Editorials

Bone health in adults with epilepsy and intellectual disability

Epilepsy is more prevalent in individuals with intellectual disability (ID) compared to the general population, and this prevalence increases with increasing severity of ID. Epilepsy affects approximately 22% of people with ID, while 25% of people with epilepsy (PWE) have an ID.[1] Epilepsy is associated with significantly impaired bone health including osteoporosis and bone fractures,[2] while individuals with ID are at increased risk of osteopenia and osteoporosis, and vitamin D deficiency.[3]

BONE HEALTH AND EPILEPSY

There has been growing interest in the association between abnormalities of bone health and epilepsy in recent years. PWE who are housebound or institutionalised, avoid sunlight for cultural reasons, or have poor nutrition are at increased risk of vitamin D deficiency. This can predispose to osteopenia/osteoporosis and proximal myopathy leading to weakness and increased fall liability. Associated conditions such as cerebral palsy with inability to weight bear, reduced physical activity, or visual impairment can be contributory factors. Anti-seizure drug (ASD) side-effects like ataxia, sedation, and seizures, especially convulsive ones, can increase the risk of falls and subsequent fractures particularly in those with reduced bone mineral density (BMD).

Attention, however, has focused mainly on ASDs and their role in abnormal bone metabolism. The relationship between abnormalities of bone health and ASDs is commonly thought to be due to the enzyme-inducing properties of many ASDs leading to reduced serum vitamin D levels, but this is not the only mechanism. Sodium valproate, an enzyme inhibitor, is also associated with reduced BMD and increased risk of fractures. Other mechanisms suggested include inhibition of intestinal calcium absorption, osteoclast cell growth, cellular response to parathyroid hormone and calcitonin secretion, and direct effects on bone cells.[4] Newer ASDs might have a more positive relationship with bone health than older ones.

The National Osteoporosis Society has adopted the definition of vitamin D deficiency used by the National Institute for Health and Care Excellence.[5] They recommend that serum vitamin D concentrations for all individuals in the UK should not fall below 25 nmol/L at any time of the year, in order to protect musculoskeletal health. They also recommend treatment for individuals with a serum vitamin D between 25 nmol/L and 50 nmol/L for certain situations. This includes the following: fragility fracture, osteoporosis, high fracture risk, and symptoms suggestive of vitamin D deficiency or increased risk of developing vitamin D deficiency including raised serum parathyroid hormone and treatment with ASDs.

BONE HEALTH IN PEOPLE WITH INTELLECTUAL DISABILITY

Risk factors identified for osteoporosis include use of ASDs (particularly older ones), immobility, and history of falls and fractures. It has been recommended that screening for risk factors associated with lower BMD in adults with ID should take place.[6] Epilepsy and ASD medication have been found to be strong predictors for fractures.[7]

Both low BMD and vitamin D deficiency are established independent risk factors for fracture, although 80% of individual variability in BMD is explained by hereditary factors including sex and ethnicity. Smoking, alcohol, hormonal status, and low levels of physical activity are also known to be associated with reduced BMD.[2]

Vitamin D deficiency, defined as a serum vitamin D level <50 nmol/L, has been found in nearly twice as many people with ID in the community, compared to controls. Winter season, dark skin pigmentation, impaired mobility, and obesity were independently associated with lower serum vitamin D levels. In most patients, 800 IU cholecalciferol daily has been shown to normalise serum vitamin D levels.[3] Another major influencer is mental disorders and psychotropic medication.[8] One in three people with ID are on psychotropics.[9] Antipsychotics, selective serotonin reuptake inhibitors, and benzodiazepines are commonly used and are considered significant culprits for leading to bone harm.[8]

The authors undertook a community study of PWE and ID attending a specialist epilepsy clinic (n = 104 participants; study currently under review). Normal serum vitamin D levels were accepted at >80 nmol/L given the complex multiple comorbidities of this patient group. This target is considered to provide 'optimal' health.[10] Of the study population, 77 (74.0%) were vitamin D insufficient (30.0%) or deficient (44.2%). Of the 76 (73.1%) who had a DEXA scan, 25 (32.9%) were osteoporotic, 30 (39.5%) osteopaenic, and only 21 (27.7%) had a normal BMD. There was a significant difference (P = 0.05) in DEXA hip T-scores between ambulant and non-ambulant patients. A raised alkaline phosphatase level significantly predicted lower vitamin D levels. An approximate dose of vitamin D 1200 IU replacement was sufficient to correct vitamin D insufficiency, or 2000 IU for deficiency.

The study showed that the rate of vitamin D deficiency/insufficiency and osteoporosis/osteopenia was very high. Non-ambulatory status was significantly associated with low BMD. Because of co-existing comorbidities such as cerebral palsy, other movement disorders, psychiatric disorders, and obesity, PWE and ID may not be able to weight bear or may be exposed to less sunlight. The management of some of these comorbidities may also contribute to poor bone health outcomes such as proton pump inhibitors, psychotropics, diuretics, diabetes medication, and ASDs. Box 1 provides a list of key factors influencing bone heath in PWE and ID.

IMPLICATIONS FOR PRIMARY CARE

A community survey of individuals with ID and their carers revealed significant shortcomings in their knowledge of the relationship between ID, epilepsy, ASDs, fracture risk, and available risk reduction strategies.[11] It was recommended that clinicians be proactive in providing PWE and their carers with information around bone health and epilepsy.

The Quality and Outcomes Framework (QOF) is a voluntary annual reward and incentive programme for all GP practices in England. It is designed to remunerate general practices for providing good-quality care to their patients, and to help fund work to further improve the quality of health care delivered. The QOF lists 19 conditions in the clinical domain including ID, epilepsy, and osteoporosis. A previous systematic review of the role of the QOF framework in long-term conditions found no evidence that the QOF influenced integration or coordination of care, holistic care, self-care, or patient experience.[12]

With advanced age, bones are more prone to fracture. Thus, the ageing ID population with epilepsy has further risk concerns. Other apprehensions include that popular osteoporosis screening tools such as Q-Fracture and FRAX have not been validated in the ID population.[13] Small-scale studies have shown that these tools regularly

Box 1. Major factors influencing bone health in people with epilepsy and intellectual disability

Factor	Examples and points of interest
Demographics	• Age, sex, skin tone, and weight
Neurodevelopmental issues	• Level of intellectual disability, presence of cerebral palsy, and ambulatory status
Existing treatment of bone conditions	• Calcium supplementation, vitamin D replacement, or bisphosphonate therapy
Biochemical markers	• Serum calcium, phosphate, alkaline phosphatase, magnesium, vitamin D, parathyroid hormone, and 24-hour urinary calcium excretion
Bone mineral density	• DEXA hip T-score
Vitamin D	• Correction of vitamin D and insufficiency/deficiency
Anti-seizure drugs	• Older anti-seizure drugs such as first generation drugs like phenytoin and phenobarbitone are considered less bone friendly
Psychotropic medication	• Antipsychotics, antidepressants, and multiple psychotropics
Other medication	• Proton pump inhibitors and diuretics

show a 'false negative' for people with ID thus putting this population at further risk of iatrogenic harm.[13]

An audit in primary care practices in the south-west of the UK looked into the quality of health checks in people with ID prescribed ASDs and antipsychotics to see if relevant blood monitoring was being done.[14] The result showed poor person-centred annual health checks. The authors highlighted the potential of patient- or carer-held records and how they could be linked to annual health checks to improve quality. Bone health screening elements could be included within this framework. A simple baseline screen consisting of bone profile, magnesium, and vitamin D levels, and a baseline DEXA scan, would identify the majority of people with ID and osteoporosis, or at risk of developing osteoporosis. An awareness of risk factors for bone health including inability to weight bear and iatrogenic causes, together with emergent signs, for example, myopathy, kyphosis, and height shortening, should also heighten clinical suspicion. An agreed local protocol involving primary and secondary Care (neurology, ID services, and endocrinology) should identify which service is responsible for actioning the screening process.

CONCLUSION

Adults with ID and epilepsy are at high risk of bone harm due to a myriad of factors including their intrinsic genetic makeup, multimorbidity, and iatrogenic influences of polypharmacy including ASDs. As the longevity in people in this vulnerable cohort increases due to better treatments and support it is important to be mindful of the changes they undergo at a bone health level to achieve and provide optimum quality of life. Thinking of bone health in this population requires a holistic and systematic approach, which has not been achieved to date. It will remain neglected and thought to be 'someone's business' leading to it being 'no one's business', unless we make this 'everyone's business'.

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REFERENCES

1. Shankar R, Rowe C, Van Hoorn A, *et al.* Under representation of people with epilepsy and intellectual disability in research. *PLoS One* 2018; **13(6):** e0198261.
2. Cock HR. Bone health in epilepsy. In: Rugg-Gunn FJ, Stapely HB, eds. *Epilepsy 2017: from bench to bedside. A practical guide to epilepsy.* London: International League Against Epilepsy (British Chapter), 2017; 433–450.
3. Frighi V, Morovat A, Stephenson MT, *et al.* Vitamin D deficiency in patients with intellectual disabilities: prevalence, risk factors and management strategies. *Br J Psychiatry* 2014; **205(6):** 458–464.
4. Arora E, Singh H, Gupta YK. Impact of antiepileptic drugs on bone health: need for monitoring, treatment, and prevention strategies. *J Family Med Prim Care* 2016; **5(2):** 248–253.
5. Arundel P, Shaw N. *Vitamin D and bone health: a practical clinical guide for patient management in children and young people.* 2018. https://theros.org.uk/media/54vpzzaa/ros-vitamin-d-and-bone-health-in-children-november-2018.pdf (accessed 21 Dec 2021).
6. Srikanth R, Cassidy G, Joiner C, Teeluckdharry S. Osteoporosis in people with intellectual disabilities: a review and a brief study of risk factors for osteoporosis in a community sample of people with intellectual disabilities. *J Intellect Disabil Res* 2011; **55(1):** 53–62.
7. Burke EA, McCallion P, Carroll R, *et al.* An exploration of the bone health of older adults with an intellectual disability in Ireland. *J Intellect Disabil Res* 2017; **61(2):** 99–114.
8. Bolton JM, Morin SN, Majumdar SR, *et al.* Association of mental disorders and related medication use with risk for major osteoporotic fractures. *JAMA Psychiatry* 2017; **74(6):** 641–648.
9. Sheehan R, Hassiotis A, Walters K, *et al.* Mental illness, challenging behavior, and psychotropic drug prescribing in people with intellectual disability: UK population based cohort study. *BMJ* 2015; **351:** h4326.
10. Pierce SH, Cheetham TD. Diagnosis and management of vitamin D deficiency. *BMJ* 2010; **340:** b5664.
11. Sawhney I, Zia A, Yazdi B, Shankar R. Awareness of bone health risks in people with epilepsy and intellectual disability. *British Journal of Learning Disabilities* 2020; **48(3):** 224–231.
12. Forbes LJL, Marchand C, Doran T, Peckham S. The role of the Quality and Outcomes Framework in the care of long-term conditions: a systematic review. *Br J Gen Pract* 2017; DOI: https://doi.org/10.3399/bjgp17X693077.
13. Redfern P, Jory C, Shankar R, *et al.* Identification of osteoporosis amongst people with intellectual disabilities (ID) being treated with antiepileptic drugs (AEDS). *Epilepsia* 2014; DOI: 10.1111/epi.12675.
14. Shankar R, Bradley-Smith G, Brigham P, *et al.* Patient- and carer-held health records: can they improve annual health checks for patients with learning disability? *Br J Gen Pract* 2016; DOI: https://doi.org/10.3399/bjgp16X684697.