

Effect of phenytoin (antiepileptic) on bone mineral density

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Abstract: Background: Long-term antiepileptic drug (AED) therapy is a postulated risk factor for bone loss and fractures. To study this we have compared cases (patients on phenytoin) with age & sex matched controls.

Objectives: A1) To determine the effect of phenytoin (> 1 year therapy) on bone mineral density in 20-50 year old epileptic patients. 2) To compare them with age & sex matched healthy controls.

Methods: We prospectively examined femoral neck & spine bone mineral density (BMD) by dual-energy x-ray absorptiometry in 50 patients, aged between 20 and 50 years old (mean age, 37 years), who were attending an outpatient epilepsy clinic or were admitted to our hospital. Low BMD values were analyzed for known risk factors for bone loss. Dual-energy x-ray absorptiometry scans (LUNAR DPX PRO) were repeated in all patients, 12 months later, to assess the rate of change in BMD over time. This was also compared with age & sex matched controls (case control study).

Result: Statistical analysis revealed that patients receiving phenytoin was an important risk factor associated with low femoral neck & spine T- score as matched with normal control group (p value <0.05). Analysis of femoral neck & spine T-score revealed that more than 50% of patient group had either osteopenia/osteoporosis as compared to control group. Females were more affected than male. T-score was low in the younger age group. But there was no significant correlation between BMD & various parameters like- 1) serum calcium level, 2) serum phenytoin level and 3) BMD after 1 year of phenytoin therapy.

Conclusion: Long-term phenytoin therapy causes significant bone loss at the hip & spine. Dual-energy x-ray absorptiometry scanning is useful in identifying patients who are particularly susceptible to rapid bone loss while taking phenytoin.

THESIS SUMMARY

Introduction

Osteoporosis has been better defined by the Consensus Development Conference as “a disease characterized by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and consequent increase in fracture risk”. Patients with epilepsy have a higher incidence of skeletal fractures due to multiple reasons. Postmenopausal women and elderly men are particularly vulnerable to osteoporosis. A

major convulsive seizure can often lead to falls and may result in fractures. Antiepileptic therapy may have seemingly contradictory effects on bone health. It can effectively reduce the incidence of major seizures and prevent the seizure related falls and fractures. Long-term antiepileptic therapy may lead to a reduction in bone mineral density, with consequent increase in bone fragility. This can increase the risk for fractures with attendant high morbidity and mortality. Dual energy X-ray absorptiometry (DEXA) is currently the gold standard for assessing bone mineral

density. Multiple pathophysiologic mechanisms have been proposed for the reduction in bone mineral density associated with antiepileptic therapy. Most of the available data are from the patients treated with conventional antiepileptic drugs (AED).

Material and Methods

We prospectively examined femoral neck & spine bone mineral density (BMD) by dual-energy x-ray absorptiometry in 50 patients, aged between 20 and 50 years old

(mean age, 37 years), who were attending an outpatient epilepsy clinic or were admitted to our hospital. Low BMD values were analyzed for known risk factors for bone loss. Dual-energy x-ray absorptiometry scans (LUNAR DPX PRO) were repeated in all patients, 12 months later, to assess the rate of change in BMD over time. This was also compared with age & sex matched controls.

Results

Statistical analysis revealed that patients receiving phenytoin was an important risk factor associated with low femoral neck & spine T-score as matched with normal control group (p value <0.05). Analysis of femoral neck & spine T-score revealed that more than 50% of patient group had either osteopenia/osteoporosis as compared to control group. Females were more affected than male. T-score was low in the younger age group. But there was no significant correlation between BMD & various parameters like- 1) serum calcium level, 2) serum phenytoin level and 3) BMD after 1 year of phenytoin therapy. What should we recommend to our epilepsy patients taking phenytoin regarding their bone health? It is becoming clear that this issue is confined not only to women with epilepsy or women in the general population but is also important for men. We have shown for the first time that Indian patients (male & female) who have seizures sustain significant bone loss at the femoral neck as well as spine while receiving AED therapy. The finding that >50% had a T-score lower than -1 at these site indicates that a substantial number are at an increased risk for hip or vertebral fractures. Thus, it is possible that the younger male skeleton with enhanced bone turnover from AED therapy may require a substantially higher calcium intake to adequately suppress bone resorption and optimize bone mineralization. Individual other drugs should also be examined for their association or otherwise with low BMD. A range of pharmacological options is available for patients with reduced BMD including HRT, biphosphonates, vitamin D; calcium etc. patients with osteoporosis identified in this study have been commenced on treatment.

Discussion

Statistical analysis revealed that patients receiving phenytoin was an important risk factor associated with low femoral neck & spine T-score as matched with normal control group (p value <0.05). Analysis of femoral neck & spine T-score revealed that more than 50% of patient group had either osteopenia/osteoporosis as compared to control group. Females were more affected than male. T-score was low in the younger age group. But there was no significant correlation between BMD & various parameters like- 1) serum calcium level, 2) serum phenytoin level and 3) BMD after 1 year of phenytoin therapy. What should we recommend to our epilepsy patients taking phenytoin regarding their bone health? It is becoming clear that this issue is confined not only to women with epilepsy or women in the general population but is also important for men. We have shown for the first time that Indian patients (male & female) who have seizures sustain significant bone loss at the femoral neck as well as spine while receiving AED therapy. The finding that >50% had a T-score lower than -1 at these site indicates that a substantial number are at an increased

risk for hip or vertebral fractures. Thus, it is possible that the younger male skeleton with enhanced bone turnover from AED therapy may require a substantially higher calcium intake to adequately suppress bone resorption and optimize bone mineralization. Individual other drugs should also be examined for their association or otherwise with low BMD.

A range of pharmacological options is available for patients with reduced BMD including HRT, biphosphonates, vitamin D; calcium etc. patients with osteoporosis identified in this study have been commenced on treatment.

Conclusion

Long-term phenytoin therapy causes significant bone loss at hip and spine as compared to age and sex matched normal control.

- In our study, those patients who were on phenytoin therapy for more than 15 years, all of them revealed significant reduction in T-score (<-1).
- BMD in females were more affected than male.
- There was no significant correlation between BMD & various parameters like- 1) serum calcium level, 2) serum phenytoin level and 3) BMD after 1 year of phenytoin therapy.
- Not only postmenopausal women but also adults with epilepsy should be encouraged to attend for bone density screening. As in our study young patients were more affected.
- Dual-energy x-ray absorptiometry scanning is useful in identifying patients who are particularly susceptible to rapid bone loss while taking phenytoin.
- These patients should be supplemented with bone calcium antiresorptive therapy to prevent osteopenia or osteoporosis.

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