Changes in serum electrolyte levels and their influence on the incidence of atrial fibrillation after coronary artery bypass grafting surgery

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Key words: *atrial fibrillation, serum electrolyte balance, coronary artery bypass grafting.*

Summary. *Objective. Our study was designed to assess the incidence of atrial fibrillation, changes of serum electrolyte concentrations following coronary artery bypass grafting surgery.*

Material and methods. After approval of Kaunas Region Ethics Committee for Biomedical Research and written informed consent of the patients the data of 82 patients undergoing elective coronary artery bypass grafting surgery in Kaunas Heart Center, Clinic of Cardiac Surgery, during the period of 2004–2005 were analyzed. Serum potassium, sodium, ionized magnesium, ionized calcium, chloride and phosphate levels were measured before cardiopulmonary bypass, on arrival to intensive care unit and 18–20 hours after the surgery. Cardiac rhythm was monitored throughout the study. All patients were divided into two groups. Group I (n=22) included patients with postoperative atrial fibrillation. Group II (n=60) included patients, who remained in sinus rhythm after the surgery.

Results. The overall incidence of atrial fibrillation was 26.83%. The patients in group I were significantly older than in group II (68.27±6.09 and 64.20±9.32 years, respectively; p=0.025). Immediately after the surgery serum chloride concentration was higher in group I comparing to group II (111.91±4.48 and 105.17±5.73 mmol/l, respectively; p<0.001). Serum phosphate level was lower in group I (0.98±0.15 and 1.09±0.19 mmol/l, respectively; p=0.013).

At 18–20 hours after the surgery in the group I ionized calcium was lower comparing to group II (0.97±0.06 and 1.00±0.05 mmol/l, respectively; p=0.021). Serum phosphate level was lower in group I also (0.81±0.16 and 0.99±0.20 mmol/l, respectively; p<0.001).

Conclusions. 1. The incidence of atrial fibrillation after coronary artery bypass surgery remains relatively high (26.83%). 2. Serum electrolyte concentration after coronary artery bypass grafting varies within normal ranges. 3. Patients with postoperative atrial fibrillation had higher chloride and lower phosphate concentration immediately after surgery and lower ionized calcium and phosphate level 18–20 hours after the surgery.

Introduction

One of the most common postoperative complications after coronary artery bypass grafting (CABG) surgery is postoperative atrial fibrillation (AF). It is rarely fatal but it may cause subjective symptoms and result in thromboembolic complications, prolong hospital stay, result in neurocognitive disorders (1–4). In patients with compromised cardiac status, this complication is associated with major morbidities, such as hemodynamic instability, increased morbidity and mortality.

The exact proarrhythmic substrate and pathogenetic mechanisms have not been identified yet. Most authors recognize that risk factors of AF include advanced age, transient atrial ischemia, arterial hypertension, dilated atria, male sex, pulmonary hypertension, previous atrial fibrillation and serum electrolyte disorders after CABG operation (5). On the other hand there is evidence that cardiopulmonary bypass (CPB) time, duration of aortic cross clamping and the time of surgery, also the type of cardioplegia and the number of constructed grafts does not influence the incidence of AF (6–9).

Electrolyte balance disorders after cardiac surgery are not widely investigated. There are only very few studies that show the depletion of electrolytes and serum electrolyte concentration changes after cardiac surgery (10–15). The role of potassium in pathogenesis of cardiac arrhythmias is well recognized. However, the role of magnesium is more and more under con-

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sideration in investigations within the field of postoperative cardiac arrhythmias. Low serum potassium level is often found in association with hypomagnesemia and predisposes atrial fibrillation. Extracellular magnesium is broadly implicated in neuronal control, neuromuscular transmission, and cardiovascular tone. It is not surprising that magnesium metabolism disturbances result in wide spectrum of clinical signs and symptoms. Also it has been shown that magnesium suppresses arrhythmias after acute myocardial infarction, and there are studies confirming correlation between hypomagnesemia and postoperative atrial fibrillation (16). The underlying mechanism of these effects is not well understood but most probably involves magnesium interaction with calcium channels within myocytes membrane. Still the role of magnesium in the pathogenesis of AF is not clear yet. Also, it is not clear if magnesium supplementation is useful for these patients, or it is useful only in hypomagnesemia patients.

Hypophosphatemia and its consequences are less investigated in patients after cardiac surgery. Common complications after cardiac surgery are cardiac and respiratory failure, and they are also among the clinical manifestations of hypophosphatemia. J. Goldstein *et al.* (17) found out that 56% of the patients after thoracic surgery and 50% of the patients after cardiac surgery were hypophosphatemic. All researchers agree that hypophosphatemia could be the cause of prolonged artificial lung ventilation and myocardial dysfunction; also they suggest that it may have influence on the incidence of arrhythmias. Anyway, there are no data confirming the arrhythmogenic effect of changes in serum phosphate level.

Our study was designed to assess the incidence of atrial fibrillation, changes of serum potassium, sodium, ionized magnesium, ionized calcium, chloride, and phosphate concentrations and effects of magnesium sulphate infusion to prevent AF following CABG surgery.

Materials and methods

The study took place in Clinic of Cardiac Surgery at Kaunas Heart Center, Kaunas University of Medicine Hospital, during 2004–2005. After approval of Kaunas Region Ethics Committee for Biomedical Research and written informed consent of the patients the data of 82 patients undergoing elective coronary artery bypass grafting surgery were analyzed. Patients' enrolment criteria were as follows: male sex, left ventricular ejection fraction >0.3, arterial hypertension grade <2, the New York Heart Association (NYHA) class <III, serum electrolytes (potassium, sodium, ionized magnesium, ionized calcium, chloride and phosphate) concentrations within normal ranges, normal liver, pulmonary and renal function, no diabetes or other metabolism disorders, normal serum cholesterol values, no pulmonary hypertension, no atrial fibrillation in the past, sinus rhythm on preoperative electrocardiogram.

The preparation of the patients before surgery, premedication, general anesthesia, cardiopulmonary bypass, cardioplegia, surgical technique, and the treatment in the intensive care unit (ICU) were the same for all patients.

The use of all medicines was continued with the exception of aspirin and steroids, which were stopped seven days before surgery. Oral diazepam at a dose of 10 mg on the eve of the surgery and 10 mg of morphine, 0.1 mg/kg of oral midazolam and half of the usual dose of beta-blocking agents directly before the transportation to the operating room were administered as premedication.

Standardized endotracheal anesthesia technique was used. When supplying 100% oxygen through the mask, 1–2 μg/kg of fentanyl, 0.05 mg/kg of midazolam, 1–3 mg/kg of thiopentone and 0.08–0.1 mg/kg of pipecuronium were used for induction of anesthesia. Fentanyl at a dose of 3 μg/kg/hour (total dose ~10–20 μg/kg), 1–4 mg/hour of midazolam and 0.6–0.7 of isoflurane were used for anesthesia maintenance according to hemodynamics. The cardiopulmonary bypass machine was primed with 2,000 ml of Ringer's acetate solution containing 10,000 units of heparin. Roller-pump with membrane oxygenator (Dideco D703, Mirandola) was used. The average flow rate varied from 2.2 to 2.4 l/min/m^2. Surgery was performed under a slight hypothermia (32–34°C). Cold crystalloid (temperature – 2–4°C) antegrade cardioplegia (St. Thomas solution) was used to protect myocardium. Initial dose was 1,000 ml. Cardioplegia was repeated every 30 min using 500 ml of St. Thomas solution. Operations were performed through the midline sternotomy; distal anastomoses were constructed first, proximal ones on beating heart and side clamp on aorta.

Serum potassium, sodium, ionized magnesium, ionized calcium, chloride and phosphate levels were measured before cardiopulmonary bypass, immediately after the surgery on arrival to ICU and 18–20 hours after the surgery. Cardiac rhythm was monitored using Siemens 900 monitors throughout the study. Any episode of irregular rhythm with the presence of f waves of variable morphology and amplitude was considered atrial fibrillation, and it was documented.

All patients were divided into two groups. Group

I (n=22) experienced at least one episode of atrial fibrillation after the surgery. Group II (n=60) remained in sinus rhythm after the surgery. Demographical and operative data of both groups are presented in Table 1.

The data did not differ significantly except the age, which was higher in group I. The dilation of left atrium and physical status according to the American Society of Anesthesiologists (ASA) classification did not differ between groups (Table 2).

Before the surgery all patients where on β-blockers, angiotensin-converting enzyme (ACE) inhibitors, nitrate and diuretics. Metoprolol was used as β-blocker, ramipril – as ACE inhibitor, isosorbide dinitrate – as nitrate, and furosemide – as diuretic in both groups. The rate and the average doses of the medications are presented in Table 3.

Statistical data analysis was performed using the "SPSS 12.0" (Statistical Package for Social Science) package. All data are presented as the means and standard deviations of the means (M±SD). The analyzed parameters were described using the general statistical status, distribution, and symmetry. The comparison of quantitative variables was performed using Student's (t) test. A test of Kolmogorov–Smirnov was used to check the normal data distribution. Mann–Whitney (U) test was used for the evaluation of the difference between two independent groups. When statistical hypothesis were verified, the following criteria were used – $p<0.05$ (statistically significant), where p is the marginal level of statistical significance in the hypothesis verification.

Results

The overall incidence of AF in our study was 26.83%. The extent of infusion therapy after the surgery in the ICU did not differ between the groups (2,272.73±1,031.96 ml in group I and 2,327.00±888.18 ml in group II, p=0.815). Patients in both groups did not receive magnesium, calcium and phosphate supplementation. KCl i/v was administered

Table 1. **The demographical and operative data of both groups**

Parameter	Group I (n=22)	Group II (n=60)	p
Age (years)	68.27±6.09	64.20±9.32	0.025*
Body mass index (kg/m^2)	27.11±5.13	27.55±4.84	0.721
LVEF (%)	45.14±10.62	41.93±8.90	0.174
Number of aorto-coronary bypasses	3.64±0.90	3.43±0.85	0.349
The time of CPB (min)	99.91±40.58	90.87±25.59	0.234
The time of aorta cross-clamping (min)	51.45±19.56	45.90±16.7501	0.207
Total volume of cardioplegic solution (ml)	1,495.45±288.22	1,508.33±316.25	0.868
Total volume of CPB priming solution (ml)	2,170.00±279.71	2,195.77±242.79	0.684

*p<0.05 between the groups. The data are presented as mean±standard deviation.
LVEF – left ventricular ejection fraction; LA – left atrium; ASA – American Society of Anesthesiologists; CPB – cardiopulmonary bypass.

Table 2. **The preoperative data of patients in both groups**

Parameter		Group I, % (n=22)	Group II, % (n=60)
The dilation level of LA	1	–	3.3
	2	54.5	56.7
	3	45.5	40
ASA class	1	–	–
	2	13.6	10
	3	59.1	73.3
	4	27.3	16.74

LA – left atrium; ASA – American Society of Anesthesiologists.

Table 3. **The rate of usage of various medications before the surgery in both groups**

Medication	The rate of the usage, %		Average daily dose, mg	
	group I (n=22)	group II (n=60)	group I (n=22)	group II (n=60)
Metoprolol	89.91	76.67	54.08±25.28	55.00±25.13
Ramipril	63.64	56	7.97±8.34	8.50±7.78
Furosemide	13.33	10	20.00±15.49	25.00±17.32
ISDN	100*	70*	41.90±17.84	38.18±20.39

*p<0.05 between the groups. The average daily doses are presented as mean±standard deviation.
ISDN – isodinitrate.

accordingly to serum potassium level in order to keep it not less than 4.5 mmol/l, but the mean dose did not differ between the groups (5.00±1.46 g in group I, 5.94±3.10 g in group II, p=0.097).

The changes in serum electrolyte (potassium, sodium, magnesium, ionized calcium, chloride and phosphate) levels during the study are presented in Table 4.

Before CPB serum potassium, sodium, magnesium, ionized calcium, chloride and phosphate concentrations did not differ between the groups and were within normal ranges. Immediately after the surgery on arrival to ICU serum potassium, sodium, and ionized calcium concentrations did not differ between the groups. Serum magnesium did not differ either, but its concentration exceeded normal ranges in both groups (1.34±0.32 mmol/l in group I and 1.38±0.37 mmol/l in group II, p=0.648). Serum chloride concentration was significantly higher in group I comparing to that in group II (111.91±4.48 and 105.17±5.73 mmol/l, respectively; p<0.001). And serum phosphate concentration was significantly lower in group I than in group II (0.98±0.15 and 1.09±0.19 mmol/l, respectively; p=0.013) though remained within normal ranges.

On the next morning after the surgery ionized calcium and phosphate levels differed significantly between the groups. In the group I ionized calcium was significantly lower than in group II (0.97±0.06 and 1.00±0.05 mmol/l, respectively; p=0.021). Serum phosphate level was lower in group I also (0.81±0.16 and 0.99±0.20 mmol/l, respectively; p<0.001).

Discussion

The overall incidence of postoperative atrial fibrillation in our study was relatively high and corresponded with the literature data. Though the problem has been analyzed by many researchers, still it remains unclear why some patients, even those having no risk factors, develop AF while others after the same sur-

Table 4. **Changes in serum electrolyte concentrations in both groups**

Parameter		Before CPB	At the ICU	18–20 hours after the surgery
K^+ (mmol/l)	group I	4.63±0.47	4.63±0.49	4.73±0.41
	group II	4.48±0.32	4.57±0.42	4.50±0.32
Na^+ (mmol/l)	group I	137.36±2.77	136.36±4.15	137.00±3.63
	group II	133.09±24.25	136.50±3.30	137.43±3.13
Mg^{++} (mmol/l)	group I	0.88±0.13	1.34±0.32	0.93±0.23
	group II	0.91±0.12	1.38±0.37	0.92±0.11
Ca^{++} (mmol/l)	group I	1.00±0.04	0.99±0.12	0.97±0.06*
	group II	0.99±0.06	1.00±0.05	1.00±0.05*
Cl^- (mmol/l)	group I	107.45±3.64	111.91±4.48*	108.68±3.05
	group II	106.47±3.36	105.17±5.73*	106.53±3.22
P^- (mmol/l)	group I	0.94±0.21	0.98±0.15*	0.81±0.16*
	group II	0.96±0.23	1.09±0.19*	0.99±0.20*

*p<0.05 between the groups. The data are presented as mean±standard deviation.
CPB – cardiopulmonary bypass; ICU – intensive care unit.

gical procedure are in sinus rhythm. Some authors suspected CPB to be the main cause of postoperative AF. K. Saatvedt *et al.* (18) reported that CPB was not the main cause for developing AF postoperatively, but patients who underwent surgery without CPB had lower incidence of AF. More studies were performed to investigate if CPB increases the incidence of AF after CABG surgery. But in most studies the incidence of AF after on-pump and off-pump CABG surgery did not differ (18–20). Y. Enc *et al.* (20) examined 328 patients, who underwent on-pump CABG surgery, and 342 patients, who underwent off-pump CABG surgery. The incidence of AF was 16.1% and 14.6%, respectively. So CPB did not influence the incidence of AF.

The patients in group I were statistically significantly older. The older age is recognized risk factor for postoperative atrial fibrillation. Incidence of postoperative AF is increased by at least 50% per decade of older age (21).

Most of the studies, designed to evaluate the changes in electrolyte levels after CPB, find enhanced electrolyte depletion and electrolyte balance disorders. Hemodilution and the use of diuretics are considered to be the main causes of enhanced electrolyte depletion (10, 15, 16). Anyway, in our study we did not find any severe electrolyte disorders during the whole study period. Measured serum electrolyte (potassium, sodium ionized magnesium, ionized calcium, chloride and phosphate) levels were within normal ranges, except serum magnesium on arrival to ICU. We did not find any hypomagnesemic patients after the surgery and we think it could be explained by the use of St. Thomas solution for cardioplegia, containing 16 mmol/l of magnesium. After the surgery on arrival to ICU ionized serum magnesium levels were similar in both groups and exceeded normal ranges. Patients in both groups received extra magnesium with cardioplegic solution. F. Amaya *et al.* (12) added 16 mmol/l of ionized magnesium into cardioplegic solution. In their study after the surgery serum ionized magnesium levels did not change without additional supplementation of magnesium.

Opinions on magnesium supplementation for prevention and treatment of atrial fibrillation are controversial. M. Kaplan *et al.* (22) in their placebo-controlled study had the same incidence of atrial fibrillation in both groups, though it well correlated with lower serum magnesium levels. However, F. Toraman *et al.* (23) in the similar study reduced incidence of AF significantly by using magnesium supplement. The data of T. Shiga's *et al.* (24) meta-analysis also support the advantage of magnesium supplementation in preventing AF. Anyway, it is not clear yet if normomagnesemic patients after coronary artery bypass grafting benefit from magnesium supplementation.

In our study on arrival to the ICU serum chloride level was significantly higher in the patients who developed atrial fibrillation. Most of solutions for intravenous infusion and cardiopulmonary bypass priming contain high content of chloride anions because the basic components are NaCl and other chloride salts. Therefore, high volume of such solutions may alter serum chloride level. The problem of iatrogenic hyperchloremic acidosis because of intensive infusion therapy was discussed in the scientific papers (25). The opinions on this point vary, but most of the data show that the phenomenon is benign, and at the end no treatment is required. In our study in spite of high volume of solutions used serum chloride levels were within normal ranges, though it was higher in the group I after the surgery. Anyway, it is not clear, why the difference appeared between the groups following the surgery.

On arrival to the ICU serum phosphate was significantly lower in the patients in group I, thought the values remained within normal ranges. This statistically significant difference between the groups increased on the first postoperative day. K. H. Polderman *et al.* (9) in their study found out that patients after cardiac surgery tend to develop hypophosphatemia more often comparing with the other patients in the ICU. J. Cohen *et al.* (14) examined severe hypophosphatemia (<0.48 mmol/l) after cardiac surgery. They found it in 34.3% of the cases, and it was already evident in the early postoperative period. Recognized risk factors include sepsis, the use of diuretics, antacids, and total parenteral nutrition. The risk factors in patients undergoing cardiac surgery are not well defined, but the surgical procedure itself predisposes for hypophosphatemia. Most authors state this fact, but the relation between decreased serum phosphate level and postoperative arrhythmias has not been established yet.

In our study ionized serum calcium level was significantly lower in the group I on the next morning after the surgery though it remained within normal ranges. The explanation for this phenomenon is not clear but it may be associated with the changes in parathyroid hormone (PTH) secretion. In the study performed by F. Carlsted *et al.* (26) ionized calcium levels decreased shortly after CABG without changes in PTH secretion, but rapid changes in ionized calcium during citrate and calcium infusion revealed a normal PTH secretory response.

We found the differences in serum electrolyte levels after CABG surgery between patients who develop and who did not develop postoperative atrial fibrillation. Anyway, it still remains unclear whether these differences determinate the incidence of postoperative arrhythmias or they are just the consequence of some arrhythmogenic factor. The changes in serum electrolyte concentrations are found in critically ill patients, in the case of sepsis. So it may be supposed that inflammatory and hormonal factors play also an important role in electrolyte balance disturbances. In spite of normal serum electrolyte levels, relatively good perioperative status, and the usage of beta-blocking agents before and early after the surgery the incidence of atrial fibrillation was high in our study. Postoperative AF remains a challenging problem that has not been resolved yet. The etiology and pathophysiology of AF after heart surgery are incompletely understood. There is still no explanation for the fact that some patients develop postoperative AF whereas others, having the same surgical intervention, remain in sinus rhythm.

Conclusions

1. The incidence of atrial fibrillation after coronary artery bypass surgery remains relatively high (26.83%).
2. Serum electrolyte concentration after coronary artery bypass grafting varied within normal ranges.
3. Patients who developed atrial fibrillation after coronary artery bypass grafting had higher chloride concentration and lower phosphate concentration immediately after surgery and lower ionized calcium and phosphate level on the next morning.

Serumo elektrolitų koncentracijos pokyčiai ir jų įtaka prieširdžių virpėjimo dažniui po aortos vainikinių jungčių suformavimo operacijų

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Raktažodžiai: prieširdžių virpėjimas, serumo elektrolitų pusiausvyra, aortos vainikinių jungčių suformavimas.

Santrauka. *Darbo tikslas.* Nustatyti prieširdžių virpėjimo po operacijos dažnumą bei serumo elektrolitų koncentracijos pokyčius po aortos vainikinių jungčių suformavimo operacijų.

Tyrimo medžiaga ir metodai. Gavus Kauno regiono biomedicininių tyrimų etikos komiteto leidimą bei raštišką ligonių sutikimą, išanalizuoti 82 ligonių, kuriems 2004–2005 metais Kauno medicinos universiteto klinikų Kardiochirurgijos klinikoje atlikta aortos vainikinių jungčių suformavimo operacija, duomenys. Tirta kalio, natrio, magnio, jonizuoto kalcio, chlorido ir fosfatų koncentracija serume prieš dirbtinę kraujo apytaką, iškart po operacijos atvežus ligonius į intensyviosios terapijos skyrių ir praėjus 18–20 val. po operacijos. Širdies veikla stebėta viso tyrimo metu, o, atsiradus ritmo sutrikimui, dokumentuota. Visi ligoniai suskirstyti į dvi grupes: I grupėje (n=22) buvo ligoniai, kuriems užfiksuoti prieširdžių virpėjimo epizodai; II grupėje (n=60) buvo ligoniai, kuriems po operacijos išliko sinusinis ritmas.

Rezultatai. Prieširdžių virpėjimo dažnis – 26,83 proc. Pirmos grupės ligoniai buvo vyresni (atitinkamai – 68,27±6,09 ir 64,20±9,32 metų, p=0,025). Iškart po operacijos chlorido koncentracija serume buvo didesnė pirmos grupės ligonių (atitinkamai – 111,91±4,48 mmol/l ir 105,17±5,73 mmol/l, p<0,001), o fosfatų koncentracija pirmos grupės ligonių buvo mažesnė (atitinkamai – 0,98±0,15 mmol/l ir 1,09±0,19 mmol/l, p=0,013).

Kitą rytą po operacijos pirmos grupės ligonių jonizuoto kalcio koncentracija serume buvo mažesnė negu antros grupės (atitinkamai – 0,97±0,06 mmol/l ir 1,00±0,05 mmol/l, p=0,021), fosfatų koncentracija serume taip pat išliko mažesnė pirmos grupės ligonių (atitinkamai – 0,81±0,16 mmol/l ir 0,99±0,20 mmol/l, p<0,001).

Išvados. Prieširdžių virpėjimas po aortos vainikinių jungčių suformavimo operacijų gana dažnas (26,83 proc.). Elektrolitų koncentracija serume aortos vainikinių jungčių suformavimo operacijos metu ir iškart po jų svyruoja normos ribose. Ligoniams, kuriems buvo prieširdžių virpėjimo epizodų po operacijos, nustatyta didesnė chlorido ir mažesnė fosfatų koncentracija iškart po operacijos, mažesnė jonizuoto kalcio bei fosfatų koncentracija prėjus 18–20 val. po operacijos.

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