CLINICAL VIGNETTE

Ionized Calcium: When to Use in Patient Care

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Case presentation

A 49-year-old male with a history of systemic sclerosis and pulmonary hypertension presented with ARDS due to aspiration pneumonia. He was intubated, developed multi-organ failure, and subsequently underwent tracheostomy. Currently on hospital day 35, he was in stable yet critical condition as he continued to have high oxygen requirements.

Notable medications at this time include methylprednisolone, treprostinil, tadalafil, bosentan, and furosemide. His heart rate was 87 beats per minute, blood pressure was 99/64 mmHg, and he was breathing comfortably with oxygen saturation of 98% on 15 liters of high flow oxygen. Examination reveals a chronically ill appearing male. Significant findings include facial telangiectasias, diffuse rhonchi in the bilateral lung fields, and slight peri-umbilical abdominal tenderness. Laboratory studies are notable for: hemoglobin 8.5 g/dL (normal 13.5-17.1 g/dL) despite a transfusion of three units of packed red blood cells at the time of admission, creatinine 3.2 mg/dL (0.5-1.3 mg/dL), and ionized calcium 1.07 mmol/L (1.09-1.29 mmol/L). Prior routine daily labs have revealed persistent ionized hypocalcemia, which has not been treated with supplemental calcium.

Discussion

Circulating calcium is divided approximately evenly as either bound to negatively charged moieties (mostly albumin) or as a free, hydrated cation, known as "ionized calcium." Multiple studies have demonstrated that ionized hypocalcemia is highly prevalent in hospitalized patients. A prospective study comparing hospitalized patients against normal age- and sex-matched controls found a prevalence of 70%.[1] Hypocalcemia is even more common among critically ill patients, estimated between 85-88%.[2,3]

Etiology for the high prevalence is unclear. It is possible that a lower calcium homeostatic set-point is an acute phase response during illness.[4] For example in one study of more than 8,000 patients, mean ionized calcium was below normal in half of all patients. In patients with hypocalcemia, ionized calcium concentrations spontaneously increased towards this lower mean, and the increase was proportional to degree of hypocalcemia.[5] A Cochrane review found no benefit in supplementing calcium in hypocalcemic critically ill patients.[6]

Despite the limitations of total serum calcium as a proxy measurement for physiologically active calcium, guidelines do not recommend routine ionized calcium measurements for several reasons.[7,8] The marginal cost of an ionized calcium can be as high as $3.28 and more than 5 times the marginal cost of a serum calcium. Moreover, while other routine laboratory tests are automated, ionized calcium must be assayed manually and requires a full, separate vial of blood to minimize measurement error.[5]

Total calcium, included in a standard basic metabolic panel, can indirectly estimate ionized (free) calcium by adjusting for albumin levels. However, the diagnostic value of serum calcium in detecting hypo- or hypercalcemia can vary in specific patient populations, such as in patients receiving massive transfusions with end stage renal disease, hypercalcemia of malignancy, or primary hyperparathyroidism.

Given the inconsistencies of serum calcium in measuring bioactive calcium, particularly in special patient populations described above, an ionized calcium measurement can identify irregularities in calcium homeostasis undetected by total serum calcium.

However, routine measurements, such as daily morning labs for hospitalized patients, serve as a screening test. The high pretest probability of hypocalcemia in hospitalized patients and the lack of benefit in addressing detected abnormalities suggest that routine ionized calcium measurements are wasteful (Table 1).

Conclusion

Given the weaknesses of the total serum calcium (even after correction for albumin) as a diagnostic tool for both hypo- and hypercalcemia, it is not unreasonable to check an ionized calcium one time for screening purposes at medical centers with available laboratory resources. This test may identify asymptomatic primary hyperparathyroidism, hypercalcemia of malignancy, or hypercalcemia in renal disease patients secondary to treatment even in the setting of a normal corrected total calcium.

However, routine ionized calcium measurements in hospitalized patients will likely reveal hypocalcemia reflecting an acute phase response to illness that does not benefit from calcium supplementation. Given the financial cost, labor requirements, and additional blood loss to the patient, ionized calcium measurements for hospitalized patients should be reserved for particular occasions rather than as part of daily morning labs.

Table 1: Recommendations for using ionized calcium in patient care

- Check ionized calcium in symptomatic patients, particularly in those with metastatic cancer to bone, or multiple myeloma, or to screen for primary hyperparathyroidism
- Monitor ionized calcium for patients with advanced kidney disease if results will alter management of calcium-regulating medications
- Always monitor ionized calcium in patients who have received massive blood transfusions
- Do not routinely monitor ionized calcium in hospitalized patients, particularly critically ill patients

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