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Original Article

Bone mineral density evaluation o epileptic children on anti-epileptic medications

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ABSTRACT

Objective: The aim of this work is to evaluate bone mineral density (BMD) in children with idiopathic epilepsy under anti-epileptic drugs and to determine the effect of the type and the duration of drug administration on BMD.

Subjects and methods: This study conducted on 120 children divided into two groups, Epileptic group included 60 children diagnosed as having epilepsy on the basis of clinical examination receiving antiepileptic drugs (AEDS). Control group included 60 healthy children.
All patients subjected to clinical examination and determination of bone mineral density.

Results: Among epileptic children, there were 35 children (58.3%) with generalized tonic clonic seizures, 11(18.3%) were partial, 10(16.7%) were partial with secondary generalization, 4(6.7%) were absence seizures. 41(68.3%) epileptic patients were on antiepileptic monotherapy while 19 (31.7%) were on polytherapy. Seventeen children with low bone mineral density state (LBMD) and 43 with normal bone density. Epileptic patients had lower BMD, Z- score, and AM compared with controls (P value < .001). Epileptic patients with LBMD had significant decrease in Z score, BMD and AM (P < .001) compared with epileptic patients with normal bone state.

Conclusion: Epileptic patients receiving polytherapy showed more decrease in BMD than that of epileptic patients receiving monotherapy with (P < .001).

1. Introduction

Epilepsy is a common medical and social disorder characterized by epileptic seizures. These seizures occur due to disruptions of electrical signals in the brain. Epilepsy also characterized by the neurobiologic, cognitive, psychological, and social consequences of this condition. These disruptions cause temporary communication problems between nerve cells, leading to seizures [1].

Most patients require long-term and sometimes lifelong therapy with antiepileptic drugs (AEDs). AEDs are associated with significant side effects not limited to, radiological evidence of rickets but decreased bone mineral density (BMD), altered bone turnover, and increased risk of fracture [2].

Osteopenia is considered a silent disease because bone loss can occur gradually without symptoms. It occurs due to inadequate mineralization of bone [3].

Osteomalacia increases fracture risk. Bone mineralization begins at birth and plateaus in the third decade of life with subsequent gradual bone loss as a natural process of aging. Many of the effects of Osteomalacia overlap with osteoporosis [4].

Many studies reported significant reduction in bone mineral density among children with epilepsy especially in patients receiving polytherapy treatment more than those on single anti-epileptic drug [5].

In addition, increasing the duration of treatment with anti-epileptic drug may increase the risk of osteopenia and fractures [6].

These observations have increased the demand for better diagnostic and therapeutic tools to address bone health in children including: laboratory investigation and dual-energy x-ray absorptiometry (DXA) [7]. The aim of this work is to evaluate bone

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mineral density (BMD) in children with idiopathic epilepsy under anti-epileptic drugs and to determine the effect of the type and the duration of drug administration on BMD.

2. Patients and methods

2.1. Study design

This is a cross sectional case-control comparative study.

2.2. Patients

This study was carried out in Pediatric outpatient Neurological Clinic, department of pediatrics; all children were referred to the Radiology Department during the period from March 2016 to December 2016. The study aimed to evaluate bone mineral density (BMD) in children with idiopathic epilepsy under anti-epileptic drugs and to determine the factors associated with diminished bone mineral density in those patients. The study included 120 children. These children were classified into two groups:

Epileptic group: (Group I): included 60 children aged 5–12 Y (mean 9.03 ± 2.02), diagnosed as having epilepsy on the basis of both clinical examination and investigation (EEG) receiving antiepileptic drugs (AEDS) for at least one year (old AEDS: Valproic acid and Carbamazepine), (new AEDS: Levetiracetam and Ethosuximide); some of them on monotherapy 41(68.3%) and others on polytherapy 19(31.7%).

Among the epileptic patients, there were 35 patients (58.3%) with generalized tonic clonic seizures, 11(18.3%) were partial, partial with 2ry generalization 10(16.7%), and absence 4(6.7%). The mean disease duration was (3.02 ± 1.74) months.

Control group: (Group II): included 60 apparently healthy children with age and sex matched to the diseased groups and without evidence of epilepsy.

2.3. Ethical approval

The goal and methodology of the study were described to all patients' parents after approval of hospital ethics committee. Both verbal and written consents were taken from the parents. The potential benefits and inconveniences of all aspects of the study were clearly stated to the parents.

Patients were selected on the basis of the following inclusion and exclusion criteria: Patients with age ranging from 5 to 12 years from both sexes, diagnosis of idiopathic epilepsy and both mono and polytherapy with antiepileptic drugs (old/new) for at least one year were included in the study.

Diseases primarily involving bone metabolism or familial history of bone metabolism disorders, chronic treatment with drugs other than anticonvulsants, poor compliance during bone density evaluation, treatment with antiepileptic drugs for less than one year, serum Ca < 9.5 mg/dl, and abnormal neurological examination were excluded from our study.

2.4. Methods

All patients were subjected to: **complete history taking** including, age, sex, type of epilepsy, age of onset of the disease, type, age of onset of the drugs, complication of treatment, other investigation, e.g.: EEG, CT, MRI, Cranial U/S, history of obstructed labor, delayed motor or mental activity and positive family history. **Clinical Examination** including general and complete neurological examination.

2.5. Laboratory investigations

The studied groups were assessed for serum level of Ca, Ph, and ALP; About 2 ml of venous blood were withdrawn from each child by sterile venipuncture and allowed to clot at 37 °C, separated after centrifugation at 3000 rpm for 10 min, the separated serum used for determination of serum total calcium, phosphorus and alkaline phosphatase using fully automated chemistry analyzer (Konelab, 20i, Finland).

2.6. Determination of bone mineral density (DXA SCAN)

Using bone Densitometer (GY lunar- DPX-Central DXA scan, USA), the children's lumbar spines (LV1–LV4) were examined while they were lying supine with their lower limbs partially raised to reduce lumbar lordosis to be straight and centered in the image, with the last rib pair and the upper sacrum visualized. The regions of interest (ROIs) are generated automatically using edge-detection software and are selected for the LV1 to LV4 vertebral segments [8].

Using these normative data for Egyptian children as a reference for distribution, age and gender specific Z-score for each subject were computed. The Z-score was calculated using the following formula:

Z-score = [Patient's BMD value – Age-matched mean value]/ Age-matched standard deviation [9].

According to the World Health Organization criteria, patients with scores that are −2 standard deviation (SD) have normal bone mineral density while those with scores that are (−2:−2.5) standard deviation below normal DXA values have osteopenia, whereas those with values <−2.5 SD below normal values are described as osteoporotic [8].

Low bone mineral mass or bone mineral density' is the phrase that is recommended for low BMC or a BMD in the absence of a fracture history suggestive of osteoporosis rather than osteopenia or osteoporosis [10].

2.7. Statistical method

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 20.

Descriptive statistics were done for numerical data by mean, standard deviation and minimum& maximum of the range, while they were done for categorical data by number and percentage.

Analyses were done for parametric quantitative data between the two groups using independent sample *t* test.

Analyses were done for qualitative data using Chi square test.

Correlation between two quantitative variables was done by using Pearson's correlation coefficient. Correlation coefficient ranges from (0 to 1): weak (r = 0–0.24), fair (r = 0.25–0.49), moderate (r = 0.5–0.74), strong (r = 0.75–1).

Simple logistic regression analysis was used to determine the risk factors of LBMD.

The level of significance was taken at (P value < .05).

3. Results

This study was carried on 120 children, classified into 2 groups;

Group I: included 60 epileptic patients 38 males (63.3%) and 22 females (36.7%) diagnosed as having epilepsy on the basis of both clinical examination and investigation receiving antiepileptic drugs (AEDS) for at least one year (Figs. 2–5).