Review Article

Photoprotection

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Recebido em: 10/09/2009
Aprovado em: 03/11/2009
Declaramos a inexistência de conflitos de interesse.

ABSTRACT

Introduction: Incidence of skin cancer has increased significantly in recent decades, corresponding to a public health problem in many countries. Skin is the organ most affected by the deleterious effects of ultraviolet radiation and the association between sun exposure and skin cancer is well-documented. **Objective:** To conduct a comprehensive review of the main photoprotection measures. **Method:** We conducted searches on MEDLINE from June 22 through August 18. Descriptive studies, review, and comparative studies were analyzed together. **Results:** Eleven articles about a review of photoprotection, effects of ultraviolet radiation on the skin, prevalence of the use of sunscreens, and behavioral measures among adults and adolescents were reported were selected. **Conclusions:** The use of broad-spectrum sunscreens, besides simple behavioral measures, appears to have a major impact on prevention of skin cancer.

Keywords: ultraviolet light, sunlight, ultraviolet filters, squamous cell carcinoma, basal cell carcinoma, melanoma, vitamin D, stability of cosmetics.

INTRODUCTION

In the USA, statistics show that 1 in 5 people in this country will develop skin cancer throughout life. About one million cases of skin cancer are diagnosed every year, and the incidence of melanoma is growing faster than any other type of cancer.[1-3]

In Brazil, according to data obtained from skin cancer prevention campaigns of the Brazilian Society of Dermatology (SBD), it is estimated that 76% of men and 62% of women expose themselves to sunlight without any protection.

Simple behavioral measures contribute significantly to reduce the risk of cutaneous neoplasias.[1-4] Current recommendations for adequate sun protection are based on the following triad: use of appropriate clothing, broad spectrum sunscreens, sun exposure avoidance from 10 AM to 4 PM.[1-2,4]

OBJECTIVE

Perform a systematic literature review on the principal measures of photoprotection, including the recent FDA guidelines and emphasizing primary prevention strategies to reduce risk of skin cancer.

MATERIAL AND METHODS

Search Strategy

The search was conducted in MEDLINE database, using the following keywords: sunscreen, photoprotection, ultraviolet rays, sunlight, ultraviolet filters, squamous cell carcinoma, basal cell carcinoma, melanoma, vitamin D, and cosmetic stability, cross-linked with other words, such as history, methods, classification, agents, efficacy, statistics, and review. Searches were carried out in English from June 22nd to August 18th, 2009.

Studies Selection Criteria

We selected 11 articles, 9 descriptive or review and 2 comparative, randomized, and blind trials.

RESULTS

Studies Main Features

Of the selected studies, 2 comprised a comprehensive review of photoprotection, including the FDA most recent guidelines for the elaboration of labels of sunscreens associated with insect repellents. Most studies (6) demonstrated the deleterious effects of ultraviolet radiation on the skin, and in 3 articles, were evaluated the prevalence of sunscreen use and behavioral measures among young adults and adolescents plus the use of artificial tanning and lights. The relationship between vitamin D synthesis and use of sunscreens has been addressed in 3 articles.

Studies Main Results

1. Physical Aspects

Ultraviolet radiation (UVR)

- Sun UVR is divided according to wavelength:
- UVA 320-400 nm: UVA 1: 340-400 nm (long wave)/ UVA2: 320-340 nm (short wave)
- UVB 290-320 nm
- UVC 270-290 nm

UVC radiation is completely filtered by the ozone layer in stratosphere, not reaching the earth's surface. UVB radiation is composed of short waves, which have a lot of energy and less penetration in the ground. Because the UVA waves are longer, they penetrate more in the earth's surface and are less influenced by atmospheric conditions, reaching deeper into the skin. The proportion of UVR reaching the earth is 20 UVA: 1 UVB.[4] The amount of UVR reaching the earth depends on several factors, including latitude, altitude, season, time of day (between 10 AM and 4 PM the sun's rays are directed more perpendicular), presence of clouds, and the ozone layer. [3-4]

Effects of UVR on skin

When UVR reaches the skin, some is reflected and some is absorbed. UVR absorbed by the skin is responsible for the production of free radicals, reactive and toxic oxygen, with consequent damage to DNA, occurrence of mutations and cancer (actinic keratoses, BCC, SCC, melanoma).[4-6] It also leads to immunosuppression and participate in pathogenesis of photodermatoses, lentigines, and photoaging.[4]

UVB radiation is the main responsible for skin damage, both acute and chronic.[2,4-6] Acute reaction is characterized by redness, swelling, burning, and pigment darkening, followed by later tanning, increased mitoses, both epidermis and dermis thickening, and vitamin D synthesis. Erythema induced by UVB starts after 4 AM, with peak between 8 and mid-night, and subsides after mid-night. UVB tanning is caused by increased melanin and occurs after 72 hours. Photoaging, immunosuppression and photocarcinogenesis occur as delayed reaction.[1,4-5]

UVA radiation can activate endogenous photosensitizing agents (porphyrin, riboflavin and quinones), producing oxygen free radicals (direct action on conjunctive tissue). It is not directly absorbed by biological targets, but drastically alters the cell function. It has stronger photosensitizing action to exogenous and systemic topical agents, and causes more tanning than erythema, requiring 1000 times more UVA than UVB to produce erythema. It also has greater immunosuppressive effect than UVB. [4,6-8] UVA tanning is caused by melanin oxidation and can be divided into: 1) immediate pigment darkening (IPD), which occurs after seconds of exposure to UVA and visible light, disappearing 2 hours after exposure; 2) persistent pigment darkening (PPD), which occurs between 2 and 24 hours after exposure.[4,9]

2. Photoprotective Agents

They are divided into:

- *natural*: occurring in nature, in the environment (ozone, clouds, fog, pollutants), and include the skin itself;
- *physical*: clothes, hats, makeup, sunglasses, glasses;
- *sunscreens*;
- *antioxidants*.

Natural photoprotective agents (atmosphere and environment)

The ozone layer allows passage of UVA and visible light, filters UVC and most UVB rays. Its thickness is not uniform, being thicker toward the poles and thinner in the region near the equator — every degree of latitude increases 3% of UVR reaching the earth. It also varies according to altitude: the higher the greater the penetration of UVR — an increase of each 300 meters increases UVR by 10%. It is estimated that a decrease of 1% in its thickness increases by 1% to 2% the mortality from melanoma.[4,6] Clouds, pollutants, fog: by dispersion, they reduce UVR reaching the earth's surface.[4] Reflective surfaces: radiation reflected by the terrestrial surface does not reach the skin. Most soils reflect about 10% of UVR. Snow, ice, white sand, glass and metal reflect 85% of UVB. Water is not a good photoprotective, since UVR can penetrate up to 60 cm below water surface. Trees with dense canopies and foliage are offer very high protection, including UVA protection.[4]

Natural biological agents

The skin reflects, diffuses, or absorbs UVR and visible light through protein (tryptophan, tyrosine), or chromophores, which are molecules that absorb light energy. The main chromophore is melanin, a large opaque molecule that blocks and diffuses UVR, turning light energy into heat.[4]

3. Physical Agents

Clothing is an excellent photoprotective measure, especially for UVB. The ability of protection is measured in ultraviolet protection factor (UPF). The test is performed in vitro and measures the fabric reflectance to UVR through spectrophotometer. In order to have good sun protection, clothing must have a minimum of SPF 30.[4] The following are some factors that influence UPF: weave (open or closed), thread thickness, moisture, new clothes, and proximity to the skin. There are already washing powder with additives that absorb UVR and increase UPF (Tinosorb). Its mechanism of action is based on the presence of ultraviolet chemical absorbers (stilbene disulfonic acid triazine backbone), which do not change the texture or color of the fabric. Clothes washed 5 times with this type of soap may have UPF increased by 400%.[4]

Large-brim hats (> 7.5 cm) provide a SPF 7 for the nose, 3 for the malar regions, 5 for the neck, and 2 for the chin; medium-brim hats (between 2.5 and 7.5 cm) offer SPF 3 for the nose, 2 for the cheeks, 2 for the neck, and 0 for the chin; small-brim hats (<2.5 cm), offer SPF 1.5 for the nose, and 0 for the other regions.[4]

Modern make-ups have associated sunscreens; those without sunscreen offer a SPF of 3 to 4.[4] Glasses protect the skin of periorbital region. Clear lenses filter only UVB. Dark lenses are needed for UVA protection.[4] Standard glass filters up to 320 nm UVR (UVB), while dark glasses with plastic filter that dim sunlight (Insulfilm) also block UVA and visible light.

4. Sunscreens

Sunscreens are composed by active ingredient and vehicle. According to chemical and physical properties of active ingredients, they attenuate UVR action by mechanisms of absorption (organic), dispersion and reflection (inorganic). The former classification included physical and chemical sunscreens; currently, they are divided into inorganic and organic, depending on the active ingredient.[4,9]

The marketing of sunscreens was regulated by the Brazilian organ of drugs administration (ANVISA) since 2002 as a cosmetic of category 2; that is, must be registered prior to marketing, backed up by studies showing its photoprotective efficacy and water resistance. Manufactured sunscreens do not have this requirement. The ideal sunscreen should has broad-spectrum protection, affordability, be stable and "be user-friendly, and cosmetically acceptable, encouraging frequent use".[9]

Organic filters (classified as UVA and UVB filters)

Mechanism of action: the active ingredients act as chromophores absorbing UVR. When the active ingredient absorbs UVR, it passes from the steady state to the excited state, then back to the steady state, releasing energy as heat. Upon returning to the steady state, it recovers the ability to repeatedly absorb UVR (photostability). The efficiency of chromophore absorption is directly related to its chemical structure. The greater the number of conjugated double bonds the greater the protection.[4,9]

Photounstable filter: undergoes transformation or degradation in its structure and quickly loses the ability to absorb and protect.[6]

Photoreactive filter: is a filter that in the excited state interacts with skin and environment, producing toxic reactions.[4]

Protection against UVB is easier; UVB sunscreens are photostable and effective. The choice is more difficult for UVA filters, which often have questionable efficacy and are more unstable.[4,7,9]

UVB filters

PABA – high UVB protection, stain clothes, induces photoallergy, carcinogen (?), and is virtually out of the market.

Padimate A – phototoxic, is no longer approved by the FDA.

Cinnamate or octylmethoxycinnamate – is one of the most used and requires additional UVB filters to achieve SPF >30.

Homomentylsalicylate or homosalate or homomentyl salicylate.

Benxyledene malonate polysiloxane – approved in Europe and other countries, not yet approved by the FDA, it has low absorption and should be combined with other filters.

Camphor derivatives – approved in Europe and other countries, not yet approved by the FDA, moderately effective for UVB, and absorption peak of 300 nm.

Ethylhexyl triazone or octyltriazone – approved in Europe and other countries, not yet approved by the FDA. One of the best filters for UVB protection with maximum absorption peak of 314 nm.

Diethylhexyl butamido triazone – approved in Europe and other countries, not yet approved by the FDA. Considered the best protection for UVB with peak absorption of 312 nm.

UVA filters

Oxybenzone or benzophenone – protects against UVB and UVA 2. Very unstable, must be combined with other active ingredients as octocrylene (Parsol 340- diphenylcyanoacrylate).

Avobenzone – protects against UVA 1, one of the best in this range. Very unstable, must be combined with another active ingredient (octocrylene).

Ecamsule – protects against UVA 2 and is photostable.

Mexoryl XL – protects against UVB and broad spectrum UVA, photostable, not yet available in the USA.

Methylene bis-benzotriazolyl and Bis-etilexiloxifenol methoxyphenyl triazine – excellent UV absorption; also protects against UVB. Photostable, stabilize avobenzone (Parsol 1789) and cinnamates. Not yet available in the USA.

Disodium phenyl dibenzimidazole tetrasulfonate – UV absorption, peak absorption 334 nm. Not yet available in the USA.

Diethylamino hydroxybenzoyl hexyl benzoate – UVA absorption, absorption peak 354 nm. It is considered the successor of avobenzone. Not yet available in the USA.

Bemotrizinol –UVA and UVB absorption. Photostable, absorption peak of 310 nm and 343 nm.

Bisoctrizole – UVA and UVB absorption. Photostable, absorption peak of 305 nm and 360 nm.

Silatriazole – UVA and UVB absorption. Photostable, absorption peak of 303 nm and 344 nm.

Inorganic filters: TiO2 and ZnO (titanium dioxide and zinc oxide)

Photostable and not sensitizing, offer protection against UVA and UVB.[4] According to the size of particles, they can reflect, scatter, or absorb UVR. Large particles (200-500 nm) are necessary for reflection, which are very effective but cosmetically unacceptable. Smaller, micronized, or ultra-fine particles (10-50 nm) are cosmetically better, however, they start to disperse or absorb UVR, reducing the protection against UVA. Moreover, due to the electrostatic effect, the micronized particles tend to aggregate, reducing the photoprotection efficacy. To decrease the aggregation of micronized particles, dimethicone or silica is added, which keeps the particles scattered, increasing photoprotection.[4,9]

5. Sunscreen Protection factors

Protection against UVB

It is measured in sun protection factor (SPF). SPF 15 means that the time of exposure required to reach the minimal erythema dose (MED) is 15 times higher than without the filter.

SPF is defined as the dose of UVR required to produce MED on protected skin after filter application, or the dose of UVR required to produce MED on unprotected skin. SPF 15 filters 94% of UVB; SPF 30 filters 97% of UVB; and SPF 50 filters 98% of UVB.

Sunscreens UVA protection (PFA)

There is no standard test for measuring UVA protection. The more accepted tests in vivo are immediate pigment darkening (IPD) and persistent pigment darkening (PPD). Both measure protection to UVA 2 with PPD being the most accepted.[4,9] PPD is measured 2 hours after application of UVA at doses between 6 and 25 J/cm2 and measures melanin oxidation after exposure to UVA.

- PPD 2 to 4 provides low protection against UVA.
- PPD 4 to 8 provides moderate protection against UVA.
- PPD ≥ 8 provides high protection against UVA.

In vivo testing measures protection against UVA 1.

- High protection in vivo and low protection in vitro: protection against UVA 2.
- High protection in vitro and low protection in vivo: protection against UVA 1.

The American Academy of Dermatology recommends that sunscreens with broad-spectrum label should have at least SPF 15, UVA with in vitro testing with minimal protection of 370 nm, and in vivo test with PPD ≥ 4.[9]

6. FDA Guidelines Proposed for Sunscreens Labels

UVB protection

It is proposed to change the acronym SPF (Sun Protection Factor) for UPF (ultraviolet protection factor), and a new method of grading UVB protection in 4 categories: 1) low UVB sunburn protection, UPF from 2 to less than 15; 2) moderate protection against UVB sunburn, UPF from 15 to less than 30; 3) high protection against UVB sunburn, UPF from 30 to 50; 4) highest protection against UVB sunburn, UPF above 50. Filters with UPF above 50 shall include only 50 +, due to lack of evidence of reproducibility and accuracy of UPF values above 50. To achieve UPF 50 +, they must have UPF 60.[9]

UVA protection

It is recommended a 0 to 4 star grading of UVA protection based on a combination of in vivo (PPD measuring UVA 2) and in vitro tests (wavelength measuring UVA 1) (Tabela 1).[9]

Water-resistant

Water-resistant sunscreen is the one that maintains its original UPF and UVA **after two** 20-min **immersions**. The highly water-resistant filter maintains protection against UVA and UVB after four 20-min immersions.[4,9]

Sunscreens that do not maintain water resistance should mention: "Reapply at least every 2 hours after swimming, sweating, or towel." Resistant or highly water-resistant sunscreens should mention: "Reapply after towel-dry and after '40 minutes' or '180 minutes' of swimming or sweating," respectively.[9]

Alerts

Exposure to UV radiation from the sun increases the risk of skin cancer, premature aging and other skin damage. To reduce the effects of ultraviolet radiation it is important to limit the time of sun exposure, wear protective clothing and sunscreen.[9]

Usage

Apply liberally and generously on any exposed skin before sun exposure and reapply at least every 2 hours to maintain protection.

7. Factors Affecting Sunscreens efficacy

Quantity is the most important factor and should correspond to 2 mg/cm^2. An adult with a body surface area of 1.73 m^2 needs 35 ml of sunscreen (equivalent to a cup of coffee to cover the entire body).[4] Substantivity is the capacity that sunscreen have to maintain its effectiveness during its use, especially after water exposure. It is very important in the vehicle composition, since it facilitates adherence of sunscreen active principle in the stratum corneum. The most effective substances for sunscreens are liposoluble. Other factors that influence the effectiveness of sunscreens are rubbing, perspiration, water immersion and repeated sun exposure.

8. Cost

The average price of the most popular sunscreens on the market of Belo Horizonte to UPF 50 + is about R$ 58.67 (50 mL), costing R$ 1.17 per mL. The correct application on the whole body (35 mL for adults with a body surface area of 1.73 m2) costs R$41.00. On the beach, a daily exposure of 6 hours (10 AM to 4 PM), reapplying every 2 hours, amounts to 3 applications in this period using 2 bottles of 50 mL at a cost of R$ 117.35. Spend a week at the beach using sunscreen 6 hours per day amounts to R$ 821.45.

9. Sunscreen Use in Children

Sunscreen molecules are very large and have virtually no absorption, but special care should be taken with children under 6 months of age because the effects of absorption in this age group are unknown.[4]

10. Vehicles

Gel and spray are the least effective, with low resistance to water, sweat, and sebaceous secretion. Emulsions are best spread, with good cosmetic results and efficacy.

11. Self-tanning

Its active ingredient, dihydroxyacetone (DHA), provides protection against UVR (UPF 2) through the stratum corneum oxidation capacity, giving the skin an orange-brown color. However, there are no studies to prove the safety of inhaled particles in spray self-tanning.

12. Combination of Insect Repellents with Sunscreen

These products combine the insect repellent DEET (N, N-diethyl-meta-toluamide), citronella oil, and IR 3535 (3-n-butyl-N-acetyl-aminocaproic acid) with sunscreen active ingredients like oxybenzone, octinoxate, octisalate, octocrylene, and padimate O.[4]

This combination is not recommended because sunscreen should be reapplied frequently, every 2 hours, which increases the toxicity of the repellent. Repellent can reduce the efficacy of sunscreens, as they thin and break the protective layer formed by sunscreen, reducing 33% of the UPF.[4] When there is an indication for use of both products, sunscreen should be applied before repellent.

13. Antioxidants: Vitamin E (tocopherol), Beta-carotene, Vitamin C

Antioxidants decrease the oxidative effects caused by exposure to ultraviolet radiation, however, they offer low UPF (5). They are found in vegetables and fruits, and there is no need of vitamin/mineral supplements in people with good eating habits.[4]

14. Other Photoprotective Agents[4]

- Calcitriol: topical.
- Ferulic acid (olive, vegetables, and seeds): topical.
- Polypodium leucotomos: oral and topical.
- Minerals (zinc, iron, cadmium): oral.
- Phenolic compounds and flavonoids (oral): blueberry (mirtilo or arándano), grapes, red wine, tomatoes, citrus fruits, cucumber, broccoli, olives, green tea, isoflavones (soy), caffeine, tamarind, fish oil (omega 3).

15. Artificial Lights

Fluorescent light has photobiological effects; it is not carcinogenic or cause photoaging, while dichroic light can be carcinogenic if it is in a distance less than 50 cm and focus directly on the skin.

Artificial tanning emits 95% UVA and 5% UVB. Some cameras have two to three times more UVA than sunlight and reflectors increase radiation power. Effects of artificial tanning are erythema, pruritus, xerosis, nausea, immediate tanning, phototoxic and photoallergic reactions, and photodermatoses triggering (lupus, porphyria, among others). Tanning does not serve as protection to the skin, since having a tan means that there has been damage to DNA.[4,10]

16. Controversies

Incidence of contact dermatitis due to sunscreens is relatively rare. Sensitization can occur through the sunscreen active ingredient, dyes, preservatives, and fragrances.[4] Several studies show that prolonged use of sunscreens has little or no effect on levels of vitamin D, not inducing hyperparathyroidism and osteoporosis.[4-5,11] Ten minutes of sun exposure twice a

week in an area the size of the face are sufficient for vitamin D synthesis. Individuals with vitamin D deficiency must trust and restore the levels of vitamin D in their diet and not with intense sunlight exposure.

The effect of estrogen is still controversial and not well defined.[4,9] Studies with experimental models demonstrating this effect have used much larger quantities than those used in humans.[9]

DISCUSSION

The incidence of skin cancer has increased significantly in recent decades, corresponding to a public health problem in many countries.[1-3] Skin is the organ most affected by deleterious effects of ultraviolet radiation, and the association between sun exposure and skin cancer is well-documented.[1,4-6] Unfortunately, studies show that most people do not adopt photoprotective measures and believes that a tanned skin is synonym of beauty and health.[1,3,5]

Studies show that UVA radiation is more immunosuppressive than UVB, while UVB is more carcinogenic than UVA. However, it should be noted that both UVA and UVB can cause immunosuppression and carcinogenesis.[4,7-8]

The risk of developing squamous cell carcinoma (SCC) and melanoma is more related to ultraviolet B (UVB) than with ultraviolet A (UVA). SCC has a higher risk with UVB at 290 nm, while melanoma has a higher risk with UVB 290-320 nm.[2-4] Non-melanoma skin cancer is more associated with UV chronic exposure, and melanoma with acute and intermittent exposures. More than five sunburns, regardless of the time, double the risk of developing melanoma.[1,2]

Use of photoprotection since childhood reduces the risk of melanoma, and the number of dysplastic nevi is significantly lower in children who use sunscreen regularly than in those who do not use. It is known that sun exposure early in childhood has more influence on the risk of developing skin cancer than late sun exposure.[2]

Simple changes in lifestyle, such as wearing appropriate clothing and avoiding sun exposure during the period from 10 AM to 4 PM, seem to have a major impact on skin cancer prevention.[1,4] Regarding sunscreens, there was major progress in their research since the first reported use of benzylsalicylate and benzylcinnamate in 1928 and the patent of PABA in 1943.[4,7,9] Recent studies with broad-spectrum sunscreens (UVA/UVB), show a decrease in the incidence of skin cancer, emphasizing the need for development and use of sunscreen with protection against UVA and UVB.[4,7-9]

Among the new FDA guidelines for sunscreen labels, we highlight the replacement of SPF for UPF (UVB protective factor), and a new grading to UVB filters (low, moderate, high and higher protection for UVB sunburn) and UVA (0 to 4 stars).[9]

It is worth noting that the association of sunscreen with insect repellent is not recommended and, according to some authors, the prolonged use of sunscreens has little or no effect on vitamin D levels.[4-5,11]

CONCLUSIONS

Educational campaigns should encourage photoprotection habits since childhood, with recommendations about time of sun exposure (avoiding the period from 10 AM to 4 PM), use of hats, appropriate clothing, sunglasses, and sunscreen, explaining the risk of photoaging, photodermatoses, and skin cancer after artificial or natural sun exposure. Regarding sunscreen, guidance on the proper amount to be used, uniform application, need to reapply every 2 hours, or after excessive sweating or immersion in water. Labels should be more illustrative regarding UPF and PPD, broad-spectrum protection, water resistance, usage, and especially regarding the amount to be used and the importance of reapplication.

This should be the education strategy used by scientific societies and government agencies in campaigns to prevent skin cancer and not simply make joint efforts for healthcare service.

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