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Original Article

Does type 1 diabetes mellitus affect bone quality in prepubertal children?

Khalid I. Khoshhal, ABOS [a,*], Salah A. Sheweita, PhD [b], Mohammad S. Al-Maghamsi, ABP [c] and Abdelhadi M. Habeb, FRCPCH [c]

[a] *Department of Orthopedic Surgery, College of Medicine, Taibah University, Almadinah Almunawwarah, KSA*
[b] *Department of Biotechnology, Institute of Graduate Studies & Research, Alexandria University, Egypt*
[c] *Endocrine and Diabetes Unit, Maternity and Children Hospital, Almadinah Almunawwarah, KSA*

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الملخص

أهداف البحث: غالبا ما يبدأ داء السكري من النوع الأول في الأطفال قبل بلوغ ذروة الكتلة العظمية، التي قد تشكل نقطة مرجعية للتنبؤ بخطر حدوث كسور العظام في وقت لاحق من حياتهم. ولذلك، تهدف هذه الدراسة إلى معرفة مستويات العلامات العظمية في البلازما عند الأطفال الذين يعانون من داء السكري من النوع الأول، مع قياس كثافة معادن العظام لديهم.

طرق البحث: ضمت عينة الدراسة الأطفال المصابين بداء السكري من النوع الأول لمدة ٣ سنوات وأكثر بدون ظهور علامات البلوغ. وكانت العينة للمجموعة الضابطة من طلاب المدارس مماثلين لعينة الدراسة، من حيث العمر وحالة البلوغ، بدون الإصابة بداء السكري. وتم قياس مستوى مجموعة من العلامات الحيوكيميائية لتكوين العظام وارتشافه في الدم. كما قيست كثافة معادن العظام بجهاز الموجات فوق الصوتية.

النتائج: ضمت الدراسة ٣٦ طفلا مصابا بداء السكري من النوع الأول، و٣٩ طفلا سليما. وأظهرت الدراسة أن ٣٦/٢٤ (٦٦.٧٪) من الأطفال المصابين بداء السكري كانت قياسات كثافة معادن العظام لهم أقل من الصفر، ومنهم ٥ كانوا أقل من -١. بينما كانت قياسات كثافة معادن العظام عند ٣٩/١٢ (٣٠.٨٪) فقط من الأطفال السليمين أقل من الصفر، ولم يصل أي منهم إلى دون -١. وبالإضافة إلى ذلك، لوحظ وجود انخفاض في بعض العلامات الحيوكيميائية لتكوين العظام، وارتفاع في بعض العلامات الحيوكيميائية لارتشاف العظام.

الاستنتاجات: تنخفض كثافة معادن العظام لدى مرضى السكري من النوع الأول، وكذلك بعض علامات تكوين العظام، بينما تزيد بعض علامات ارتشاف العظام. إن قياس كثافة معادن العظام والعلامات العظمية يفيدان في الكشف المبكر عن أي تغييرات في نوعية العظام عند المصابين بداء السكري من النوع الأول، التي بدورها إن عولجت قد تقلل من قابليتهم للكسور العظمية.

الكلمات المفتاحية: كثافة معادن العظام؛ الموجات فوق الصوتية الكمية؛ أوسيتوكالسين؛ هشاشة العظام؛ فيتامين د

Abstract

Objectives: Type 1 diabetes mellitus (T1DM) in children often starts before the achievement of peak bone mass. This may constitute a landmark in predicting bone fracture risk later in their lives. This study aims to determine the serum levels of bone markers in children with T1DM in combination with their bone mineral density (BMD).

Methods: Children diagnosed with T1DM for 3 years or more without signs of puberty were included in the diabetic group. Another group of age-matched healthy non-diabetic controls was recruited from a local school. The serum levels of a group of biochemical markers for bone formation and resorption were determined in both study groups, and BMD was measured by ultrasound absorptiometry.

Results: Thirty six children with T1DM and 39 normal children were included in this study. The results showed that 24/36 (66.7%) diabetic children had a Z score below zero. Of these, five scored below −1. In contrast, 12/39 (30.8%) children from the control group had a Z score below zero, but none had a score below −1. Significantly lower levels of osteocalcin and procollagen N-terminal peptide were detected in the diabetic group. The serum levels of bone resorption markers were significantly higher in the diabetic group.

* Corresponding address: College of Medicine, Taibah University, P.O. Box 879, Almadinah Almunawwarah, KSA.
E-mail: kkhoshhal@hotmail.com (K.I. Khoshhal)

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Conclusion: T1DM decreases BMD and some bone formation and increases some bone resorption biomarkers. BMD and bone markers are useful diagnostic tools for the early detection of alterations in the bone quality of children with T1DM. This, if treated in a timely manner, may decrease future bone fracture susceptibility.

Keywords: Bone mineral density; Osteoporosis; Osteocalcin; Quantitative ultrasound; Vitamin D

Introduction

Osteoporosis has become an alarming health problem throughout the entire world, and approximately 200 million people in the world are threatened by this deleterious disease.[1,2] Osteoporosis is often described as a silent disease because it is typically asymptomatic until a fracture occurs.[3] Like osteoporosis, diabetes mellitus (DM) is a pandemic and a chronic metabolic disorder. In fact, 374 million people in the world may suffer from diabetic complications.[3–6] As a chronic condition, DM adversely affects many different parts of the body including bones, nerves, muscles, eyes, and kidneys.[4] As increased rates of bone fractures and osteoporosis have been found among patients with type 1 DM (T1DM),[5,7–11] in both children[12,13] and adults,[14] and because the mechanisms of diabetic effects on bone cells are very complex, several researchers have described different mechanisms that showed how DM induces osteoporosis and bone fractures through multiple pathways.[6,14,15]

Bone marrow-derived endothelial progenitor cells (EPCs) play a significant role in bone healing.[5,16] DM was found to down-regulate the expression of EPCs through different mechanisms and thereby decrease bone formation at fracture sites.[5,17,18] DM is also responsible for the deposition of lipid in the bone marrow, thereby leading to the expansion of the marrow cavity and a decrease in the rate of blood flow to the bone, which is required for the transfer of nutrients.[5] The transformation of osteoblast to adipocyte leads to the reduction of osteoblasts available for bone formation.[5,19] It is known that DM is responsible for the over expression of advanced glycation end products (AGE) and has roles in bone rigidity.[20,21] Pancreatic β cells also produce other osteoporotic factors including amylin and preptin. Amylin and preptin induce bone formation and sequester bone resorption and reduce the apoptosis of osteoblasts.[4] Osteocalcin is a peptide that positively regulates osteogenesis. DM limits the production of osteocalcin through the negative regulation of osteoblasts by decreased synthesis of insulin, amylin and preptin.

Dual energy X-ray absorptiometry and peripheral quantitative computed tomography may be used to measure bone mineral density (BMD) in children who are exposed to an increased risk of osteoporosis in their adulthood, but both expose children to unnecessarily ionizing radiation, which is a limiting factor for preventive studies in children. Therefore, in recent years, quantitative ultrasound (QUS) methods have been developed to assess bone mineral status in some peripheral skeletal sites such as hand phalanges, tibia and calcaneus. QUS techniques are safe, easy to use, radiation-free, and come with portable devices so they are particularly suitable and indicated to assess bone mineral status in children.

The optimal use of bone marker measurement with assessment of BMD using QUS of the calcaneum in predicting osteoporosis has not yet been established. Therefore, the present study aims to investigate the levels of bone markers in plasma of children with T1DM in combination with their BMD.

Materials and Methods

Setting

This study was conducted in the Maternity and Children Hospital (MCH), Almadinah Almunawwarah, Kingdom of Saudi Arabia and was approved by the MCH research and ethics committee. The diabetes unit at MCH provides comprehensive services for children with DM up to the age of 12 years, and the city has one of the highest incidences of childhood T1DM in the world.[22]

Inclusion and exclusion criteria

Patients diagnosed with T1DM for 3 years or more without signs of puberty were included. We excluded patients with a history of fractures of less than 1 year and those with associated bone/joint problems, liver disease or patients on long-term steroid therapy. Patients with incomplete data were also excluded.

Control and diabetic groups

Informed written consent was obtained from all of the families of the participating children. All 36 T1DM patients were included from the Endocrine and Diabetes Unit, MCH, from February to May 2013. 39 age-matched healthy non-diabetic controls were recruited from a local school. The study included 75 children (age 4–12 years), with 49 males and 26 females. Biochemical markers for bone formation and resorption and QUS for BMD were utilized for all patients and the control group.

Measurement of bone mineral density (BMD)

BMD in the current study was measured using The Lunar Achilles (InSight, GE Healthcare, USA), which is a proven bone ultrasonometer to avoid exposing the children to unnecessarily ionizing radiation. In this study, BMD was measured using QUS of left calcaneum according to the method of Valerio et al.[23] All measurements were converted to Z-scores using a data bank for age-matched speed of sound values supplied by the manufacturer.