Sunscreen use in organ transplant patients

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Introduction

Non-melanoma skin cancer, specifically basal cell carcinoma and squamous cell carcinoma, is the most frequent type of cancers diagnosed in fair-skinned populations. Their respective incidence is increasing worldwide by 3–5% per year [1].

Ultraviolet radiation is a major environmental cause. Both the total cumulative lifetime exposure to UV radiation and sporadic patterns of sun exposure (i.e. chronic, during work versus intermittent, during leisure time) are determinants for the individual risk of skin cancer. Increased cumulative lifetime sun exposure is associated with an increased risk of squamous cell carcinoma and actinic keratosis, the latter representing possible precursors of invasive squamous cell carcinoma [2].

Epidemiology in organ transplant recipients

Organ transplant recipients have particularly high rates of squamous cell carcinoma with a relative risk ∼100-fold higher than that in the immunocompetent population [3].

In an Irish study of renal transplant recipients, 93.5% of all squamous cell carcinomas occurred on the traditional ‘sunny terraces’ of the body, mainly head, neck, dorsum of the hands and forearms (Figure 1) [4]. Basal cell carcinoma is increased ‘only’ by a factor of 10 in organ transplant recipients. The reason for this is that the preferential sites of basal cell carcinoma are infrequently exposed to UV radiation, which could explain their occurrence on areas like the trunk that are less frequently exposed to the sun [5]. While basal cell carcinomas are believed to develop de novo, the development of cutaneous squamous cell carcinomas is viewed as a multi-step process that is initiated by p53 mutations of single cells leading to p53-mutated clusters and patches in clinically nonsuspicious skin and gradually progressing via different stages of actinic keratoses to invasive squamous cell carcinoma. Whereas, in immunocompetent patients, only ∼10% of individual lesions of actinic keratosis advance to invasive squamous cell carcinoma during a 5- to 10-year time frame, in organ transplant recipients the rate of progression of actinic keratoses is apparently accelerated (months) and the incidence of progression higher (>20–30%) [6]. Unfortunately, standardized data on the progression of actinic keratosis in organ transplant recipients are still missing.

The role of immune suppression

Apart from the direct effect of UV radiation causing DNA damage in keratinocytes, increasing evidence supports the hypothesis that UV radiation has also a negative effect on
the local immunosurveillance of exposed skin and even on systemic immunity [7]. UV radiation inhibits the function of antigen-presenting cells (Langerhans cells) and T-cells with suppressor activities. This inhibition enables previous UV radiation-induced mutant clones to escape from local immunosurveillance and to proliferate [7]. Systemic immunosuppression is mainly supported by the induction and release of IL-10 by keratinocytes caused by UV radiation [7].

Is UV radiation-induced skin damage avoidable?

UV radiation is not only the major risk factor for non-melanoma skin cancer in organ transplant recipients, but it is also presumably the only factor that is ‘avoidable’ in the immunocompromised organ transplant recipients. Two studies from Australia have shown good evidence that sunscreen use reduces the prevalence of actinic keratosis and of recurrent squamous cell carcinoma in immunocompetent populations [8,9]. Sun avoidance and sun protection measures, including sunscreen application techniques, are usually cornerstones of dermatological education programmes designed for organ transplant recipients worldwide [10,11]. Indeed, >90% of 128 renal transplant recipients surveyed by the transplant centre in Swansea, UK, were aware of the dangers of the sun, and 77% knew that they were more susceptible since receiving their transplant. However, 31% were not taking any precautions to reduce exposure to the sun and only 39% of the interviewed organ transplant recipients used sunscreens [12]. In 90% of those who used sunscreen, the sun protection factor (SPF) (which reflects only the protection level against UVB, not UVA radiation) was <10. In the USA, similarly alarming figures have been found: in a telephone survey, 79% of all 200 interviewed organ transplant recipients believed that the appearance of a tan was attractive and only 35% reported regularly using sunscreens. Episodes of sunburning were reported by 35% of the organ transplant recipients [13]. A study of 270 renal transplant recipients from Ireland found that more than 25% of the patients never applied sunscreen on a sunny day, compared to 68% prior to transplantation. Eighty percent of organ transplant recipients who subsequently developed keratinocyte skin cancer (KSC) following transplantation reported taking no precautions against sun exposure ($P = 0.03$). Especially, organ transplant recipients in the very high risk group, i.e. older patients, males and patients who worked outdoors or enjoyed outdoor hobbies, were less likely to apply sunscreen. Interestingly, the study showed a decreased KSC risk associated with the pre-transplant use of sunscreen, highlighting the need for early education of all transplant candidates entering the organ transplant waiting list [4].

Sunscreens—could they be the solution?

Sunscreens are topical preparations that attenuate the effects of UV radiation on the skin. A perfectly balanced combination of medical as well as cosmetic requirements dictates that an ideal sunscreen should meet the following criteria: easy to apply in a uniform layer, effective in blocking close to 100% of incident UV radiation,
invisible on the skin (no-whitening effect), non-greasy and non-sticky. When evaluating the reasons given by those patients denying regular sunscreen use despite the knowledge of the deleterious effects of UV radiation, two main groups of ‘reasons’ usually arise. The largest group describes sunscreens as ‘cosmetically and socially unacceptable’. Indeed, the physical inorganic filters (titanium or zinc oxide), which are the protective compounds in most broad-spectrum sunscreens recommended to organ transplant recipients, require a more greasy formulation; they are difficult to rub in and are comedogenic. Cyclosporine induces sebaceous gland hyperplasia, leading to a seborrheic (oily) skin with folliculitis and acne. Steroids, and also newer immunosuppressive agents such as everolimus and sirolimus (mTOR-inhibitors), are also able to induce or promote acne. Patients therefore usually try to avoid or reduce application of any additional fatty emollients to the face, including sunscreens. The final result of this cosmetic drawback is that much smaller amounts of sunscreens are used. Consequently, the SPF values are well below those indicated on the bottle, giving the patient a false sense of security.

The second most frequently heard reason for not using sunscreens on a regular basis is the cost of high-quality sunscreens. In Germany, as well as in most other Western countries, health insurance companies still consider sunscreens to be ‘cosmetic’ products. Consequently, they are not reimbursed even for patients at high risk of skin cancer such as organ transplant recipients.

Nevertheless, the compliance of patients will hopefully be increased by new sunscreen formulations: gel, spray or newer filters embedded in liposomes and delivered into the upper level of the epidermis [14].

**Is there evidence of benefit?**

In a single-centre, matched pairs observational study, a group of 60 organ transplant recipients (20 heart, 20 kidney, 20 liver-grafted patients) with daily application of a highly protective, liposomal sunscreen (2 mg/cm²) as part of their regimen and sirolimus (mTOR-inhibitors), are also able to induce or promote acne. Patients therefore usually try to avoid or reduce application of any additional fatty emollients to the face, including sunscreens. The final result of this cosmetic drawback is that much smaller amounts of sunscreens are used. Consequently, the SPF values are well below those indicated on the bottle, giving the patient a false sense of security.

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synthesis is maximal at suberythemal UV doses and further UV exposure only increases the conversion of pre-vitamin D3 to lumisterol and tachysterol, both biologically inert compounds [18]. Furthermore, continued sun exposure degrades the active form of the photolabile vitamin D3 [19].

**Conclusion**

For individuals with an increased risk of skin cancer development, such as dialysis patients and organ transplant recipients, sun protective measures must be employed throughout the life of the patient. Sunscreens, as part of a conclusive sun protection strategy, are an important pillar of preventive healthcare. Since posttransplantation skin cancer becomes an increasingly important cause of morbidity and mortality in organ transplant recipients, the cost for sunscreens with medically proven efficacy should be covered by healthcare providers.

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**References**


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