

The Effect of Lidocaine and Magnesium Sulfate on Prevention of Ventricular Fibrillation in Coronary Artery Bypass Grafting Surgery

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Abstract

Background: One of the most common events, after the release of aortic cross-clamp in patients undergoing coronary artery bypass grafting surgery is reperfusion induced ventricular fibrillation, which occurs in 74% of 96% of patients. Regarding the controversies over the use of lidocaine or magnesium sulfate for the prevention of ventricular fibrillation following the release of aortic cross-clamp, this study was designed to compare the effectiveness of magnesium sulfate and lidocaine to suppress ventricular fibrillation.

Methods: In a double blind, prospective, randomized, controlled trial study, 76 patients who were candidates for elective coronary artery bypass grafting surgery were divided into three groups including Group A (lidocaine, n=26), group B (magnesium sulfate, n=25), and group C (normal saline, n=26). Lidocaine (1.5 mg/Kg), magnesium sulfate (30 mg/Kg) and normal saline were administered 5 minutes before the release of aortic cross clamp.

Results: The incidence of ventricular fibrillation significantly decreased in patients receiving magnesium sulfate (12% vs. 26.9% and 44% in patients who received lidocaine and normal saline, respectively) There was no statistically significant difference between the groups with respect to age, ejection fraction (L/ min), anesthetic time (min), cross-clamping time (min), PH, HCT (%), and serum K⁺ level (meq).

Conclusion: The administration of lidocaine and magnesium sulfate before the release of aortic cross-clamp reduces the incidence of postoperative ventricular fibrillation in adult patients undergoing coronary artery bypass grafting surgery with cardiopulmonary bypass. In our study, magnesium sulfate was more efficient in prevention of ventricular fibrillation than lidocaine. Administration of magnesium sulfate (30 mg/kg) caused no toxic effect and was safe for patients undergoing coronary artery bypass grafting surgery with cardiopulmonary bypass.

Keywords: Coronary artery bypasses grafting surgery; Magnesium sulfate; Lidocaine; Ventricular fibrillation

Introduction

One of the most common events after the release of aortic cross-clamp in patients undergoing coronary artery bypass grafting surgery is reperfusion induced ventricular fibrillation, which occurs in 74% of 96% of patients.¹ Ventricular fibrillation increases myocardial oxygen consumption, myocardial wall tension

and intramyocardial damage and so deteriorates cardiac output.² Myocardial damage induced by ischemic reperfusion injuries is believed to be due to the production of reactive oxygen species and calcium overload.³

Various approaches have been used to prevent or treat reperfusion-induced ventricular fibrillation. Lidocaine has been used primarily for patients with ventricular tachyarrhythmia, as it has been effective in patients after coronary revascularization and in patients resuscitated from out-of-hospital ventricular fibrillation.⁴ Lidocaine, an amide local anesthetic,⁵ has been shown to increase the threshold for ventricular fibrillation by binding to sodium channels,⁵ decreasing the

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slope of phase 4 depolarization⁶ and increasing the diastolic threshold potential in purkinje fibers.⁷

The use of lidocaine as an additive to cold hyperkalemic crystalloid cardioplegia at a dose of 500 mg/Liter was associated with a lower incidence of ventricular fibrillation. However, it was associated with an extremely high incidence of high degree atrioventricular block, which required temporary pacing and inotropic support.⁸ Moreover, the administration of lidocaine (100 mg) two minutes before the release of aortic cross-clamp not only decreased the incidence of reperfusion ventricular fibrillation, but also increased the cardiac output.⁹

Another approach to prevent ventricular fibrillation after the release of aortic cross-clamp has been the use of magnesium sulfate. The use of magnesium was indicated in several reports suggesting that patients undergoing coronary revascularization with cardiopulmonary bypass have significantly lower serum magnesium levels.¹⁰ The prophylactic use of magnesium after cardiac surgery was better than placebo in reducing the risk of atrial fibrillation, supraventricular and ventricular arrhythmia.¹¹ Moreover, magnesium supplementation before aortic cross-clamp could stabilize the plasma membrane of the myocardium and thereby offer a protective effect.¹² The cardiac protective effects of magnesium are induced by activation of the Na⁺K⁺ ATPase, which stabilizes the membrane potential, and thereby raises the ventricular fibrillation threshold.¹³

Regarding the controversies over the use of lidocaine or magnesium sulfate for the prevention of ventricular fibrillation following the release of aortic cross-clamp, in this study we investigated the efficacy of lidocaine and magnesium sulfate on prevention of ventricular fibrillation in patients undergoing elective coronary artery bypass grafting surgery.

Materials and Methods

The study was conducted at a university-affiliated hospital from Feb. 2004 to Dec. 2005, recruiting 76 patients undergoing coronary artery bypass grafting surgery. The study was approved by the University Ethics Committee and informed consent was obtained from all patients. Exclusion criteria included any cardiac rhythm other than sinus rhythm, on the basis of preoperative 12-lead electrocardiography (ECG) and Antiarrhythmic drug consumption (e. g. Digoxin, Lidocaine) other than B-receptor antagonists. The use

of drugs causes electrolyte imbalance (e.g. magnesium sulfate, diuretics). Poor left ventricular function was defined as an ejection fraction of less than 50% or metabolic, surgical or endocrine disease. We did not include patients with severe type of hyperkalemia at the time of aortic cross-unclamping.

After inserting the radial arterial line, the patients were anesthetized using intravenous (IV) midazolam (0.04 mg/kg), sufentanyl (0.6 ug/kg); thiopental (2.5 mg/kg), and pancuronium (0.1 mg/kg). Anesthesia was maintained using diazepam. After intubation, controlled ventilation was started with 100% oxygen. The patients were monitored with pulse oximeters, ECG, capnometer, radial artery catheter and esophageal thermometer. In operations, standard cardiopulmonary bypass was used with systemic cooling between 30-32°C. All patients were perfused by a sarns roller pump at a flow rate of 2.4L/min/m². After application of the aortic cross-clamp, cardioplegic solution was infused into the aortic root at 10-15 ml/Kg of body weight.

Computerized randomization was done for patients to receive lidocaine (1.5 mg/Kg; Group A, n=26), magnesium sulfate (30 mg/Kg; Group B, n=25), or an equal volume of normal saline (Group C, n=25) 5 minutes before releasing the aortic cross-clamp.

Then, all the patients were monitored for 15 minutes after release of aortic cross-clamp and any abnormal electrical rhythm (including ventricular fibrillation) was registered, and if prolonged ventricular fibrillation (more than 2 minutes) or repeated ventricular fibrillation was encountered, electrical defibrillation or antiarrhythmic medication was administered. At the time of aortic cross-clamp release, pH count of the blood, arterial O₂ and CO₂ tensions, hemoglobin, hematocrit (HCT) and serum potassium levels (K⁺) were recorded. The patients' demographic characteristics including ECG, ejection fraction and numbers of grafts were also obtained.

The statistical analyses were performed using SPSS software (version 14.0, Chicago, IL, USA). Chi Square was used to compare the rate of the occurrence of ventricular fibrillation. Analysis of Variance was used to compare K⁺, pH, Hct, cross-clamping time (min) and ventricular fibrillation.

Results

Intraoperative data are shown in Table 1. There was no statistically significant difference between the groups A, B, and C with respect to age ($p=0.38$).

Table 1: Demographic characteristics and perioperative data

Variable	Group A(n=26)	Group B (n=25)	Group C (n=25)	P value
Age (year)	56.7±7.5	60.12±89	60.8±10.48	$p=0.38$
Anesthetic time (min)	252.0±66	266.4±66	267.0±51	$p=0.55$
Cross-clamping time (min)	48.6±9.5	46.0±7.9	47.2±6.6	$p=0.51$
pH	7.4±0.05	7.4±0.05	7.4±0.06	$p=0.214$
HCT (%)	37.0±5.92	39.1±6.14	35.5±6.09	$p=0.115$
K ⁺ (meg/l)	4.3±0.67	4.3±0.57	4.4±0.89	$p=0.712$
Ventricular fibrillation	26.9%	12.0%	44.0%	$p=0.410$

Also, there was no statistically significant difference between the groups A, B and C with respect to ejection fraction. The rate of occurrence of ventricular fibrillation in groups A, B and C were 26.9%, 12% and 44%, respectively. The difference between the groups was statistically significant ($p=0.041$). There was no high degree AV block, or intra-aortic balloon counter pulsation. The same number of patients in the three groups required inotropic agent after the termination of cardiopulmonary bypass.

Discussion

The findings of the present study indicated that prophylactic treatment with magnesium sulfate was associated with a lower incidence of ventricular fibrillation in comparison to treatment with lidocaine or placebo.

England *et al.* showed that there will be a decrease in the incidence of ventricular arrhythmias up to 50% when 2 grams of prophylactic magnesium was administered intraoperatively, while this had no effect on supraventricular arrhythmias.¹⁴ Also, Shiga *et al.* showed that prophylactic treatment with magnesium after cardiac surgery was better than placebo for reducing atrial fibrillation, supraventricular and ventricular arrhythmias.¹⁵ Moreover, Kurian *et al.* showed that administration of 2 grams magnesium before aortic cross-clamp could stabilize the plasma membrane of the myocardium and thereby mediate the protective effect.¹⁷ On the other hand, Wistbacka *et al.* showed that magnesium at a dose greater than 4 grams was associated with bradycardia requiring pacing for 24 hours and mild hypotension which is responsible for fluid administration.¹⁶ This dose of magnesium sulfate in the present study was safe and had no toxic complication such as bradycardia requiring temporary pacing. The mechanisms of antiarrhythmic effect of magnesium include increasing

threshold membrane potential and maintaining intracellular/extracellular K⁺ ratio. The findings of the present study indicated that prophylactic treatment with lidocaine was associated with a lower incidence of ventricular fibrillation in comparison to the use of placebo.

Techervenkov *et al.*, using lidocaine as an additive to cold hyperkalemic crystalloid cardioplegia in a dose of 500 mg/L demonstrated a lower incidence of ventricular fibrillation (4% versus 96%). However, an extremely high incidence of high grade atrioventricular block (83% in the lidocaine treated group versus 4% in the control group) required temporary pacing and an increased requirement for inotropic support.¹⁸ Anis *et al.* showed that a bolus of 100 mg of lidocaine 2 minutes before the release of the aortic cross-clamp not only significantly decreased reperfusion ventricular fibrillation (70% in the control group versus 11% in the lidocaine group) but also caused higher cardiac output after weaning from cardiopulmonary bypass.¹⁹ Also, Fall and colleagues were able to significantly reduce the incidence of ventricular fibrillation immediately after the removal of aortic cross-clamp using lidocaine.²⁰ The absence of the high grade of atrioventricular block in our study was probably due to a lower dose of lidocaine in comparison to what Techervenkov *et al.* found.

The mechanism of antiarrhythmic action of lidocaine has been attributed to the decrease in automaticity, action potential duration, and increase in ventricular fibrillation threshold. Lidocaine also binds to sodium channels,⁵ attenuating phase 4 depolarization and increasing the diastolic electric current threshold in Purkinje fibers.⁶

The administration of lidocaine and magnesium sulfate before the release of aortic cross-clamp reduces the incidence of ventricular fibrillation postoperatively in adult patients undergoing coronary ar-

tery bypass grafting surgery with cardiopulmonary bypass. Magnesium sulfate was more efficient in prevention of ventricular fibrillation than lidocaine. Administration of magnesium sulfate (with a dose 30 mg/Kg) did not have any toxic effect and was safe for patients undergoing coronary artery bypass grafting surgery with cardiopulmonary bypass.

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Conflict of interest: None declared.

References

- Hamid M, Kamal RS, Sami SA, Atiq F, Shafquat A, Naqvi HI, Khan FH. Effect of single dose magnesium on arrhythmias in patients undergoing coronary artery bypass surger. *J Pak Med Assoc* 2008;**58**:22-7. [182 97971]
- Boyd WC, Thomas SJ. Pro: Magnesium should be administered to all coronary artery bypass graft surgery patients undergoing cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 2000;**14**:339-43. [10890493] [doi:10.1016/S1053-0770(00)90137-X]
- Brackbill ML, Moberg L. Magnesium sulfate for prevention of postoperative atrial fibrillation in patients undergoing coronary artery bypass grafting. *Am J Health Syst Pharm* 2005;**62**:397-9. [15745892]
- Stuhlinger HG. Magnesium in cardiovascular disease. *J Clin Basic Cardiol* 2002;**5**:55-9.
- Jian W, Su L, Yiwu L. The effects of magnesium prime solution on magnesium levels and potassium loss in open heart surgery. *Anesth Analg* 2003;**96**:1617-2. [12760983] [doi:10.1213/01.ANE.0000065444.21593.23]
- Wilkes NJ, Mallett SV, Peachey T, Di Salvo C, Walesby R. Correction of ionized plasma magnesium during cardiopulmonary bypass reduces the risk of postoperative cardiac arrhythmia. *Anesth Analg* 2002;**95**:828-34. [12351253] [doi:10.1097/00000539-200210000-00008]
- Wyman MG, Wyman RM, Cannom DS, Criley JM. Prevention of primary ventricular fibrillation in acute myocardial infarction with prophylactic lidocaine. *Am J Cardiol* 2004;**94**:545-51. [15342281] [doi:10.1016/j.amjcard.2004.05.014]
- Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med* 2002;**346**:884-90. [11907287] [doi:10.1056/NEJMoa013029]
- Kurian GA, Paddikkala J. Effect of Intra-Operative Magnesium Supplementation in Plasma Antioxidant Levels, Trace Elements and Electrolyte Balance in Serum of Coronary Artery Bypass Graft Patients. *J Clin Basic Cardiol* 2007;**10**:11-15.
- Satoh N, Kitada Y. Cardioprotective effect of MCC-135 is associated with inhibition of Ca²⁺ overload in ischemic/reperfused hearts. *Eur J Pharmacol* 2004;**499**:179-87. [153 63965] [doi:10.1016/j.ejphar.2004.07.095]
- Treggiari-Venzi MM, Waeber JL, Perneger TV, Suter PM, Adamec R, Romand JA. Intravenous amiodarone or magnesium sulphate is not cost-beneficial prophylaxis for atrial fibrillation after coronary artery bypass surgery. *Br J Anaesth* 2000;**85**:690-5. [11094581] [doi:10.1093/bja/85.5.690]
- Polderman KH, Girbes AR. Severe electrolyte disorders following cardiac surgery: a prospective controlled observational study. *Crit Care* 2004;**8**:R459-66. [15566592] [doi:10.1186/cc2973]
- Dorman BH, Sade RM, Burnette JS, Wiles HB, Pinosky ML, Reeves ST, Bond BR, Spinale FG. Magnesium supplementation in the prevention of arrhythmias in pediatric patients undergoing surgery for congenital heart defects. *Am Heart J* 2000;**139**:522-8. [10689268] [doi:10.1016/S0002-8703(00)90097-8]
- Azar RR, Berns E, Seecharran B, Veronneau J, Lippman N, Kluger J. De novo monomorphic and polymorphic ventricular tachycardia following coronary artery bypass grafting. *Am J Cardiol* 1997;**80**:76-8. [9205025] [doi:10.1016/S0002-9149(97)00287-7]
- England MR, Gordon G, Salem M, Chernow B. Magnesium administration and dysrhythmias after cardiac surgery. A placebo-controlled, double-blind, randomized trial. *JAMA* 1992;**268**:2395-402. [1404796] [doi:10.1001/jama.268.17.2395]
- Shiga T, Wajima Z, Inoue T, Ogawa R. Magnesium prophylaxis for arrhythmias after cardiac surgery: a meta-analysis of randomized controlled trials. *Am J Med* 2004;**117**:325-33. [15336582] [doi:10.1016/j.amjmed.2004.03.030]
- Wistbacka JO, Koistinen J, Karlqvist KE, Lepojärvi MV, Hanhela R, Laurila J, Nissinen J, Pokela R, Salmela E, Ruokonen A, et al. Magnesium substitution in elective coronary artery surgery: a double-blind clinical study. *J Cardiothorac Vasc Anesth* 1995;**9**:140-6. [7540058] [doi:10.1016/S1053-0770(05)80184-3]
- Tchervenkov CI, Symes JF, Sniderman AD, Lisbona R, Derbekyan VA, Novick RJ, Wynands JE, Dobell AR, Morin JE. Improvement in resting ventricular performance following coronary bypass surgery. *Ann Thorac Surg* 1985;**39**:340-5. [3872642]
- Baraka A, Kawkabani N, Dabbous A, Nawfal M. Lidocaine for prevention of reperfusion ventricular fibrillation after release of aortic cross-clamping. *J Cardiothorac Vasc Anesth* 2000;**14**:531-3. [11052433] [doi:10.1053/jcan.2000.9484]
- Fall SM, Burton NA, Graeber GM, Head HD, Lough FC, Albus RA, Zajtchuk R. Prevention of ventricular fibrillation after myocardial revascularization. *Ann Thorac Surg* 1987;**43**:182-4. [3492974]