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Do Ionized Calcium and Phosphorus Levels have any Prognostic Value in Patients with ST-Segment Elevation Myocardial Infarction?

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Abstract

Introduction: The significance of serum calcium and phosphorus levels in patients with acute myocardial infarction is not entirely clear.

Objective: To assess the potential predictive value of ionized calcium (iCa) and phosphorus levels in acute ST-segment elevation myocardial infarction (STEMI) patients treated using primary percutaneous coronary intervention.

Design and Methods: A total of 256 patients included in the STEMI-RADIAL study were evaluated. Calcium and phosphorus levels were measured on admission, and after 6 h and 12 h. Correlations of these values with other laboratory and clinical parameters were assessed.

Results: Within the first 12 h of admission we observed a statistically significant increase in iCa and phosphorus levels; none of the patients received iCa or phosphorus supplementation. Hypocalcemia was present in 14% of patients at baseline and was associated with increased troponin I levels (P<0.0018). After adjustment for confounders, a higher left ventricular ejection fraction was associated with increased iCa levels after 12 h (P=0.010) and lower values of peak troponin I (P<0.0001) and C-reactive protein (CRP; P<0.006) levels. Baseline hypophosphatemia was associated with longer chest pain duration (P=0.044) and lower CRP levels after 24 h (P=0.040). The mortality rate of the group after one month and one year was 1.32% and 3.08%, respectively. Of the biochemical parameters studied, only the CRP level was associated with higher one-month mortality (odds ratio [OR] 4.01 [95% confidence interval (CI) 1.16 to 13.9]; P=0.029). Twelve-month mortality was associated with CRP level (OR 2.21 [95% CI 1.00 to 4.89]; P=0.049) and also patient age (OR 1.08 [95% CI 1.00 to 1.17]; P=0.045).

Conclusion: We did not find any prognostic value with regard to baseline levels of ionized calcium and phosphorus. We observed an association between iCa levels 12 h after admission and left ventricular systolic dysfunction in STEMI patients. However, the clinical relevance of this finding is not yet clear. Patients with longer chest pain duration had lower baseline phosphorus levels.

Keywords: Ionized calcium; Left ventricular ejection fraction; Phosphorus; STEMI; Troponin I

Abbreviations

BMI: Body Mass Index; CK: Creatine Kinase; CRP: C-Reactive Protein; Ica: Ionized Calcium; IHD: Ischemic Heart Disease; LVEF: Left Ventricular Ejection Fraction; PCI: Percutaneous Coronary Intervention; STEMI: ST-Segment Elevation Myocardial Infarction

Introduction

The significance of serum calcium and phosphorus levels in relation to myocardial necrosis markers, C-reactive protein (CRP) levels, and clinical presentation in acute myocardial infarction patients has not been fully established.

Hypocalcemia (ionized Ca [iCa] ≤ 1.12 mmol/L) is a relatively common problem in critically ill patients, particularly those with sepsis, acute necrotizing pancreatitis, rhabdomyolysis, trauma, and systemic inflammatory response syndrome [1-7], and the etiology appears to be multifactorial. Data published to date suggests several different mechanisms may be involved: (i) cytokine-mediated inflammatory response [8], (ii) increased binding to proteins (albumin) [9], (iii) relative parathormone deficiency, or (iv) reduced renal hydroxylase activity [10]; however, simple changes in bone metabolism and renal excretion are not considered viable options. An alkaline change acid-base balance is also a significant and well-known mechanism that can lead to hypocalcemia. Alkalosis induces hypocalcemia by promoting increased calcium binding to proteins. It has been reported that each 0.1 unit increase in pH leads to a decrease in iCa by approximately 0.05 mmol/L [11]. 'Significant' fluid replacement (especially Ca-free fluids) can also lead to dilutional hypocalcemia. It is also know that calcium supplementation, in

critically ill patients with reduced calcium levels, has been shown to increase systolic blood pressure and stroke volume [12].

Phosphorus metabolism is closely associated with calcium metabolism. Plasma phosphorus levels are also affected by pH, and alkalosis supports cellular uptake of phosphorus. Hypophosphatemia is classified as moderate (0.3 mmol/L to 0.7 mmol/L) or severe (<0.3 mmol/L). In critically ill patients, significant hypophosphatemia may contribute to rhabdomyolysis and leukocyte dysfunction as well as respiratory and heart failure [13-16]. Severe hypophosphatemia is typically observed in alcoholic patients, septic patients and patients with malnutrition or diabetic ketoacidosis, and is associated with an increased mortality risk [17,18]. Hypophosphatemia in patients with acute myocardial infarction may be caused by a stress response that requires addition energy and involves the transfer of phosphorus into cardio-myocytes, where it is transformed into adenosine triphosphate, which binds to the damaged cellular membranes of necrotic myocytes. Increased serum catecholamine levels or metabolic acidosis can also lead to increased phosphorus loss in the urine, which can lead to or contribute to hypophosphatemia [14,19]. A positive association between increased phosphorus levels and the severity of coronary angiography findings in patients with chronic ischemic heart disease, as well as risk of death, has been found in previous studies [20,21]. In our pilot study, hypophosphatemia was present more frequently in STEMI patients than in the control group, which was comprised of patients without acute coronary syndrome [22].

The objective of the present study was to establish calcium and phosphorus levels in the acute phase of STEMI, and to assess a possible association with laboratory markers of myocardial necrosis.

Material and Methods

Study population

The present study was a prespecified laboratory substudy of the multicenter randomized STEMI-RADIAL (ST-Elevation Myocardial Infarction treated by RADIAL or femoral approach) study [23]. The STEMI-RADIAL study compared radial and femoral PCI approaches in patients presenting, within 12 h of symptom onset, with an ST-segment elevation myocardial infarction (STEMI), who were then treated using primary percutaneous coronary intervention (PCI) performed by experienced surgeons familiar with both access sites. Neither calcium nor phosphorus was administered during the study period.

Age, years	61.20 ± 10.54
Male sex, n (%)	197 (77)
Body mass index, kg/m²	28.31 ± 4.10
Hypertension, n (%)	153 (60)
Dyslipidemia, n (%)	95 (37)
Diabetes mellitus, n (%)	46 (18)
Current smoker, n (%)	158 (62)
Previous MI, n (%)	28 (11)
Previous stroke, n (%)	8 (3)
Symptoms to balloon, min	205 (148-285)
Anterior MI, n (%)	105 (41)
Inferior MI, n (%)	116 (45.3)
Lateral MI, n (%)	34 (13.3)
Posterior MI, n (%)	1 (0.4)

Table 1: Basic characteristics of the study participants (n=256). Data presented as mean ± standard deviation or median (interquartile range), unless otherwise indicated. MI: Myocardial Infarction.

The present substudy included 286 patients in one (Pilsen, Czech Republic) of four participating centres (patients were enrolled between October 2009 and February 2012). Six patients with normal coronary angiography findings and 24 patients with incomplete laboratory results were excluded; thus, a total of 256 patients were included in the final evaluation. The relationships among left ventricular ejection fraction (LVEF) and various laboratory parameters were assessed in 228 patients (28 patients with a history of ischemic heart disease were excluded from echocardiography analysis). The study was approved by the local ethics committee. Written informed consent was obtained in the catheterization laboratory immediately before the invasive procedure.

Laboratory

Levels of phosphorus and iCa were measured before coronary angiography, and 6 h and 12 h after the procedure. Acid-base values were measured on admission and after 12 h. Troponin I and creatine kinase (CK) levels were measured on admission and after 6 h and 12 h; baseline and peak values are presented in Table 3 and 4. Myoglobin and lactate levels were determined at baseline. CRP levels were evaluated in blood samples obtained 24 h after admission. Cardiac troponin I was determined using a chemiluminescent assay kit (STAT Troponin I; Abbott Laboratories Chicago, Illinois, USA) on an Architect i-2000 immunoassay analyzer (Abbott).

Levels of CK, total calcium, inorganic phosphorus, myoglobin, and CRP were measured using an Olympus AU 400 (Beckman Coulter, Prague, Czech Republic). Levels of iCa, lactate and pH were measured using a blood gas analyser (Radiometer, ABL 800, Kobenhavn, Denmark). For the study, reference ranges were set as 2.2 mmol/L to 2.6 mmol/L for total calcium, 1.13 mmol/L to 1.32 mmol/L for iCa and 0.7 mmol/L to 1.6 mmol/L for phosphorus.

Echocardiography was performed four to seven days after the STEMI event.

Statistical analysis

SAS version 9.3 software (SAS Institute Inc., Cary, North Carolina, USA) was used to perform all statistical analyses. The characteristics of the study population and laboratory parameters are presented as mean ± standard deviation, median and interquartile range, or as a percentage. We compared means and proportions using a standard paired Student's t test, Kruskal-Wallis test and Fisher's exact test, respectively. To perform regression analysis, variables with distributions skewed to the right were normalized using logarithmic transformation. We performed single and stepwise linear (left ventricular ejection fraction, CRP) and stepwise logistic (mortality) regression to identify correlates of the outcome variables. In further

analyses we investigated whether the change in iCa levels over time might be associated with LVEF.

Results

The basic characteristics of the study group, existing comorbidities, location of the infarction and time from the onset of chest pain to the opening of the coronary artery are presented in Table 1. There was a statistically significant increase in iCa (P=0.0009) and phosphorus levels (P<0.0001) after 6 h and 12 h (recall that there was no calcium or phosphorus supplementation (Table 2)). It should be noted that pH decreased over the first twelve hours after admission (P=0.0007). Reduced baseline iCa levels (<1.13 mmol/L) were observed in 36 (14%) patients; these patients were compared with patients who had normal iCa levels on admission (Table 3). Of the studied variables, only baseline troponin I levels were higher in patients with reduced baseline iCa levels compared to patients with normocalcemia. Baseline hypophosphatemia (<0.70 mmol/L) was present in 76 (30%) patients (Table 4). Patients with baseline hypophosphatemia were younger (P=0.036), had longer durations of chest pain (P=0.044), and lower CRP levels (P=0.040).

	Baseline	After 6 h	After 12 h	P for trend
Calcium, mmol/L	2.34 ± 0.11	2.30 ± 0.09	2.30 ± 0.12	0.0003
iCa, mmol/L	1.17 ± 0.06	1.19 ± 0.09	1.19 ± 0.06	0.0009
Phosphorus, mmol/L	0.84 ± 0.24	1.10 ± 0.25	1.07 ± 0.22	<0.0001

Table 2: Biochemical parameters and changes over time. iCa: Ionized Calcium.

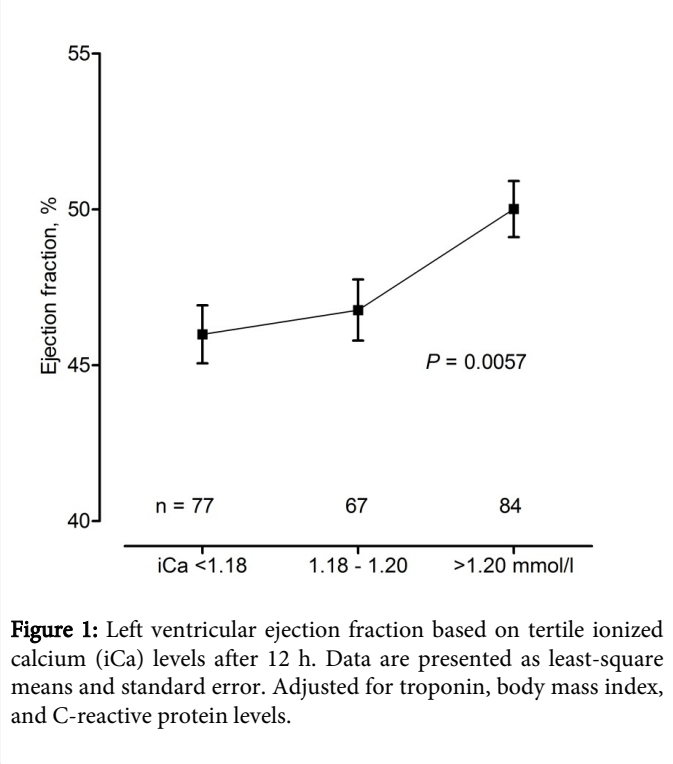

Figure 1: Left ventricular ejection fraction based on tertile ionized calcium (iCa) levels after 12 h. Data are presented as least-square means and standard error. Adjusted for troponin, body mass index, and C-reactive protein levels.

	Baseline iCa<1.13 mmol/L (n=36)	Baseline iCa ≥ 1.13 mmol/L (n=220)	P
Age, years	60.55±8.67	61.19 ± 11.19	0.69
CRP after 24 h, mg/L	13 (4-23)	9 (4-18)	0.23
Symptoms to balloon, min	197 (145-262)	209 (150-287)	0.21
Baseline TnI, µg/L	1.40 (0.25-3.92)	0.18 (0.05-1.35)	0.0018
Peak TnI, µg/L	79.0 (18.0-186.5)	64.87 (19.0-114.4)	0.27
Lactate, mmol/L	1.95 (1.25-2.95)	1.80 (1.30-2.4)	0.48
LVEF, %	45.93 ± 9.92	48.68 ± 9.70	0.16
Baseline creatinine, µmol/L	103.0 (81.5-108.0)	96.0 (87.0-108.0)	0.66
One-month mortality, n (%)	1 (2.8)	3 (1.4)	0.46
Twelve-month mortality, n (%)	2 (5.6)	7 (3.2)	0.62

Table 3: Characteristics of the study participants relative to baseline ionized calcium (iCa) levels. Data are presented as mean ± standard deviation or median (interquartile range), unless otherwise indicated. The P for differences between the groups was calculated using the Student's t test, Kruskal-Wallis test and Fisher's exact test. Bolded values indicate statistical significance. CRP: C-Reactive Protein; LVEF: Left Ventricular Ejection Fraction; TnI: Troponin I.

We also investigated determinants of left ventricular ejection fraction and mortality. In the multivariate linear regression analysis, higher LVEF were associated with lower peak troponin I (P<0.0001), larger body mass indexes (BMI; P=0.033), and higher iCa levels after 12 h (P=0.039; Table 5). The relationship between LVEF and iCa levels was also confirmed in an analysis in which the group was divided into tertile levels relative to iCa (Figure 1). After adjusting for troponin I, CRP, and BMI, the patients with the lowest iCa levels had the lowest LVEF.

The mortality rate of the group after one month was 1.32%. Of the biochemical parameters studied, only higher CRP was associated with higher mortality. The twelve-month mortality was 3.08% and was associated with higher CRP levels, age, and with marginally higher serum creatinine levels.

Additionally, we examined whether the increase in iCa over a 12 h period was associated with changes in LVEF. After adjusting for troponin I and CRP levels, BMI and baseline iCa levels, patients with the lowest ratio of iCa increase (1st tertile, iCa ratio after 12 h/baseline iCa level ≤ 1.0081) had lower LVEF than patients who experienced a steeper increase in iCa (3rd tertile, iCa ratio after 12 h/baseline iCa level ≥ 1.0261), LVEF 47.1% ± 1.0% versus 49.9% ± 1.1%, P=0.029.

After adjusting for confounders, higher iCa after 12 h was correlated with lower CRP (P=0.010) and peak CK levels (P=0.014). A similar trend was observed for the relationship between iCa levels and peak troponin I levels (P=0.061). Neither baseline iCa levels (P ≥ 0.058) nor change in iCa levels over time (P ≥ 0.35) affected these biochemical parameters.

Discussion

In our study involving STEMI patients treated using primary PCI we found a statistically significant increase in iCa and phosphorus levels during the first 12 h of hospitalization. Patients with baseline hypocalcemia had higher baseline troponin I levels, but we did not observe a correlation with peak troponin I levels or LVEF and baseline iCa. A statistically significant association between iCa levels and LVEF was found 12 h after admission. However, the clinical relevance of this association is not yet clear.

	Baseline P<0.7 mmol/L (n=76)	Baseline P ≥ 0.7 mmol/L (n=180)	P
Age, years	58.9 ± 11.2	62.0 ± 10.6	0.036
CRP after 24 h, mg/L	7.5 (3.0-14.0)	10 (4-23)	0.04
Symptoms to balloon, min	232 (161-310)	199 (145-273)	0.044
Baseline TnI, µg/L	0.14 (0.06-1.35)	0.30 (0.05-2.04)	0.25
Peak TnI, µg/L	60.3 (17.0-117.9)	71.0 (20.1-126.8)	0.59
Lactate, mmol/L	1.8 (1.3-2.6)	1.7 (1.3-2.4)	0.37
LVEF, %	48.8 ± 9.4	48.1 ± 9.9	0.62
Baseline creatinine, µmol/L	97.0 (85.5-110.0)	96.5 (86.5-106.5)	0.76
One month mortality, n (%)	1 (1.3)	3 (1.7)	0.99
Twelve-month Mortality, n (%)	1 (1.3)	8 (4.4)	0.29

Table 4: Characteristics of the group relative to baseline phosphorus levels. Bolded values indicate statistical significance. CRP: C-Reactive Protein; LVEF: Left Ventricular Ejection Fraction; TnI: Troponin I.

	β ± SE	P
Peak troponin I, µg/L	-3.30 ± 0.40	<0.0001
iCa after 12 h, mmol/L	18.82 ± 9.09	0.039
C-reactive protein, mg/L	-0.98 ± 0.51	0.054
Body mass index, kg/m²	0.30 ± 0.14	0.033

Table 5: Determinants of left ventricular ejection fraction. β=Regression coefficient; iCa: Ionized Calcium; SE: Standard Error.

Xin Lu et al. [24] analyzed baseline calcium levels in 1,431 STEMI patients. In patients with reduced calcium levels, they found higher hospital mortality (hazard ratio 0.267 [95% CI 0.164 to 0.433]; P<0.001). In our study, we measured total calcium and iCa levels; however, unlike the results reported by Xin Lu et al., neither baseline iCa levels nor iCa levels after 12 h, were associated with hospital mortality. After 12 h we found that iCa levels were significantly positively correlated with LVEF and negatively correlated with myocardial necrosis markers in our study. As success rate of primary PCI in our study was very high (TIMI flow ≥ than 2 was achieved in 98.6% of patients), it is not likely that our findings might be affected by the results of intervention procedure.

We can only speculate that the cause of reduced calcium levels during the first several hours after an acute myocardial infarction may be the result of an increased concentration of intracellular calcium in blood platelets and platelet aggregation during coronary thrombus formation [25]. The administration of dual antiplatelet therapy (acetylsalicylic acid and clopidogrel in our study) together with coronary revascularization is the likely cause of the subsequent rise in calcemia after 6 h and 12 h. An elevation of iCa levels in the cytosol of platelets, after stimulation by an agonist, is essential for proper platelet activation and the subsequent cascade of events associated with hemostasis and the immune response. In addition to known sources of iCa (dense granules), a significant influx of iCa through the platelet plasma membranes has been observed in recent years. A series of mechanisms mediating this transit of bivalent calcium ions have been described [25]. Despite this information, a firm connection cannot be made between the ongoing or completed thrombosis of a coronary artery (or other locations) and mild hypocalcemia. As previously mentioned, the etiology of this phenomenon is likely multifactorial and involves many variables.

Our previous pilot study showed that STEMI patients exhibited hypophosphatemia more frequently than a control group of non-myocardial infarction patients on admission to the intensive cardiac care unit; in all patients with baseline hypophosphatemia, the value normalized within the subsequent 6 h [26]. It is possible that renal function may have had an impact on phosphatemia. In the present study, we did not see any differences in baseline phosphorus levels relative to creatinine levels. We also observed that at admission, hypophosphatemia was unrelated to myocardial necrosis markers or LVEF. However, baseline hypophosphatemia was more often associated with longer chest pain duration and was also associated with lower CRP levels after 24 h. CRP has been shown to be an independent predictor of increased 14-day mortality in acute myocardial infarction patients [27].

While not numerous, there have been other studies that monitored phosphorus levels in myocardial infarction patients. Gould et al. [28] described a significant drop in phosphorus levels on the third and fourth post-infarction days compared with a control group. In contrast, the difference between the groups on the first day of hospitalization was not significant. Ognibene et al. [29] found a positive association between reduced phosphorus and bicarbonate levels in relation to the incidence of coronary arrhythmia in myocardial infarction patients. In 2000, while monitoring phosphorus levels in acute myocardial infarction patients, Vaidyanathan et al. [30] found an association between hypophosphatemia and left ventricular systolic dysfunction as well as 30-day mortality. In our study however, left ventricular systolic dysfunction, after 12 h, was associated with decreased iCa levels but not decreased phosphorus levels.

Acetylsalicylic acid administered in the early phase of acute coronary syndrome has a protective impact on myocardial high-energy phosphates during ischemia and reperfusion [28] and indirectly reduces phosphatemia by inducing respiratory alkalosis [31,32]. In our study, all patients were given dual antiplatelet therapy before the baseline sample was obtained, which may have had an impact on phosphatemia.

Conclusion

Baseline hypocalcemia in STEMI patients treated with primary PCI was associated with higher baseline, but not peak, troponin I levels. It was also observed that hypocalcemia 12 hours after admission was associated with left ventricular systolic dysfunction. Additionally, lower baseline phosphorus levels were observed in patients with longer

chest pain duration. Further studies are needed to elucidate role of ionized calcium and phosphorus in STEMI patients.

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References

1. Hadjis T, Grieff M, Lockhat D, Kaye M (1993) Calcium metabolism in acute renal failure due to rhabdomyolysis. Clin Nephrol 39: 22-27.
2. Müller B, Becker KL, Kränzlin M, Schächinger H, Huber PR, et al. (2000) Disordered calcium homeostasis of sepsis: association with calcitonin precursors. Eur J Clin Invest 30: 823-831.
3. Cherry RA, Bradburn E, Carney DE, Shaffer ML, Gabbay RA, et al. (2006) Do early ionized calcium levels really matter in trauma patients? J Trauma 61: 774-779.
4. Szyfelbein SK, Drop LJ, Martyn JA (1981) Persistent ionized hypocalcemia in patients during resuscitation and recovery phases of body burns. Crit Care Med 9: 454-458.
5. Hästbacka J, Pettilä V (2003) Prevalence and predictive value of ionized hypocalcemia among critically ill patients. Acta Anaesthesiol Scand 47: 1264-1269.
6. Frick TW (2012) The role of calcium in acute pancreatitis. Surgery 152: S157-163.
7. Choi YC, Hwang SY (2008) The value of initial ionized calcium as a predictor of mortality and triage tool in adult trauma patients. J Korean Med Sci 23: 700-705.
8. Lind L, Carlstedt F, Rastad J, Stiernström H, Stridsberg M, et al. (2000) Hypocalcemia and parathyroid hormone secretion in critically ill patients. Crit Care Med 28: 93-99.
9. Zaloga GP, Chernow B, Cook D, Snyder R, Clapper M, et al. (1985) Assessment of calcium homeostasis in the critically ill surgical patient. The diagnostic pitfalls of the McLean-Hastings nomogram. Ann Surg 202: 587-594.
10. Zaloga GP, Chernow B (1987) The multifactorial basis for hypocalcemia during sepsis. Studies of the parathyroid hormone-vitamin D axis. Ann Intern Med 107: 36-41.
11. Wang S, McDonnell EH, Sedor FA, Toffaletti JG (2002) pH effects on measurements of ionized calcium and ionized magnesium in blood. Arch Pathol Lab Med 126: 947-950.
12. Vincent JL, Bredas P, Jankowski S, Kahn RJ (1995) Correction of hypocalcaemia in the critically ill: what is the haemodynamic benefit? Intensive Care Med 21: 838-841.
13. Gaasbeek A, Meinders AE (2005) Hypophosphatemia: an update on its etiology and treatment. Am J Med 118: 1094-1101.
14. Geerse DA, Bindels AJ, Kuiper MA, Roos AN, Spronk PE, et al. (2010) Treatment of hypophosphatemia in the intensive care unit: a review. Crit Care 14: R147.
15. Amanzadeh J, Reilly RF Jr (2006) Hypophosphatemia: an evidence-based approach to its clinical consequences and management. Nat Clin Pract Nephrol 2: 136-148.
16. O'Connor LR, Wheeler WS, Bethune JE (1977) Effect of hypophosphatemia on myocardial performance in man. N Engl J Med 297: 901-903.
17. Camp MA, Allon M (1990) Severe hypophosphatemia in hospitalized patients. Miner Electrolyte Metab 16: 365-368.
18. Shor R, Halabe A, Rishver S, Tilis Y, Matas Z, et al. (2006) Severe hypophosphatemia in sepsis as a mortality predictor. Ann Clin Lab Sci 36: 67-72.
19. Kjeldsen SE, Moan A, Petrin J, Weder AB, Julius S (1996) Effects of increased arterial epinephrine on insulin, glucose and phosphate. Blood Press 5: 27-31.
20. Narang R, Ridout D, Nonis C, Kooner JS (1997) Serum calcium, phosphorus and albumin levels in relation to the angiographic severity of coronary artery disease. Int J Cardiol 60: 73-79.
21. Tonelli M, Sacks F, Pfeffer M, Gao Z, Curhan G; Cholesterol And Recurrent Events Trial Investigators (2005) Relation between serum phosphate level and cardiovascular event rate in people with coronary disease. Circulation 112: 2627-2633.
22. Khetagurov AD (1963) Changes in the calcium and inorganic phosphorus of the blood in patients with acute myocardial infarct developing after coronary thrombosis. Terapevtichesky Arkhiv 35: 15-20.
23. Bernat I, Horak D, Stasek J, Mates M, Pesek J, et al. (2014) ST-segment elevation myocardial infarction treated by radial or femoral approach in a multicenter randomized clinical trial: the STEMI-RADIAL trial. J Am Coll Cardiol 63: 964-972.
24. Lu X Wang Y, Meng H, Chen P, Huang Y, et al. (2014) Association of admission serum calcium levels and in-hospital mortality in patients with acute ST-elevated myocardial infarction: an eight-year, single-center study in China. PLoS One 9: e99895.
25. Varga-Szabo D, Braun A, Nieswandt B (2009) Calcium signaling in platelets. J Thromb Haemost 7: 1057-1066.
26. Lhotska J, Pechman V, Cech J, Hromádka M, Opatrny J, et al. (2012) Early phosphatemia changes in acute cardiac care patients. Cor et Vasa 54: e232-e236.
27. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, et al. (1998) C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes: A TIMI 11A substudy. J Am Coll Cardiol 31: 1460-1465.
28. Gould L, Reddy CV, Swamy CR, Oh KC, Kim SG (1979) Decline of serum phosphorus in acute myocardial infarction. Angiology 30: 219-222.
29. Ognibene A, Ciniglio R, Greifenstein A, Jarjoura D, Cugino A, et al. (1994) Ventricular tachycardia in acute myocardial infarction: the role of hypophosphatemia. South Med J 87: 65-69.
30. Vaidyanathan D, Venkatesan S, Ramadesikan VK (2000) Serum phosphate in acute myocardial infarction. Indian J Physiol Pharmacol 44: 225-228.
31. Gomaa AA, Hassan HA, Ghaneimah SA (1990) Effect of aspirin and indomethacin on the serum and urinary calcium, magnesium and phosphate. Pharmacol Res 22: 59-70.
32. Buckley MS, Leblanc JM, Cawley MJ (2010) Electrolyte disturbances associated with commonly prescribed medications in the intensive care unit. Crit Care Med 38: S253-264.