

LETTERS

Association between thiazide diuretics and skin cancer: still nebulous

I read with interest the article by Drucker and colleagues,¹ which concludes, “higher cumulative exposure to thiazides was associated with increased risk of skin cancer.” No doubt an important study, and I agree that efforts should be made in identifying modifiable risk factors to prevent this. However, Table S7 in the supplementary appendix of the article shows that the hazard ratios for all 3 types of skin cancers were similar or higher with angiotensin receptor blockers when compared with thiazides (keratinocyte carcinoma: 1.09 v. 1.08; advanced keratinocyte carcinoma: 1.49 v. 1.07; and melanoma: 1.73 v. 1.34; angiotensin receptor blockers v. thiazide diuretics),¹ yet the association between thiazides is highlighted in the manuscript. This association between thiazide diuretics and skin cancer was raised in some studies^{2,3} and refuted⁴⁻⁶ in others, and the study by Drucker and colleagues does not resolve this issue conclusively. Although the Pottegård study published in 2017³ showed an association with lip cancer, another study by the same authors 2 years later⁴ failed to demonstrate or confirm this association. In fact, both hypertension and all antihypertensive agents are associated with increased risk of cancer, and 2 meta-analyses of observational studies failed to show evidence of association with the use of thiazide diuretics, but did show an association between calcium channel blockers and β -blockers.^{5,6} Furthermore, although diuretics were first-line agents in the treatment of hypertension, they have not held this status for uncomplicated hypertension for at least 2 decades,⁷ and any of the classes of antihypertensive agents, except β -blockers, may be used as first-line therapy.⁷ The use of thiazides for treatment of hypertension has been declining,⁸⁻¹⁰ defined daily dose of thiazide diuretics is decreasing,¹¹ and prescriptions for thiazides failed to increase despite the distribution of printed educational materials

to primary care providers in Ontario.¹² The effective control of blood pressure often requires multiple agents,¹³ increasing the cost and number of agents, and strategies to contain cost and number of pills should be considered.¹⁰

Since the publication of this article, the media have exaggerated this association in the population, and to clarify this issue, Hypertension Canada a week later posted a statement¹⁴ that such observational studies generate hypotheses and cannot provide proof of causality, and hypertension itself is associated with cancer risk. The organization advised the public that those who are concerned about this hypothetical risk should speak with their physician and, more importantly, should use measures to prevent skin cancer. Thiazides are important agents in controlling blood pressure and in reducing risk of death, stroke, heart failure and heart attack, and should not be stopped or withheld without assessing the risk–benefit ratio.

The incidence of skin cancer increased by 10% between 2005 and 2015, and focus should be on factors responsible for this increase in risk, rather than creating anxiety in the population about an important, cost-effective therapy for control of hypertension whose utilization is already decreasing worldwide.^{10,11}

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