

The APACHE II Score and Mortality in Relation to Hypocalcaemia in Critically Ill Patients

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ABSTRACT

Background: Electrolyte imbalance is commonly seen in the intensive care unit (ICU) patients. Hypocalcaemia is one of the most common electrolyte deficiencies found in these patients.

Methods: This study was conducted on 110 critically ill patients who were admitted to the ICU (71 males and 39 females). The patients were classified into two groups, group I (patients expired) and group II (patients completely recovered). We further sub-classified the patients, based on the APACHE II score into three groups as group A (APACHE II score <15), group B (APACHE II score 15-25) and group C (APACHE II score >25). The serum calcium, magnesium and albumin levels were determined by

using a clinical chemistry auto analyzer. Corrected calcium was calculated by using formula.

Type of study: Prospective/Retrospective

Results: There was a significant decrease in the calcium and the corrected calcium levels in the group I patients as compared to those in group II ($p < 0.05$). There was significant hypocalcaemia in the group C patients as compared to the group A and group B patients ($p < 0.01$). The calcium levels correlated negatively with the APACHE II score.

Conclusions: There is a direct correlation between hypocalcaemia and mortality in the critically ill patients. Hypocalcaemia and the APACHE II score were negatively correlated.

Key Words: Critical illness, APACHE II score, Mortality, Hypocalcaemia, Calcium, Corrected calcium, Electrolyte imbalance

INTRODUCTION

Electrolytes play a major role in most of the physiological processes, from maintaining electrical properties across the membranes to the release of many hormones and muscle contraction. Small electrolyte imbalances are very harmful to the human systems and have to be monitored very carefully in the patients. The assessment of the serum electrolyte values is of vital importance in caring for the critically ill patients [1, 2].

Hypocalcaemia is a common finding in the critically ill patients who are admitted to the adult as well as the paediatric intensive care units (ICU) [3-9] and in patients who are admitted with trauma [10, 11]. Critically ill surgical patients and leukaemic patients with infections have been shown to present with hypocalcaemia [12, 13]. The ionized and total calcium levels were also found to be lower in children with meningococcal infections and were found to be well related to the severity of the disease [14]. There are only few studies on the correlation between hypocalcaemia and mortality [6, 15].

In the current study, we determined the calcium, magnesium and albumin levels in all the critically ill patients who were admitted to the ICU, to find the correlation between these biomolecules and the mortality in these patients.

MATERIALS AND METHODS

A prospective study was conducted on 110 critically ill patients who were admitted in the ICU at the Kasturba Hospital, Manipal, India. The subjects included 71 males and 39 females in the age group of 14 to 80 years. The serum calcium [16, 17], magnesium [18-20] and albumin [21] levels were measured by using a clinical chemistry auto-analyzer (Magnesium-Roche Cobas Integra 400, Serum Calcium and Albumin-Hitachi 912). Corrected calcium i.e.

the total calcium which is bound to albumin and ionized calcium was also calculated by using the following formula: Corrected calcium = ionized calcium + $0.8 (4 - \text{albumin})$ [19]. The acute physiology and the chronic health evaluation (APACHE) II score were also assigned to be evaluated in all the patients.

Statistical analysis was done by using the SPSS, version 16 (Chicago, USA). The independent sample t test was used to compare the parameters with the mortality status of the patients. One way analysis of variance (ANOVA) was used, followed by multiple comparisons by the post-hoc test to compare the subdivision of the APACHE II score with the determined parameters. Pearson's correlation was used to correlate between the parameters.

RESULTS

We classified the 110 cases into two groups, group I as the expired cases and group II as the completely recovered cases. As depicted in [Table/Fig-1], there was a significant decrease in the calcium ($p < 0.05$) and the corrected calcium ($p < 0.05$) levels in group I as compared to those in group II. However, there was no significant difference in the magnesium and the albumin levels between these two groups.

We further classified the 110 cases into three subdivisions according to the APACHE II score: group A having an APACHE II score of <15, group B having an APACHE II score of 15-25 and group C having an APACHE II score of >25. As depicted in [Table/Fig-2], there was a significant decrease in the calcium ($p < 0.05$, $p < 0.001$) and the corrected calcium ($p < 0.05$, $p < 0.001$) levels in group C (93% of them were hypocalcaemic) and group B (75% of them were hypocalcaemic) as compared to those in group A (60% of them were hypocalcaemic), respectively. However, there was no significant difference in the calcium and the corrected calcium levels of group B and group C.

Categories	Calcium (mM/L)	Corrected Calcium (mM/L)	Magnesium (mM/L)	Albumin (g/L)
Group I (Expired)	1.956 ± 0.054*	2.071 ± 0.037*	0.702 ± 0.056	34.235 ± 1.484
Group II (completely recovered)	2.099 ± 0.025	2.195 ± 0.021	0.759 ± 0.019	35.247 ± 0.588

[Table/Fig-1]: Comparison between the determined parameters in expired and completely recovered patients expressed in (Mean ± SEM)

*(p < 0.05 when compared to completely recovered patients (group II))

Categories	Calcium (mM/L)	Corrected Calcium (mM/L)	Magnesium (mM/L)	Albumin (g/L)
Group A [APACHE II score (<15)]	2.177 ± 0.033* ^ψ	2.511 ± 0.030* ^ψ	0.743 ± 0.031	36.317 ± 0.798
Group B [APACHE II Score (15-25)]	2.511 ± 0.039	2.163 ± 0.029	0.764 ± 0.029	34.80 ± 0.977
Group C [APACHE II Score (>25)]	1.960 ± 0.039	2.085 ± 0.037	0.741 ± 0.040	33.758 ± 1.062

[Table/Fig-2]: Comparison between the determined parameters in different APACHE II score groups (Mean ± SEM)

^ψ(p<0.001 when compared to Group B), * (p<0.05 when compared to Group C)

On applying Pearson's correlation, the calcium ($r = -0.346$, $p < 0.001$) and the corrected calcium ($r = -0.324$, $p < 0.001$) levels were found to be correlated inversely with the APACHE II score (Table/Fig-1 and 2).

DISCUSSION

Hypocalcaemia is common among critically ill adults as well as in children and is associated with increased mortality. However, the mortality depends on the severity of the underlying chronic disease [7]. A number of critical cases like end stage renal disorder (ESRD), severe trauma, leukaemia and meningococcal infections have been found to be associated with hypocalcaemia [13-15].

Previous studies have reported hypocalcaemia in critically ill patients [3-5]. In line with the previous authors, we observed significant hypocalcaemia in the critically ill patients who expired as compared to the patients who completely recovered after the treatment ($p < 0.05$). The observation of hypocalcaemia in all the expired cases in our study, along with the reports of other authors raises the possibility of calcium playing a critical role in the electrolyte derangement in these patients. Changes in the physiological pH and in the albumin levels may cause an altered binding affinity of calcium to albumin [3]. We calculated the corrected calcium levels and considered the possibility of such an alteration in the current study. Previous authors had noted changes in the magnesium levels in critically ill patients [7]. However, we did not find any significant change in the magnesium levels in our study.

Previous authors used various systems for classifying the severity of the illness, like the base deficit, the systemic inflammatory response syndrome (SIRS) score, and the triage-revised trauma score (t-RTS) [10]. They reported a direct correlation between hypocalcaemia and increased mortality in the critically ill patients. The APACHE II score and the simplified acute physiology score (SAPS) are the most commonly used scoring systems to predict the outcomes in critical illness [16-22]. Recently, Iqbal M et al used the APACHE II score to classify the severity of the illness, they sub grouped the critically ill patients into three groups and reported that hypocalcaemia and disease severity (APACHE II scores) were negatively correlated [23]. Out of the 17 expired cases in the current study, 14 of them (82%) were in group C, having an APACHE II score of >25 and 13 out of the 14 who expired in group C (93%) had hypocalcaemia. These observations indicated that there was increased mortality with increasing APACHE scores and decreasing calcium levels.

In the current study, we used the APACHE II score to classify the critically ill patients. In line with Iqbal M et al's report, we observed that there was significant hypocalcaemia in the patients with an

APACHE score of >15, compared to the patients with an APACHE score of <15. On grouping, based on the APACHE II score, it was observed that group C (APACHE II score >25) have the lowest mean calcium and corrected calcium levels as compared to group A and group B, who had an APACHE II score of <15 and 15-25, respectively.

In conclusion, our study has shown a negative trend of hypocalcaemia with respect to the APACHE II score, and a direct positive correlation between hypocalcaemia and mortality in the critically ill patients. This study may help in checking for hypocalcaemia as an indicator of mortality in the critically ill patients. However, the pathophysiological cause effect mechanism has to be worked out by further consideration.

REFERENCES

- [1] Elgart HN. Assessment of fluids and electrolytes. *AACN Clin Issues* 2004; 15:607-21.
- [2] Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. *Am J Health Syst Pharm* 2005; 62:1663-82.
- [3] Lee JW. Fluid and electrolyte disturbances in critically ill patients. *Electrolyte Blood Press* 2010; 8(2):72-81.
- [4] Zivin JR, Gooley T, Zager RA, Ryan MJ. Hypocalcemia: a pervasive metabolic abnormality in the critically ill. *Am J Kidney Dis*. 2001; 37:689-98.
- [5] Hastbacka J, Pettila V. Prevalence and predictive value of ionized hypocalcemia among critically ill patients. *Acta Anaesthesiol Scand*. 2003; 47:1264-9.
- [6] Singhi SC, Singh J, Prasad R. Hypocalcaemia in a paediatric intensive care unit. *J Trop Pediatr*. 2003; 49:298-302.
- [7] Soliman HM, Mercan D, Lobo SS, Mélot C, Vincent JL. Development of ionized hypomagnesaemia is associated with higher mortality rates. *Crit Care Med*. 2003; 31(4):1082-7.
- [8] Singhi SC, Singh J, Prasad R. Hypocalcaemia in a paediatric intensive care unit. *J Trop Pediatr*. 2003; 49:298-302.
- [9] Egi M, Kim I, Nichol A, Stachowski E, French CJ, Hart GK et al., calcium concentration and outcome in critical illness. *Crit Care Med*. 2011; 39(2):314-21.
- [10] Choi YC, Hwang SY. The value of initial ionized calcium as a predictor of mortality and triage tool in adult trauma patients. *J Korean Med Sci*. 2008; 23:700-5.
- [11] Vivien B, Langeron O, Morell E, Devilliers C, Carli PA, Coriat P et al., Early hypocalcemia in severe trauma. *Crit Care Med*. 2005; 33:1946-52.
- [12] Iqbal M, Rehmani R, Hijazi M, Abdulaziz A, Kashif S. Hypocalcemia in a Saudi intensive care unit. *Ann Thorac Med*. 2008 Apr;3(2):57-9.
- [13] Yu HY, O'Brien JJ, Magnani B. Conflicting calcium concentrations in the presence of low albumin after bone marrow transplantation. *Clin Chem*. 2010; 56(11):1777-8.
- [14] Baines PB, Thomson AP, Fraser WD, Hart CA. Hypocalcaemia in severe meningococcal infections. *Arch Dis Child*. 2000; 83:510-3.
- [15] Miller JE, Kovesdy CP, Norris KC, Mehrotra R, Nissenson AR, Kopple JD et al., Association of cumulatively low or high serum calcium levels with mortality in long-term hemodialysis patients. *Am J Nephrol*. 2010; 32(5):403-13.

- [16] Gitelman, H.J.: An improved automated procedure for the determination of calcium in biological specimens. *Anal Biochem.* 1967; 18:521-531.
- [17] Gindler E M, King J D. The rapid colorimetric determination of calcium in biological fluids with methylthymol blue. *Am J Clin Pathol* 1972; 58:376-82.
- [18] Jacob R A. Trace elements. Teitz N W, ed. *Fundamentals of Clinical Chemistry*, 3rd ed. Philadelphia: W B Saunders; 1987: 517-532.
- [19] Ryan M F. The role of magnesium in clinical biochemistry: An overview. *Ann Clin Biochem* 1991; 28; 19-26.
- [20] Gauder W G, Narayanan S, Wisser H, Zawta B. List of Analytes; Pre-analytical variables. Brochure in: *Samples: From the patient to the laboratory*. Darmstadt, Verlag, 1996.
- [21] Teppo, A M.: Immunoturbidimetry of albumin and immunoglobulin G in urine. *Clin Chem* 1982; 28:1359-1361.
- [22] Kress J P, Hall J B. Respiratory critical care, *Critical care medicine*. In: *Principles of internal medicine*. 17th edition, McGraw Hill: Medical Publishing division: 2006, 1673-1674.
- [23] Iqbal M, Rehmani R, Hijazi M, Abdulaziz A, Kashif S. Hypocalcemia in a Saudi intensive care unit. *Ann Thorac Med* 2008; 3:57-9.

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