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Hydrochlorothiazide and the risk of skin cancer: a word of caution Statement by the swiss society of hypertension and Swiss Society of Dermatology and Venereology

Two recent papers examined the association between the use of hydrochlorothiazide (HCTZ) and the risk of basal cell, squamous cell carcinoma and nodular melanoma in a case-control study using data from the Danish Cancer Registry and the Danish Prescription Registry. These two studies showed that high cumulative doses of HCTZ (> 50 g) were associated with a dose-dependent increase in the risk of non-melanoma skin cancer, but not of melanoma. The increase of risk was only small for squamous cell carcinoma, and negligible for basal cell carcinoma. It has to be realized that the risk reduction of death due to lower blood pressure by HCTZ was much higher than the small risk increase for squamous cell carcinoma by HCTZ.

These studies presented several limitations. First, statistical associations from observational studies do not prove a causal relationship. Hypertension is associated with other risk factors (e.g. smoking) that increase cancer risk. Nevertheless, a causal relationship is potentially possible through photosensitization by HCTZ. Second, a cumulative dose of 50 g of HCTZ is high. This corresponds to 12.5 mg HCTZ daily taken over more than 10 years. Therefore, the results of the study are only true for patients taking HCTZ over a long period. Third, antihypertensive drugs such as HCTZ prolong life and, therefore, the time of being at risk of developing cancer is increased. To the best of our knowledge, this kind of potential confounding was not statistically properly excluded in the aforementioned studies. Fourth, the Danish population is a pale-skinned population. People with pale skin have higher risk of skin cancer. Information on genetic predisposition (e.g. mutations), sun habits and ultraviolet exposure, which are major risk factors for all skin cancers, was missing in the studies. Therefore, the results from this Danish population should be generalized to other populations only with caution.

Nonetheless, these new data have to be taken into consideration. As there is a potential risk increase of squamous cell carcinoma with long-term prescription of HCTZ, the Swiss Society of Hypertension recommends using alternatives to HCTZ in young patients. Also, in patients who had squamous cell cancer previously, HCTZ should be avoided as a precaution. The Swiss Society of Hypertension discourages the use of HCTZ in patients with a family history of or genetical predisposition to skin cancers, pre-cancer skin lesions or a previous skin cancer, as well as in patients taking immunosuppressive drugs. However, for most patients with hypertension, there is no reason to stop HCTZ as the risk of developing this skin cancers is pretty low - and negligible as compared to the risks of untreated hypertension.

The Swiss Society of Hypertension and the Swiss Society of Dermatology and Venereology recommend evaluating benefits and risk of HCTZ on an individual basis. The choice of antihypertensive drug should still be chosen according to the current

guidelines (www.swisshypertension.ch). For patients on a prescription of HCTZ, the skin should be checked annually by the general practitioner. Use of protection against UV as recommended in general by dermatologists for preventing all skin cancers and a regular check of your skin, is always suggested, even if you do not have HCTZ!

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