Clinical Dermatology Research Journ

Short Communication A SCITECHNOL JOURNAL

Advances in Photodynamic Therapy for Non-Melanoma Skin Cancers

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Citation: Samantha K (2025) Advances in Photodynamic Therapy for Non-Melanoma Skin Cancers. Clin Dermatol Res J 10:241

Received: 01-Mar-2025, Manuscript No. CDRJ-25-170291, **Editor assigned:** 03-Mar-2025, PreQC No. CDRJ-25-170291(PQ), **Reviewed:** 17-Mar-2025, QC No. CDRJ-25-170291, **Revised:** 21-Mar-2025, Manuscript No. CDRJ-25-170291(R), **Published:** 28-Mar-2025, DOI: 10.4172/2576-1439.1000241

Abstract

Non-melanoma skin cancers (NMSC), primarily basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are among the most prevalent malignancies worldwide. Photodynamic therapy (PDT) has emerged as a minimally invasive alternative to surgery, offering targeted tumor destruction with excellent cosmetic outcomes. This review explores the principles of PDT, recent advancements in photosensitizer formulations, light delivery systems, and combination therapies. The advantages, limitations, and clinical success rates of PDT in NMSC management are discussed, along with future research directions aimed at improving efficacy and patient outcomes. Enhanced treatment specificity and reduced recurrence rates remain key goals in the field.

Keywords: Photodynamic therapy; Non-melanoma skin cancer; Basal cell carcinoma; Squamous cell carcinoma; Photosensitizers; Dermatologic oncology

Introduction

Non-melanoma skin cancers account for a significant proportion of global cancer incidence, with BCC and SCC being the most common types. While surgical excision remains the standard of care, it is not always suitable for patients with comorbidities, large or multiple lesions, or those seeking better cosmetic results. Photodynamic therapy (PDT) has gained prominence as a non-invasive, outpatient-based treatment that offers high precision and reduced scarring compared to surgery.

Principles of photodynamic therapy

PDT involves the application of a photosensitizing agent to the lesion, followed by illumination with a specific wavelength of light. The photosensitizer absorbs the light energy, generating reactive oxygen species (ROS) that selectively destroy tumor cells while sparing surrounding healthy tissue. This selectivity makes PDT particularly attractive in dermatology for treating lesions in cosmetically sensitive areas [1].

Photosensitizers in dermatology

First-generation photosensitizers such as porfimer sodium had limitations due to prolonged photosensitivity. The introduction of second-generation agents, such as methyl aminolevulinate (MAL) and 5-aminolevulinic acid (ALA), has significantly improved tolerability and reduced downtime. Recent research has focused on nanoparticle-based delivery systems to enhance skin penetration and target specificity.

Light sources and delivery systems

Advances in LED technology have revolutionized PDT by providing more efficient and portable light sources. Adjustable wavelengths and intensity control allow better tailoring of treatment to lesion depth and size. Daylight PDT has also gained popularity, especially in Europe, offering a less painful and more patient-friendly approach for superficial NMSC [2].

Clinical applications in BCC

PDT has shown high efficacy in treating superficial BCC, with clearance rates exceeding 80% in some studies. For nodular BCC, pretreatment methods such as curettage or fractional laser can improve photosensitizer penetration and treatment outcomes. The cosmetic results are generally superior to those achieved with surgery, especially in facial lesions.

Clinical applications in SCC

While SCC in situ (Bowen's disease) responds well to PDT, invasive SCC is less sensitive due to deeper dermal invasion. Combination therapy approaches, including PDT followed by topical immunomodulators such as imiquimod, have demonstrated improved efficacy. This strategy enhances tumor destruction and reduces recurrence risk [3].

Combination therapies

Recent trials have explored PDT combined with targeted therapies like epidermal growth factor receptor (EGFR) inhibitors, which can sensitize tumor cells to ROS damage. Additionally, fractional laser-assisted PDT has been effective for thicker lesions by improving drug penetration.

Advantages of PDT

The key advantages of PDT include:

Minimally invasive approach suitable for elderly or frail patients.

Superior cosmetic outcomes with minimal scarring.

Ability to treat multiple lesions simultaneously.

Repeatability without cumulative toxicity. These benefits make PDT an attractive alternative in select patient populations [4].

Limitations and challenges

PDT has limitations, including pain during illumination, incomplete clearance for thick or deeply invasive tumors, and the need for patient compliance regarding post-treatment light avoidance.

Further refinement of protocols and development of more potent yet selective photosensitizers are necessary to address these challenges.

Future directions

Future research in PDT for NMSC is likely to focus on:

Third-generation photosensitizers with tumor-targeting ligands.

AI-guided imaging to monitor treatment progress in real time.

Personalized PDT protocols based on tumor biology and genetic profiling.

These innovations aim to maximize efficacy, minimize recurrence, and broaden PDT's applicability in dermatologic oncology [5].

Conclusion

Photodynamic therapy has established itself as an effective, cosmetically favourable, and minimally invasive option for selected cases of non-melanoma skin cancer. Advances in photosensitizers, light delivery, and combination regimens have expanded its role beyond superficial lesions. Continued innovation and integration with other therapeutic modalities are expected to further enhance its clinical value.

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