Letter to the Editor

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Antiepileptic Drug-Induced Osteopenia and Fracture Risk: A Preventable Clinical Burden

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1. Letter to the Editor

Antiepileptic Drugs (AEDs) remain the foundation of long-term epilepsy management, yet their consequences often receive minimal clinical attention. Over the last two decades, substantial evidence has emerged linking chronic AED therapy, particularly with enzyme-inducing and valproate-based agents, to impaired bone mineralization and increased fracture risk. Despite this, bone health assessment remains notably absent from standard epilepsy care pathways in many low and middle-income countries.

Zhong[1] et al. showed in a meta-analysis of 19 reports that patients who had been on valproate monotherapy have a statistically significant decrease in Bone Mineral Density (BMD) when compared with matched controls, with loss further increasing after 36 months of uninterrupted therapy. The results were uniform across the adult and pediatric populations, emphasizing that skeletal weakness occurs early in the course of treatment. Long-term exposure to valproate inhibits osteoblast activity and collagen production, changing bone microarchitecture and resulting in brittle bones even in young persons[1].

Systematic review by Griepp[2] et al. brought together the wider range of AED effects on bone, showing that both traditional and newer drugs adversely affect calcium homeostasis and vitamin D balance. Enzyme-inducing AEDs like phenytoin, carbamazepine and phenobarbital promote vitamin D catabolism via cytochrome P450 induction, whereas valproate disrupts bone matrix protein production. The cumulative effect, osteopenia, osteoporosis and increased fracture risk, represents a preventable, chronic burden to patients already potentially beset by physical and social disability from epilepsy.

At a regional level, a study emphasized that vitamin D deficiency is already epidemic in South Asians, reaching over half of Pakistan's adults[3]. In such environments, long-term use of AEDs adds to an underlying nutritional deficiency, which makes the patient prone to premature skeletal fragility. Socio-cultural practices, restricted exposure to sunlight and absence of dietary fortification add to this risk. The authors recommend context-based protocols for vitamin D monitoring and supplementation in the management of epilepsy in the setting of resource-constrained environments[3].

Clinically, the implications are simple but poorly applied.

Baseline and regular checks on serum calcium, phosphate, alkaline phosphatase and vitamin D should be standard for patients placed on AEDs for more than six months. Dual-Energy X-Ray Absorptiometry (DEXA) screening, if available, can detect early demineralization of bones prior to the development of irreversible changes. Calcium and vitamin D supplementation, lifestyle therapy and weight-bearing exercise are the foundation of prevention. Notably, clinicians should reevaluate the long-term need for valproate or enzyme-inducing therapy in patients with other risk factors for osteoporosis and use alternative AEDs when feasible.

This problem has implications beyond the individual patient to healthcare economics. Fragility fractures have high costs of rehabilitation and surgery, especially in developing countries where preventive surveillance is cheap by comparison. Incorporation of bone health assessment into guidelines for epilepsy management is an inexpensive, high-reward intervention. As our knowledge of AED-induced metabolic effects increases, so must our clinical awareness.

2. Conclusion

In summary, the skeletal consequences of long-term AED therapy represent a preventable iatrogenic condition. Preventive screening, early supplementation and heightened clinician awareness can collectively minimize osteopenia and fractures in individuals with epilepsy. It is thus essential for neurologists, family physicians and policy-makers to prioritize bone health as a standard component of epilepsy care, one that is both evidence-based and morally obligatory.

3. References

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