VITAMIN D
UpDates

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EDITORIAL

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Dear Readers,
I don't know about you, but I'm beginning to wonder whether in the uncritical application of statistical methodology at the base of evidence-based medicine we haven't forgotten the presupposition that is supposed to guide it: the physiopathological and clinical rationale. Let me explain more clearly: in the *Journal of the American Medical Association* (JAMA) were recently published the recommendations of the United States Preventive Service Task Force (USPSTF) on the use of vitamin D and/or calcium supplements for primary prevention of fractures in adults living in senior communities [1]. The report concludes that on the basis of available studies there is insufficient evidence in terms of a risk-benefit evaluation for recommending calcium or vitamin D supplementation; indeed, the task force advises against supplements of vitamin D and calcium doses ≤ 400 IU or 1000 mg/day, respectively, in postmenopausal women because of the increased risk of kidney stones.
Pity that these recommendations are not applicable to persons with a history of osteoporotic fractures, with a high risk of falls, or with diagnoses of osteoporosis of vitamin D deficiency (!), given that these subjects were largely excluded from the examined studies! Seeing that common sense tells us, based on our knowledge of physiopathology, that vitamin D is only needed when it is lacking, such an assertion, to my mind, is much like proving that turning on a light in a well-lit room is useless (if not harmful)! Was it then necessary to employ a task force and to conduct a complex analysis to reach this conclusion?
I worry also about the media effect of the concluding message, which I imagine might be simplified and communicated or received uncritically for editorial reasons or for basic incompetence.
And what about people who are at risk of deficiency? Let's not worry about prevention and let's wait to find evidence for the deficiency, with all the costs involved, or let's take action only when the person becomes a patient with a symptomatology. We also have to consider that the task force in question – justifiably in my view – defines the evidence as insufficient in terms of a risk-benefit analysis to warrant screening of vitamin D deficiency in asymptomatic adults.
On the other hand, I believe that it is also justifiable to aim to reduce the exorbitant costs of vitamin D supplementation by lowering expectations and refining our judgement of when action needs to be taken; we need to simplify our procedures and use common sense to avoid having recourse to expensive solutions which are ultimately of little use. A new development in this sense is represented by the recent authorization of the Agenzia Italiana del Farmaco (AIFA) for the marketing of a new calcifediol formula in gel capsules. We certainly welcome new solutions, especially if they are low cost, which expand the range of therapeutic options for doctors in the interest of patients, at the same time keeping in mind that calcifediol is the form of vitamin D which is produced and metabolized physiologically.
What puzzles me is the package insert of this new calcifediol-based product. In particular I am concerned about:

- the inappropriate expression of the contents in IUs of vitamin D, when it is known that calcifediol is not at all comparable to cholecalciferol in terms of pharmacokinetics and perhaps of pharmacodynamics as well; indeed, the extent of the equivalence relationship between them is still a topic of discussion today [2]. This could create another element of confusion about vitamin D

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dosages, which could be dangerous in terms of safety;
- the instruction and the recommended dose for the "treatment of vitamin D deficiency in cases in which it is necessary to initially administer high doses…" Are we to consider 0.266 mg of calcifediol once a month as a high dose if it is half of what has been deemed necessary in recent studies conducted by the school of Prof. Minisola [3,4] and given that the half-life of calcifediol is 2-3 weeks [5]?
- the instruction that "the treatment of vitamin D deficiency in cases … in which an administration that extends over time is preferable, as in the following conditions: as a coadjuvant treatment of osteoporosis, in patients suffering from malabsorption syndrome, renal osteodystrophy, and in corticosteroid-bone induced diseases." On the basis of what evidence are calcifediol treatments extended over time preferable in these pathologies?
- the need – repeated several times – for a "regular control of serum concentrations of 25-OH-cholecalciferol." This caution may derive from the fact that the increase of serum levels of 25-OH-cholecalciferol following the use of calcifediol is not physiologically regulated, unlike what occurs with cholecalciferol. It is a pity that the use of this calcifediol formula, which is indeed more expensive, may be compromised by the high management costs in clinical practice;
- the statement that "in case of hepatic insufficiency, the absence of the production of bile salts will prevent absorption of the calcifediol," when in fact it is reported that intestinal absorption of calcifediol, unlike that of cholecalciferol, takes place mostly through the portal vein [6] and is not dependent on the presence of bile acids [7]. It is therefore justifiable, also given the possible deficit of 25OH-hydroxylase in conditions of serious hepatic insufficiency, to prefer the use of calcifediol in this case [2].

What do you think?

I hope you enjoy reading this issue.

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