Original Article

Role of ionized calcium in critically ill patients

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Abstract

Background: Ionized calcium (iCa) is the calcium that is present in the blood in a free form and not attached to proteins. It is the physiologically active form of calcium. Abnormalities of ionized calcium concentration are common in critically ill patients and the vast majority of these abnormalities are due to hypocalcemia. **Aim and Objective:** The aim of the study was to see how ionized calcium values differ in critically ill patients before treatment compared to after treatment, it was done to show the importance of ionized calcium in critically ill patients as one of the marker of effectiveness of the treatment as well as to show how abnormally low values can be fatal. **Method:** The present study was conducted on 30 patients admitted to the ICU and 10 health check-up patients. Measurement of ionized calcium was done using ABL 800 Basic analyser and the values were correlated with parameters like magnesium, albumin, total calcium, creatinine, whole blood count and platelet count. **Results:** After analysing the data obtained it was observed that when ionized calcium was very low, the patient was in poor state and the prognosis was bad. After treatment, the ionized calcium levels improved. When ionized calcium was higher than the initial value, the patient was in a good state and the prognosis was good. **Conclusion:** The findings in the study suggest that ionized calcium can be considered as one of the markers in showing the effectiveness of treatment. In good prognosis the values of ionized calcium are raised while in bad prognosis hypocalcaemia is associated with mortality. A direct measurement of ionized calcium is a must for critically ill patients. Estimation of ionized calcium can be routinely done to check how a patient is responding to treatment.

Key Words: Calcium Ion Selective Electrode, Complete blood count (CBC), Hypocalcaemia, Ionized calcium.

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INTRODUCTION

Ionized calcium (iCa) is the calcium that is present in the blood in a free form and not attached to proteins. It is also called as free calcium. It is the physiologically active form of calcium which comprises approximately 45-50% of the total calcium in plasma. There might be a need to have a separate ionized calcium test if there are factors that increase or decrease total calcium levels. If abnormal levels of proteins, such as albumin, or immunoglobulins are present in the blood, it may be important to know the ionized calcium levels. A normal ionized calcium (iCa) concentration in blood is important to many fundamental physiologic regulatory mechanisms. However, abnormalities of ionized calcium concentration are common in critically ill patients and the vast majority of these abnormalities are due to hypocalcemia. Moritoki Egi *et al* in their past studies assessed the association of abnormalities of ionized calcium levels with mortality in a heterogeneous cohort of critically ill patients. Thus they concluded that extreme abnormalities of ionized calcium concentrations are independent predictors of mortality[1]. There was convincing evidence which demonstrates that ionized calcium and not total calcium is the physiologically relevant component of blood calcium. Because ionized calcium is the most important physiologic component of calcium and is controlled by stringent endocrine regulation, strategies either to measure it directly or to estimate it from measurements of total calcium have emerged. In the critical care setting, ionized calcium should be the routine measurement as well as where procedures such as continuous venovenous hemofiltration mandate the direct measurement of ionized

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calcium[2]. David F Westenkirchner *et al* undertook a study to determine the frequency and significance of abnormalities of ionized calcium in critically ill paediatric patients. They concluded that derangements in ionized calcium occur frequently in critically ill children and hypocalcemia is associated with increased mortality[3]. Zaloga GP *et al* in their past studies assessed calcium homeostasis in the critically ill surgical patients. Their studies state that hypocalcemia is a common problem in critically ill surgical patients and that direct measurement of serum ionized calcium is a good indicator of the clinical condition and prognosis of critically ill patients than measuring total calcium alone[4]. The aim of the present study was to see how ionized calcium values differ in critically ill patients before treatment compared to after treatment. It was done to show the importance of ionized calcium in critically ill patients as one of the marker of effectiveness of the treatment as well as to show how abnormally low values can be fatal and life threatening. Various biochemical parameters were taken into consideration while studying ionized calcium. Biochemical comparison was done to give a better view of the topic. The differences observed in the various parameters considered are being noted. This helped to give a better understanding of the topic and carry out research in systematic way to produce correct results and conclusions.

MATERIALS AND METHODS

The present study was conducted at Breach Candy Hospital on 30 patients admitted to the intensive care unit of the hospital and 10 health check-up patients (control group). Institutional Ethics Committee approval was taken before publishing this research paper. For analyzing serum Ionized calcium, direct measurement of ionized calcium is done using ion selective electrodes on a specialized instrument called ABL 800 Basic analyzer from Radiometer (Blood Gas Analyzer). The instrument is fully automated and thus gave direct values of ionized calcium; human errors are reduced in this test and the test was also useful in early detection of the patient's state. Ionized calcium values were analysed for each of the 40 patients in correlation with other parameters like magnesium, albumin, total calcium, creatinine, whole blood count and platelet count. 3-5 ml of the blood is collected in ready-made Green Top Sodium Heparin tube (BD Ltd India) to acquire plasma and Red top (plain tube) to acquire serum. ROTOFIX 32A is used to centrifuge the sample. The ionized calcium test was carried out on 40 patients using ion selective electrodes on Radiometer ABL 800 basic analyser. The parameters like magnesium, albumin, total calcium, creatinine, etc, were analyzed on the VITROS 5,1 FS chemistry system. The complete blood count (CBC) carried out on Symex XT-2000i. Auto check levels 1, 2, 3(from Radiometer Denmark) were used as quality control material. They are low, normal and high levels controls to check whether the levels of ionized calcium are up to the mark in our studies. Performance verifiers level 1 and 2 from Ortho Clinical Diagnostics were used as internal quality control materials for calcium, magnesium, albumin and creatinine. The external quality control material was EQAS from Bio-Rad Laboratories. A complete blood count (CBC) is a test that gives information about the cells in a patient's blood. The quality control material used was from Span Diagnostics (R and D). The external quality control is from Randox.

OBSERVATIONS AND RESULTS

Biochemical analysis of normal samples

In 10 normal health check-up patients, the value of ionized calcium was within the normal range. All the other parameters including magnesium, albumin, total calcium, creatinine, white blood count (WBC) and platelet count were also in the normal range. Hence, in healthy patients, with good clinical conditions, the ionized calcium is found within the normal range.

Table 1: Critically ill patients in ICU with high base line ionized calcium

Parameters	Control Group(n=10) Mean ± S.D	Patients with high base line ionized Ca (n=10) Mean ± S.D	P Value
Ionized Calcium	1.20 ± 0.047	1.09 ± 0.13	0.0216*
Albumin	4.25 ± 0.58	2.98 ± 0.94	0.0019*
Magnesium	1.82 ± 0.218	2.37 ± 0.43	0.0020*
Creatinine	0.83 ± 0.518	3.74 ± 2.16	0.0006*
Total calcium	9.65 ± 0.60	9.53 ± 2.48	0.8834 NS
White blood count	9.24 ± 4.04	16.99± 8.41	0.0171*
Platelet count	241.7 ± 72.27	161 ± 89.12	0.0392*

Results were compared at 5% level of significance

As seen in the above table, ionized calcium, albumin and platelet values were found decreased significantly as compared to control group. In malnourished and critically ill patients with cardiac arrhythmia who have hypoalbuminemia the corrected calcium is generally normal, however, the ionized calcium or the free calcium is low and administration of intravenous calcium gluconate or calcium chloride would help in correction of cardiac arrhythmia in such patients. Thus, ionized calcium is considered to be one of the markers in improving the clinical condition of such patients. 10

critically ill patients with high base line when treated with intravenous calcium gluconate and calcium chloride, responded well to the treatment and their clinical condition improved.

Table 2: Critically ill patients in icu with low base line ionized calcium

Parameters	Control Group(n=10) Mean ± S.D	Patients with low base line ionized Ca (n=10) Mean ± S.D	P Value
Ionized Calcium	1.20 ± 0.047	0.84* ± 0.09	0.0001*
Albumin	4.25 ± 0.58	2.5 ± 0.74	0.0001*
Magnesium	1.82 ± 0.218	2.37 ± 1.21	0.1742 NS
Creatinine	0.83 ± 0.518	2.36 ± 1.46	0.0059 *
Total calcium	9.65 ± 0.60	7.32 ± 0.86	0.0001*
White blood count	9.24 ± 4.04	11.78 ± 10.98	0.5011 NS
Platelet count	241.7 ± 72.27	110.6 ± 145.0	0.0197*

Results were compared at 5% level of significance

In 10 critically ill patients, the ionized calcium levels were abnormally low and these patients were suffering from severe hypocalcaemia. Total calcium and protein albumin was also lowered while magnesium was slightly on the higher side. These patients had raised creatinine and WBC levels. The platelet count was also low in these patients. These patients though treated with intravenous calcium gluconate and calcium chloride succumbed to the illness. The association between hypocalcaemia and mortality was highly significant ($p<0.001$). These patients did not respond to treatment.

Table 3: Biochemical analysis of patients with good prognosis (before treatment)

Parameters	Control Group(n=10) Mean ± S.D	Patients with good prognosis(before treatment) (n=10) Mean ± S.D	P Value
Ionized Calcium	1.20 ± 0.047	0.93 ± 0.20	0.0006*
Albumin	4.25 ± 0.58	3.32 ± 0.48	0.0010*
Magnesium	1.82 ± 0.218	1.92 ± 0.36	0.4621 NS
Creatinine	0.83 ± 0.518	1.67 ±1.79	0.1711 NS
Total calcium	9.65 ± 0.60	8.019 ± 1.61	0.0077*
White blood count	9.24 ± 4.04	14.6 ± 6.39	0.0378*
Platelet count	241.7 72.27	302.6 137.9	0.2320 NS

Results were compared at 5% level of significance

10 serum samples of patients with critical illness and prolonged ICU stay were subjected to ionized calcium test on Radiometer ABL 800 Basic analyzer. In these patients, the levels of ionized calcium were very low before treatment. The total calcium and albumin was also on the lower side, while the patients showed raised creatinine and WBC levels. As hypocalcaemia is common in critically ill surgical patients, these patients had low levels of ionized calcium.

Table 4: Biochemical analysis of patients with good prognosis (after treatment)

Parameters	Control Group(n=10) Mean ± S.D	Patients with good prognosis(after treatment) (n=10) Mean ± S.D	P Value
Ionized Calcium	1.20 ± 0.047	1.10* ± 0.107	0.0145*
Albumin	4.25 ± 0.58	3.52 ± 0.59	0.0121*
Magnesium	1.82 ± 0.218	1.91 ± 0.41	0.5476 NS
Creatinine	0.83 ± 0.518	1.07 ± 0.74	0.4118 NS
Total calcium	9.65 ± 0.60	9.11* ± 1.135	0.2001 NS
White blood count	9.24 ± 4.04	12.76 ± 4.429	0.0798 NS
Platelet count	241.7 ± 72.27	271.9 ± 90.243	0.4196 NS

Results were compared at 5% level of significance.

After treatment, the ionized calcium levels were improved. The values of all the other parameters - magnesium, albumin, total calcium, creatinine, and whole blood count (WBC) and platelet count were in the normal range after treatment. Thus, when ionized calcium was higher (improved) than the initial value the prognosis was good. The response to treatment in patients with good prognosis was statistically significant ($p<0.01$), as both, ionized calcium and total calcium values improved with treatment.

DISCUSSION

A normal ionized calcium (iCa) concentration in blood is important to many fundamental physiologic regulatory mechanisms. The present study was carried out to see how ionized calcium values differ in critically ill patients before treatment compared to after treatment, to show the importance of ionized calcium in critically ill patients as a marker of effectiveness of the treatment as well as to show how abnormally low values can be fatal and life threatening. In 30 patients with hypocalcaemia, 10 patients with severe hypocalcaemia were associated with ICU mortality. The probability of ICU mortality was high for patients with a mean ionized calcium value less than 0.85 mmol/L. The results were in accordance with the studies of Moritoki Egi *et al* which stated that an ionized calcium <0.8 mmol/L or an ionized calcium >1.4 mmol/L were independently associated with intensive care unit

and hospital mortality and that extreme abnormalities of ionized calcium concentrations are independent predictors of mortality[1]. The results obtained from the present study showed that patients with multi organ failure had normal levels of total calcium, while the ionized calcium levels were on the lower side. Also direct measurement of ionized calcium was done during this study which was more superior and sensitive to total calcium measurement. The results were in accordance with the studies of Laura M. Calvi *et al*[2] and Zaloga GP *et al*[4]. Their studies stated that direct measurement of ionized calcium was more sensitive than estimation of ionized calcium based on total calcium. David F Westenkirchner *et al* concluded that derangements in ionized calcium occur frequently in critically ill children and hypocalcemia is associated with increased mortality [3]. The results of the present study were in accordance with the study of David F Westenkirchner *et al*. In the present study that was carried out on 30 critically ill patients, 75% hypocalcemic patients had low albumin values. The results were in accordance with the studies conducted by Desai TK *et al*[5]. In case of multi organ failure, good prognosis and bad prognosis, the value of ionized calcium was low before treatment. The values of creatinine and WBC were raised, while the albumin and total calcium levels were lowered before treatment. When the values of ionized calcium were abnormally low, the patient was in poor state and the prognosis was bad. This hypocalcaemia was associated with mortality in patients. After the treatment, the values of ionized calcium improved. Though they did not fall within the normal range, they were higher than the initial values which indicated an improvement in the condition of the patient. All the other parameters like albumin, magnesium, total calcium, creatinine, WBC and platelet count were also normal after treatment. Thus when ionized calcium values improved with treatment, the patient was in good condition and the prognosis was good. In most of the critically ill patients, ionized calcium levels increased after treatment showing that ionized calcium is one of the markers that indicates the effectiveness of treatment. Also in patients with multi organ failure, though the ionized calcium levels fell outside the normal range, the total calcium levels were normal. This indicates that total calcium is a less accurate measure of calcium status and ionized calcium is the physiologically active form of calcium. Critically ill patients in the intensive care unit (ICU), such as those with infections and sepsis, pancreatitis, burns, or major trauma, are highly susceptible to hypocalcaemia. Because of its importance in maintaining cardiac output, arterial pressure, and systemic vascular resistance, adequate ionized calcium concentrations are especially important. Also hypocalcaemia has been associated with increased mortality in critically ill patients and hence normal serum ionized calcium levels are crucial to many aspects of physiologic stability.

CONCLUSION

The findings in the study suggest that ionized calcium can be considered as one of the markers in showing the effectiveness of treatment of critically ill patients. In good prognosis the values of ionized calcium are improved while in bad prognosis hypocalcaemia is associated with mortality. A direct measurement of ionized calcium is a must for critically ill patients. Estimation of ionized calcium can be routinely done to check how a patient is responding to treatment.

REFERENCES

1. Moritoki E, Inbyung K, Alistair N, Edward S, Craig JF, Graeme KH, Colin H, Michael B, Rinaldo B: Ionized calcium concentration and outcome in critical illness: Critical Care Medicine 2011;39(2):314-21.
2. Laura MC, David AB: When is it appropriate to order ionized calcium? : Journal of the American Society of Nephrology 2008; 19(7):1257-60.
3. Cynthia WB, Gregory LS and David FW: Significance of ionized calcium measurements in critically ill children: Pediatric Research 1987; 21(4):198A.
4. Zaloga GP, Chernow B, Cook D, Snyder R, Clapper M, O'Brian JT: Assessment of calcium homeostasis in the critically ill surgical patient: The diagnostic pitfalls of the McLean-Hastings nomogram. Annals of Surgery 1985; 202: 587 –94.
5. Desai TK, Carlson RW, Gaheb MA: Prevalence and clinical implications of Hypocalcaemia in acutely ill patients in a medical intensive care setting. American Journal of Medicine 1988; 84: 209-14.

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