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Environmental factors' contribution to skin cancer etiology

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Abstract
Skin cancers are the most frequent types of malignant tumors worldwide, being mostly found in light-skinned populations, with a ratio of 30%. Approximately 3 million non-melanoma skin cancers and 132000 melanoma cases are diagnosed globally each year. The most frequent skin cancers are basal cell carcinoma, squamous cell carcinoma, and malignant melanoma. The incidence, morbidity, and mortality of skin cancers are on the rise and have become a major public health concern. We aim to review the most important environmental factors involved in the development of skin cancers, along with the incidence rates and preventive behaviors or strategies (including personal behavioral changes and public educational initiatives). Ultraviolet radiation (UVR) is a well-known physical hazard, responsible for photoaging, photoallergy, and phototoxic reactions, being heavily involved in carcinogenesis, including melanoma development. Overexposure to natural and artificial UVR is a public health problem. Sunburns, especially in childhood, are an important risk factor for melanoma development. Excessive exposure causes cumulative damage which determines immune suppression and skin cancer initiation. Transplant patients and AIDS patients have an increased incidence of skin cancer. Some treatment methods, including radiotherapy, phototherapy, and psoralen and ultraviolet A (PUVA) therapy can lead to skin cancer development. Viral infections such as those with human papillomavirus can trigger the initiation of squamous cell carcinoma. Patients with familial genetic syndromes are highly sensitive to certain types of skin cancers. Ionizing radiation, environmental pollutants, chemical carcinogenic agents, and work exposure have been associated with skin cancer. Artificial UV radiation exposure (tanning beds and lamps), aging, skin color, personal diet, and smoking are important risk factors. Ultraviolet radiation is the main etiological agent in skin cancer development. A better understanding of the causative factors is an essential step in skin cancer prevention.

Keywords: skin cancer, environmental factors, cancer etiology

1. INTRODUCTION

Skin cancers are the most frequent types of malignant tumors on the entire globe, found especially in light-skinned populations, with a world ratio of approximately 30-40%. Approximately three million non-melanoma skin cancers and 132000 new melanoma cases are diagnosed globally each year. Our country has also registered alarming numbers of skin cancer patients. The incidence, morbidity, and mortality of skin cancers are on the rise and a major public health problem. [1]

2. EXPERIMENTAL

We aim to present the most important environmental factors, incidence rates, and preventive behaviors or strategies involved in skin cancer development, including personal behavioral modifications and public education initiatives.

3. RESULTS AND DISCUSSION

Among the unmodifiable/uncontrollable factors we mention: skin color, genetic inheritance, number of nevi located on the skin. Thus, people with white skin, blond or red hair, and light-colored eyes are known to have a low degree of protection against the damage exerted by ultraviolet rays. Over the short term, solar burns can develop, even in cases with brief exposures, which then disappear rapidly. Over the long run though, these sunburns constitute a risk for skin cancer development at an advanced age. With time, the DNA necessary for solar-induced injuries begins to not function properly and mutations appear, giving rise to malignant/cancerous cell development. [2]

The most frequent modifiable risk factor for skin cancer development is ultraviolet radiation (UV) exposure. UV radiation is a well-known physical danger, responsible on one hand for photo-aging, photo-allergies, and phototoxic reactions, and on the other hand for carcinogenesis, including melanoma. Overexposure to natural and artificial UV rays is a public health problem.

Sunburns, especially during childhood, are a highly important risk factor for melanoma development. Excessive exposure determines cumulative damage which in turn can induce immune suppression and skin cancer developing.

UVA radiation has the longest wavelength – 315 to 400 nm. They are being absorbed by the ozone layer and can penetrate deep into the skin through the epidermal junction where melanocytes locate basally and are responsible first and foremost for premature skin aging. [3]

UVB radiation is shorter – 280 to 315 nm. Both UVA and UVB exposure can give the tan look. UVB makes the bronzed/tanned look appear by increasing melanin production which acts as minimal photo-protection, equivalent with an SPF of approximately 3, and is at the same time a sign for skin deterioration. UVA-induced tan is not considered photo-protective. Most UVB radiation is absorbed by the ozone layer, but climactic conditions can affect the quantity which is absorbed. UVB overexposure develops characteristic sunburn signs which take several hours to appear – erythema, edema, and pain.

UVC rays are the shortest – 100 to 280 nm and are absorbed by the ozone layer and the atmosphere.

Various types of UV exposures have been associated with different types of skin cancers and various anatomic distribution patterns. Cumulative chronic exposure, including open-air professional exposure, has been associated more frequently with skin cancer, more specifically with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). BCC distribution by anatomic site varies with the histologic type; thus, nodular BCC is more frequent on the scalp, while superficial BCC is found more often on the trunk.

As opposed to SCC, melanoma is associated in general with intermittent exposure and a history of sunburns [4].

Similar to BCC, although melanoma can take various pathways of development, a study done by Gallagher, Garland, found that women with multiple nevi on the arms have an increased risk of developing melanoma on the trunk, while those with fewer nevi have developed head and neck melanomas. Although outdoor workers are traditionally considered to have an increased risk for BCC and SCC, but not for melanoma development, a cumulative analysis that combined 15 studies has proven that outdoor workers in intense UV areas had an increased risk for melanoma. [5,6]

If we only talk about UV radiation variability according to time and location, we find that people who live closer to the Equator or at higher altitudes are considered to have the highest risk for melanoma development.

Professional UV exposure can increase the risk of skin cancer among outdoor workers. Research has clearly demonstrated that outdoor workers have an increased risk for BCC and SCC developing. That being said, some studies reported finding no increased risk for melanoma among outdoor workers or finding a lowered risk as compared to indoor workers. [7]

Several studies on workers in intense UV areas have shown that they do not seem to have an increased risk for head and neck melanoma. Research linking melanoma and occupation is frequently limited due to the lack of information linked to other interconnected factors such as – recreational exposure, protection devices used, and socio-economic factors.

Altitude is another factor able to influence the skin, which is even more affected by UV radiation as the altitude rises, UV rays becoming more powerful. NHIS data (National Health Interview Survey) has proven that sunburns are frequent among adults. In 2010, approximately 38% of the adult population (37% women and 39% men) reported suffering sunburns in the last year. Sunburns were more frequent among the non-Hispanic white population (47%) and among adults less than 25 years of age (51%). [8]

Interior tanning exposes users to intense UV radiation in order to tan the skin for cosmetic reasons. Meta-analyses found that interior tanning has the capacity to increase the risk of developing BCC, SCC, and melanoma. UV exposure from tanning devices is usually more intense than natural, outdoor UV, especially concerning UVA levels. For example, tanning devices have been found to expose users to approximately 4 to 13 times the quantity of UVA found during the afternoon sun in Washington DC, some registering even higher quantities. The extent of the link found between interior tanning and melanoma varies between studies, as a reflection of various populations and locations; however, frequent tanning at young ages is constantly associated with a high risk for melanoma development. A recent study from Minnesota found that among women under 30 years of age, diagnosed with melanoma, a ratio of 97% took part in interior tanning, reflecting a 6 times increase in melanoma risk. Thus being said, interior tanning is most frequent among white, non-Hispanic women with ages between 16 and 25 years, with a ratio of over 30% of the demographic group. [9]

Patients with multiple nevi are at a greater risk of melanoma development from preexisting nevi or in normal skin. At the same time, birthmarks or congenital nevi, have an increased risk for malignant transformation during a patient's lifespan. Dermatoscopic and mole mapping investigation of nevi are important tools for early diagnosis in such cases. [10]

Precancerous skin lesions such as actinic keratosis can increase the risk for skin cancer development. These precancerous skin growths have a clinical appearance of rough, scaly patches with color variation from brown to dark pink, being frequently located on the face, head, and hands of light-skinned patients. [11,12]

Age is a risk factor as important as skin phototype. Most skin cancers, such as BCC or SCC, develop more frequently from the 5^{th} decade of life, although melanoma can develop earlier, in adolescents or, rarer in children. Organ transplant patients or those suffering from AIDS have an increased incidence of skin cancer.

Patients undergoing immunosuppressive treatment for various systemic diseases are susceptible to developing skin cancer. Some treatment methods, including radiotherapy or psoralen and ultraviolet A phototherapy (PUVA), can also increase the risk for skin cancer. PUVA interventions are associated with an increased risk for BCC and also SCC, while photosensitizing agents are associated with increased risk for developing all non-melanoma skin cancers (NMSC). Some authors suggested that concerning BCC, important risk factors are UVB and/or ionizing radiation exposure. [13]

Viral infections such as human papillomavirus (HPV) are known factors for skin cancer development, more specifically SCC.

Patients with familial genetic syndromes are sensitive to some types of skin cancers. Ionizing radiation, environmental pollutants, chemical carcinogenic agents, and work environment exposures are risk factors associated with skin cancers. [14]

The family medical history is also highly important in melanoma. First degree relatives of melanoma patients have a greater predisposition than the general population for melanoma development. Things are different for BCC and SCC, in such cases the family history being much less important.

There are some genetic syndromes that are capable of predisposing the patient to multiple skin cancer development. They are, in general, diagnosed before cancer has yet developed, but the reported cases of skin cancers developed in the young population, cancers which are found usually in the elderly (such as BCC), raise the question for such syndromes. [15]

As part of the evidence based treatment strategies for lowering the skin cancer risk, the first objective aims at increasing the opportunities for open-air solar protection, for example by increasing the availability of shading in recreational, professional, and educational environments. The second objective aimed at providing people with exact information on UV exposure, by applying strategies such as elaborating specific messages on UV exposure and skin cancer developing, and/or ensuring an efficient education on solar safety is available in schools and in the workplace. A strategy linked to this objective, which is relevant for nurses and other medical services providers, is making use of the recommended preventive services, especially of the US Preventive Services Task Force (USPSTF). The third strategic objective for appealing to action was linked to promoting policies that support the national skin cancer prevention objective – such as supporting the inclusion of solar protection in school education and in the workplace, consolidating policies that allow the electronic reporting of skin cancer, and supporting policies concerning shading. The fourth strategic objective aimed at decreasing the damage caused by interior tanning, by communicating its ill-effects, ensuring the implementation of the current protective measures and policies, and considering the new ones. The fifth one aimed at consolidating skin cancer research, surveillance, monitoring, and evaluation. [16,17]

What can we do in order to reduce skin cancer incidence? At first, primary prevention strategies must be implemented, in the form of personal, institutional, and government efforts for protecting the healthy population against developing some form of skin cancer! Secondary prevention consists of an early diagnosis of skin cancer by incidental finding during a periodical check-up or a medical examination for another pathology. At the same time, regular examination of people or population groups exposed to a high risk of skin cancer development, or the regular medical examination of patients with suspicious-looking lesions are efficient methods for the early diagnosis of various types of skin cancer. Tertiary prevention consists of a regular and routine examination of the entire skin surface in patients diagnosed with a form of skin cancer. [18]

Early diagnosis of melanoma, in particular, is based on the well-known rule of ABCDE, an acronym with the meaning: A = Asymmetry, B = Border irregularity, C = Color variegation – respectively color changes and the presence of black, blue, red, or white colors, and D = Diameter, because most melanomas are at least 6 mm at diagnosis. E = Evolution – is characterized by changes in the shape, size, and symptoms (pruritus, pain, etc.), bleeding or nodular lesion development, pigmentation changes, or recent development. Not all melanomas have ALL those 5 elements listed and a combination of these parameters must raise the suspicion of melanoma. [19, 20]

4. CONCLUSIONS

The environmental factors involved in skin cancer development are solar UV radiation (especially for BCC and SCC). HPV is a contributing factor towards the development of BCC and SCC; in these types of skin cancers, some other risk factors have been associated, such as iatrogenic immune suppression, HIV infection/AIDS, and non-Hodgkin lymphoma. UV radiation is, in the end, the main etiologic agent in skin cancer development.

Light skin and UV exposure (natural – solar light, and artificial – from tanning salons) increase the risk for skin cancer, being considered the main risk factors involved in its development.

The multitude of associated risk factors increases the risk of skin cancer and acts as prognostic indicators.

A more clear understanding of the causative risk factors is an essential step in skin cancer prevention.

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