Comment on “Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case–control study from Denmark”

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To the Editor: We were intrigued by the findings from a case–control study that showed a minor association between long-term hydrochlorothiazide use and risk of basal cell carcinoma (BCC) and a strong association with squamous cell carcinoma (SCC).[1] The publication played an important role in the decision making on a subsequent warning by the European Medicines Agency.[2] However, a meta-analysis performed by Gandini et al did not find a significant association between the use of thiazide-diuretics and skin cancer risk (melanoma as well as nonmelanoma).[3]

The data source used in this case–control study (Danish National Data) might have been suboptimal, considering that an important potential confounder, smoking status, is not available in this database.[1] The study data were not statistically adjusted for smoking status, which is a known risk factor of SCC.[4] We recognize that the analyses were adjusted for chronic obstructive pulmonary disease; however, this might not reflect smoking status accurately.

Another important issue is the possibility of diagnostic bias. Patients who are treated for a condition for which hydrochlorothiazide is prescribed are likely to visit their general practitioner more often, and consequently, they might be more likely to receive a skin cancer diagnosis. The supplemental tables show increased risk of BCC (bendroflumethiazide, calcium channel blockers, angiotensin II receptor antagonists) and SCC (furosemide) associated with the use of other drug classes as well. Although these increased risks were not as high as those from the main analyses, it should be noted that the supplementary analyses were adjusted for hydrochlorothiazide use and the main analyses were not adjusted for concomitant use of other antihypertensive drugs. Therefore, we question the association found between hydrochlorothiazide use and risk of BCC and SCC.

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Funding sources: None.

Conflicts of interest: None disclosed.

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https://doi.org/10.1016/j.jaad.2019.01.087