Qeios

Peer Review

Review of: "Vitamin D Deficiency in Smokers: A Major Risk Factor in Lung Carcinogenesis"

Tobias Niedermaier[1]

1. Ludwig-Maximilians-Universität München, Germany

Abstract: „Vitamin D deficiency in smokers is due to VDR gene polymorphism.“ à This statement is too strong in my opinion. Polymorphisms probably only account for a very small proportion of the actual vitamin D serum levels.

Introduction: Should be shortened, unless the (generally well-established) summary of LC risk factors and subtypes (NSCLC etc.) is relevant for the remainder of the article.

“It is already mentioned that two-thirds of lung cancer deaths are associated with smoking.” à repetitive, delete.

“lung cancer patients carry remarkably low levels of vitamin D in their blood” à Even if so, what is the cause and what is the consequence?

Consider doing a systematic review. A systematic review, even in only 1 or 2 databases, would be better than a narrative review using 5 databases.

Ref. 17: A difference in vitamin D levels between 54.7 nmol/L (smokers) and 58.3 nmol/L (non-smokers) is not clinically relevant, especially since both are well above the threshold for adequate/optimal levels of 50 nmol/l. It would be more interesting to know the proportion of individuals in each group that fall below 50 nmol/l (suboptimal) and below 30 nmol/l (deficient).

The section about the mechanisms by which tobacco smoke causes LC is overly long. I would suggest omitting everything that is not related to vitamin D. Or at least focus on the (supposedly) most important mechanisms.

The fact that 46% of stage IV LC patients are vitamin D deficient does not really prove anything. First, because also in the general population, a high percentage is vitamin D deficient; second, because LC

doi.org/10.32388/432A1A

patients might be deficient as a consequence of their cancer or simply because of being hospitalized; and third, because of the numerous other possible confounders (age, physical activity, supplementation, etc.).

It would be interesting to know if the supplementation of 30,000 IU/day for 14 days actually improved any clinically relevant outcome in those patients, such as survival, quality of life, etc. If not, it wouldn't make sense to supplement them with vitamin D, even if it raises their serum levels to the normal range. (We are treating patients, not laboratory measurements.)

"However, the function of vitamin D to suppress lung cancer is yet to be explored." à This is very speculative unless you can cite studies (ideally randomized studies) that demonstrate better survival in patients receiving vitamin D supplementation.

In fact, from what I found in a quick PubMed search, I would not think that vitamin D lowers lung cancer incidence. See the following PMIDs: 28676217, 29748306. But it might improve survival, at least in some cancers, see PMID 30018118, 30964526, at least in those who are vitamin D deficient and/or with daily supplementation (rather than e.g., monthly), see PMID 37004841.

"Neurofibromatosis 1 (NF1) is a tumor suppressor" à As far as I know, Neurofibromatosis is the disease, caused by a mutation of the Neurofibromin 1 gene (see https://en.wikipedia.org/wiki/Neurofibromatosis_type_I), but I'm not a physician. Please double-check and clarify. Furthermore, NF1 is a rare condition, as far as I know. As you wrote, the overwhelming majority of LC cases can be attributed to smoking and other environmental factors, not (primarily) to genetic mutations. So I wouldn't emphasize that too much.

Declarations

Potential competing interests: No potential competing interests to declare.