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Research Article

A Comparison of the Effects of Lidocaine or Procaine containing St. Thomas No. 2 Cardioplegia Solution on Post-operative Renal Function

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Abstract

Acute kidney injury (AKI) is one of the most common complications after cardiac surgery and is thought to result as a complex interplay between peri-operative factors. The effects of cardioplegia on renal function have not been well defined. We compared the effects of St. Thomas No. 2 cardioplegia solution modified with lidocaine or procaine and found no statistically significant difference in between the two groups. We carried out further multivariate testing adjusting for diabetes and found no statistically significant changes in renal function between the two groups.

Keywords: Cardioplegia; Renal failure; Lidocaine; Procaine; St. Thomas No. 2

Introduction

Acute kidney injury (AKI) is one of the most common complications after cardiac surgery and has been reported at various rates between 1-30% and is associated with increased morbidity and mortality [1-3]. The mechanism behind AKI after cardiac surgery is not well defined and is thought to be the result of a complex interaction between peri-operative factors [1,2,4].

Whilst many studies that look at pre-operative risk factors for the development of renal failure exist, intraoperative factors have not been well investigated [5-7]. Currently in global literature, the association between different cardioplegia solutions and AKI has not been examined.

In this study, we look at the effects of St-Thomas Solution No. 2 cardioplegia modified with lidocaine or procaine on post-operative renal function. We also hypothesise that diabetes will have an additive effect in addition to cardioplegia in negatively affecting renal function.

Study Design

Institutional approval was gained for the modification of our standard cardioplegia solution with either lidocaine or procaine. Both solutions were compounded by Baxter International (Deerfield, IL, USA).

The standard cardioplegia solution composition is given below in Table-1 to which either 1mmol lidocaine (AHK 5560) or procaine Hydrochloride (CP 5537) was added.

All patients undergoing cardiac surgery at our institution between March 2016 – 2017 were included in this study. Cases that were done without the use of CP 5537 or AHK 5560 were excluded. Our database contained 126 patients with 79 people being administered CP 5537 and 47 individuals receiving AHK 5560. Randomisation was not possible due to surgeon preference.

The anaesthetic and perfusion protocols were the same between both groups. Non pulsatile cardiopulmonary bypass was used to provide a mean arterial pressure of 50mm Hg. All operations were done using a LivaNova S5 pump using cold blood cardioplegia at a ratio of four parts blood and one part cardioplegia solution. Antegrade and retrograde delivery routes were used where possible and re-dosing was done at 20 minute intervals with half strength (8:1) solutions. Patients were passively cooled to 28°C and actively warmed to 37°C on separation from bypass.

Renal function (viz. creatinine, urea and eGFR) was measured on post-operative days 0, 1 and 5 in keeping with unit protocols. CKD was diagnosed as defined in the 2012 KIDGO guidelines.

Results were analysed in SPSS v.26 and are presented as mean ± standard deviation unless specified otherwise. For brevity, comparisons have been reported as CP 5537 results vs. AHK 5560 results.

Two statistical tests were used in this study: one way repeated measures ANOVA using Mauchly's test of sphericity and a 2-way ANOVA using Levene's test of Equality. A p value of 0.05 was considered statistically significant.

Results

Sodium 77mmol
Potassium 40mmol
Magnesium 15mmol
Chloride 149mmol
Glucose 11mmol
Sodium bicarbonate 25mL 8%

Table 1: Standard Cardioplegia Solution (added to 1L normal saline by volume)

		Cardioplegia Type			
		CP 5537		AHK 5560	
		Mean	Count	Mean	Count
Age of patient		65		67	
Sex	Male		58 (73.4%)		39 (83%)
	Female		21 (26.6%)		8 (17%)
Diabetic Status	Diabetic		24 (30.4%)		13 (27.7%)
	Not Diabetic		55 (69.6%)		34 (72.3%)
Chronic Kidney Disease	Stage 2		38 (48.1%)		25 (53.2%)
	Stage 3a		9 (11.4%)		7 (14.9%)
	Stage 3b		6 (7.6%)		4 (8.5%)
	Stage 4		2 (2.5%)		0
	Stage 5		2 (2.5%)		1 (2.1%)
Preoperative Dialysis			2		1
AXC Time		63		59	
CPB Time		98		92	
Pre Op Creatinine		112		110	
Pre Op Urea		7.3		7.0	
Pre Op eGFR		70		71	

CPB: Cardiopulmonary Bypass Time (min); AXC: Aortic Cross Clamp Time (min); Creatinine (µmol/L); Urea (mmol/L); estimated GFR as calculated by the Cockcroft-Gault Equation (mL/min/1.73m^2)

Table 2: Clinical Characteristics.

		df	Mean Square	F	P	Partial η2
Creatinine	Time*CP	1.540	1464.479	.889	.389	.007
	Error	187.887	1646.473			
Urea	Time*CP	1.596	2.434	.241	.735	.002
	Error	193.084	10.084			
eGFR	Time*CP	2.493	64.901	.761	.494	.006
	Error	301.602	85.265			

Time: Repeated measures on post operative days 0, 1 and 5; CP: cardioplegia; df: degrees of freedom

Table 3: Repeated measures ANOVA after Greenhouse-Geisser Correction

Discussion

Our patient base had a similar demographic profile compared to other major centres in Australia, having a mean age of 65.6±10.6 years and a male majority (n=97; 76.9%). 37 (29.4%) patients were diabetic with comparable spreads across both cardioplegia groups.

94 (74.6%) patients had some degree of CKD and three patients had stage 5 CKD requiring dialysis. Stage 1 CKD was not reliably identified in our study group. Pre-operative creatinine, urea and eGFR were similar between both groups (112±121 vs. 110±122 μmol/L; 7.3±3.4 vs. 7±3.9 mmol/L; 70±21 vs. 71±20 mL/min/1.73m^2).

Although not mentioned explicitly in the results section, there were a mix of cases including coronary artery bypass grafts, valve replacements and aortic operations including emergency management of Type – A dissections. All urgency classifications as per the ANZSCTS database were included in the study [8]. Total cardiopulmonary bypass and aortic cross clamp times were similar between both groups (98±38 vs. 92±32 mins; 63±33 vs. 59±28 minutes).

A one-way repeated measures ANOVA was performed to determine if there was a statistically significant difference in the post-operative day 0, 1, 2 and 5 creatinine, urea and eGFR tests between the two cardioplegia groups. The assumption of sphericity was not met in all three tests (Mauchly's test of sphericity: $\chi^2(5) = 194.2$, $p < 0.001$; $\chi^2(5) = 200.8$, $p < 0.001$; $\chi^2(5) = 40.9$, $p < 0.001$). Epsilon was calculated according to Greenhouse and Geisser in all three cases and used to correct the ANOVA. Statistically significant changes were not noted in creatinine [$F(1.540, 187.887) = 0.889$, $p=0.389$], urea [$F(1.596, 193.084) = 0.241$, $p=0.735$] and eGFR [$F(2.493, 301.602) = 0.761$, $p=0.494$] between the two cardioplegia types. Further post-hoc tests were therefore not carried out.

A 2 way ANOVA was then performed to examine the effects of diabetes on the change of creatinine, urea and eGFR between pre-operative and post-operative day 5 levels. Statistically significant interactions between diabetic status and cardioplegia type were not noted in creatinine [$F(1, 122) = 2.709$, $p = 0.102$, partial $\eta^2 = 0.22$], urea [$F(1, 122) = 2.312$, $p = 0.131$, partial $\eta^2 = 0.19$] and eGFR [$F(1, 122) = 2.709$, $p = 0.102$, partial $\eta^2 = 0.22$]

In conclusion, we have found no significant differences in the post-operative renal function when using procaine or lignocaine enriched cardioplegia solutions. Patients with pre-existing CKD remained within their classification and any transient AKI resolved by the 5th postoperative day without targeted therapy. Neither group had cases who had to be commenced on temporary or new long-term dialysis.

There are several limitations to this study and the field in general that need to be addressed. First, the lack of randomisation due to institutional factors is sub-optimal even though this was a prospective study. Pre-existing CKD caused a significant number of outliers making statistical modelling difficult. Cardiopulmonary bypass may contribute to AKI in various ways including activation of pro-inflammatory cytokines, hypoperfusion etc. Temperature has also not shown to be a significant factor in the development of renal failure but may affect hypoperfusion in general. Finally, as with all but the largest of studies, larger patient cohorts can improve the power of the study [5].

Conclusion

No statistically significant reduction in renal function was seen when comparing St. Thomas No. 2 cardioplegia solution modified with lidocaine vs. procaine. We also did not find a statistically significant reduction in renal function when adjusting for the presence or absence of diabetes.

Ours is the first study that we are aware of that has investigated relatively common modifications to the St. Thomas No. 2 cardioplegia solution within the context of renal dysfunction after cardiac surgery. The authors hope that further studies can be undertaken to build on these results.

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