. Studies on the interaction between environmental factors and genetic predispositions have contributed significantly to the advancement of therapeutic strategies and the identification of new forms of intervention [6,7]. This knowledge also promotes awareness campaigns and preventive measures, which are fundamental to reducing the incidence of BCC and improving treatment outcomes [8].

OBJECTIVES

The aim of this integrative review is to evaluate the different therapeutic approaches for the treatment of Basal Cell Carcinoma (BCC), considering factors such as efficacy, precision in the removal of tumor cells, aesthetic and functional preservation, as well as the implications for the patient. Methods such as Mohs surgery, surgical excision, curettage and electrodissection, cryotherapy and topical treatments, photodynamic therapy (PDT) and radiotherapy will be analyzed, taking into account their advantages and limitations. The review aims to provide a broader understanding of the options available, highlighting the importance of personalizing treatment according to the characteristics of the tumour, its location, size and the patient's clinical conditions [9].

Another aim of this review is to highlight the importance of early diagnosis and prevention of Basal Cell Carcinoma, especially in relation to sun exposure and self-examination. Early identification of lesions, combined with appropriate treatment, can reduce recurrence rates, avoid complications such as deformities and scarring and improve patient prognosis. In addition, the review seeks to emphasize the importance of preventive strategies, such as the use of sunscreen and regular dermatological follow-up, as well as promoting awareness of the need for a proper differential diagnosis, differentiating BCC from other dermatological conditions with similar presentations [9].

METHODOLOGY

The survey of studies was carried out in the PUBMED, VHL and MEDLINE databases, covering articles published between 2018 and 2023, in English. The keywords used included: "Basal Cell Carcinoma", "Epidemiology", "Surgical Treatment", "Skin Cancer Prevention", and "UV Exposure". The article selection process was structured in three stages. In the first stage, 643 articles were identified by combining the descriptors, applying filters for date, language and type of publication [10]. In the second stage, an initial screening was carried out based on the titles and abstracts, excluding duplicate studies, narrative reviews, experimental animal studies, dissertations, theses and articles that did not directly address the surgical treatment of BCC. As a result, 192 studies were selected for full reading. In the third stage, the remaining articles were fully evaluated and 45 studies were included in the final analysis, after excluding publications with incomplete data, redundant information or insufficient methodology for the objectives of the review [10].

RESULTS AND DISCUSSION

Basal cell carcinoma (BCC) is the most common type of skin cancer, originating in the cells of the basal layer of the epidermis, the most superficial layer of the skin. Although it is slow-growing and rarely metastatic, BCC is locally invasive and can cause significant damage to surrounding tissues and deformities if left untreated [11]. Its main cause is prolonged exposure to the sun's ultraviolet rays, but factors such as age, genetic predisposition and family history also play an important role [11]. BCC lesions are variable, but common features include pearly papules, non-healing ulcerations, crusts and telangiectasias, often located on sun-exposed areas such as the face, neck and ears. Early identification and treatment are essential to

prevent complications such as deformities and loss of function, ensuring that the tumor is removed completely and effectively [11,12].

Basal cell carcinoma (BCC) is a slowgrowing skin cancer that often goes unnoticed for long periods due to the absence of symptoms [13]. In the early stages, the lesion can be small, with gradual growth, and is often mistaken for benign macules and papules or other skin changes [13]. In addition, the lack of symptoms such as pain or itching makes early recognition difficult. Given this insidious nature, a detailed clinical assessment and biopsy are essential to confirm the diagnosis and differentiate BCC from other conditions [13,14]. By analyzing the lesion at the histopathological level, the biopsy identifies specific characteristics of the cancer cells, allowing for an accurate diagnosis [13,14].

Early diagnosis of BCC is essential, as it facilitates simpler and more effective treatments, reducing the risk of complications, such as deformities and scarring, and increasing the chances of a cure with low recurrence rates [15,16]. Factors such as lack of self-examination, confusion with benign lesions and difficulties in accessing health services can delay diagnosis, reinforcing the importance of prevention [17]. Measures such as using sunscreen, protective clothing, avoiding excessive sun exposure and regular dermatological consultations are fundamental [17,18]. Skin self--examination also plays a crucial role, helping in the early identification of alterations and contributing to a better prognosis [19].

The treatment of BCC depends on several factors, including the size, location, type and aggressiveness of the lesion, and ranges from less invasive interventions to specialized surgical techniques [19,20]. One of the most effective techniques is Mohs surgery, which allows precise removal of the tumor with a minimal margin of healthy tissue. Mohs Surgery is widely recognized as a precise

and effective approach to treating Basal Cell Carcinoma (BCC) [21].

Unlike conventional surgery, this technique is carried out in stages, where the tissue is removed in very thin layers [21,22]. Each layer removed is immediately analyzed under a microscope, allowing the exact identification of cancer cells at the margins of the lesion [23]. This detailed analysis continues until all margins are free of tumor, ensuring complete removal of the cancer with minimal removal of healthy tissue. This precision is especially advantageous in delicate areas such as the face, nose and eyelids, where aesthetic and functional preservation is crucial [24].

The main advantage of Mohs surgery is its high cure rate, which makes it the gold standard for high-risk tumors or in difficultto-treat sites [25]. Furthermore, by removing only the affected tissue, this technique minimizes scarring and the need for extensive reconstructions, resulting in a lower functional and aesthetic impact for the patient [25]. Precise tumor removal significantly reduces the risk of recurrence, promoting a safe and efficient approach. For patients with invasive or recurrent tumours, Mohs surgery offers a highly reliable and specialized alternative [25,26].

Indications for Mohs surgery include high--risk tumors, such as those that are large, invasive or have poorly defined margins [26,27]. In addition, it is indicated for BCCs located in sensitive areas, where the preservation of healthy tissue is essential, such as the face, ears and nose [26,27]. Recurrent tumors, which have grown back after previous treatment, also benefit from this technique, as it ensures greater precision in the complete removal of the cancer [27]. Mohs Surgery thus combines the precision of microscopic analysis with a minimally invasive surgical approach, offering superior results in terms of cure and aesthetic preservation. It is an indispensable tool for the management of complex BCCs, reinforcing the importance of a personalized and targeted approach, especially for tumours in delicate regions or those that are difficult to manage [27,28].

Surgical excision is one of the most widely used options for treating BCC, especially in cases of localized and moderate-sized tumours. The procedure involves the complete removal of the tumor, along with a margin of surrounding healthy tissue, to ensure that all the cancer cells are removed [28]. After removal, the tissue is sent for pathological analysis, where a specialist checks for the presence of tumor cells in the margins, confirming that the excision was effective [28,29]. Finally, the wound is closed with sutures or other surgical techniques, depending on the size and location of the lesion [28,29].

Among the advantages of surgical excision are the simplicity of the procedure and its wide availability, making it an effective option for smaller tumors in less complex areas of the body [30]. Because it is performed in a single stage, with subsequent follow-up limited to pathological analysis, the technique is more accessible and requires less initial recovery time compared to more complex approaches [30]. However, surgical excision has some limitations, such as the need to remove a larger margin of healthy tissue, which can result in larger scars, as well as less precision in removing tumor cells in lesions with poorly defined margins [30,31].

Surgical excision is indicated for small tumors located in areas where the skin has less tension, such as the trunk or limbs [31]. It is also often recommended for patients who are not candidates for Mohs surgery due to comorbidities or personal preferences [31]. Despite being effective, in cases of larger, recurrent tumors or those located in delicate regions such as the face, surgical excision may not offer the same safety in terms of tumor control and aesthetic preservation [32]. When comparing surgical excision with Mohs surgery, some important differences emerge [33]. Mohs surgery is more precise and indicated for tumors in sensitive areas, offering a lower recurrence rate and reduced scarring, but it is a more expensive and time-consuming procedure [33,34]. On the other hand, surgical excision is more affordable and has a faster recovery time, making it an excellent choice for simple tumors. The decision between the two techniques should be based on factors such as the size, location and characteristics of the tumor, as well as the clinical conditions and preferences of the patient [33,34].

Curettage and Electrodissection is a technique widely used in the treatment of Basal Cell Carcinoma, especially for superficial and small tumors [35]. The procedure consists of two stages: first, the doctor uses a curette to scrape the lesion, removing most of the cancer cells [35]. Then, with an electric scalpel, electrodissection is performed, which cauterizes the base of the lesion, destroying residual cells and controlling bleeding. This method is quick, effective in selected cases and can be carried out in a doctor's office, without the need for hospitalization [35,36].

Among the main advantages of curettage and electrodissection are the affordable cost, reduced recovery time and simplicity of the procedure. Because it is less invasive, it is often indicated for patients with comorbidities or who wish to avoid larger scars [36]. However, the technique has limitations, being less precise for tumors with ill-defined margins or located in critical areas, such as the face [36]. In addition, the risk of recurrence is relatively higher compared to surgical excision or Mohs surgery, especially in deeper or more aggressive tumors [36].

When compared to Surgical Excision and Mohs Surgery, Curettage and Electrodissection stands out because it is less invasive and less expensive, but has significant disadvantages in terms of precision and tumor control [37]. Mohs Surgery, for example, offers the highest cure rate and preservation of healthy tissue, making it ideal for high-risk tumors or in delicate areas, while Surgical Excision is more suitable for localized tumors with clear margins [37]. The choice between these techniques should take into account the characteristics of the tumor, its location, the patient's clinical conditions and therapeutic priorities, balancing cost, efficacy and aesthetic preservation [37].

Cryotherapy is an effective and minimally invasive technique for the treatment of Basal Cell Carcinoma, especially for superficial and small lesions [37]. The procedure uses liquid nitrogen, which is applied directly to the tumor. Extreme freezing causes necrosis of the cancer cells, destroying them through the process of repeated freezing and thawing [37,38]. This approach is performed quickly, without the need for anesthesia, and can usually be done in an outpatient setting [37,38].

Among the main advantages of cryotherapy are its practicality, low cost and rapid recovery. Furthermore, the procedure involves minimal bleeding, due to the immediate coagulation caused by the cold, making it an attractive option for patients who cannot undergo invasive surgery [37,38]. However, cryotherapy has important limitations, such as a higher risk of recurrence for more aggressive tumors or those with poorly defined margins. Aesthetic changes, such as hypopigmentation or scarring, are also possible, especially in more sensitive or highly visible areas [37,38].

The technique is mainly indicated for superficial BCCs, less than 1 cm in diameter and located in regions that tolerate changes in skin texture or pigmentation well. It can also be an alternative for patients who have contraindications to more invasive procedures [37,38]. However, its reduced effectiveness in deeper tumors and the lack of histological evaluation of the margins limit its use in complex cases, such as lesions in critical areas or with a high risk of recurrence [37,38].

Compared to surgical excision and Mohs surgery, cryotherapy is less invasive, more accessible and associated with a shorter recovery time. However, the accuracy in removing cancer cells is inferior, as there is no analysis of the tumor margins [37,38]. While Mohs surgery is the most precise, with the lowest risk of recurrence and preservation of healthy tissue, and surgical excision offers a balance between effectiveness and cost, cryotherapy stands out for its comfort and speed in smaller lesions [37,38]. The choice of the ideal method must take into account factors such as the type and location of the tumor, as well as the patient's preferences and clinical conditions [37,38].

Topical treatments, such as Imiquimod and Fluorouracil, are important options for the management of superficial basal cell carcinomas (BCC), especially in patients who wish to avoid surgical procedures [37,38]. Imiquimod acts as an immunomodulator, stimulating the local immune system to recognize and destroy cancer cells, while Fluorouracil directly interferes with the cellular replication of tumour cells. Both substances offer the advantage of being non-invasive treatments, applied directly to the skin, which makes them convenient for patients with lesions in aesthetically delicate locations [37,38].

Although they have benefits, topical treatments have limitations that must be considered. They are mainly effective for superficial and low-risk tumors, but are less effective for deep or more aggressive lesions [39]. In addition, prolonged use can cause skin irritation, with redness, itching and sensitivity to the sun [39]. These local adverse reactions can compromise patient adherence to treatment, which generally requires weeks of daily application. The lack of complete removal of diseased tissue can, in some cases, make histopathological assessment difficult and increase the risk of recurrences.

The choice of topical treatments should be based on a careful assessment, taking into account the patient's profile, the characteristics of the tumor and the clinical context [39]. For lesions located in areas that are difficult to access by surgery or for patients who cannot tolerate invasive procedures, Imiquimod and Fluorouracil offer a viable solution. However, regular follow-up with a dermatologist is essential to monitor the response to treatment and ensure that the tumor has been completely eradicated [39].

Photodynamic Therapy (PDT) is an advanced and minimally invasive approach to treating BCC, especially superficial lesions. The treatment combines the use of a photosensitizing agent, such as methylaminolevulinate (MAL) or 5-aminolevulinate (ALA), with a specific light source, usually blue or red, which activates the compound applied to the skin. This activation generates free radicals and reactive oxygen species, leading to the selective destruction of tumor cells, with minimal aggression to healthy tissues [40]. As well as offering excellent aesthetic results due to the preservation of the skin, PDT is effective in areas that are difficult to access, such as the face and neck, and allows multiple lesions to be treated simultaneously [40,41].

Despite its advantages, PDT has some limitations, such as reduced efficacy in deep lesions due to limited light penetration and the need for strict care with sun exposure after treatment, due to the increased sensitivity of the treated skin [40,41]. The cost of the procedure and the requirement for specialized equipment can also be a challenge in some contexts [40,41]. However, new trends, such as the development of more potent and less toxic photosensitizing agents and the combination with other therapeutic modalities, are expanding the reach and efficacy of PDT, consolidating it as a promising option in the management of BCC [40,41].

Radiotherapy is an effective option for treating Basal Cell Carcinoma (BCC), especially in cases where surgery is not feasible, such as tumors located in areas that are difficult to access or in patients with comorbidities that contraindicate surgery. Its mechanism of action involves the use of high-energy X-rays to damage the DNA of cancer cells, preventing them from multiplying and promoting their death [40,41]. Radiotherapy is indicated for inoperable tumors, recurrences after other treatments or when the surgical margins are compromised, resulting in remaining cancer cells. For these cases, radiotherapy has shown a high cure rate and is an important alternative when surgery is not the best option [41,42].

Among the advantages of radiotherapy is its non-invasive nature, since it does not require incisions, as well as its ability to preserve healthy tissue around the treated area, compared to surgical procedures. Radiotherapy can also be applied to areas where surgery is more complex or risky, offering an effective treatment for localized tumours [42]. However, the therapy is not without its drawbacks, such as common side effects, which include redness, swelling and pain in the treated area, as well as the risk of ulceration in more severe cases. Treatment may also require several sessions, which implies a longer period of treatment and recovery, as well as a greater chance of recurrence, especially when compared to Mohs surgery, which has a lower recurrence rate [42].

Prevention of Basal Cell Carcinoma (BCC) is essential to reduce the risk of developing this condition. The main preventive strategy is sun protection [41,42]. Daily use of sunscreen with SPF 30 or higher, even on cloudy days, is essential to protect the skin from damage caused by ultraviolet (UV) rays, which are the main culprits in the development of BCC [41,42]. It is also important to reapply sunscreen every two hours, especially after swimming or sweating, and to wear clothing that covers the skin, such as long-sleeved shirts and wide-brimmed hats. Sun protection also includes avoiding direct exposure to the sun, especially between 10am and 4pm, when UV radiation is most intense.

In addition to sun protection, skin self-examination and regular visits to the dermatologist are crucial preventative measures. Performing regular skin self-examinations can help identify changes in existing spots or patches, such as changes in size, color or shape, which can be early signs of skin cancer [41,42]. If any changes are detected, it is important to see a dermatologist for evaluation and early diagnosis. Seeing a dermatologist at least once a year is especially recommended for people with a family history of skin cancer or characteristics such as fair skin, which tends to burn easily. Early detection is key to increasing the chances of effective treatment and avoiding complications associated with Basal Cell Carcinoma [41,42].

CONCLUSION

Basal cell carcinoma (BCC) is the most common type of skin cancer and, although it is slow-growing and rarely metastatic, it can cause significant local damage if not treated properly [43]. Early identification is essential for successful treatment and to prevent complications such as deformities or recurrences. The various therapeutic options, such as Mohs Surgery, Surgical Excision, Curettage and Electrodissection, Cryotherapy, Topical Treatments, PDT and Radiotherapy offer varied approaches that should be chosen based on the type, size, location and characteristics of the tumor, as well as the patient's clinical conditions [43]. Mohs surgery stands out for its precision, especially in tumors in sensitive areas, guaranteeing high cure rates and aesthetic preservation [44,45]. Surgical excision, curettage, cryotherapy and topical treatments are more suitable for smaller or superficial cases, with each method having its advantages and limitations. Choosing the right treatment requires a careful assessment by the dermatologist, taking into account the risks, benefits and preferences of the patient [44,45]. Prevention, such as the use of sunscreen and regular dermatological consultations, also plays a crucial role in reducing the incidence of BCC and improving treatment results [44,45].

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