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EDITORIAL COMMENTARY

Vitamin D Supplementation in Children on Antiseizure Medications: High Time to Have Proper Guidelines

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A recent meta-analysis highlighted significantly reduced serum vitamin D levels in epileptic children receiving valproate monotherapy compared to healthy controls. Although it is not a conventional hepatic enzyme inducer, there are reports of valproate inducing CYP3A4 and CYP24A1, both involved in vitamin D catabolism [1]. Valproate activates pregnane X receptor which regulates the expression of vitamin D responsive genes [2]. Apart from its importance in bone growth and development, vitamin D also plays a significant role in the functioning of muscular, immune, and cardiovascular systems [1].

Studies by Viraraghavan et al. and Mikati et al. have shown the utility of vitamin D supplementation in children on antiseizure medications (ASMs) [3, 4]. The present study by Mishra et al. is a welcome addition in that direction, evaluating the utility of vitamin D supplementation in children on valproate monotherapy [5].

Mishra et al. studied children aged 2–12 y with new onset epilepsy on valproate monotherapy with vitamin D–sufficient status at baseline. They were randomized into 2 arms: intervention arm receiving vitamin D (600 IU/d) for a period of 90 d and a control group receiving only ASM. The median vitamin D level significantly increased and decreased, respectively, in the intervention and control arms over 3 mo [5].

Mikati et al. and Viraraghavan et al. included cases of a variety of ASMs as mono- or polytherapy. Although Viraraghavan included new-onset epilepsy cases, subjects in the study by Mikati et al. were on ASM for at least 6 mo. Viraraghavan et al. prescribed 60,000 IU/mo of vitamin D in the intervention arm, whereas Mikati et al. had two arms, one receiving 400 IU/d and another receiving 2000 IU/d of vitamin D. Contrary to the study by Mishra et al., both of these studies included cases of vitamin D deficiency at baseline [3, 4]. Viraraghavan et al. demonstrated maintained serum vitamin D levels at 6-mo follow-up in the intervention arm compared to a significant decrease in the control arm [3]. Mikati et al. found a significant increase in both intervention groups at 1-y follow-up; however, the values were comparable in both groups. They also documented increases in bone mineral density at multiple skeletal sites in both arms [4]. The study by Mishra et al. reinforces the fact that even children with vitamin D–sufficient status show a significant fall in serum levels on ASM therapy that can be prevented by vitamin D supplementation.

The Endocrine Society recommends at least 2–3 times the RDA of vitamin D on ASM polytherapy [6]. Recent literature has unveiled possible anticonvulsant effects of vitamin D mediated by reduction in voltage-sensitive calcium channel expression, inhibition of iNOS, and suppression of inflammatory cytokines [7]. Mishra et al. did not show any difference in breakthrough seizures between the control and intervention arms; however, the follow-up is only for 90 d [5].

Thus, the current study further reiterates the utility of vitamin D supplementation in children with epilepsy and paves the way for future studies on various ASM mono- and polytherapies, including the long-term effect of vitamin D on seizure control.

Declarations

Conflict of Interest None.

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