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Short Communication

Severe Sunburn as the Overwhelming Risk Factor for 3 Common Skin Cancers: New Prevention Strategy

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Abstract

Re-analysis of published data from two large prospective cohort studies by Wu et al provides hitherto most unequivocal evidence showing Severe Sunburn (SS) as an overwhelming risk factor (> 90%) for all incidences of melanoma, Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC). Low incidence rates such as 0.77% for melanoma, 1.3% for SCC and 16% for BCC in women with 1-5 SSs reveal extremely efficient repair mechanisms of body to counter DNA damages caused by SS. A new SS prerequisite theory is proposed for skin cancer formation. Since use of sunscreen during intense intermittent sun exposure can cause unintended SS, a false security phenomenon, sunscreen is postulated as a major risk factor for causing exponential increases of all 3 skin cancers in recent decades. Because chronic exposure to non-burning sunlight is protective against melanoma and can enhance immunity, this protective effect is expected to occur also with less serious BCC and SCC. Therefore, regular exposure to non-burning sunlight may serve as a new strategy for skin cancer prevention and general health promotion. It is theorized that in addition to immunity enhancement, regular exposure to non-burning sunlight can result in skin tanning that will protect against sunburn and thereby protect against skin cancer. The role of erythema, a mild sunburn, in cancer development appears relatively limited due to our body's extremely efficient repair mechanisms. Since skin aging in ordinary people is predominantly caused by the intrinsic factor, and SS is predominantly caused by intense ultraviolet (UV) B rays, the need of using broad-spectrum sunscreens or organic sunscreen ingredients for protection against UVA may need to be re-considered. Based on an earlier modeling analysis, a sunscreen with an SPF of

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about 8 and 2 to 6 for white and non-white populations, respectively, may be adequate. Also, use of non-absorbable, non-degradable mineral sunscreens should be considered as first choices. Information on UV Index, non-cumulative UV damage and SPF concepts should be widely promoted.

Keywords

Severe Sunburn; Ultraviolet Rays; Skin Cancers; Skin Lesions; Sunscreen; UV Index; Skin Cancer Theory; Incidence Rate of Skin Cancer

Introduction

Exposure to ultraviolet (UV) rays from the sun or tanning devices has been commonly regarded as the major risk factor for skin cancer development [1,2]. Well-designed studies on the relative role of cumulative sun exposure and sunburn caused by acute intense UV radiation (often regarded as a skin cancer biomarker, ref. 2) in contributing to incidences of the 3 most common skin cancers, namely, melanoma, Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC) appear limited to date. Furthermore, there is a different degree of sunburn ranging from mild sunburn showing only skin reddening or inflammation (i. e., erythema) to severe sunburn (SS) with pain, swelling, peeling and/or blistering; conceivably different degrees of sunburn may have different impacts on cancer development [3]. Delineation of the above scenarios may be useful to the design of an effective strategy to prevent skin cancer. This communication reports, for the first time, quantitative data clearly demonstrating that SS is the overwhelming risk factor or even is a prerequisite for all 3 skin cancers in the same large populations in the United States and briefly discusses its potential implications in skin cancer prevention.

Relationship between the Number of Severe Sunburn and Percent Incidence of 3 Skin Cancers

The data are based on quantitative re-analysis of an extensive well-designed prospective study on the history of SS and the risk of skin cancer reported by Wu et al in 2016 (4). In their study, 87,166 female nurses and 32,959 male health professionals were enrolled and most the participants had red/blonde hair. The total number of SS incidences for each subject in 6 years prior to cancer monitoring (28 years for females; 18 years for males) was obtained. Monitoring of skin cancers was limited to skin areas exposed to UV radiation [4]. Relationships between the number of SS incidences and number of cancer cases were obtained directly from their

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Table 2 that were then converted to percent of total case number as summarized in Table 1 and illustrated in Fig. 1.

Mean Incidence Rate of 3 Skin Cancers in Participants with Different Number of Severe Sunburns

This was estimated by dividing the number of skin cancer cases reported in their Table 2 by the number of participants reported in their Table 1 for both sexes with different numbers of SSs [4]. Only results from 1-5 SSs and ≥ 16 SSs are summarized in Table 2.

Female			
# of Severe Sunburns	Melanoma (%)	BCC (%)	SCC (%)
0 (never sunburned)	6.1	8.1	7.8
1-5	32.7	32.8	31.3
6-10	15.5	17.4	15.7
11-15	17.8	19.7	22.1
≥ 16	27.9	22	23.1
Male			
# of Severe Sunburns	Melanoma (%)	BCC (%)	SCC (%)
0 (never sunburned)	2.8	6.9	5.3
1-5	35.5	40.8	40.1
6-10	15.9	15.9	15.3
11-15	13.6	12.2	12.9
≥ 16	32.2	24.2	26.4

Table 1: Relationship between the number of severe sunburns incurred and the number of female cancer cases reported in terms of percent of total cases (N = 774 for invasive melanoma, 16,092 for BCC and 1,366 for SCC) and male cancer cases reported in terms of percent of total cases (N = 391 for invasive melanoma, 5,454 for BCC and 798 for SCC) based on data reported in Table 2 of reference 4 for melanoma, BCC and SCC.

Figure 1: Illustration of remarkable similarity in the number of severe sunburns incurred and the percent of total skin cancer cases reported for melanoma, BCC and SCC in males and females in spite of dramatic differences in the total cases of 3 cancers based on data from Table 1.

Female			
# of Severe Sunburns	Melanoma MIR (%)	BCC MIR (%)	SCC MIR (%)
1-5	0.77	16.1	1.31
≥ 16	1.53	25.1	2.24
Male			
# of Severe Sunburns	Melanoma MIR (%)	BCC MIR (%)	SCC MIR (%)
1-5	1.0	16	2.3
≥ 16	1.97	18.5	3.0

Table 2: Mean Incidence Rate (MIR) in % of participants with 1-5 severe sunburns (SSs) or ≥ 16 SSs for women and men with each of 3 common cancers calculated based on data from Reference 4.

Discussion

Melanoma incidences without SS were remarkably low, only 2.8% and 6.1% for men and women, respectively. BCC and SCC incidences without SS were also low ranging from 5.3% to 8.1%. The above data clearly indicate that SS was a common overwhelming (all > 90%; 97.2% for melanoma in men) risk factor for all 3 skin cancers. In this study, SS was only monitored during the 6-year period of childhood and adolescence and the likeliness of SS occurring during the long (18 and 28 years) cancer monitoring was not followed [4]. It is almost certain that some incidences of SS could have occurred for participants reported as “never sunburned” (12.4% and 8.5% of the total number of participants in female and male studies, respectively) during these very long periods and hence, it is very possible that virtually all the skin cancer cases could have been associated with one or more SSs. In other words, it is logical to postulate that incurring SS is most likely a prerequisite for all skin cancer incidences. Such a hypothesis (i.e., no SS no skin cancer) is unique and different from most other studies reported to date that regard chronic exposure to non-burning sunlight or high long-term UV flux as an important contributing factor to skin cancer incidences [1,2,4]. However, such a hypothesis is consistent with the classical intense intermittent sun exposure theory predicting that melanoma incidences are proportional to the number of intense intermittent sun exposure that would result in SS and melanoma incidences [4,5].

The data on Mean Incidence Rates (MIRs) (Table 2) are quite revealing. For melanoma in women, MIRs for the 1-5 SSs and ≥ 16 SSs are 0.77% and 1.53%, respectively. This means that women having 1-5 SSs and ≥ 16 SSs, on average, would only have 0.77% and 1.53% of chance to get a melanoma, respectively, and a very overwhelming majority, about 98% to 99%, of women would be able to successfully fight against the mutated or damaged DNAs incurred by SS. For melanoma in men (Table 2), the corresponding values are 1.00% and 1.99%, respectively and they also indicate similar extremely-high healing rates. For SCC in women and men, the corresponding values are 1.31% and 2.24% versus 2.3% and 3.0%, respectively, all indicating very high healing rates. For BCC, they are 16.1% and 25.1% versus 16.0% and 18.5%, respectively. These values are about 10 to 20 times higher compared with those for melanoma and SCC, reflecting much higher incidence rates of the BCC cases in the studies [4]. For women with ≥ 16 SSs, about 75% of them would not get BCC. The above data clearly suggest that we need to alter the conventional concept that UV damage is cumulative and not reversible [3].

Comparison of MIR data between 1-5 SSs and ≥ 16 SSs in Table 2 shows that although the difference in mean SS numbers between them is more than 6 times, the MIRs for most of them differ only by about 2 times. For BCC and SCC in men, the differences are only 15% and 30%, respectively. These data may suggest that the body had developed resistance to counter damages caused by more SS. It is to be noted that for BCC in men, the MIRs for 6-10 and 11-

16 SSs are 17% and 16.9%, respectively, thus hardly showing any dose-dependent response as anticipated [4]. Potential clinical significance of the above findings remains to be studied.

When the MIR is calculated from the entire male or female study for the 3 cancers, it is found that both sexes essentially yield the same results, 20.2% for males and 21.4% for females. The slightly higher (6%) for the female study may be related to the fact that the cancer monitoring was carried out 10 years longer in this study compared with the male study (28 vs 18 years). The above discussion may suggest that overall, in the real world in the reported study, the effects of UV radiation on total skin cancer incidences in both sexes were virtually the same [4]. Such view seems consistent with the remarkable similarity of relationship between the number of SSs and percent of cancer cases for all 3 cancers in both sexes (Fig. 1). As shown in Table 1, in spite of their large differences in the number of the total case (e.g., 20.8 fold for women between melanoma and BCC), about 33%, 33%, and 31% of the total melanoma, BCC and SCC cases were associated with 6-10 SS, respectively, and about 28%, 20% and 23% were associated with ≥ 16 SS in women, respectively. The above great similarity patterns among the three totally different cancers appear very intriguing. Their potential significance and reasons for such occurrences remain to be studied especially at the molecular level.

The above data suggest that we may need to focus more on avoiding SS and less on decreasing chronic or cumulative UV exposure in cancer prevention. For example, intense intermittent sun exposure at the beach and ski resort may be discouraged as this has been shown to be positively correlated with melanoma incidences due to SS; obviously, a prudent method is to have direct sun exposure in non-peak hours such as after 3 or 4 p.m. or when sun exposure is non-burning [5]. Use of sunscreen during intermittent exposure can result in unintended sunburns due to factors such as prolonged use and virtually unavoidable SPF-and-site-independent missing applications (even on 1% of the intended area) [3,7]. The resulting unintended or unexpected sunburn may be regarded as a false security phenomenon. Interestingly, it was reported by Petersen, et al., that “A sun holiday is a sunburn holiday” for all 25 people who used sunscreen with an SPF of 30 and developed unintended sunburn after spending one week of sunbathing at a subtropical resort [8]. Therefore, the present work also suggests sunscreen use for intense intermittent sun exposure as a potential major risk factor for all skin cancers that may primarily account for the reported exponential increase of incidences of melanoma and BCC and SCC in the United States and other countries with a temperate climate in the last two or three decades [3,9,10]. It is recommended that the potential unintended risk of sunburn and skin cancer when using sunscreen for intense intermittent sun exposure be urgently conveyed to the general public as an effort to help prevent SS and skin cancer. As of now, it seems that the more people use sunscreen for recreational purpose as being aggressively advertised in news media by drug industry or recommended by clinicians, the more people would get SS and skin cancer. It is noted that use of sunscreen was not found to be a risk factor in skin cancers in the study by Wu, et al., potential reasons for this may remain to be explored [4]. As expected, sunscreen

was also not found to help reduce skin cancer in their study as claimed on the label. This issue has been extensively discussed in my recent article [3]. The present work also suggests that monitoring of long-term UV flux may not be sensitive to the study of risk factors for or etiology of skin cancers.

The present work suggests that erythema may play a much less important role in cancer development than commonly assumed. Although erythema can cause damage to DNA, its visible inflammatory sign on the skin can usually disappear with minimum intervention in days [3]. Also, virtually all damaged DNAs may be completely repaired or eliminated by our body's extremely efficient repair mechanisms in weeks or months [3,6,7]. The above incidence rate analyses seem to confirm such a scenario. However, erythema may serve as an early sign or warning to avoid getting SS by changing the sun exposure behavior.

Chronic exposure to non-burning sunlight (including UVA and UVB rays) that damages DNAs and other tissue components is ironically protective against melanoma and some other non-dermatological cancers, this kind of unexpected protective phenomenon may likely also occur with the less serious BCC and SCC [3,5,7]. In other words, the observed protective phenomenon of non-burning UV radiation against melanoma may suggest that in theory, cumulative or chronic non-burning UV exposure should not be a risk factor for BCC and SCC incidences as commonly implied [1,4]. It is theorized that in addition to immunity enhancement, regular exposure to non-burning sunlight can result in skin tanning that will protect against sunburn and thereby protect against skin cancer. As discussed above, our body is able to successfully repair the DNA damage caused by SS 98 to 99% of the time. Therefore, it seems very reasonable to assume that our body can easily repair relatively mild damages incurred by erythema or non-burning sunlight. In view of the above discussions and reported numerous health benefits from exposure to non-burning sunlight, it is suggested that regular daily exposure to non-burning sunlight should be recommended as a new important strategy to help prevent skin cancer in our public health policy [3,7,11]. In reversing the traditional zero tolerance toward sunlight Australia and New Zealand, two countries with the highest incidence rates of melanoma, have recently encouraged their residents to go out and enjoy sunshine when the UV Index is below 3 [3,7,11].

It is possible that SS, not erythema nor non-burning chronic sun exposure, may predominantly cause precancerous skin lesions such as actinic keratosis and mole. However, one obviously needs to avoid getting erythema as much as possible in our daily lives. It is known that numerous confounding factors can also contribute to development of skin cancers that may account for why someone may need only one SS to get a melanoma, BCC or SCC while others may need up to 16 or more SSs to develop a skin cancer (Table 1) [1,2].

Because SS is known to be predominantly caused by intense UVB radiation and chronic non-burning sun exposure may not have significant adverse effects on skin aging, the need of using

organic sunscreen ingredients in our daily lives for protection against UVA may need to be re-considered, especially in view of their potential percutaneous absorption and long-term adverse effects [3,7,12-15]. It is hoped that the present work may stimulate further debate and study on the need of using broad-spectrum sunscreens in our daily lives. It may be of use to mention here that the importance of intense UVB rays and the relative insignificance of UVA rays in the etiology of melanoma in animal models have been recently reviewed [3]. Also, the dominant or prominent role of UVA rays in causing photoaging in ordinary people and in causing skin cancer seems to have been the main-stream thinking worldwide in the last two or three decades [3,15-17].

Based on an earlier pharmacodynamic modeling analysis, a sunscreen with an SPF of about 8 and 2 to 6 for white and non-white populations, respectively, may be adequate for regular use. A new concept of Skin UV Index has been employed in this modeling analysis [7]. In an effort to avoid getting sunburned, people are strongly recommended to monitor regularly UV index information for their own living areas and places they intend to travel [11]. Also, use of non-absorbable, non-degradable, safety-proven mineral sunscreens should be strongly recommended as first choice [3]. Contrary to the common assumption, to my best knowledge, the efficacy of mineral or inorganic sunscreens has also not been clinically proven to be effective to help reduce sunburn and skin cancer for intense intermittent sun exposure that appears to be the major occasion for using sunscreen especially for males.

Conflict of Interest

There is no conflict of interest to declare.

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