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Original research

Incidence of hypocalcemia and hypercalcemia in hospitalized patients: Is it changing?

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ABSTRACT

Disorders of calcium metabolism are frequently encountered in routine clinical practice. However limited data are available on the epidemiology of hypocalcemia and hypercalcemia in hospitalized patients. Our aim was to evaluate the frequency of hypocalcemia and hypercalcemia in hospitalized patients.

This is a retrospective study based on the laboratory results of all hospitalized subjects (n = 12,334) whose calcemia was determined between January 1st, 2011 and December 31st, 2014. Measurements of serum calcium were carried out by a single centralized laboratory. Hypocalcemia was defined as serum calcium levels < 8.2 mg/dl and hypercalcemia as serum calcium levels > 10.4 mg/dl. Albumin correction was applied to adjust serum calcium values.

Overall, hypocalcemia accounted for 27.72% (n = 3420) and hypercalcemia for 4.74% (n = 585) of the 12,334 inpatients. The highest prevalence of hypocalcemia was found in patients over 65 yr. (n = 2097, 61.31%) vs. younger subjects, while the highest prevalence of hypercalcemia was observed in patients aged 0–18 yr. (n = 380, 64.95%). Hypocalcemia was more often encountered in males (n = 1952, 57.07%) while no gender differences were found regarding hypercalcemia. Incidence of hypocalcemia changed over time varying from 35.42% (n = 1061) in 2011 to 21.93% (n = 672) in 2014 (r = −0.98; p = 0.01). Differently, incidence of hypercalcemia did not significantly increase significantly from 3.47% (n = 104) in 2011 to 6.92% (n = 211) in 2014 (r = 0.94; p = 0.052).

Despite increased awareness about electrolytes disturbance, physicians should consider calcium levels because of life-threatening consequences associated to hypo- and hypercalcemia. Patient's gender and age could be associated to a different risk of calcium disturbance in hospitalized patients.

Introduction

Calcium is the most abundant mineral in the body and participates with phosphorus to form calcium phosphate in bones and teeth. It is involved in many biological processes since it is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation and in several enzymatic processes [1,2].

As expected perturbation of calcium homeostasis may have a deep impact on human pathology [2]. Serum calcium levels are usually maintained within a normal range and ionized calcium is tightly regulated by the actions of parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (1,25$[OH]_2$D) on the kidney, bone and gastrointestinal tract [3,4].

PTH stimulates calcium release from bone and calcium resorption in the kidney, moreover it stimulates 1α-hydroxylation of 25-hydroxyvitamin D leading to the production of active 1,25-dihydroxyvitamin D (calcitriol) which modulates gastrointestinal calcium absorption [3].

In a clinical setting, either elevation (hypercalcemia) or reduction (hypocalcemia) of serum calcium concentrations could depend by several pathologies and could be associated with life-threatening consequences [2].

Increasing life expectancy and improvement of standard medical

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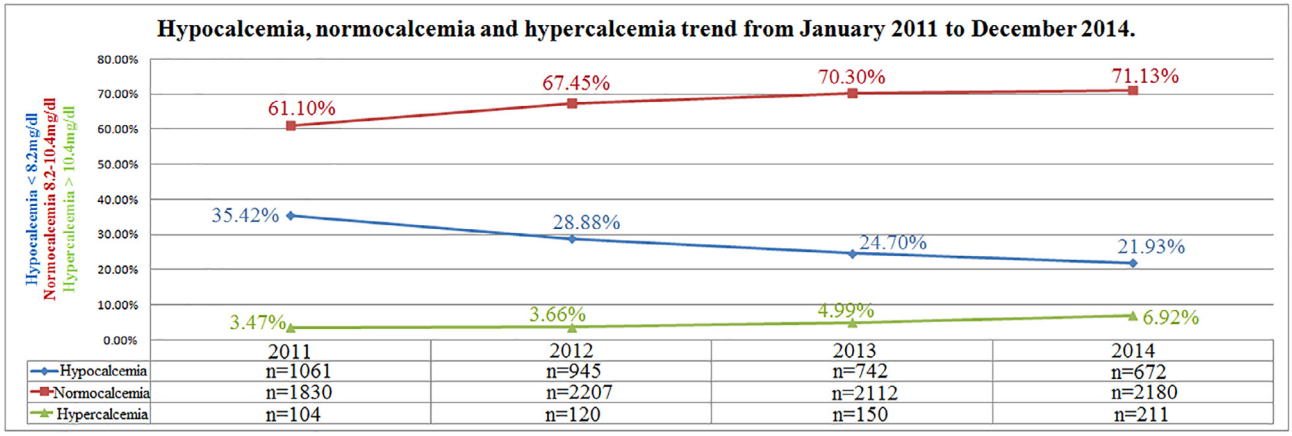

Fig. 1. Hypocalcemia, normocalcemia and hypercalcemia trend from January 2011 to December 2014.

care have modified the epidemiology of some human diseases (e.g. renal failure, cancer). Thus, the incidence of calcium related disorders could be challenging over time [5–8].

However, the prevalence of hypo- and hypercalcemia is dependent by the specific setting of patients [6–8].

Persistent hypercalcemia has been reported to occur in up to 1% of individuals in general population [9,10] whereas the prevalence of hypocalcemia in hospital setting has been observed up to 3% [10]. Differently, hypocalcemia has been described to reach a prevalence of 18% in hospitalized patients and up to 85% in the intensive care units [5].

The main aim of our study was to update the incidence of hypocalcemia and hypercalcemia in a large cohort of inpatients subjects. The secondary aim was to explore whether age and gender could be associated with serum calcium alterations.

Materials and methods

This is a retrospective study considering all the patients whose calcium concentrations were determined during hospital recovery at the University Hospital of Messina, Messina, Italy, over the period from January 2011 to December 2014. Any age and gender were considered.

Total calcium levels were detected by a Centralized Laboratory of our hospital through an automated analyzer (Roche Modular Analytics P 800). All the measurements were corrected with serum albumin levels in accordance with the formula: corrected serum calcium = measured calcium + [(4.1-albumin) × 0.8] if albumin is < 4.1 g/dl, or measured calcium − [(4.1-albumin) × 0.8] if albumin is > 4.1 g/dl [11,12].

Hypercalcemia was defined for calcium levels above 10.4 mg/dl, whereas hypocalcemia was defined for calcium levels under 8.2 mg/dl in accordance with the reference range of our Laboratory.

Recruited subjects came from multiple medical and surgical department clinics within our hospital.

The study was conducted in accordance with the ethical standards of our institutional research committee and with the 1964 Declaration of Helsinki and its later amendments. Written informed consent was not required. Statistical analyses were performed using MedCalc software (version 10.2.0.0; Mariakerke, 173 Belgium).

Statistical analyses were performed using MedCalc software (version 10.2.0.0; Mariakerke, 173 Belgium). The χ^2 test was performed to calculate differences in the proportion of categorical variables. Linear regression was used to describe changes of incidences over time. Values of $p < 0.05$ were considered to indicate statistical significance.

Results

In the period from January 1st, 2011 to December 31st, 2014 we evaluated a sample of 12,334 internal patients whose calcium level was measured. We found 27.72% (n = 3420) of patients showing hypocalcemia and 4.74% (n = 585) showing hypercalcemia. Concerning patients with hypocalcemia we observed 42.93% of cases (n = 1468) in females and 57.07% (n = 1952) in males ($\chi^2 = 136$, $p < 0.0001$). Adult subjects were more likely to exhibit low calcium levels: in fact, hypocalcemia was found in 61.31% (n = 2097) of subjects over 65 yr., in 33.3% (n = 1139) of subjects aged 19–65 yr., finally in 5.38% (n = 184) of subjects aged 0–18 yr. ($\chi^2 = 2407$, $p < 0.0001$). At the same time, we detected 585 cases of hypercalcemia of whom 50.95% (n = 298) were observed in female and 49.05% (n = 287) in male patients ($\chi^2 = 0.34$, $p = 0.55$). The higher incidence of hypercalcemia was found in subjects aged 0–18 (64.95%, n = 380), whereas in the age range19–65 yr. was 16.92% (n = 99) and in patients over 65 yr. (n = 106) was 18.11% ($\chi^2 = 395$, $p < 0.0001$).

Incidence of hypocalcemia changed over time varying from 35.42% (n = 1061) in 2011 to 21.93% (n = 672) in 2014 ($r = -0.98$; $p = 0.01$); differently, incidence of hypercalcemia increased from 3.47% (n = 104) in 2011 to 6.42% (n = 211) in 2014 ($r = 0.94$; $p = 0.052$); normocalcemia cases increased from 61.10% (n = 1830) in 2011 to 71.13% (n = 2180) in 2014 ($r = 0.93$; $p = 0.06$) (Fig. 1). Incidence of hypocalcemia according to gender was reduced during the observation period in both genders ($r = -0.96$, $p = 0.03$ and $r = -0.99$, $p = 0.006$ in females and males respectively) (Fig. 2). Differently, incidence of hypercalcemia increased over time in males ($r = 0.99$, $p = 0.006$) but not in females ($r = 0.67$, $p = 0.32$) (Fig. 3).

Distribution of cases of hypocalcemia according to age remained unchanged over time in the group of subjects in the age range 0–18 yr. ($r = -0.52$, $p = 0.47$) while in subjects between 19 and 65 yr. and in those ones over 65 yr. a reduction of cases was observed ($r = -0.96$, $p = 0.04$ and $r = -0.99$, $p = 0.007$, respectively) (Fig. 4). A tendency of increasing incidence of hypercalcemia was observed in the age ranges 0–18 yr. ($r = 0.92$, $p = 0.07$) and 19–65 yr. ($r = 0.97$, $p = 0.02$), while incidence of hypercalcemia remained unchanged in the subjects aged over 65 yr. ($r = 0.17$, $p = 0.82$) (Fig. 5).

Discussion

Our research study shows the temporal trend of serum calcium abnormalities observed in hospitalized patients. As known total calcium includes ionized calcium, protein-bound calcium and calcium complexed with inorganic and organic anions. Since about 80% of the protein-bound calcium is associated with albumin, albumin levels could influence calcemia. Thus we considered only patients whose calcium serum concentration was corrected taking in account albumin levels [11–13].

Hypo- and hypercalcemia are calcium disorders commonly observed