Original Article

Perioperative Coronary Artery Spasm in Off-pump Coronary Artery Bypass Grafting and its Possible Relation with Perioperative Hypomagnesemia

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Purpose: We experienced 3 cases of serious perioperative coronary artery spasm in off-pump coronary artery bypass grafting (OPCAB). In consideration of the causes, we directed our attention to hypomagnesemia, one of the triggers of coronary artery spasm. This study was performed to confirm the tendency to hypomagnesemia in OPCAB.
Methods: First, we report 3 patients having severe coronary artery spasm immediately after OPCAB with consideration of the causes. Second, serial magnesium (Mg) value (xylidyl blue method, normal 1.9-3.1 mg/dl) was measured in 45 consecutive patients with OPCAB between April and October 2002, 1) before starting the operation, and 2) after the patient's entrance into the intensive care unit.
Results: Preoperative and postoperative values of Mg (mg/dl) were 2.1±0.3, 1.7±0.3, respectively ($p<0.01$). Postoperative incidence of hypomagnesemia was as high as 89% of the patients (40 out of 45 patients). In this study and thereafter, we corrected hypomagnesemia with magnesium sulfate during and after OPCAB, and no perioperative coronary artery spasm occurred.
Conclusion: Hypomagnesemia, one of the triggers of coronary artery spasm, is very common in OPCAB. We strongly recommend the correction of hypomagnesemia during and after OPCAB for the prevention of perioperative coronary artery spasm. (Ann Thorac Cardiovasc Surg 2006; 12: 32–6)

Key words: magnesium, hypomagnesemia, coronary artery spasm, coronary artery bypass grafting, off-pump coronary artery bypass grafting

Introduction

The surgical results of off-pump coronary artery bypass grafting (OPCAB) are reported to be equal to those of conventional on-pump coronary artery bypass grafting (CABG).[1,2] However, perioperative coronary artery spasm still remains a serious problem also in OPCAB.[3,4] We report 3 patients with postoperative severe coronary artery spasm in OPCAB. In consideration of the causes of the postoperative coronary artery spasm, we directed our attention to hypomagnesemia, one of the triggers of coronary artery spasm.[5,6] We studied the serial magnesium (Mg) change to confirm a tendency for hypomagnesemia in patients with OPCAB.

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Patients and Methods

First, we report 3 cases with severe perioperative coronary artery spasm in patients with OPCAB and analyzed their conditions. Next, a serial Mg study was performed in 45 consecutive patients with OPCAB.

Case 1

A 48 year-old man with angina and an old anterior myocardial infarction was referred for CABG. Coronary angiography (CAG) revealed a 50% stenosis of the left main

trunk (LMT), a 90% in-stent restenosis of the left anterior descending artery (LAD) and a 75% stenosis of the circumflex artery (Cx). Under general anesthesia with fentanyl, diazepam, vecuronium bromide and enflurane, he underwent triple vessel OPCAB in November 2001. The graft flow was 20 ml/min for a left internal thoracic artery (LITA) to the LAD, 27 ml/min for a right internal thoracic artery (RITA) to the diagonal branch (Dg), and 35 ml/min for a radial artery from the ascending aorta to the Cx. All the grafts showed good diastolic flow waves. Nitroglycerin (NTG) and diltiazem were routinely infused for the prevention of spasm with a low dose of dopamine for hemodynamic support during and after the surgery. The patient was hemodynamically stable in the intensive care unit (ICU). However, one hour after his entrance into the ICU on awakening from anesthesia, sudden hypotension with bradycardia occurred, followed by ventricular fibrillation (Vf). A percutaneous cardio-pulmonary support (PCPS) system with a centrifugal pump and an oxygenator was immediately established under cardiac massage and intra-aortic balloon pumping (IABP) was initiated in the ICU. Emergency CAG revealed a spastic occlusion of the non-targeted right coronary artery (RCA), spasm of the targeted LAD and Cx. The grafts were all patent but spastic. Direct injection of diltiazem, nicorandil and papaverine hydrochloride into the native coronary arteries and the grafts effectively relieved the spasm without perioperative myocardial infarction. The patient was weaned from PCPS and IABP 46 and 64 hours later, respectively. No further episode of spasm occurred thereafter, and he was discharged from the hospital on postoperative day 43. The graft patency of the LITA to LAD and the RITA to Dg was confirmed by detecting their good systolic and diastolic flow waves and velocities with vascular ultrasonography (Radial artery to Cx was not confirmed by this method).

Case 2

A 76 year-old man with a recent history of inferior myocardial infarction was referred for CABG due to a 75% stenosis of LMT, a 75% stenosis of LAD and a 90% stenosis of Cx. He underwent uneventful double vessel OPCAB in January 2002. The graft flow was 50 ml/min for a LITA to LAD, and 37 ml/min for a lengthened RITA graft with a radial artery to Cx. Both grafts showed good diastolic flow waves. NTG, diltiazem and additional nicorandil were continuously administered for the prevention of spasm, as well as a low dose of dopamine for hemodynamic support during and after the surgery. The patient was hemodynamically stable in the ICU. However, 3 hours after entrance into the ICU on awakening from anesthesia, an electrocardiogram (ECG) showed an elevation of the ST segment in leads II, III, aVF, and a depression of the ST segment in leads V2-6 with bradycardia (50 beats/min) and wide QRS. IABP was immediately performed and emergency CAG was administered, showing spasm of the non-targeted RCA at the distal portion of the previous stenting site [segment 3-4]. The LITA was patent without spasm. The composite graft of the RITA-radial artery was patent with spasm. Direct injection of papaverine hydrochloride and nicorandil into the RCA and RITA effectively improved the spasm and normalized the ST changes on ECG. He was weaned off IABP 35 hours later. No further episode of spasm occurred thereafter. However, pneumonia of the lung appeared and deteriorated with hypoxemia. Veno-venous extracorporeal lung assistance was performed for 20 days, but the patient died of multi-organ failure 30 days after the surgery.

Case 3

A 45 year-old woman was referred for CABG due to 75% stenosis of LMT with unstable angina. Double vessel OPCAB was uneventfully performed in February 2002. The graft flow was 25 ml/min for a LITA to LAD, and 65 ml/min for a radial artery to Cx from the ascending aorta. Both grafts showed good diastolic flow waves. NTG, diltiazem and nicorandil for the prevention of spasm, and low dose of dopamine for hemodynamic support were continuously administered during and after the surgery. The patient was hemodynamically stable in the ICU. One and a half hours after entrance into the ICU on awakening from anesthesia, a sudden hypotension with ST segment depression in leads I, aVL, V2-4 appeared on ECG, followed by Vf. PCPS was immediately established under cardiac massage. IABP was also inserted. Emergency CAG revealed severe spasm on the native LAD. The LITA and the radial artery graft were patent with spasm. RCA was normal. Direct injection of nitroglycerin, papaverine hydrochloride, and nicorandil into the native left coronary artery (LCA) and the grafts improved the spasm; however, a perioperative myocardial infarction occurred with an elevation of MBCK (100 IU/L). She was weaned off PCPS and IABP 45 hours and 124 hours later, respectively. No further episode of spasm occurred thereafter and she was discharged from the hospital on postoperative day 75. The graft patency of the LITA to LAD was confirmed by detecting good systolic and diastolic flow waves and velocities on vascular ultrasonography (radial

Table 1. Details of 3 patients with perioperative coronary artery spasm

Case	Age/ Sex	Operation	Graft	When	Body temp. blood gas electrolytes before spasm	Drug used before spasm	ECG change	Cardiac collapse	IABP PCPS	Spasm site on EmCAG	Graft patency on EmCAG	Results
1	48/M	OPCAB 3	LITA RITA RA	1 hour after ICU entrance (awakening)	37.4°C pH7.41 $PaCO_2$ 40.4 mmHg PaO_2 258 mmHg K 4.1 mEq/L Ca 0.90 mmol/L	NTG diltiazem dopamine	Bradycardia Vf	Yes	PCPS IABP	LCA, all grafts, non-targeted RCA	All patent	Alive
2	76/M	OPCAB 2	LITA RITA RA	3 hours after ICU entrance (awakening)	37.8°C pH7.36 $PaCO_2$ 40.3 mmHg PaO_2 204 mmHg K 4.3 mEq/L Ca 0.83 mmol/L	NTG diltiazem nicorandil dopamine	ST elevation (II, III, aVF), ST depression (V2-6), bradycardia	No	IABP	LITA, non-targeted RCA	All patent	Dead 30th day (MOF)
3	45/F	OPCAB 2	LITA RA	1.5 hours after ICU entrance (awakening)	34.4°C pH7.50 $PaCO_2$ 24.9 mmHg PaO_2 278 mmHg K 2.6 mEq/L Ca 1.03 mmol/L	NTG diltiazem nicorandil dopamine	ST depression (I, aVL,V2-4), Vf	Yes	PCPS IABP	LCA, all grafts	All patent	Alive

OPCAB, off pump coronary artery bypass; LITA, left internal thoracic artery; RITA, right internal thoracic artery; RA, radial artery; ICU, intensive care unit; NTG, nitroglycerine; Vf, ventricular fibrillation; IABP, intra-aortic balloon pumping; PCPS, percutaneous cardio-pulmonary support; EmCAG, emergency coronary angiography; RCA, right coronary arery; LCA, left coronary artery; MOF, multi-organ failure; ECG, electrocardiogram; temp., temperature.

artery to Cx was not confirmed by this method).

OPCAB had been the standard method of CABG since October 1999 by one surgeon in our hospital with good results and without serious problem until these 3 episodes of spasm occurred in the short period of time between November 2001 and February 2002. NTG and diltiazem had been routinely used for the prevention of spasm during and after OPCAB since the beginning of our OPCAB experience. After the first experience of spasm in case 1, nicorandil was added for the prevention of spasm; however, other episodes occurred in case 2 and 3. All the patients with OPCAB were anesthetized by neuroleptanesthesia with fentanyl, diazepam, vecuronium bromide and enflurane from the start of OPCAB without any change in anesthesia.

All the cases presented sudden ischemic ST-T changes on ECG with or without cardiac collapse in the perioperative period between 1 and 3 hours after entrance into the ICU. Emergency CAG, performed in all 3 patients, revealed spasm of the non-targeted RCA in 2 patients, and the targeted LCA in 2, including both coronary arteries in 1 patient. Three patients were just awakening from anesthesia in the ICU when coronary artery spasm occurred, suggesting some sympathetic nerve stimulation. The patients' data immediately before spasm occurrence are listed in Table 1. Case 3 had low body temperature (34.4°C) and respiratory alkalosis with hypocapnea and hypopotassemia (pH7.50, $PaCO_2$ 24.9 mmHg, K 2.6 mEq/L) just before the coronary artery spasm occurred. These factors could be the triggers of coronary artery spasm in case 3. However, other patients showed no abnormality in body temperature, blood gas, and serum potassium. Thus, we considered that there must be some additional important factors that strongly induce coronary artery spasm especially in OPCAB procedure. Although serum Mg concentration had not been routinely measured in the hospital duration of the presented patients, we directed our attention to hypomagnesemia, one of the triggers provoking coronary artery spasm, and studied the serial Mg change in patients with OPCAB.

Serial magnesium study

Between April and October 2002, 45 consecutive patients with OPCAB were included in this study and written informed concent was obtained from each patient. Patients with chronic renal failure requiring homodialysis were excluded. There were 35 men and 10 women. The age ranged from 44 to 85 years (mean 68±10). The patients consisted of 35 elective and 10 emergency cases with 2.6±0.9 bypass grafts per patient (mean ± standard derivation (SD)). Blood sampling was performed from the arterial line, and serial Mg concentration (normal 1.9-3.1

Table 2. Serial magnesium value, mg/dl

	n	pre operative	post operative	Mg-sulfate supplement	1st day
Mean±SD	45	2.1±0.3	1.7±0.3**	Yes	2.0±0.3*
Range		1.7-3.3	1.1-2.9		1.3-2.7

*p<0.05, **p<0.01 compared with preoperative value.

mg/dl) was measured according to the xylidyl blue method; 1) immediately before starting the operation, 2) just after patient's entrance into the ICU, and 3) at 6 a.m. on postoperative day 1. Hypomagnesemia was defined when serial Mg is less than 1.9 mg/dl. When hypomagnesemia occurred immediately after the operation in the ICU, Mg sulfate was administered intravenously over an hour to elevate the serial Mg value to a normal range. The data were expressed as mean±SD. Statistical evaluation of the data was performed using the Student's *t*-test. The paired *t*-test was used between the data at each blood sampling time. A p value less than 0.05 was considered to be statistically significant.

Results

Table 2 indicates the serial Mg value in consecutive patients with OPCAB. The postoperative Mg values were significantly lower than those in the preoperative values. The incidence of preoperative hypomagnesemia less than 1.9 mg/dl were 11% (5 out of 45 patients). However, the postoperative incidence of hypomagnesemia was 89% (40 out of 45 patients). Mg values on postoperative day 1 recovered to the normal range by the supplement of Mg sulfate in the ICU. In this study and thereafter, we noticed a significant decrease in serial Mg concentration during and after OPCAB, and started to correct the serial Mg value with the supplement of Mg sulfate during and after OPCAB. No perioperative coronary artery spasm has occurred thereafter.

Comment

Coronary artery spasm is an important cause of myocardial ischemia that leads to life-threatening arrhythmias, cardiac collapse and death after conventional CABG[7] and also after OPCAB.[3,4] It may occur during surgery or in the immediate postoperative period of CABG, and may occur on the targeted vessels or on the non-targeted vessels.[8] Many factors have been listed as the etiology of coronary artery spasms after CABG: manipulation of coronary arteries during CABG, endogenous cathecolamine elevation, exogenous cathecolamine administration, hyperventilation, alkalosis, low body temperature, release of vasospastic factors such as thromboxane A2 from platelets, and autonomic nerve stimulation.[9] These factors are intricately related with each other to induce spasm in the presented cases, and the prophylactic use of coronary dilators and calcium antagonists during and after surgery failed to prevent the severe coronary artery spasms after OPCAB.

Hypomagnesemia has been reported as a trigger of coronary artery spasm.[5,6,10-12] Turlapaty and Altura[5] reported that extracellular Mg ion plays a critical role in the regulation of vasomotor tone. They experimentally proved that a sudden decrease of extracellular Mg ion resulted in a rapid increase in coronary arterial tone and that in contrast a sudden increase in extracellular Mg resulted in rapid relaxation of coronary arterial tone. Additionally the withdrawal of Mg potentiated the constrictor actions of vasoactive agents such as angiotensin, serotonin, norepinephrine, acetylcholine, and potassium in coronary arteries. Thus, perioperative hypomagnesemia will easily evoke coronary artery spasm in OPCAB, in which some vasoactive agents are routinely used perioperatively.

Perioperative hypomagnesemia is common in patients who have undergone on-pump cardiac operations without Mg-contained cardioplegic solution and priming,[13] and in patients with OPCAB,[14] and is associated with atrial and ventricular dysrhythmias.[14-16] Perioperative hypomagnesemia has been attributed mainly to hemodilution by non Mg-containing crystalloid solution and renal loss,[17] intracellular transfer of Mg,[18] metabolic responses to surgical trauma[19] and pain.[20]

Serial Mg changes in the perioperative period showed that the occurrence of hypomagnesemia was 89% in our patients with OPCAB, and this was much higher than that (35%) reported by Maslow et al.[14] In a search of the English literature, we found no reports to caution of a strong relation between perioperative hypomagnesemia and coronary artery spasm in OPCAB. Native coronary arteries and bypassed grafts may be highly sensitive to spasm due to the tendency for perioperative hypomagnesemia especially in OPCAB.

Cohen reported that a bolus of Mg sulfate promptly ter-

minated vasospastic angina attacks.[21] The preventive effect of the intravenous administration of Mg sulfate on coronary artery spasm has been demonstrated by CAG[22] and by Thallium scintigraphy.[23] We have experienced no spasm in OPCAB since we started the supplement of Mg sulfate during this study, in spite of having no changes in the other perioperative conditions.

The limitations to this study include the lack of measurement of serial Mg values in the 3 cases presented here, and also the lack of randomized comparative data to prove that perioperative Mg supplement for hypomagnesemia reduced the occurrence of the perioperative coronary artery spasm in OPCAB.

In conclusion, hypomagnesemia is very common in the perioperative period of OPCAB, which can be a trigger of life-threatening perioperative coronary artery spasms. We strongly recommend frequent measurement of serial Mg value and proper supplement of Mg sulfate during and after OPCAB to correct hypomagnesemia to the normal value for the prevention of perioperative coronary artery spasm.

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