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Myocardial protection with histidine-tryptophan-ketoglutarate solution in comparison with hypothermic hyperkalemic blood solution in the correction of acyanotic congenital heart diseases

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Abstract

Background: Intraoperative myocardial preservation is essential in pediatric cardiac surgeries. The combination of hypothermia and hyperkalemic cardioplegia is commonly used. Histidine-tryptophan-ketoglutarate (HTK–Custodiol) is a long-acting crystalloid cardioplegia which induces cardiac arrest by reducing the extracellular sodium concentration. Cold blood cardioplegia has many modifications differing in the blood: crystalloid ratio, buffers, substrates, and final potassium concentration which induces cardiac arrest in diastole as the main role. We compared cold histidine-tryptophan-ketoglutarate crystalloid (HTK) solution with hypothermic hyperkalemic blood (HHB) cardioplegia solution regarding their efficacy in myocardial preservation in patients undergoing total repair of non-cyanotic congenital cardiac defects. We assessed postoperative cardiac troponin level, myocardial function, inotropic support, intensive care unit (ICU) length of stay, hospital length of stay, and the incidence of prolonged postoperative mechanical ventilation as indicators of myocardial protection.

Results: This interventional, single-blinded, randomized, comparative, and prospective clinical study was conducted randomly on 60 patients, aged between 6 and 24 months undergoing total surgical repair. We found no statistically significant difference regarding patients' personal, demographics, and operative details (surgery duration, cardiopulmonary bypass time, aorta clamp time). However, patients who were given HTK cardioplegia were found to stay less in the ICU (with a p value <0.05). However, there was no statistically significant difference between both groups as regards hospital length of stay. Also, all patients were extubated in less than 24-h duration. There was a statistically significant difference between both groups regarding troponin levels after 8, 12, and 24 h post-bypass in favor of the HHB solution. Interestingly, no significant correlation was proved between both groups regarding myocardial function (EF%, FS) and level of inotropic support (assessed by maximum vasoactive inotropic score).

Conclusions: Hypothermic hyperkalemic blood cardioplegia showed better results in myocardial preservation than the cold histidine-tryptophan-ketoglutarate solution in the repair of noncyanotic congenital cardiac defects.

Trial registration: Pan African Clinical Trial Registry, PACTR202109777317416. Registered on 28 September 2021—Retrospectively registered, https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=16154

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Keywords: Myocardial preservation, Cardioplegia, Vasoactive inotropic score

Background

Intraoperative myocardial preservation is essential in pediatric cardiac surgeries as after elective ischemia, depletion of adenosine triphosphate occurs, and this leads to myocardial acidosis, cell swelling, and irreversible structural damage (Angeli 2011).

The combination of hypothermia and hyperkalemic cardioplegia has become the most common method of myocardial protection (Talwar et al. 2013).

In 1987, Buckberg and colleagues put six physiologic requirements in the design of a cardioplegic solution, which are used to compare each solution as regards its effectiveness (Buckberg 1987).

Cardioplegia solutions protect the myocardium by decreasing the metabolic demands, as well as avoiding osmotic, electrolytic, and pH imbalances (Yamamoto and Yamamoto 2013).

Buckberg's blood cardioplegia is a 4:1 blood to crystalloid, glucose-based cardioplegia with a potassium chloride (KCl) concentration of about 36 mmol/l and given in 20-min intervals. As the blood is an inherent component, it has higher oxygen carrying capacity than conventional crystalloid cardioplegia, has its own inherent buffering system like histidine, contains natural buffers of the blood part, results in less hemodilution in patient's circulation, keeps the oncotic pressure of the plasma around normal levels, and includes free radical scavenging molecules. Blood cardioplegia can be administered as warm (37°C), tepid (29°C), and cold (4°C) (Mick et al. 2015).

Blood cardioplegia is advantageous and more commonly used as it induces cardiac arrest in an oxygenated environment. It is unnecessary to add anaerobic substrates or oncotic constituents as the blood component contains them (Kotani et al. 2013).

HTK solution contains tryptophan (for membrane stabilization), ketoglutarate (for increased energy production during reperfusion—a precursor to adenosine triphosphate), mannitol (osmotic agent for cell membrane regulation), and histidine buffer (supports anaerobic glycolysis and maintains a normal pH). Its osmolality is 310 milliosmoles/liter, and it is prepared in 1000 ml of sterile water for injection (Buckberg 1987).

Histidine-tryptophan-ketoglutarate (HTK) cardioplegia induces cardiac arrest by reducing the extracellular sodium concentration which minimizes the transsarcolemmal gradients of this ion and hyperpolarizes the plasma membrane (Preusse 2016).

Reduced oxygen supply "or blood flow" and increased demand are usually the basic mechanisms of myocardial ischemia. A decrease in blood flow can occur in cases with congenital coronary malformations, acquired coronary artery diseases, or post-surgical repair (Carmona et al. 2013).

Ischemic myocardium shows coagulation necrosis and contraction bands which represent compressed sarcomeres and develop after reperfusion following ischemia (Morita et al. 2015).

Cardioplegia solutions divide into crystalloid (HTK) and blood cardioplegia (plegisol, Del Nido). Del Nido cardioplegia has been widely used as it acts as a long-acting non-glucose, blood-based solution which can give ischemia time nearly 90 min and can be used for a single-dose myocardial preservation during congenital cardiac procedures. It is composed of 1 l Plasmalyte-A, KCl 26 mmol/l, mannitol, $NaHCO_3$, lidocaine, and magnesium sulfate. It is mixed with the blood and delivered in a 1:4 blood: crystalloid ratio. Its inherent advantage is the number of dosing intervals. So, it is recommended in long procedures with the anticipation of multiple dosing or in surgeries where it is not feasible to do that frequently (Charette et al. 2012).

Regarding cold blood cardioplegia, a simple safe easy low-cost modification has been studied and introduced as a long-acting, single-dose cold blood cardioplegia rather than depending on a well-recognized HTK solution as a long-acting method but lacks the characteristics of conventional blood-based cardioplegia with multi-dosing intervals. This is a 4:1 blood to the crystalloid solution, and the crystalloid part was made by adding a 40-ml potassium chloride (80 mmol) and 30-ml $NaHCO_3$ (30 mmol) to 930 ml Ringer's lactate. Thus, the final potassium concentration was 20–24 mmol/l (Molina et al. 2018).

We aimed to compare the efficacy of HTK solution with hypothermic hyperkalemic blood (HHB) solution in myocardial protection in children.

Methods

We enrolled 60 patients in our study, aged between 6 and 24 months. All of them had received the same anesthetic protocol under similar conditions and undergone elective total surgical repair using CPB.

Ethical considerations

After the approval of the Ethical Committee of Ain Shams University with FMASU MD 64/2020, this interventional, randomized, and prospective clinical study

was conducted at Ain Shams University Hospitals from February 2020 to February 2021. Written informed consent was obtained from the patients' legal guardians after explaining the procedure and its potential complications.

Inclusion criteria

We enrolled 60 patients, aged from 6 months to 2 years of both sexes, diagnosed with non-cyanotic congenital heart diseases underwent total repair under cardiopulmonary bypass (CPB), and scheduled for elective operations.

Exclusion criteria

Patients who were scheduled for palliative surgeries, reoperation, underwent emergency surgeries, patients with reduced left ventricular function as determined by left ventricular ejection fraction less than 40%, patients with renal or liver impairment as determined by elevated creatinine levels or liver enzymes more than normal values for age, or patients with any neurological dysfunction as epilepsy and cerebral palsy were excluded.

Patients for both groups were admitted to the hospital the night before the procedure. In the morning, the patients were shifted to the operating room, and the peripheral intravascular access was inserted. After applying the standard monitoring devices with pulse oximetry, 5 leads electrocardiogram, capnography (end-tidal CO_2), and non-invasive blood pressure, all operations were performed using a standard general anesthesia protocol with using intravenous induction with ketamine (1–2 mg/kg) and atropine (0.01–0.02 mg/kg) after the intravenous blood access was obtained, then injection of midazolam (0.05–0.1 mg/kg), fentanyl (10–20 mcg/kg), and cisatracurium (0.15 mg/kg) were followed.

After induction, the endotracheal tube was inserted; its position was confirmed with chest auscultation and capnography tracing. An intraarterial catheter using a femoral puncture was inserted. The central venous catheter was inserted using a transjugular (or femoral) approach with ultrasound guidance. The maintenance of anesthesia was done with sevoflurane inhalational (1–2%), infusion of morphine (20 mcg/kg/h), and cisatracurium (2 mcg/kg/min).

A median sternotomy approach and CPB with mild systemic hypothermia (32–28 °C) were used. Topical cooling with ice was used in both groups.

Conventional ultrafiltration was performed by the end of CPB in all patients, to increase hematocrit to 40%, and was started earlier in the group of patients who received HTK solution.

Patients were randomly allocated by computer-generated randomization and using opaque-sealed envelopes into two groups according to the type of the cardioplegic solution used.

Patients who were allocated to the HTK group received the cold HTK solution (4–8 °C), administered as a single dose for up to 3 h of ischemia, antegrade in the aortic root, for 6–8 min, with an infusion of 30 mL/kg.

Patients who were allocated to the HHB group received the HHB solution; the crystalloid solution was obtained by adding 15 ml of 15% KCL (30 mEq), 25 ml of 8.4% $NaHCO_3$ (25 mEq), and 5ml of 2% lidocaine (100 mg) to a 1L Ringer's lactate. A blood cardioplegia circuit was added to the CPB machine. The perfusionist added 60 mEq KCL to the crystalloid solution via using the cardioplegia delivery system. The HHB cardioplegia was given by the perfusionist on CPB with a heat exchanger as the temperature was regulated to 4 °C and a pressure control (up to 200 mmHg prior to the heat exchanger). The dilution ratio was a 4:1 (4 parts autologous blood to 1 part crystalloid) mixture. The cardioplegia was delivered at a dose of 30 ml/kg initially, administered into the aortic root for 4–5 min, followed by repeated doses of (15 ml/kg) at 20–25 min intervals using the same pattern.

We compared HTK cardioplegia with HHB cardioplegia regarding their effectiveness in pediatric myocardial preservation. The parameters which were evaluated in this study are age (months), weight (kilogram), gender, duration of surgery, CPB, aortic clamping time (minutes), left ventricular function (EF%), level of cardiac troponin, maximum vasoactive inotropic score, ICU length of stay (LOS) (days), hospital LOS, and the incidence of prolonged postoperative mechanical ventilation more than 24 h.

The primary outcome was cardiac troponin level which was measured preoperatively (basal) once then at the end of the procedure (0 h post-CPB) and at 4, 8, 12, 18, 24, and 48 h postoperatively.

The secondary outcomes were the left ventricular ejection fraction (EF%) and the fractional shortening (FS) percentage, the maximum vasoactive inotropic score, ICU-LOS (days), the incidence of prolonged postoperative mechanical ventilation (>24 h), and the hospital LOS (days).

The left ventricular systolic function was estimated by using transesophageal echocardiography pre- and post-CPB. And by using transthoracic echocardiography after 24 and 48 h postoperatively, M Mode modality was applied to measure the left ventricular ejection fraction (EF) and fractional shortening (FS).

The inotropic support for each patient was estimated according to the maximum vasoactive inotropic score (VIS). Maximum VIS for both the first 24 h and the next 24 h were calculated. It was calculated according

to Gaies et al.'s study as follows: VIS= dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100 × epinephrine dose (mcg/kg/min) + 10 × milrinone dose (mcg/kg/min) + 10,000 × vasopressin dose (U/kg/min) + 100 × norepinephrine dose (mcg/kg/min) (Gaies et al. 2010).

Inotropes and vasopressors were added after CPB if the systolic blood pressure is less than 90 mmHg in adequately preloaded patients.

Statistical analysis

The collected data was revised, coded, tabulated, and introduced to a PC using the Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro Wilk's test was used to evaluate the normal distribution of continuous data (Ghasemi and Zahediasl 2012). The mean, standard deviation (± SD), and range were used for parametric numerical data, while the median and interquartile range (IQR) was used for non-parametric numerical data. Student's *T* test was used to assess the statistical significance of the difference between the two study group means. Mann-Whitney test (*U* test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. Regarding the level of significance, *P* value < 0.05 was considered significant, *P* value < 0.001 was considered highly significant, and *P* value > 0.05 was considered insignificant.

Sample size

The sample size was calculated using the G*power program, setting the type-1 error (α) at 0.05 and the power (1-β) at 0.8. Results from the previous study (Caputo et al., 2002) showed that the mean (95% confidence interval (CI)) of Troponin I in the cold blood cardioplegia group (CBC) was 2.4(0.7), while for cold crystalloid cardioplegia (CCC) group, it was 4.3 (1.8). The CI was transformed to standard deviation through the formula: SQRT (n)* CI/ (t alpha, df *2) to be ±1.14 and±2.82 for CBC and CCC, respectively. Calculation according to these values produced a sample size of 30 cases per group taking into consideration a 20% dropout rate.

Results

After the exclusion of two patients, the surgical plan changed and the total correction could not be done. Sixty patients were randomly allocated into two groups: HTK group and HHB group.

In groups HTK and HHB, we included cases with atrial septal defect, ventricular septal defect, atrioventricular septal defect, and partial anomalous pulmonary venous drainage ($N = 8$ and 7, 9 and 10, 10 and 7, and 3 and 6, respectively).

There was no statistically significant difference between the study groups regarding personal and demographic data as shown in Table 1.

Also, there was no statistically significant difference regarding operative details (surgery duration, CPB time, aorta clamp time). As in the HTK group, duration of surgeries, CPB time, and aorta cross-clamp time were higher as shown in Table 1.

Regarding postoperative details, ICU-LOS showed a statistically significant correlation between both groups. Group A has shown lower mean and standard deviation values with *P* value (<0.05). Patients who were given HTK cardioplegia were found to stay less in the ICU. However, there was no statistically significant difference between both groups as regards hospital LOS, as shown in Table 2. Also, all patients were extubated in less than 24-h duration. In general, fast-track extubation was planned in our center.

Regarding the study outcomes, it was found that HHB cardioplegia does not elevate troponin levels as much as HTK solution at all times of measurement. And there was a statistically significant difference between both groups regarding troponin levels after 8, 12, and 24 h post-bypass in the HHB group. This outcome raised the assumption that HHB cardioplegia is more effective in the myocardial preservation. This correlation was described in Table 3. However, by comparing both solutions in the matter of myocardial function (EF% and fractional shortening), no significant correlation was proved as shown in Tables 4 and 5. Also, both groups showed no statistically significant difference as regards inotropic support as shown in Table 6.

Discussion

In our study, there is a statistically significant difference between both groups regarding troponin levels after 8, 12, and 24 h post-bypass (p=0.023), (p=0.034), and (p=0.034), respectively. This was supported by Caputo et al. (Caputo et al. 2002), while comparing cold crystalloid (St. Thomas' I crystalloid cardioplegia, Kcl=16 mmol/l) solution (CCC) with cold blood cardioplegia (CBC) ((4:1 dilution blood/St. Thomas' I crystalloid cardioplegia, KCl adjusted to 15 mmol/L). Postoperative troponin level release was 42% lower in the CBC than the CCC group, p= 0.015).

Also, in the study done by Giordano et al. (Giordano et al. 2016) who compared HTK with cold blood

Table 1 Personal, demographic, and operative data

		Group										*P*
		HTK					HHB					
		Mean	±SD	Median	IQR		Mean	±SD	Median	IQR		
Age (months)		15.53	5.57	16.50	10.00	21.00	14.80	5.94	14.50	10.00	21.00	0.624*
Weight (kg)		7.69	0.84	7.85	7.20	8.30	7.70	1.07	7.95	7.20	8.60	0.988*
Surgery duration (min)		208.60	24.41	215.00	210.00	225.00	202.07	28.25	210.00	190.00	220.00	0.342
CPB time (minutes)		115.87	5.73	115.00	110.00	120.00	112.07	22.38	114.50	110.00	120.00	0.374
Ao clamp time (min)		84.83	4.19	85.00	83.00	88.00	78.93	18.74	82.00	75.00	87.00	0.102
		Number			%		Number			%		*P*
Sex	Male	18			60.0%		14			46.7%		0.301**
	Female	12			40.0%		16			53.3%		
Operation	Atrial septal defect	8			26.7%		7			23.3%		0.648
	Ventricular septal defect	9			30%		10			33.3%		
	Atrioventricular septal defect	10			33.3%		7			23.3%		
	Partial anomalous pulmonary venous drainage	3			10%		6			20%		

HTK histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Student *t* test; **Chi-square test. *P* value < 0.05 was considered significant

Table 2 Postoperative details

	Group										*P**
	HTK					HHB					
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR		
ICU LOS (days)	2.80	0.71	3.00	2.00	3.00	3.20	0.76	3.00	3.00	4.00	0.04
Hospital LOS (days)	8.90	1.88	8.50	8.00	10.00	9.67	2.20	9.00	8.00	11.00	0.153

ICU intensive care unit, *LOS* length of stay, *HTK* histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Student *t* test

P value < 0.05 was considered significant

Table 3 Troponin level

	Group										*P*
	HTK					HHB					
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR		
Preoperative troponin level (ng/ml)	0.01	0.02	0.00	0.00	0.01	0.09	0.44	0.00	0.00	0.01	0.341*
Postoperative troponin level (post CPB) at 0 h (ng/ml)	6.54	2.71	7.05	3.90	8.70	6.22	2.65	6.97	4.30	8.60	0.645**
Postoperative troponin level at 4 h (ng/ml)	6.50	2.52	7.10	4.50	8.60	5.31	2.11	5.54	3.97	6.67	0.051**
Postoperative troponin level at 8 h (ng/ml)	6.10	2.31	6.90	4.60	7.70	4.81	1.92	5.19	3.80	6.20	0.023**
Postoperative troponin level at 12 h (ng/ml)	5.20	2.12	5.90	3.80	6.50	4.12	1.72	4.42	3.20	5.12	0.034**
Postoperative troponin level at 18 h (ng/ml)	4.23	1.71	4.38	3.20	5.40	3.37	1.65	3.23	2.40	4.23	0.053**
Postoperative troponin level at 24 h (ng/ml)	2.97	1.29	2.85	2.10	3.80	2.29	1.11	2.10	1.60	2.90	0.034**
Postoperative troponin level at 48 h (ng/ml)	1.43	.93	1.31	.67	1.92	1.13	.80	.85	.60	1.30	0.184**

CPB cardiopulmonary bypass, *HTK* histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Mann-Whitney test; **Student's *t* test

P value < 0.05 was considered significant

Table 4 Ejection fraction % in both groups

	Group									*P**
	HTK					HHB				
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR	
Preoperative EF%	60.50	3.95	60.00	58.00	62.00	61.17	7.10	60.00	56.00	64.00	0.655
Postoperative EF% (post CPB) at 0 h	60.90	4.26	62.00	58.00	63.00	61.83	10.41	62.00	58.00	66.00	0.652
Postoperative EF% at 24 h	58.67	3.30	59.00	57.00	62.00	59.13	7.47	59.00	55.00	63.00	0.756
Postoperative EF% at 48 h	59.73	3.62	61.00	57.00	63.00	59.80	6.36	61.50	56.00	63.00	0.960

EF ejection fraction, *CPB* cardiopulmonary bypass, *HTK* histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Student's *t* test

P value < 0.05 was considered significant

microplegia in arterial switch operations, a higher peak troponin level in the custodial group was found, with a non-significant correlation, p=0.19.

Also, Demmy et al. (Demmy et al. 2008) compared to HTK solution with modified St. Thomas' Hospital Solution (Plegisol). Cardiac troponin was less in the Plegisol group than the HTK group in patients undergoing CABG operation.

Our study did not find any significant correlation regarding myocardial function determined using EF% and FS% between both groups.

Table 5 Fractional shortening in both groups

	Group										*P**
	HTK					HHB					
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR		
Preoperative FS%	30.17	2.02	30.00	29.00	32.00	31.33	5.25	30.00	28.00	32.00	0.263
Postoperative FS% (post CPB) at 0 h	30.20	2.22	30.00	28.00	32.00	32.20	8.27	32.00	28.00	32.00	0.206
Postoperative FS% at 24 h	29.20	2.04	29.00	27.00	32.00	29.20	7.12	29.00	27.00	32.00	1.0
Postoperative FS% at 48 h	29.37	2.27	30.00	28.00	32.00	30.40	4.09	30.00	28.00	32.00	0.231

FS fractional shortening, *CPB* cardiopulmonary bypass, *HTK* histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Student's *t* test

P value < 0.05 was considered significant

Table 6 Maximum vasoactive inotropic score

	Group										*P**
	HTK					HHB					
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR		
Maximum VIS at 24 h	14.07	2.26	15.00	13.00	15.00	12.93	3.38	14.00	12.00	15.00	0.133
Maximum VIS at 48 h	4.27	1.68	5.00	3.00	5.00	3.90	2.06	4.00	3.00	5.00	0.453

VIS vasoactive inotropic score, *HTK* histidine-tryptophan-ketoglutarate, *HHB* hypothermic hyperkalemic blood, *SD* standard deviation, *IQR* interquartile range; *Student's *t* test

P value < 0.05 was considered significant

This was supported by Mimic et al. (Mimic et al. 2016) who compared cold blood cardioplegia (a mixture of one part of potassium-enriched crystalloid Cp (60 ml of KCl added to 1000 ml of CCp) and four parts of autologous blood, KCl=20 mmol/l) with cold crystalloid solution (KCl=40 mmol/l).

However, Amark et al. (Amark et al. 2005) found that myocardial function was better in the blood cardioplegia group in the first hour post-CPB (p=0.046). They used cold blood cardioplegia composed of 1 part K-enriched Plegisol (60 mmol KCl added to 1000 mL Plegisol): 4 parts of the blood from the CPB circuit (final K concentration: 15 mM) and cold crystalloid cardioplegia (St. Thomas' II, KCl=16 mmol/l).

Also, Bibevski et al. (Bibevski et al. 2020) found that there was no difference as regards biventricular function assessed using echocardiography (LVEF, LVFS, RVFAC) between cold blood microplegia (blood with K+ at 30 mEq and magnesium 10 mL/L) and HTK crystalloid solution group.

Young et al. (Young et al. 1997) compared antegrade cold blood cardioplegia (4:1 dilution, blood/Plegisol, KCl concentration was 15 mEq/L) with cold crystalloid (Plegisol) cardioplegic solution in patients undergoing repair of a variety of cyanotic and non-cyanotic cardiac conditions. By using echocardiography in the assessment of ventricular function, it was revealed that blood cardioplegia did not prove a significant difference in myocardial protection. However, it was an early study, it used mild systemic hypothermia for ischemic periods, 30 °C, and a large scale of cyanotic and non-cyanotic conditions with different cellular metabolic effects was studied. Interestingly, the crystalloid cardioplegia group showed less postoperative inotropic support, mean= 5.14 (p=0.005).

As regards inotropic support in this study, maximum VIS was lower in the HHB group, after 24 h and 48 h (p=0.133 and 0.453, respectively). However, there was no statistically significant difference between both groups

Bibevski et al. (Bibevski et al. 2020) proved that there was a significantly lower inotrope score in the custodiol (9.3 ± 2.6) in comparison with the blood group (10.4 + 3), p= 0.03. In their study, scores were calculated for all patients within the first 48 h after surgery, and the highest calculated score was recorded. But we differently assessed the inotropic support as the maximum score in the first 24 h and in the 48 h were taken.

Caputo et al. (Caputo et al. 2002) while comparing St. Thomas' I crystalloid cardioplegia with cold blood cardioplegia in patients undergoing ventricular septal defect repair, concluded that a significant postoperative inotropic support was required more frequently in the crystalloid cardioplegia group than in the cold blood cardioplegia group. They defined significant inotropic support as using dopamine in a dose of 5–10 microgram/kg/min with or without another inotropic agent (p=0.23).

The crystalloid cardioplegia group showed less postoperative inotropic support in the study done by Young et al. (Young et al. 1997), (p=0.005).

Regarding ICU length of stay (LOS), we found a significant positive correlation among the HTK group. It was shorter with a mean of 2.8 days and p= 0.04 (HHB group ICU LOS mean= 3.2 days). Also, hospital length of stay (LOS) was less in HTK, p= 0.153.

This was supported in the study done by Giordano et al. (Giordano et al. 2016), as ICU LOS and hospital LOS were less in the HTK group with a non-significant correlation, p=0.49 and 0.07.

In addition, Young et al. (Young et al. 1997) did not find any significant correlation between blood and crystalloid cardioplegia regarding ICU LOS, p=0.08.

Also, Caputo et al. (Caputo et al. 2002) proved that there was no difference between ICU LOS and hospital LOS (p= 0.22 and 0.98, respectively).

Conclusions

Hypothermic hyperkalemic blood cardioplegia showed better results in myocardial preservation than cold histidine-tryptophan-ketoglutarate solution in the repair of noncyanotic congenital cardiac defects.

Abbreviations

CPB: Cardiopulmonary bypass; HHB: Hypothermic hyperkalemic blood; HTK: Histidine-tryptophan-ketoglutarate; ICU: Intensive care unit; IQR: Interquartile range; KCl: Potassium chloride; LOS: Length of stay; VIS: Vasoactive inotropic score.

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Authors' contributions

AA, GS, MK, EA, and SA have full access to all the data in the study and take responsibility for the integrity of the data. Study concept and design: GS and MK; acquisition of data: AA, EA, and SA: and analysis of data and critical revision of the manuscript: AA and GS. The authors have read and approved the final manuscript.

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Availability of data and materials

We intend to share the study protocol as well as the individual de-identified participants' data. Data will be accessible through direct contact with the corresponding author, beginning 12 months and ending 24 months following article publication.

Declarations

Ethics approval and consent to participate

The study obtained approval from the Ethical Committee of Ain Shams University (FMASU MD 64/2020). The study was registered at the Pan African Clinical Trial Registry (**PACTR202109777317416**; September 28, 2021; https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=16154). Informed written consents were obtained from the legal guardians of the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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