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Comparison of serum and urinary calcium profile of immobilized and ambulant trauma patients

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ABSTRACT

Background: Hypercalcemia occurs more frequently than is recognized in patients who are immobilized, but most of these patients are asymptomatic. This study is to determine serum and urinary calcium levels, incidence of hypercalcemia and hypercalciuria in immobilized and ambulant trauma patients.

Methods: A prospective comparative study was carried out over a period of seven months. Total serum calcium level and 24-hour urinary calcium output were measured weekly over 4 weeks in 55 immobilized trauma patients as study group and 51 ambulant trauma patients as control group.

Results: Mean total serum calcium of immobilized patients increased progressively (on admission: 2.315 ± 0.056 mmol/l and week 4: 2.552 ± 0.231 mmol/l, $p < .001$) while that of ambulant patients did not change significantly (on admission: 2.306 ± 0.041 mmol/l, and week 4: 2.300 ± 0.028 mmol/l, $p = .348$). There is a significant difference in overall mean total serum calcium between immobilized and ambulant patients ($p < .001$). In immobilized and ambulant patients, mean 24-hour urinary calcium increased progressively from baseline (3.044 ± 0.480 mmol/day and 3.056 ± 0.540 mmol/day respectively), till the end of the study (8.543 ± 2.142 mmol/day and 6.783 ± 1.372 mmol/day respectively). Overall mean 24-hour urinary calcium is significantly different between immobilized and ambulant patients {multivariate Pillai F (5,100) = 883.124, $p < .001$}. Incidence of hypercalcemia increased progressively in immobilized patients (end of week 1 = 7.27% and end of week 4 = 29.09%) while none of the ambulant patients had hypercalcemia. Incidence of hypercalciuria also increased progressively in immobilized patients (end of week 1 = 7.27% and end of week 4 = 63.64%) while ambulant patients only had hypercalciuria at the end of week 3 (9.8%) and week 4 (21.57%).

Conclusion: Mean total serum calcium increased with increased duration of immobilization in trauma patients. Both immobilized and ambulant trauma patients developed hypercalciuria but it is worse and earlier in the immobilized trauma patients.

Introduction

Calcium exists in three distinct pools in the body, and its metabolism is strictly regulated. The largest pool is in the skeleton, followed by the extracellular calcium pool and the intracellular space [1]. The homeostasis of calcium is complex; the bone, gastrointestinal tract, and kidney are all involved in calcium metabolism. Alteration of calcium homeostasis from any of these organ systems can lead to changes in the serum calcium level [2]. Disuse osteoporosis in clinical practice could result from prolonged immobilization with release of calcium into the extracellular fluid and the excess calcium is excreted mainly via the kidney. It has been noted that hypercalcemia occurs more frequently than is recognized in patients who are immobilized, but most of these patients are asymptomatic [3]. However, hypercalcemia and hypercalciuria secondary to immobilization can be occasionally severe, producing variety of symptoms: anorexia, constipation, nausea, vomiting, pruritus, seizures and respiratory arrest have been recorded [3]. In the first reported case of hypercalcemia due to immobilization by Albright et al. [4] in 1941, the patient was subjected to array of investigations and treatment including parathyroidectomy before the diagnosis was made as cited by Conley et al. [3], thereafter, Winters JL et al., Lawrence GD et al. and Dodd K et al. has reported similar cases [5–7].

Accidents and injuries are major public health problems worldwide [8]. Nigeria, the most populous country in Africa [8], has one of the highest road traffic accident rates in the world [9]. A significant number

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of victims of road traffic accidents in this environment are immobilized in the course of their treatment and they are prone to develop hypercalcemia and hypercalciuria. It is also a common practice in this environment, especially among the general medical practitioners, to administer calcium to patients with bone related problems.

This could worsen the background hypercalcemia.

There is paucity of studies on serum and urinary calcium profile of immobilized trauma patients. The aim of this study is to determine serum and urinary calcium levels, incidence of hypercalcemia and hypercalcuria in immobilized and ambulant trauma patients.

Materials and methods

Study design

This is a prospective comparative study designed to determine the effect of immobilization on serum and urinary calcium levels in trauma patients. The study was conducted at Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria. The hospital is located in southwestern Nigeria along the busy road networks linking southwestern Nigeria to the oil rich Niger Delta region and Abuja, the capital of Nigeria. The study group was trauma patients that required immobilization, that is the nature of injury and/or the need of treatment kept the patient in bed while the control group were trauma patients that ambulated immediately after skeletal stabilization. Ethical approval was obtained and the study was carried out over a period of seven months from October 2008 to April 2009.

Patient selection

Fifty eight consecutive patients with bony injury to the limb, that is anywhere from shoulder joint down to the fingers in the upper limb and anywhere from hip joint down to the toes in the lower limb, who required immobilization in bed for four weeks or more during the course of their treatment were recruited into the study group while fifty nine consecutive patients with bony injury to the limb who did not require immobilization in bed in the course of treatment were recruited into the control. Excluded from the study were: patients or parents of patients who refuse to give consent for the study; patients with metabolic bone disease; patients with primary or metastatic bone tumor; patients on steroid, calcium or vitamin D supplements; and patients with abnormal baseline serum or urinary calcium level.

Methods

The authors were informed when a trauma patient presented at the study center. The patient was resuscitated and evaluated and once stable, an informed consent was obtained from the patient or the parent/guardian. Patient's bio-data, medical and surgical history, drug history, history of the injury, and the affected limbs were entered into a structured information sheet. Patient was allocated to the study group when immobilized in bed and to the control group when ambulated immediately after skeletal stabilization.

Sample collection

The first samples collected were initiated within 24 h of presentation after an overnight fast to serve as the base-line values and subsequent samples were collected weekly. Ten milliliters (ml) of venous blood was collected from each of the patients without the use of tourniquet into a plain specimen bottle. The blood sample was processed and the serum separated. The serum of the first sample collected from patient was divided into five aliquots for serum electrolyte, urea, creatinine, calcium, phosphate, total protein and albumin analysis while subsequent weekly serum was divided into four aliquots for serum calcium, phosphate, total protein and albumin analysis The bottles were appropriately labeled for each patient.

Each patient had a 5 l plastic container for 24-hour urine sample collected once a week when blood sample was collected. The volume was noted and sample taken from the first 24-hour urine sample for urinalysis to screen for diabetes mellitus, which is a cause of polyuria that could occur if there is hypercalciuria. The remaining urine was processed to dissolve the calcium oxalate and a representative sample was taken into a universal bottle. The sample was appropriately labeled for each patient.

Both serum and urine samples were stored frozen at −20 °C in a deep freezer. The samples were analyzed in batches by the same laboratory scientists and each batch was under quality control. Serum and urinary calcium were estimated using o-Cresolphthalein Complexone (CPC) method [10]. Serum phosphate was estimated using Phosphomolybdate complex technique [11], serum total protein was estimated using biuret technique and serum albumin was estimated using Bromcresol green technique [12].

The analyses of the samples were done at the study center chemical pathology laboratory.

Data analysis

Data collected from the study were entered into a worksheet and analyzed using Statistical Package for Social Science (SPSS) software for window. Frequency distribution of the variables, means and standard deviations of the values were presented in tables and charts. Multivariate and univariate tests were used to compare mean values between the groups. The level of statistical significance was determined at $p < 0.05$.

Results

Over the study period, 626 patients presented at the study center following trauma. Four hundred and forty eight were males and one hundred and seventy eight were females, with male:female of 2.5:1.

One hundred and seventeen patients met the criteria for inclusion into the study, with 58 patients in the immobilized group and 59 patients in the ambulant group. However, only 106 (90%) patients completed the study with 55 patients in the immobilized group and 51 patients in the ambulant group, 8 (7%) dropped out of study, 2 (2%) took their discharge, and 1 (1%) died before the end of study.

The ages of the patients in the immobilized group ranged from 6 to 52 years and mean = 28.02 ± 12.56 years while that in the ambulant group ranged from 7 to 50 years and mean = 24.24 ± 11.89 years. No statistical significant difference in the mean age of the two groups (t(df = 104) = 1.589, p = .115). In the immobilized group, 35 (63.6%) were male (M) and 20 (36.4%) were female (F) with M: F = 1.75:1, while in the ambulant group, 41 (80.4%) were male and 10 (19.6%) were female with M: F = 4.1:1.

The serum electrolyte, urea and creatinine of all the patients recruited into the study and control group were within the laboratory normal reference range and none of the patients had glucose in their urine. The mean total serum protein and mean serum albumin of both groups were within the laboratory reference range during the study period.

More than half of the immobilized patients had femoral fractures (60%) while the ambulant patients had mainly humeral fracture (37.25%) and leg/foot injury (41.18%). The distribution of the immobilized and the ambulant patients by the site of the injury as shown in Tables 1 and 2, the immobilized patients had from one (56.4%) to five (5.5%) bones fractured while the ambulant patients had either one (52.9%) or two (47.1%) bones fractured.

From Table 3 and Fig. 1, the mean total serum calcium of the immobilized patients increased progressively (on admission: 2.315 ± 0.056 mmol/l and week 4: 2.552 ± 0.231 mmol/l, t(df = 54) = −7.783, p < .001) while that of ambulant patients did not change significantly (on admission: 2.306 ± 0.041 mmol/l, and week 4: 2.300 ± 0.028 mmol/l, t(df = 50) = .948, p = .348). Using multivariate test,