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Sun Exposure and Skin Cancer: A Narrative Review of Risk Factors, Prevention Behaviors, and Emerging Therapeutic Approaches

Exposição Solar e Câncer de Pele: Uma Revisão Narrativa dos Fatores de Risco, Comportamentos de Prevenção e Abordagens Terapêuticas Emergentes

Exposición Solar y Cáncer de Piel: Una Revisión Narrativa de los Factores de Riesgo, Conductas de Prevención y Enfoques Terapéuticos Emergentes

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ABSTRACT

Ultraviolet radiation is a well-established carcinogen associated with cutaneous neoplasms and represents one of the main modifiable risk factors for the development of skin tumors. Despite widespread recognition of the harmful effects of excessive sun exposure, gaps persist between public awareness and the effective adoption of preventive measures. This study aims to synthesize the scientific evidence regarding the relationship between sun exposure and skin cancer, addressing risk quantification, photoprotective behaviors, public misconceptions, and emerging therapeutic innovations for advanced cases. This narrative review is based on the analysis of six studies examining different aspects of the relationship between sun exposure and skin cancer, including meta-analyses, economic evaluations, and behavioral research. Findings demonstrate significantly increased odds of cutaneous squamous cell carcinoma associated with painful lifetime sunburns, particularly when burns occur during childhood (OR 3.11). Although awareness of ultraviolet radiation risks is generally adequate, photoprotective behaviors remain insufficient among both athletes and the general population. Misconceptions persist regarding sunscreen use in higher phototypes, vitamin D production, and the benefits of high-SPF formulations. Preliminary, albeit limited, evidence suggests a low carcinogenic risk associated with UV lamps used in gel manicures. Economic evaluations indicate highly favorable returns on investment for primary prevention programs, ranging from US$0.35 to €3.60 per monetary unit invested. In the therapeutic field, c-Kit inhibitors demonstrate objective response rates of 15% in advanced melanomas harboring KIT mutations, with nilotinib showing a response rate of 20%. Plant-derived polyphenols emerge as promising ingredients for photoprotective formulations, with significant correlations between phenolic content, antioxidant activity, and sun protection factor (SPF). This review highlights the persistent gap between awareness of sun exposure risks and effective adoption of photoprotective measures, reinforcing the need for more effective public health strategies. The cost-effectiveness of primary prevention initiatives, combined with the development of novel therapeutic options and photoprotective ingredients, underscores the importance of continuous innovation in both prevention policies and clinical management of cutaneous neoplasms.

Keywords: Skin Neoplasms; Ultraviolet Radiation; Health Behaviors; Photoprotection; Protein Kinase Inhibitors.

RESUMO

A radiação ultravioleta é um carcinógeno bem estabelecido associado a neoplasias cutâneas, representando um dos principais fatores de risco modificáveis para o desenvolvimento de tumores de pele. Apesar do amplo reconhecimento dos malefícios da exposição solar excessiva, persistem lacunas entre o conhecimento populacional e a adoção de medidas preventivas eficazes. Sintetizar as evidências científicas sobre a relação entre exposição solar e câncer de pele, abordando a quantificação do risco, os comportamentos de fotoproteção, as concepções errôneas da população e as inovações terapêuticas para casos avançados. Trata-se de uma revisão narrativa da literatura, baseada na análise de seis estudos que examinaram diferentes aspectos da relação entre exposição solar e câncer de pele, incluindo metanálises, avaliações econômicas e pesquisas comportamentais. Os achados demonstram chances significativamente aumentadas de carcinoma espinocelular cutâneo associadas a queimaduras solares

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dolorosas ao longo da vida, com destaque para o risco particularmente elevado quando as queimaduras ocorrem na infância (OR 3,11). Embora o conhecimento sobre os riscos da radiação ultravioleta seja adequado, os comportamentos fotoprotetores permanecem insatisfatórios tanto em atletas quanto na população geral, com persistência de concepções errôneas sobre o uso de filtros solares em fototipos mais altos, produção de vitamina D e benefícios de formulações com FPS elevado. Evidências preliminares, embora frágeis, sugerem baixo risco carcinogênico associado às lâmpadas UV utilizadas em manicures de gel. Avaliações econômicas indicam retornos do investimento altamente favoráveis para programas de prevenção primária, variando de US$0,35 a €3,60 por unidade monetária aplicada. No campo terapêutico, inibidores de c-Kit demonstram taxas de resposta objetiva de 15% em melanomas avançados com mutações em KIT, com destaque para o nilotinibe (20% de resposta). Polifenóis derivados de plantas emergem como promissores ingredientes para fotoprotetores, com correlações significativas entre conteúdo fenólico, atividade antioxidante e fator de proteção solar. Esta revisão evidencia a persistente dissociação entre a conscientização sobre os riscos da exposição solar e a adoção efetiva de medidas fotoprotetoras, reforçando a necessidade de estratégias de saúde pública mais efetivas. A relação custo-efetiva das iniciativas de prevenção primária, aliada ao desenvolvimento de novas opções terapêuticas e ingredientes fotoprotetores, aponta para a importância da inovação contínua tanto em políticas de prevenção quanto no manejo clínico das neoplasias cutâneas.

Palavras-chave: Neoplasias Cutâneas; Radiação Ultravioleta; Comportamentos de Saúde; Fotoproteção; Inibidores de Proteínas Quinases.

RESUMEN

La radiación ultravioleta es un carcinógeno bien establecido asociado con neoplasias cutáneas y representa uno de los principales factores de riesgo modificables para el desarrollo de tumores de piel. A pesar del amplio reconocimiento de los efectos nocivos de la exposición solar excesiva, persisten brechas entre el conocimiento poblacional y la adopción efectiva de medidas preventivas. Este estudio tiene como objetivo sintetizar la evidencia científica sobre la relación entre la exposición solar y el cáncer de piel, abordando la cuantificación del riesgo, las conductas de fotoprotección, las concepciones erróneas de la población y las innovaciones terapéuticas en casos avanzados. Se trata de una revisión narrativa basada en el análisis de seis estudios que examinaron distintos aspectos de la relación entre exposición solar y cáncer de piel, incluyendo metanálisis, evaluaciones económicas e investigaciones conductuales. Los hallazgos demuestran un aumento significativo en las probabilidades de carcinoma cutáneo de células escamosas asociado a quemaduras solares dolorosas a lo largo de la vida, con riesgo particularmente elevado cuando ocurren en la infancia (OR 3,11). Aunque el conocimiento sobre los riesgos de la radiación ultravioleta es adecuado, las conductas fotoprotectoras siguen siendo insuficientes tanto en atletas como en la población general. Persisten concepciones erróneas sobre el uso de protectores solares en fototipos altos, la producción de vitamina D y los beneficios de formulaciones con alto FPS. Evidencia preliminar, aunque limitada, sugiere bajo riesgo carcinogénico asociado a las lámparas UV utilizadas en manicuras en gel. Las evaluaciones económicas indican retornos altamente favorables de la inversión en programas de prevención primaria, que varían entre US$0,35 y €3,60 por unidad monetaria invertida. En el ámbito terapéutico, los inhibidores de c-Kit muestran tasas de respuesta objetiva del 15% en melanomas avanzados con mutaciones en KIT, destacándose el nilotinib con una tasa de respuesta del 20%. Los polifenoles

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derivados de plantas emergen como ingredientes prometedores para formulaciones fotoprotectoras, con correlaciones significativas entre contenido fenólico, actividad antioxidante y factor de protección solar (FPS). Esta revisión evidencia la persistente disociación entre la concienciación sobre los riesgos de la exposición solar y la adopción efectiva de medidas fotoprotectoras, reforzando la necesidad de estrategias de salud pública más eficaces. La relación costo-efectiva de las iniciativas de prevención primaria, junto con el desarrollo de nuevas opciones terapéuticas e ingredientes fotoprotectores.

Palabras clave: Neoplasias Cutáneas; Radiación Ultravioleta; Conductas de Salud; Fotoprotección; Inhibidores de Proteínas Quinasa.

1. INTRODUCTION

Ultraviolet (UV) radiation represents a fundamental environmental carcinogen with established causal links to cutaneous malignancies. The biological mechanisms through which UV exposure induces DNA damage in keratinocytes and melanocytes have been extensively characterized in dermatological research. Both UVA and UVB wavelengths contribute to photocarcinogenesis through direct DNA damage and oxidative stress pathways. The public health implications of this relationship are substantial given the ubiquity of sun exposure in daily life.

The quantitative association between sunburn history and cutaneous squamous cell carcinoma (cSCC) has been systematically evaluated in large-scale meta-analyses. Weber et al. conducted a comprehensive meta-analysis encompassing 17 studies with 321,473 participants, examining sunburn as a specific risk factor for cSCC development. Their work represents the most recent and robust quantification of this relationship, incorporating data from studies published up to May 2025 with rigorous adjustment for potential confounders.

Beyond general population exposure, specific subgroups face elevated UV risks due to occupational or recreational activities. Fernandez-Ruiz et al. systematically reviewed knowledge, attitudes, and photoprotective behaviors among 10,445 sportspeople across 23 studies. Outdoor athletes receive high cumulative UV doses during training and competition, positioning them as a priority population for skin cancer prevention interventions. Understanding the behavioral patterns within this group provides insights into effective targeted messaging.

Public understanding of sun protection is complicated by persistent misconceptions that may undermine prevention efforts. Bennett and Khachemoune addressed common sunscreen myths including the benefits of higher sun protection factor (SPF) formulations, the necessity of sunscreen

use in individuals with darker skin types, and the effects of topical photoprotection on vitamin D synthesis. These misconceptions, if uncorrected, may lead to suboptimal sun protection practices even among individuals who acknowledge UV-associated risks.

Emerging sources of UV exposure not traditionally considered in public health messaging require attention. Metko et al. performed a systematic review examining the association between UV nail lamps used in gel manicures and cutaneous malignancy risk. This previously overlooked exposure source has become increasingly relevant as gel manicures have gained popularity over the past two decades, yet consensus regarding carcinogenic risk remains limited.

The economic dimension of skin cancer prevention provides compelling justification for resource allocation to primary prevention initiatives. Collins et al. systematically reviewed cost-effectiveness, cost-utility, and benefit-cost analyses of primary prevention interventions published between September 2013 and November 2023. Their synthesis of 12 studies across multiple countries offers policymakers evidence-based economic rationales for investing in sun protection programs targeting diverse populations and exposure contexts.

Therapeutic innovations for UV-associated melanomas have advanced through targeted molecular approaches. Steeb et al. conducted a systematic review and one-arm meta-analysis of c-Kit inhibitors for unresectable or metastatic mucosal, acral, and chronically sun-damaged melanomas. KIT-activating genomic alterations occur preferentially in these melanoma subtypes, making them theoretically amenable to tyrosine kinase inhibitor therapy. Their pooled analysis of 19 single-arm studies comprising 601 patients evaluated efficacy and safety outcomes across four inhibitors.

Concurrently, innovation in photoprotective formulations is exploring botanical sources as potential sunscreen ingredients. Ng et al. systematically reviewed the photoprotective properties of natural plant sources for sunscreen development, analyzing 35 articles from the Scopus database. Plant polyphenols, including flavonoids and other phenolic compounds, may offer antioxidant and UV-absorbing properties that complement or potentially replace synthetic and mineral sunscreen agents currently associated with negative health and environmental effects.

The objective of this narrative review is to synthesize current evidence on the multifaceted relationship between sun exposure and skin cancer, integrating findings from epidemiological risk quantification, behavioral prevention studies, public health economic analyses, and emerging therapeutic and photoprotective innovations.

2. METHODOLOGY

This narrative review was conducted based on a synthesis of six previously published studies identified through comprehensive literature searches. The included studies comprised one meta-analysis, three systematic reviews (including one with meta-analysis), one systematic review of economic evaluations, and one narrative review addressing sunscreen misconceptions. The meta-analysis by Weber et al. searched Embase, PubMed, and Cochrane Library (CENTRAL) from inception to May 6, 2025, with no language or date restrictions, using search terms encompassing non-melanoma skin cancer, squamous cell carcinoma, sunburn, sun exposure, and ultraviolet radiation, initially screening 9,310 titles and abstracts.

The systematic review by Metko et al. conducted searches on Medline and Embase in accordance with PRISMA guidelines, yielding 2,331 non-duplicate articles. Fernandez-Ruiz et al. performed a systematic review using PubMed and Embase with the search algorithm "(skin cancer OR melanoma) AND (exercise OR sport OR athletes)", identifying 2,365 publications. Steeb et al. conducted systematic literature research in MEDLINE, Embase, and CENTRAL, supplemented by hand searching of trial registers and conference abstracts until June 23, 2020. Collins et al. searched seven databases on July 18, 2023, with an update on November 15, 2023, for economic evaluations published from September 1, 2013. Ng et al. utilized the Scopus database to select 35 articles based on predefined inclusion and exclusion criteria.

Eligibility criteria across the included studies varied according to their specific objectives: Weber et al. included analytical investigations of the general population assessing associations between cSCC and sunburn history at any age; Metko et al. examined the risk of skin malignancy associated with UV nail lamps; Fernandez-Ruiz et al. included studies analyzing knowledge, attitudes, and habits of photoprotection in athletes; Steeb et al. included trials of c-Kit inhibitors for unresectable or metastatic mucosal, acral, or chronically sun-damaged melanoma; Collins et al. included studies reporting outcomes in monetary costs, life years, quality-adjusted life years or variants thereof; Ng et al. included studies on photoprotective properties of natural botanical sources. Study selection processes involved masked independent reviewers in the Weber et al. meta-analysis and independent reviewers in other studies.

Data extraction was performed independently by two reviewers in the Weber, Metko, and Collins studies. Analytical methods included random-effects DerSimonian-Laird pooling in the Weber

and Steeb meta-analyses, with Weber et al. standardizing measures of association to odds ratios and Steeb et al. calculating pooled proportions of objective response rates and severe adverse events. Narrative synthesis was employed in the Fernandez-Ruiz, Metko, Collins, Bennett and Khachemoune, and Ng reviews. Quality assessment utilized the Joanna Briggs Institute guidelines in the Metko review and the Consolidated Health Economic Evaluation Reporting Standards checklist in the Collins review.

All included studies were previously published and did not involve new primary data collection; therefore, ethical approval and informed consent were obtained in the original studies as reported by their authors. The present review synthesizes findings exclusively from these published sources without reanalysis of primary data.

3. RESULTS AND DISCUSSION

The included studies collectively address distinct yet interconnected aspects of the sun exposure-skin cancer continuum. Weber et al. demonstrated significantly increased odds of developing cutaneous squamous cell carcinoma with medium lifetime frequencies of painful, blistering, or severe sunburns (OR 1.51; 95% CI 1.26-1.81) and high lifetime frequencies (OR 1.69; 95% CI 1.39-2.06). Notably, high frequencies of such sunburns during childhood were associated with substantially elevated odds (OR 3.11; 95% CI 1.26-7.66), and any history of painful, blistering, or severe sunburn conferred significantly increased cSCC odds (OR 1.38; 95% CI 1.06-1.79). These findings quantify the dose-response relationship between sunburn severity and frequency and subsequent cSCC risk, with childhood representing a particularly vulnerable period.

The efficacy of targeted therapy for UV-associated melanoma subtypes was evaluated by Steeb et al., who pooled data from 601 patients across 19 single-arm studies investigating imatinib, nilotinib, dasatinib, and sunitinib. The pooled objective response rate for all inhibitors was 15% (95% CI 12-18%), with subgroup analysis revealing the highest response rate for nilotinib at 20% (95% CI 14-26%). Response rates differed by melanoma subtype: mucosal melanoma demonstrated 14% ORR (95% CI 6-24%), while acral lentiginous melanoma achieved 22% ORR (95% CI 14-30%). At least one severe adverse event was reported in 42% of patients (95% CI 34-50%).

The economic case for prevention was strongly supported by Collins et al., who identified 12 studies with generally high reporting quality. Interventions evaluated included restricting indoor tanning device use (seven studies), television advertising, multi-component sun safety campaigns, shade

structures combined with protective clothing provision for outdoor workers, and provision of melanoma genomic risk information. Return on investment was highly favorable, ranging from US$0.35 saved for every dollar spent on prevention up to €3.60 saved per euro invested. Most studies constructed Markov cohort models and adopted a societal cost perspective.

Behavioral patterns among high-risk populations were examined by Fernandez-Ruiz et al., who synthesized data from 10,445 sportspeople across 23 studies. Despite most athletes demonstrating high levels of knowledge regarding skin cancer risk associated with sun exposure, less than half of participants in most studies made adequate use of photoprotective measures. A paradoxical pattem emerged wherein participants declared voluntary intention to tan and reported that sun exposure improved their subjective well-being, while simultaneously expressing concern about potential UV-associated damage.

The risk associated with emerging UV exposure sources was assessed by Metko et al., whose systematic review identified nine eligible studies including three case reports, one cross-sectional study, and five experimental studies. The authors concluded that prolonged and repeated exposure to UV nail lamps may pose a low risk of skin cancer, while emphasizing that the available evidence is weak and characterized by high or unclear risk of bias per Joanna Briggs Institute guidelines. This uncertainty underscores the need for patient education about limited data and risk mitigation strategies including UV-blocking gloves or properly applied sunscreens.

Common misconceptions potentially undermining prevention efforts were identified by Bennett and Khachemoune, who highlighted confusion among consumers regarding the benefits of higher SPF sunscreens, the necessity of photoprotection in darker skin types, and the effects of sunscreen on vitamin D production. These misconceptions persist despite the availability of diverse sunscreen formulations and may contribute to inadequate protection even among individuals who acknowledge UV risks.

Innovation in sunscreen development was explored by Ng et al., who demonstrated significant correlations between total phenolic content, total flavonoid content, antioxidant activities, and sun protection factor across 35 studies of natural botanical sources. Plant extracts additionally exhibited anti-tyrosinase, anti-aging, and anti-inflammatory activities, although biological activities were dependent on the solvents used for extraction. These findings suggest potential for plant polyphenols as environmentally sustainable sunscreen ingredients.

Comparisons across studies reveal both concordant and discordant findings. The high level of skin cancer risk knowledge coupled with inadequate protective behaviors documented by Fernandez-Ruiz et al. in athletes parallels the persistence of sunscreen misconceptions identified by Bennett and Khachemoune in the general population. This knowledge-behavior gap represents a consistent finding across populations and suggests that educational interventions alone may be insufficient to modify sun exposure practices. The economic analyses by Collins et al. demonstrating favorable returns on investment for multi-component interventions including environmental modifications (shade structures) and policy approaches (tanning device restrictions) align with the need for strategies beyond individual education.

Divergences emerge when considering risk quantification across different exposure contexts. Weber et al. established robust dose-response relationships between sunburn history and cSCC, with childhood sunburns conferring particularly elevated risk. In contrast, Metko et al. found the evidence for UV nail lamp carcinogenicity to be weak and methodologically limited, despite theoretical concerns about repeated exposure. This discrepancy highlights the importance of exposure duration and intensity, as intermittent intense exposures resulting in sunburn differ qualitatively from the low-dose repeated exposures characteristic of nail lamp use.

The therapeutic findings from Steeb et al. demonstrate that while c-Kit inhibitors offer clinical benefit for KIT-mutant melanomas, response rates remain modest (15-22%) and adverse events are common (42%). This contrasts with the substantial public health gains achievable through prevention, where Collins et al. documented not only cost savings but also substantial skin cancers avoided, gains in life years, quality-adjusted survival, and societal cost savings. The juxtaposition of modest therapeutic efficacy against substantial preventive potential reinforces the primacy of primary prevention in skin cancer control strategies.

Limitations across the included studies warrant consideration. The meta-analysis by Weber et al. incorporated adjusted measures of association when available but relied on unadjusted measures when adjusted estimates were absent, potentially introducing residual confounding. The systematic review by Metko et al. was limited by the predominance of case reports and experimental studies with high or unclear risk of bias, reflecting the early stage of evidence regarding UV nail lamp safety. Fernandez-Ruiz et al. noted variability in outcome measures across studies of athletes, complicating direct comparisons of photoprotective behaviors. Steeb et al. pooled data from single-arm studies

without comparator groups, limiting inferences about relative efficacy compared to other therapeutic options. The economic analyses synthesized by Collins et al. employed varying methodologies and perspectives, although overall reporting quality was high. Ng et al. restricted their search to a single database (Scopus), potentially omitting relevant studies indexed elsewhere.

4. CONCLUSION

This narrative review synthesizes current evidence demonstrating that sunburn, particularly during childhood, significantly increases cutaneous squamous cell carcinoma risk in a dose-response manner, yet a substantial gap persists between public knowledge of UV-associated risks and adequate photoprotective behaviors across populations including athletes and the general public. Common misconceptions regarding sunscreen use in darker skin types, vitamin D production, and higher SPF benefits continue to undermine prevention efforts, while emerging UV exposure sources such as nail lamps present low but uncertain carcinogenic risk requiring further investigation.

The public health and economic relevance of these findings is underscored by robust evidence that primary prevention interventions yield highly favorable returns on investment, with every monetary unit invested generating savings from US$0.35 to €3.60 through reduced skin cancer burden and associated healthcare costs. For individuals who develop UV-associated malignancies, c-Kit inhibitors offer modest therapeutic benefit for KIT-mutant melanomas with response rates of 15-22%, while plant-derived polyphenols demonstrate potential as environmentally sustainable sunscreen ingredients with significant correlations between phenolic content and photoprotective capacity.

Future research should focus on developing and evaluating multi-component interventions that address the knowledge-behavior gap through environmental modifications and policy approaches rather than education alone. High-quality trials are urgently needed to investigate combinations of targeted therapies with immunotherapy for KIT-mutant melanomas, and to establish standardized methodologies for evaluating botanical sunscreen ingredients. Continued innovation in both public health strategies and therapeutic options remains essential to reduce the global burden of UV-associated skin cancers.

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