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Systematic Review

Effectiveness of topical sunscreen use to prevent skin cancers: systematic review

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ABSTRACT

Topical sunscreen is a potential modality to prevent skin cancer development in vulnerable people although few study has evaluated its effectiveness in clinical setting. This study is aimed to review most recently available evidence on the clinical effectiveness of topical sunscreen in preventing skin cancers. We identified literature from online databases including Pubmed and Google Scholar and included population-based study evaluating the effect of sunscreen usage and risk of skin cancers, including melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) either as primary objective or as a confounder in multivariate analysis. Data form included articles was harvested and analyzed with thematic analysis. Final analysis included 11 articles. Of these, 6 reported results on melanoma, 4 reported on BCC, and 3 on SCC. Overall, there was conflicting evidence on the effectiveness of topical sunscreen in preventing skin cancer. Available evidence found that topical sunscreen was most effective in preventing melanoma and SCC. However, there was considerable heterogenicity in study design and definition of sunscreen treatment between included articles that may affect the results. There are no consensus among included articles, including among RCTs, on the ideal topical sunscreen regiment to prevent skin cancer. There are conflicting evidence on the clinical effectiveness of topical sunscreen to prevent skin cancer although evidence suggest that it would be effective in preventing melanoma and SCC. More clinical studies should be conducted with special emphasis on ensuring subject apply the sunscreen correctly and consistently.

Keywords: Sunscreen, Skin cancer, Melanoma, Squamous cell carcinoma, Basal cell carcinoma

INTRODUCTION

Skin cancers are one of the most prevalent cancer in the world. Global data in 2018 showed there was a combined 1.3 million new cases of skin cancer in the world. This figure includes 280 thousand new of melanoma and over 1 million cases of non-melanoma skin cancers, which included squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Skin cancers also contributed significantly to cancer-related mortality, with melanoma contributing 60 thousand mortality and non-melanoma skin cancers contributing 65 million mortality in 2018.[1]

Ultraviolet (UV) light exposure from sunlight has been known as one of the primary risk factor for melanoma, especially on fair skinned people. UV light has been described as "complete carcinogen" as it has been found causing both mutation and molecular damage, inducing neoplastic and malignant change to the cells. As sunlight intensity varies across the globe, incidence and risk of skin cancer related to sunlight exposure also varies. Meanwhile, melanin pigmentation in the skin give some protection. As such, regions with intense sunlight populated by fair-skinned people have higher risk of skin cancer.[2]

Application of topical sunscreen has been proposed as one way to prevent skin cancers, especially to those especially vulnerable. Some substances have been identified to be safe in topical preparation while effective to block or filter UV light. Most commercial sunscreen contain inorganic and cheaply available UV filters as their active substances, such as zinc oxide and titanium oxide.[3] Further studies have identified organic substances that would be effective as active substances in sunscreen while being more environmentally safe.[4]

A recent study showed that sunscreen application has been proven effective in vitro and in vivo preventing DNA damage from UV exposure.[5] However, few studies has been conducted to prove the clinical potential of topical sunscreen application to prevent skin cancers. Thus, we conducted this review to study the effectiveness of topical sunscreen application in preventing skin cancer in clinical setting.

METHODS

Literature identification

Literature searches was conducted on online databases, including Pubmed, ScienceDirect, and Google Scholar. Keywords utilized in literature search was developed based on population, intervention, comparison, and outcome (PICO) criteria detailed in Table 1. Identified literature was then exported and sorted to remove duplicates. The results were then filtered based on inclusion and exclusion criteria.

The final keywords utilized included:

"topical sunscreen" AND "skin cancer" AND "prevention", "topical sunscreen" AND "melanoma" AND "prevention", "topical sunscreen" AND "squamous cell carcinoma" AND "prevention", "topical sunscreen" AND "basal cell carcinoma" AND "prevention".

Table 1: PICO criteria for literature identification.

Population	General population
Intervention	Topical sunscreen preparation
Comparison	Irregular sunscreen use OR no sunscreen use
Outcome	Skin cancers, including: melanoma, squamous cell carcinoma, basal cell carcinoma

We filtered search results based on eligibility criteria for analysis inclusion which was based on methodology employed, year of publication, and variables studied. Methodology criteria for inclusion was clinical trial or observational studies with outcome of interest being diagnosis of skin cancers, including melanoma, squamous cell carcinoma, and basal cell carcinoma. Due to limited literature with clinical skin cancer diagnosis as the outcome identified in preliminary search, we use extended timeframe for inclusion criteria which extended from 2000 to 2020. We excluded review articles from analysis. However, reference from these articles was mined for further literatures that might have been missed in initial literature search. We also excluded case reports, case series, as well as in vitro and in vivo studies that does not involve human subjects.

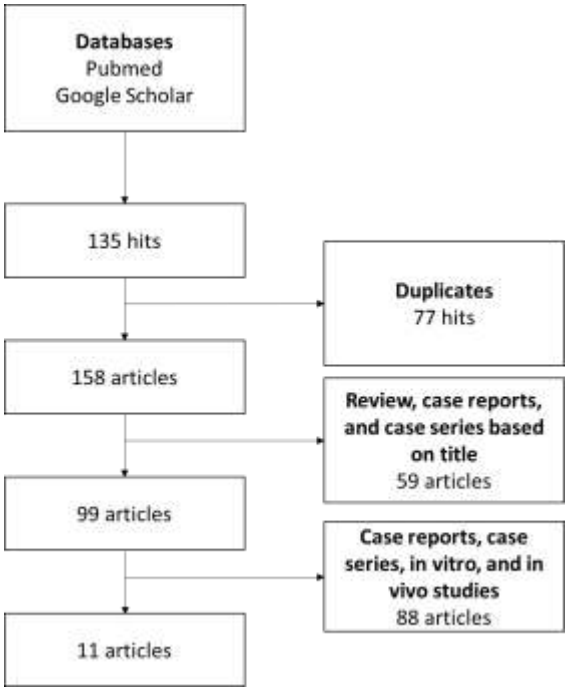

Figure 1: Literature identification process through searching and filtering.

Quality appraisal

Articles that passed filtering underwent quality appraisal before data extraction and analysis. Quality appraisal was conducted based on CASP (Critical Appraisal Skills Programme) Checklist for the appropriate study design employed in each particular articles. Quality appraisal was aimed to review validity of methodologies as well as importance of the reported results before further extraction and analysis.

Data extraction and synthesis

Articles that passed eligibility criteria and quality appraisal was extracted for variables of interest. Main variable of interest in this review are types of topical sunscreen preparation used in each study as well as incidence of skin cancer reported. To characterize each study, we also extracted information on methodologies, sample size, and study location. Afterward, we analyzed the results with thematic analysis to synthesize the common theme of results reported from these studies in order to answer the research question.

RESULTS

Characteristics of included studies

The final analysis included 11 articles which have passed through eligibility filtering and quality appraisal. These articles included 3 RCTs, 3 observational cohorts, and 5 case-control studies. The largest included study was an observational cohort involving over 140 thousand samples.[6] The method of reporting risk also varies between included studies. RCTs and observational cohorts reported risk difference by presenting the adjusted relative risk (aRR) or adjusted hazard ratio (aHR) figure from multivariate analysis. Meanwhile, case-control studies reported risk difference by presenting adjusted odds ratio (aOR).

Most studies involved did not specify the sunscreen preparation specifically used in their study. This is especially true for case-controls and observational cohort studies which only assessed the frequency of sunscreen use with a Likert scale. Some studies specified the sunscreen use to have SPF value of over 15.[6–10]

Table 2: Characteristics of included studies.

Sr. No.	Author	Year of publication	Title	Design	Sample Size
1	**Sanchez and Nova[15]**	2013	Risk factors for squamous cell carcinoma, a study by the national dermatology centre of Colombia	Case-control	Case = 166 Control = 166
2	**van der Pols et al[7]**	2006	Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use	RCT	Treatment for BCC = 1,296 Control for BCC = 1,270 Treatment for SCC = 546 Control for SCC = 811
3	**Dyer et al[8]**	2012	Predictors of basal cell carcinoma in high-risk patients in the VATTC (VA topical tretinoin chemoprevention) Trial	Observational cohort	1,131 people with previous history of keratinocyte carcinoma
4	**Ghiasvand et al[6]**	2016	Sunscreen use and subsequent melanoma risk: a population-based cohort study	Observational cohort	143,844 women aged 40-65 in database
5	**Gon et al[14]**	2011	Risk factors for basal cell carcinoma in a southern Brazilian population: a case–control study	Case-control	Case = 127 Control = 280
6	**Green et al[9]**	2011	Reduced melanoma after regular sunscreen use: randomized trial follow-up	RCT	Intervention = 812 Control = 809
7	**Youl et al[11]**	2002	Melanoma in adolescents: a case-control study of risk factors in Queensland, Australia	Case-control	Cases = 201 Control = 205
8	**Lazovich et al[10]**	2011	Melanoma risk in relation to use of sunscreen or other sun protection methods	Case-control	Cases = 1,158; control = 1,101
9	**Olsen et al**	2015	Sun protection and skin examination practices in a setting of high ambient solar radiation a population-based cohort study	Observational cohort	40,172 population-based cohort
10	**Luiz et al[13]**	2012	Ethnicity and cutaneous melanoma in the city of Sao Paulo, Brazil: a case-control study	Case-control	Case = 202 Control = 222
11	**Ulrich et al[16]**	2009	Prevention of non-melanoma skin cancer in organ transplant patients by regular use of a sunscreen: a 24 months, prospective, case–control study	RCT	Treatment = 191 Control = 191

Table 3: Effect of sunscreen use in melanoma prevention.

Sr. No.	Author	Treatment	Comparison	Outcome
1	**Ghiasvand et al[6]**	Sunscreen SPF ≥ 15	No sunscreen or SPF < 15	aHR: 0.67 (95% CI 0.53 – 0.83)
2	**Green et al[9]**	Daily sunscreen SPF16 use	Discretionary use	aHR: 0.50 (95% CI 0.25 – 1.02)
3	**Youl et al[11]**	Often/always use sunscreen	Rarely/never use sunscreen	aOR: 1.00 (95% CI 0.50 – 1.70)
4	**Lazovich et al[10]**	Frequently use sunscreen with SPF ≥ 15	Does not use sunscreen	aOR: 0.83 (95% CI 0.62 – 1.12)
5	**Olsen et al[12]**	Regular sunscreen use	Irregular sunscreen use	aPR: 0.57 (95% CI 0.51 – 0.67)
6	**Luiz et al[13]**	Often/always use sunscreen	Rarely/never use sunscreen	aOR: 0.33 (95% CI 0.11 – 0.97)

Table 4: Effect of sunscreen application on BCC prevention.

Sr. No.	Author	Treatment	Comparison	Outcome
1	**van der Pols et al[7]**	Broad spectrum SPF 16 applied to head, neck, arms, and hands every morning	Discretionary use	aRR: 1.02 (95% CI 0.78 – 1.35)
2	**Dyer et al[8]**	Sunscreen SPF ≥ 15 use in the week prior to enrollment	No sunscreen use reported	aHR: 1.25 (95% CI 1.01 – 1.54)
3	**Gon et al[14]**	Frequent sunscreen use	Rarely/never use sunscreen	aOR: 0.59 (95% CI 0.29 – 2.22)
4	**Ulrich et al[16]**	Frequent SPF > 60 sunscreen with training how to apply it correctly	Discretionary use	Incidence: In treatment group: 2 new cases out of 191 subjects In control group: 10 new cases out of 191 subjects

Table 5: Effect of sunscreen application on SCC prevention.

Sr. No.	Author	Treatment	Comparison	Outcome
1	**Sanchez and Nova[15]**	Failure to use sunscreen in three life phases: < 15 years old 15 - 30 years old > 30 years old	Use of sunscreen in each life phases	OR for melanoma in each life phases: 2.96 (95% CI 0.15 – 176.9) 0.00 (95% CI 0.00 – 3.25) 1.74 (95% CI 0.22 – 13.60)
2	**van der Pols et al[7]**	Broad spectrum SPF 16 applied to head, neck, arms, and hands every morning	Discretionary use	aRR: 0.65 (95% CI 0.45 – 0.94)
3	**Ulrich et al[16]**	Frequent SPF > 60 sunscreen with training how to apply it correctly	Discretionary use	Incidence: In treatment group: 0 new cases out of 191 subjects In control group: 8 new cases out of 191 subjects

There was also variation based on the types of skin cancers observed. Most included articles studied melanoma as the primary observed outcome.[6,9–13] The second most studied type of skin cancer was BCC which was the observed outcome in two studies while SCC was the observed outcome in one study.[8,14,15] Meanwhile, two further articles reported both BCC and SCC as observed outcomes.[7,16]

Sunscreen application in prevention of melanoma

Six included articles studied the effectiveness of sunscreen to prevent melanoma, either as the main or secondary objective of the study. It included 1 RCT, 2 observational cohorts, and 3 case-control studies. There are also relatively high heterogenicity on sunscreen treatment and controls among included articles on melanoma. Five articles specified the frequency of sunscreen use while 3 articles specified SPF value for the sunscreen for treatment.

There are also heterogenicity of the effectiveness of sunscreen to prevent melanoma. Three included articles reported favorable results where sunscreen reduced melanoma risk.[6,12,13] One study give less clear results, showing daily sunscreen SPF16 usage reduce melanoma risk but with confidence interval bordering not statistically significant.[9] Two more included articles showed no association between sunscreen use and melanoma risk.[10,11]

Sunscreen application in prevention of BCC

Four included studies reported the results of sunscreen use on prevention of BCC. Three of these studies employed observational cohort or RTC design while only one employed case-control design. The results here are more uniform. Three out of four studies reporting BCC as an outcome reported no significant difference of risk between people who use topical sunscreen and control group. These include 1 RCT, 1 observational cohort, and 1 case-control study.[7,8,14] Only one RCT study reporting significant difference in risk between the two groups although this study did not provide any relative risk or hazard ratio figure.[16]

Sunscreen application in prevention of SCC

There were three included articles that reported the effect of sunscreen use on SCC risk. It included 2 RCTs and 1 case-control study. Out of these three articles, two reported that sunscreen use is effective to reduce risk of SCC incidence. Both RCTs reported similar results showing effectiveness of sunscreen use in preventing SCC. One RCT reported reduction of risk with adjusted risk ratio (RR) of 0.65 (95% CI 0.45 – 0.94).7 Meanwhile, the other RCT reported lower incidence in treatment group without reporting relative risk or hazard ratio figure.[16] The only study reporting no significant effect of sunscreen use was the case-control study.[15]

DISCUSSION

Our review found conflicting evidence on the effectiveness of topical sunscreen to prevent skin cancers. Out of the three types of skin cancers reviewed in this study, melanoma, BCC, and SCC, sunscreen seems to be most effective in prevention of melanoma and SCC. Even so, the evidences were not conclusive. Out of 6 articles reporting the effect of sunscreen in melanoma prevention, 3 reported that it was effective. Meanwhile, 2 out of 3 included articles reporting the effect on SCC risk showed that sunscreen was effective.

This finding somewhat opposed the previous findings from in vitro and animal studies. In vitro studies have repeatedly showed the effectiveness of sunscreen in protecting against UV lights, both UVA and UVB. Molecular components of commercially available topical sunscreens, such as titanium dioxide, zinc dioxide, and avobenzone, are effective in blocking or filtering UVA and UVB wavelengths, preventing it from damaging the molecular integrity of the tissue underneath.[17,18] Further animal studies showed similar results. A recent study combining in vitro model of human skin and mouse animal models showed that topical sunscreen application prevent the formation of SCC in animal model.[19]

The difficulties in replicating in vitro and animal model results in human could be attributed to the level of consistency in sunscreen usage required to effectively prevent skin cancer in human. Not only the person should use the right sunscreen product, conferring adequate UV protection, the person should also use the sunscreen appropriately and consistently to feel the full benefit of sunscreen use. Supporting this hypothesis, RCTs that provided training on how to use the sunscreen instead of merely supplying the subjects with sunscreen showed more significant risk reduction for skin cancers.[7,16]

The results of prior in vitro and animal model study, compounded by the results of this review, showed the potential of sunscreen use in reducing risk of skin cancers as long as it is used correctly and consistently. Consequently, health promotion approach should address the correct and consistent use of sunscreen instead of merely focusing on frequency of use. Approaches intended to increase awareness of skin cancer risk in appropriate population may help to increase frequency and consistency of sunscreen usage.[20,21] Meanwhile, active engagement with individuals would be required both to improve knowledge on effective sunscreen application technique as well as to improve adherence to sunscreen use regiment.[22,23]

Despite these findings, this review is not without its limitation. We found high level of heterogenicity of methods between included articles in this review. Other than variation of study design, we also found variation in groups being compared in each study. This heterogenicity may partially explain the conflicting results we found on

the issue of sunscreen effectiveness in preventing skin cancer.

CONCLUSION

We found conflicting evidence on the effectiveness of sunscreen use in preventing skin cancers, including melanoma, BCC, and SCC. However, evidence in this review support that sunscreen is somewhat effective in preventing some skin cancer, especially melanoma and BCC. More population-based study and RCTs are required to further ascertain this effectiveness with special emphasis in behavior modification to achieve correct and consistent sunscreen use for optimal benefit.

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