ELSEVIER

CrossMark

The Spine Journal 14 (2014) 1132–1138

THE SPINE JOURNAL

Clinical Study

Bone biomarkers in patients with chronic traumatic spinal cord injury

Hadis Sabour, MD, PhD[a], Abbas Norouzi Javidan, PhD[a,*], Sahar Latifi, MD[a], Bagher Larijani, MD[b], Farzad Shidfar, PhD[c], Mohammad Reza Vafa, PhD[c], Ramin Heshmat, MD, MPH, PhD[b], Hassan Emami Razavi, MD[a]

[a]*Brain and Spinal Injury (BASIR) Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Keshavarz Avenu, Tehran, Iran*
[b]*Endocrinology and Metabolism Research Institute (EMRI), Endocrinology Department, Tehran University of Medical Sciences, North Kargar St, Tehran, Iran*
[c]*Department of Nutrition, Iran University of Medical Sciences, Hemat Highway, Tehran, Iran*

Received 23 December 2012; revised 27 June 2013; accepted 25 July 2013

Abstract

BACKGROUND CONTEXT: Bone loss after spinal cord injury (SCI) occurs because of pathologic changes in osteoblastic and osteoclastic activities due to mechanical unloading. Some biochemical changes in bone metabolism after SCI are described before that were related to bone mineral loss.

PURPOSE: Our purpose was to determine bone markers' changes and related effective factors in patients with chronic traumatic SCI.

STUDY DESIGN: This investigation was designed as an observational cross-sectional study.

PATIENT SAMPLE: All patients with chronic SCI who were referred to Brain and Spinal Injury Research Center and did not meet our exclusion criteria entered the study.

OUTCOME MEASURES: Self-reporting measures including patient's demographic features and date of accident were obtained using a questionnaire and physiologic measures including spinal magnetic resonance imaging to determine the level of injury accompanied with physical examination along with dual-energy X-ray absorptiometry were performed. Blood samples were analyzed in the laboratory.

METHODS: Dual-energy X-ray was used to determine bone mineral density in femoral and spinal vertebrae bone sites. Serum level of C-telopeptide cross-linked Type 1 collagen (CTX), parathyroid hormone, calcitonin, osteocalcin, and bone alkaline phosphatase (BALP) were measured.

RESULTS: We detected a negative association between CTX level and bone mineral density in femoral and spinal bone sites that confirms that CTX is a bone resorption marker. C-telopeptide cross-linked Type 1 collagen and BALP levels did not show any significant correlation with post-duration injury. Patients with spinal injury at lumbar level had the highest calcitonin level ($p<.04$). C-telopeptide cross-linked Type 1 collagen was positively related with osteocalcin and BALP ($p<.0001$, $r=0.51$), and osteocalcin was positively related with BALP ($p<.0001$, $r=0.44$). Osteocalcin was related negatively only to femoral intertrochanteric zone bone mineral density.

CONCLUSIONS: Some bone biomarkers undergo noticeable changes after SCI. C-telopeptide cross-linked Type 1 collagen was positively correlated with BALP and osteocalcin that shows the coincidental occurrence of osteoblastic and osteoclastic activities. Our data also support this fact that although bone reduction after 2 years is slower than acute phase after SCI, bone resorption rate is higher than bone formation. These bone markers also revealed different site of action as osteocalcin level only affected femoral intertrochanteric bone mineral density. Generally, it seems that

FDA device/drug status: Not applicable.

Author disclosures: ***HS:*** Nothing to disclose. ***ANJ:*** Nothing to disclose. ***SL:*** Nothing to disclose. ***BL:*** Nothing to disclose. ***FS:*** Nothing to disclose. ***MRV:*** Nothing to disclose. ***RH:*** Nothing to disclose. ***HER:*** Nothing to disclose.

Funding of this study was provided by Tehran University of Medical Sciences and up to our knowledge no conflict of interest exists.

* Corresponding author. Brain and Spinal Injury Research (BASIR) Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Keshavarz Avenu, Tehran, Iran. Tel.: (98) 21-665-81560; fax: (98) 21-669-38885.

E-mail address: noroozia@tums.ac.ir (A. Norouzi Javidan)

http://dx.doi.org/10.1016/j.spinee.2013.07.475

the coincidental consideration of these factors that influence bone mineral density can lead to a better understanding of bone changes after SCI.

Keywords: Bone biomarkers; Bone mineral density; Spinal cord injury; Bone alkaline phosphatase

Introduction

Bone loss after spinal cord injury (SCI) is a known complication that starts immediately after injury and is described with a rapid progression in acute phase [1–4]. This reduction occurs because of mechanical unloading of sublesional areas along with biochemical changes in bone metabolism. Structural changes of collagen and neurovascular disorders are proposed etiologies for bone loss [5,6]. Some studies have shown the decreased level of parathyroid hormone (PTH) and 25-hydroxy vitamin D despite normal level of ionized calcium in long-standing spinal cord–injured patients, whereas calcitonin levels were increased [7]. Besides, some changes in bone resorption markers in SCI have been reported so far. Increased level of C-telopeptide cross-linked Type 1 collagen (CTX) in individuals with chronic SCI has been shown previously [8]. Osteocalcin, which is a specific parameter in bone formation has been shown to be increased in some studies [9], whereas other investigations showed decreased level of osteocalcin in patients with SCI [8]. These changes may vary through time as it has been shown that PTH levels remain lower than normal range in patients with SCI but increase gradually after the first year since injury [10]. Decreased level of ionized calcium, PTH, and osteocalcin accompanied with increased level of phosphorus and CTX has been reported so far [8]. Parathyroid hormone that influences bone metabolism undergoes some changes after SCI. Parathyroid hormone suppression is frequently reported [5,9], and persistent suppressed level of PTH has been observed even after 3 to 5 years since SCI [7]. All these changes lead to high incidence of pathologic fracture especially in femoral and proximal tibia because of higher bone demineralization in these sites [11–13]. Whereas CTX and urinary calcium present osteoclastic activity, bone alkaline phosphates and osteocalcin reflect bone formation. Osteocalcin has been used as a marker indicating mature osteoblastic activity and bone overall turnover. Despite all these facts, these correlations between bone mineral changes and bone indexes are compromised in SCI in which loss of interactions of neurohypophysis and serum fluid-electrolyte balance is proposed as an etiology [14]. Because our knowledge in bone marker changes after SCI is still so limited and by considering the potential predicting value of these markers to indicate fracture risk, further investigations of these markers are essential. Our purpose was to investigate bone biomarkers and their probable associations with bone mineral density in chronic cases of SCI, and we also tried to evaluate PTH and calcitonin changes.

Material and methods

Study design

We investigated patients with chronic traumatic SCI who were referred to Brain and Spinal Injury Research Center in a descriptive cross-sectional study. Written consent was obtained from each participant after explaining adequate information about the study. The study was approved by the research ethics committee of Tehran University of Medical Sciences.

Participants

Patients with chronic traumatic SCI who did not have the following exclusion criteria were asked to enter the study: pregnancy, lactation, any rehabilitation therapy, amputation, and nontraumatic SCI etiology. Patients with history of diabetes, cancer, endocrinology disease, acute infection, and use of special medications were also excluded.

Anthropometric measurements

We used questionnaire to obtain patients' demographic features such as gender, age, weight, height, body mass index (BMI), and injury duration. Body weight was measured using a digital wheelchair scale, and body height was obtained measuring the supine length. Body mass index was calculated as body weight (in kilograms) divided by height (in meters) squared.

Bone densitometry

Dual-energy X-ray was used to determine patients' bone mineral density using Lunar DPX-MD device (Lunar Corporation, Madison, WI, USA). According to the diagnostic categories of the World Health Organization/Osteoporosis Foundation, we defined osteoporosis as a T score of BMD more than −2.5 SD below the young adult mean, BMD between −1 and −2.5 SD was defined as osteopenia, and BMD within 1 SD (−1 to +1) of young adult mean was considered as normal. In patients with spinal implant, the involved lumbar vertebrae were excluded and the mean bone density of noninvolved vertebrae was entered into the analysis. Femoral bone mineral density was calculated in three bone sites including neck, trochanter, and intertrochanteric zone.

Clinical measures

Completeness was classified as either complete (no sensory or motor function preserved in the sacral segments