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Review Article

Comparison of Procaine and Lidocaine in Cardioplegia for Preventing Ventricular Fibrillation After Aortic Cross-Clamping Release in Coronary Artery Bypass Graft

Rach Pongseeda
Komkrit Komuttarin, MD
Monthian Nithithanakul
Nathamon Srivirojmanee

Department of Surgery, Maharat Nakhon Ratchasima Hospital

Abstract

Background: The use of Procaine hydrochloride in cardioplegia has been discontinued due to challenges importing the product from outside the country despite its crucial role in preserving myocardium during heart surgery. However, Lidocaine hydrochloride, an anti-arrhythmic medication, functions similarly to Procaine hydrochloride. Both medications are compared regarding their effectiveness in preventing ventricular fibrillation, the most common type of heart arrhythmia, after releasing the aortic cross-clamp in cardiac surgery.

Materials and Methods: This is a retrospective study in which data was collected from medical records of patients who were operated on with coronary artery bypass grafts between May 2017 and August 2023. Patient demographics and early outcomes between the two groups were analyzed.

Results: A total of 328 patients who underwent CABG were divided into 2 groups, respectively. Group "P" received cardioplegia solutions with Procaine hydrochloride, whilst group "L" received cardioplegia solutions with Lidocaine hydrochloride. The average age of the participants was 64.19 years old in group P and 64.24 years old in group L. The duration of the aortic cross-clamp was significantly different between the two groups, with durations of 76.06 minutes and 87.79 minutes, respectively, showing a *p*-value of less than 0.01 in statistical analysis. Following the release of aortic cross-clamping, the occurrence of ventricular fibrillation was observed in 37 patients (43%) in the first group and 49 patients (56.9%) in the second group, with no significant difference noted. After defibrillation at 10 joules, there were 21 patients (24.4%) in the first group and 13 patients (15.1%) in the second group, indicating a significant difference. Additionally, no significant difference was observed in the duration of the CCU stay between both groups.

Conclusion: Cardioplegic solution containing Lidocaine hydrochloride provides the same clinical result as Procaine hydrochloride in coronary artery bypass grafting surgery.

Keywords: Coronary artery bypass graft, Lidocaine hydrochloride, Procaine hydrochloride, Ventricular fibrillation

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Corresponding author: Rach Pongseeda, Department of Surgery, Maharat Nakhon Ratchasima Hospital, Thailand; E-mail: de_sharp@hotmail.co.th

Introduction

Coronary artery disease (CAD) is a common heart condition where a narrowing of the coronary artery has been partially or entirely blocked, causing insufficient delivery of blood to the heart. There are alternative management strategies to reduce the risk of further problems, commonly involving medication and lifestyle modification. However, once the patient has developed a tolerance to medication, surgical correction and coronary artery bypass grafts (CABG) should be the next consideration for physicians.[1]

Arrhythmias and ventricular fibrillation (VF) likely occur after cardiac surgery, which has a deteriorating impact on mortality and morbidity rates.[2,3] Research has shown a correlation between the incidence of ventricular fibrillation and the ischemic time of the heart after an aortic cross-clamp has been removed. Therefore, we rely on the cardioplegic solution to play an essential role in protecting the myocardium during the operation.[4] Several additives, such as beta-blockers and calcium blockers, can be used to prevent arrhythmia after aortic declamp.[5] Lidocaine and Procaine hydrochloride are additives used in cardioplegic solutions to induce cardiac arrest. They work by reducing extracellular sodium levels, thereby depriving the cells of the sodium needed for action potential. Additionally, they help stabilize the cell membrane and maintain a small amount of extracellular potassium, facilitating the restoration of heart rhythm following ischemic periods.[4,6] In addition, the risk of seizure as a complication of Lidocaine toxicity is particularly concerning for patients undergoing cardiac surgery because postoperative seizure in cardiac patients is a known independent risk factor for permanent neurologic deficits and operative mortality.[7]

Procaine hydrochloride, which was used in cardioplegia, has been discontinued for import from outside the country. As a result, many cardiology centers in Thailand have developed their cardioplegia solution in hospitals, where Lidocaine Hydrochloride is an anti-arrhythmic medicine that works in the same way as Procaine Hydrochloride.[8]

In this study, we studied the prevalence of ventricular fibrillation by using Lidocaine hydrochloride and Procaine hydrochloride in cardioplegia reagents to determine if there is an arrhythmia after the release of an aortic cross-clamp. Also, we investigated the complications that may occur during and after surgery.

Materials and Methods

Ethical committee approval was obtained from the Maharat Nakhon Ratchasima Hospital Institutional Review Board (090/2023). After informed consent, since this is a retrospective study, data from three hundred and twenty-eight patients who underwent CABG and were divided into two groups was collected retrospectively from May 9th, 2017, to August 25th, 2023, to study the incidence of cardiac arrhythmia after the removal of artery clamping in arrest reagents combined with Procaine hydrochloride and Lidocaine hydrochloride.

The primary outcome was ventricular fibrillation (VF) after aortic cross-clamping release. Secondary outcomes were defibrillation requirement, use of the temporary pacemaker, intra-aortic balloon pump, creatinine values, intubate time, and 30-day hospital mortality.

Data Collection

The authors collected demographic data, echocardiographic data, cardiopulmonary bypass time, aortic cross-clamp time, cardiac arrhythmia post-aortic clamp off, Number of defibrillations, inotropic drug support duration transfers, cardiac care unit stay, hospital stay, and lastly, in-hospital mortality from the medical records.

Surgical Technique

All patients were operated on under standard CPB after median sternotomy and aortic arterial and two-stage right atrial venous cannulation with mild to moderate hypothermia (temperature 32–34 ˚C). Cold-blood cardioplegia was used for myocardial protection. Antegrade cardioplegia was given. At this stage, patients in Group P were administered cardioplegia containing Procaine hydrochloride, initially at a dose of 20 cc/kg, followed by a maintenance dose of 10 cc/kg every 20 minutes. Patients in Group L received cardioplegia with Lidocaine hydrochloride, administered at the same initial and maintenance doses. The heart was vented through the aortic root, followed by clamping of the ascending aorta. Subsequently, distal anastomosis of coronary artery bypass grafts was performed, followed by the completion of aortocoronary bypass under a double clamp technique. Once rewarming was completed, cardiopulmonary bypass was discontinued, and decannulation was performed, along with checking for bleeding points and placement of drains. Finally, the chest was closed, and the patient was transferred to the cardiac critical care unit.

Statistical analysis

The data were analyzed using SPSS version 29.0. Continuous variables were reported as mean ± standard deviation and compared using the independent sample t-test. Categorical variables were reported as frequency and percentage of the total group and compared using the chi-square test. All *p*-values ≤ 0.05 were considered significant.

Results

A total of 328 patients were studied: 164 in cardioplegia solution with Procaine hydrochloride (group P) and 164 in cardioplegia solution with Lidocaine hydrochloride (group L). No statistically significant difference was determined between the groups regarding diabetes mellitus, hypertension, and ejection fraction over 40% ($p = 0.50$, 0.60, and 0.16, respectively) (Table 1).

Table 1 Baseline patients' characteristics

Factor	Cardioplegia			*p*-value
	All	Group P	Group L	
Mean age; mean ± SD	64.44 ± 8.8	64.19 ± 8.20	64.24 ± 10.6	0.963
Male gender; n (%)	227 (69.2)	110 (67)	117 (71.3)	0.402
Comorbid; n (%)				
DM	153 (46.6)	73 (44.5)	79 (48.1)	0.506
HT	291 (88.7)	144 (87.8)	147 (89.6)	0.602
Laboratory finding; mean ± SD				
EF	48.33 ± 15.96	49.40 ± 15.89	46.93 ± 16.40	0.166
Creatinine	1.65 ± 6.59	2.24 ± 12.01	3.01 ± 15.92	0.622
Creatinine Clearance	58.76 ± 26.98	58.15 ± 27.13	59.08 ± 27.26	0.757
NYHA; n (%)				
Class I	27 (8.2)	12 (7.3)	15 (9.1)	0.547
Class II	230 (70.1)	116 (70.7)	114 (69.5)	0.809
Class III	66 (20.1)	33 (20.1)	33 (20.1)	1
Class IV	5 (1.5)	3 (1.8)	2 (1.2)	0.652

The duration of cardiopulmonary bypass time showed an insignificant difference between groups (groups P 120.51 vs. groups L 145.81 minutes). However, the period of aortic clamping significantly differed in both groups (groups P 76.07 vs. groups L 87.79 minutes) at $P < 0.01$. There was no difference in ventricular fibrillation occurrence after the aortic clamping was released between groups (groups P 22.6% vs. groups L 29.9%). The defibrillation results (10 joules) of the ECG returned to normal and showed that the difference between groups was statistically significant (group P 24.4% vs. group L 15.1%; $p = 0.005$). and defibrillation greater than 10 joules in group P (18.6%) was lower than in group L (41.9%), and the difference between the two groups was statistically significant ($p = 0.005$). There was no significant difference in the number of defibrillations between groups (groups P = 0.35 vs. groups L = 0.46), respectively. There was also no significant difference in bradycardia between groups (groups P 1.8% vs. groups L 4.3%). With the dysfunctional heart patients who were eligible for an intra-aortic balloon pump, there was no significant difference between groups (groups P 1.8% vs. groups L 4.9%). The use of inotropic medication during the transfer of both groups showed no significant difference (groups P 56.7% vs. groups L 53.7%), respectively (Table 2).

There was no significant difference in intubation periods between groups (groups P 2.25 vs. groups L 2.31 days). after being discharged from the cardiac operating room to the cardiac care unit (CCU). Creatinine levels after surgery did not increase as much between groups (groups P 1.15 vs. groups L 1.56 mg/dl). There was no significant difference in CCU stay between groups (groups P 7.48 vs. groups L 6.61 day) or the proportion of patients within 30-day mortality rates between groups (groups P 6.1% vs. groups L 6.1%) (Table 3).

Table 2 Variables and indicators related to arrhythmia during surgery in the two studied groups

Factor	Cardioplegia		*p*-value
	All	With Procaine	With Lidocaine	
Operate; n (%)				
CABG x 2	14 (4.3)	7 (4.3)	7 (4.3)	1
CABG x 3	116 (35.4)	56 (34.1)	60 (36.6)	0.644
CABG x 4	181 (55.2)	93 (56.7)	88 (53.7)	0.579
CABG x 5	17 (5.2)	8 (4.9)	9 (5.5)	0.803
Bypass time; mean ± SD	133.68 ± 85.45	120 ± 29.58	145.81 ± 116.41	0.07
Aortic cross-clamp time; mean ± SD	82.21 ± 21.52	76.07 ± 17.92	87.79 ± 24.04	**< 0.01**
VT/VT; n (%)	86 (26.3)	37 (22.6)	49 (29.9)	0.123
Defibrillation; n (%)	86 (26.3)	37 (22.6)	49 (29.9)	0.123
Defibrillation 10 Joule	34 (39.5)	21 (24.4)	13 (15.1)	**0.005**
Defibrillation > 10 Joule	52 (60.5)	16 (18.6)	36 (41.9)	**0.005**
Number of defibrillation	0.41 ± 0.84	0.35 ± 0.75	0.46 ± 0.91	0.265
Anesthesia uses drugs; n (%)				
Lidocaine hydrochloride	42 (12.8)	17 (10.4)	25 (15.2)	0.186
Cordarone	6 (1.8)	1 (0.6)	5 (3)	0.099
Magnesium sulfate	12 (3.7)	4 (2.4)	8 (4.9)	0.239
Temporary pacemaker; n (%)	10 (3)	3 (1.8)	7 (4.3)	0.199
Intra-aortic balloon pump (IABP); n (%)	11 (3.4)	3 (1.8)	8 (4.9)	0.125
Inotropic drug during transfer; n (%)	249 (75.9)	114 (69.5)	135 (82.3)	0.07

Table 3 Postoperative parameters and outcomes

Factor	Cardioplegia		*p*-value
	All	With Procaine	With Lidocaine	
Intubate time (day); mean ± SD	2.28 ± 3.79	2.25 ± 4.18	2.31 ± 3.38	0.873
Laboratory finding: mean ± SD				
Creatinine day 1	1.36 ± 3.85	1.15 ± 0.95	1.56 ± 5.3	0.336
Creatinine day 2	1.44 ± 1.17	1.46 ± 1.09	1.42 ± 1.26	0.748
CCU stay, day; mean ± SD	7.05 ± 7.55	7.48 ± 8.86	6.61 ± 5.97	0.297
Hospital stays, day; mean ± SD	12.23 ± 12	12.11 ± 14.47	12.34 ± 8.9	0.862
30 days in hospital mortality; n (%)	20 (6.1)	10 (6.1)	10 (6.1)	1

SD: standard deviation, DM: diabetes mellitus, HT: hypertension, EF: ejection fraction, NYHA: New York Heart Association, CABG: coronary artery bypass graft, VT: ventricular tachycardia, VF: ventricular fibrillation, CCU: critical care unit, IQR: interquartile range

Discussion

Cardiac arrhythmias are one of the most common complications after open heart surgery and are an important factor in mortality and morbidity.[2,9] The incidence of post-operative ventricular arrhythmias may range from 1.8% to 13%.[10] Ventricular fibrillation status and attempts for treatment by internal defibrillation may injure the myocardium during reperfusion.[11] Lidocaine affects the sodium channels and decreases late depolarization. By increasing the diastolic electric current, shock works as an anti-arrhythmic agent.[12] Procaine hydrochloride is also a local anesthetic agent that may have an antiarrhythmic role and has a similar action mechanism to Lidocaine.

Therefore, a cardioplegic solution is used to prevent myocardial damage and develop its protection, and choosing a cardioplegic solution is important in this regard.[2,13]

The cardioplegic solution protects the myocardium against ischemia and events during reperfusion.[4] Lidocaine and Procaine hydrochloride are two additives commonly included in cardioplegic solutions. These agents function by reducing extracellular sodium levels, thereby inducing cardiac arrest by depriving the heart of the sodium needed for action potential generation. Additionally, they facilitate a small increase in extracellular potassium, aiding in stabilizing cell membranes. This mechanism helps restore normal heart rhythm following periods of ischemia.[4,6]

In the recent investigation, no significant difference was noted between the two groups regarding the spontaneous return to sinus rhythm after declamping. However, the group treated with Procaine hydrochloride showed a higher rate of spontaneous return. Additionally, there was a notable decrease in the need for Lidocaine, cordarone, magnesium, and inotropic drugs during transfers for sinus rhythm in the Procaine hydrochloride group. These results mirror those found in Sellevold's study,[6] which compared the effectiveness of two cardioplegic solutions – one containing 1 mM Procaine hydrochloride and the other 0.9% normal sodium in the Lidocaine group. Sellevold's research focused on the occurrence of ventricular fibrillation after aortic declamping and the potential of Procaine hydrochloride to reduce such incidents post-declamping. In our study, the percentage of ventricular arrhythmias between the two groups was 10%–24%, and there was no significant difference between the two groups regarding the occurrence of ventricular arrhythmias.[14] Previous studies have explored that Lidocaine causes a reversible, concentration-dependent increase in the energy requirements for successful defibrillation.[15] Previously published studies have evaluated the effects of Lidocaine hydrochloride and Procaine hydrochloride in cardioplegia. There was no variation in postoperative kidney function between the two groups that resulted in acute kidney injury.[16]

Despite the fact that Procaine hydrochloride in cardiac arrest reagents has been extensively investigated and that arrhythmia following aortic clamping has not varied drastically, it was determined to continue coronary artery bypass surgery.

Limitations

This retrospective observational study cannot control past relevant variables and data collected from a single center; therefore, it cannot be used to represent most of the population. Coronary heart disease is a life-threatening condition, sometimes concomitant with valvular heart disease. There were only 328 cases over the seven-year recording period, so extending the data collection time to allow a broader population may impact the results that differ from prior research, such as demographic characteristics, surgical teams, and patient care patterns. This study compared fibrillation following aorta clamping to Procaine hydrochloride and lidocaine hydrochloride in a cardioplegia solution that required comparable environmental variables as feasible. Different circumstances may vary over time, resulting in comparable unpredictability.

Conclusion

Lidocaine can be an alternative agent for Procaine hydrochloride with a similar incidence of ventricular fibrillation.

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