Original Article

Conventional hemofiltration during cardiopulmonary bypass increases the serum lactate level in adult cardiac surgery

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ABSTRACT

Objective: To evaluate the effect of hemofiltration during cardiopulmonary bypass on lactate level in adult patients who underwent cardiac surgery. **Design:** An observational study. **Setting:** Prince Sultan cardiac center, Riyadh, Saudi Arabia. **Participants:** The study included 283 patients classified into two groups: Hemofiltration group (*n*=138), hemofiltration was done during CPB. Control group (*n* = 145), patients without hemofiltration. **Interventions:** Hemofiltration during cardiopulmonary bypass. **Measurements and Main Results:** Monitors included hematocrit, lactate levels, mixed venous oxygen saturation, amount of fluid removal during hemofiltration and urine output. The lactate elevated in group H than group C ($P < 0.05$), and the PH showed metabolic acidosis in group H ($P < 0.05$). The mixed venous oxygen saturation decreased in group H than group C ($P < 0.05$). The number of transfused packed red blood cells was lower in group H than group C ($P < 0.05$). The hematocrit was higher in group H than group C ($P < 0.05$). The urine output was lower in group H than group C ($P < 0.05$). **Conclusions:** Hemofiltration during cardiopulmonary bypass leads to hemoconcentration, elevated lactate level and increased inotropic support. There are some recommendations for hemofiltration: First; Hemofiltration should be limited for patients with impaired renal function, positive fluid balance, reduced response to diuretics or prolonged bypass time more than 2 hours. Second; Minimal amount of fluids should be administered to maintain adequate cardiac output and reduction of priming volumes is preferable to maintain controlled hemodilution. Third; it should be done before weaning of or after cardiopulmonary bypass and not during the whole time of cardiopulmonary bypass.

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INTRODUCTION

The hematocrit (HCT) value is low during cardiac surgery with cardiopulmonary bypass (CPB) because of the surgical blood loss, positive fluid balance as a result of prebypass fluid loading, prime fluids of CPB and crystalloid cardioplegia returned into the pump,[1-4] and to keep hemoglobin levels above 7 g/dl in patients during CPB either by transfusing blood or by doing hemofiltration.[5-7]

Hemofiltration is used to remove extra fluids as well as to induce hemoconcentration and elevation of HCT value to minimize blood transfusion.[8-10]

It was found that serum lactate level increased in some patients and not in others during adult cardiac surgery and by reviewing the

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data of patients, this problem was mainly in the patients who did hemofiltration during CPB. One study reported the occurrence of metabolic acidosis with hemofiltration,[11] and another study reported that lactic acidosis cannot be excluded during hemofiltration,[12] therefore the present study was done to evaluate the effect of hemofiltration on the serum lactate level in adult cardiac surgery.

MATERIALS AND METHODS

The present study was an observational study done in Prince Sultan Cardiac Center, Riyadh, Saudi Arabia (2009–2012). The number of patients enrolled in the study was 637 adult patients. The inclusion criteria were patients with:

- Cardiac surgery with CPB
- Ejection fraction >35% from.

Exclusion criteria included patients with:

- Acute myocardial infarction
- Emergency operation
- Liver or kidney dysfunction.

The excluded patients were 354 according to the exclusion criteria. The present study included 283 patients classified into two groups:

- Hemofiltration group (Group H), included 138 patients who did hemofiltration during CPB
- Control group (Group C), included 145 patients without hemofiltration during CPB.

Data measurements

Blood sugar, HCT, arterial blood gases, and lactate levels were measured before CPB, every 15 min during CBP and after weaning from CPB. Also, the heart rate, mean arterial pressure, central venous pressure (CVP), mixed venous oxygen saturation (VO_2) (it was measured by withdrawing blood samples from pulmonary artery catheter), and temperature in addition to the duration of cross-clamping, CPB, cooling and rewarming during CPB.

The amount of fluid removal during hemofiltration and urine output was measured. The using of intraoperative vasopressors was reported.

Anesthesia technique

All patients were premedicated with diazepam 5–10 mg orally (at midnight before surgery and also 1 h before surgery). An arterial line was inserted under local anesthesia before induction, after induction; five-lumen central venous catheter and pulmonary artery catheter were inserted for all patients.

A standardized anesthetic technique was used for all patients. The induction was done by fentanyl 5–10 mcg/kg, etomidate 0.3 mg/kg and cisatracurium 0.2–0.3 mg/kg and after endotracheal intubation, oxygen:air 50% was maintained. Anesthesia was maintained with sevoflurane 1–2%, fentanyl infusion 1–2 mcg/kg/h, and cisatracurium 1–2 mcg/kg/min. At the beginning of CPB, sevoflurane was stopped, and propofol was infused 50–100 mcg/kg/min, in addition to fentanyl and cisatracurium infusion as before CPB. The serum blood sugar was controlled with insulin infusion during the procedures.

Cardiopulmonary bypass

The pump (Roller pump, Stockert S5 Germany) was primed with 1000 ml of Ringer lactate, 300 ml hetastarch 6%, 100 ml albumin 20%, 50 mEq of sodium bicarbonate, 5000 IU of heparin and 200 ml of mannitol 20%. Packed red blood cells were added, if the HCT value was <20% during CPB. A nonpulsatile flow (2.4 L/min/m^2) was achieved during CPB using a twin roller pump. Myocardial preservation protocol included mild systemic hypothermia (nasopharyngeal temperature 34–32°C) and potassium cardioplegia solution.

The initial dose of cardioplegia was 15–20 ml/kg, followed by half the initial dose every 30 min or earlier if the electrocardiogram showed electrical activity. Arterial blood gases were done every 15–30 min. At the end of surgical procedures, patients were rewarmed to 37°C and weaned from CPB. Hypotension during CPB was managed with bolus doses of phenylephrine (50–100 μg) given by perfusionist. The inotropes (dopamine, epinephrine, and norepinephrine) and nitroglycerine were added to help weaning from CPB in addition to intra-aortic balloon pump.

Hemofiltration

After the initiation of CPB and stabilizing the hemodynamics according to the standardized parameters during CPB, the hemofiltration was started and continued up to 10 min before weaning from CPB to keep the HCT value to 25–30%.

A Hemofilter (Hemofiltration DHFO2 System, Sorin Group, Italy), was placed in the CPB circuit. The inlet of hemofilter was connected to venous reservoir and outlet was connected to oxygenator. Blood was

withdrawn from venous reservoir at a rate 100 to 200 ml/min to be filtered through hemofilter, and then the concentrated blood was returned to the oxygenator. Through this technique about 1–2 L/h of the blood was hemofiltrated.

The statistical analysis

Data were statistically described in terms of mean ± standard deviation, median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's *t*-test for independent samples. For comparing categorical data, Chi-square (χ^2) test was performed. Exact test was used instead when the expected frequency is <5. $P < 0.05$ was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

RESULTS

Figure 1 shows number of patients evaluated and enrolled. All included patients have completed the study. There was no significant difference regarding the age, weight, gender, preoperative co-morbidities, ejection fraction and Euro score between the patients of two groups ($P > 0.05$) [Table 1]. There was no difference in the heart rate, mean arterial blood pressure and CVP between the two groups ($P > 0.05$) [Table 2]. The number of required patients to inotropic support and intra-aortic balloon pump to help the weaning from CPB was significantly higher in Group H than Group C ($P < 0.05$) [Table 2]. The total urine output was lower in patients of Group H than Group C ($P < 0.001$) [Table 2]. The comparison of temperature, SPO_2, $PaCO_2$, blood sugars, CPB duration, cross-clamping time, type of surgery, cooling, and rewarming durations during CPB were insignificant between the two groups ($P > 0.05$) [Tables 2 and 3].

The lactate level before CPB was insignificant between the two groups ($P > 0.05$), but elevated in Group H patients more than Group C after CPB and through the first 12 h in the Intensive Care Unit (ICU) ($P < 0.05$) and decreased gradually to be around the baseline at the 24^{th} h in the ICU ($P > 0.05$) [Table 3]. The mixed VO_2 was lower in patients of Group H than Group C after CBP and through the first 12 h in the ICU ($P < 0.05$) and increased to be around the baseline at the 24^{th} h in the ICU ($P > 0.05$) [Table 3]. The pH showed metabolic acidosis in patients of Group H due to increased level of serum lactate after weaning from CPB and through the first 12 h in the ICU ($P < 0.05$) [Table 3]. The number of transfused packed red blood cells during surgery was significantly lower in Group H than Group C ($P = 0.005$) [Table 2]. Regarding the HCT, the results showed no difference in the HCT value between the two groups before, after CPB, and

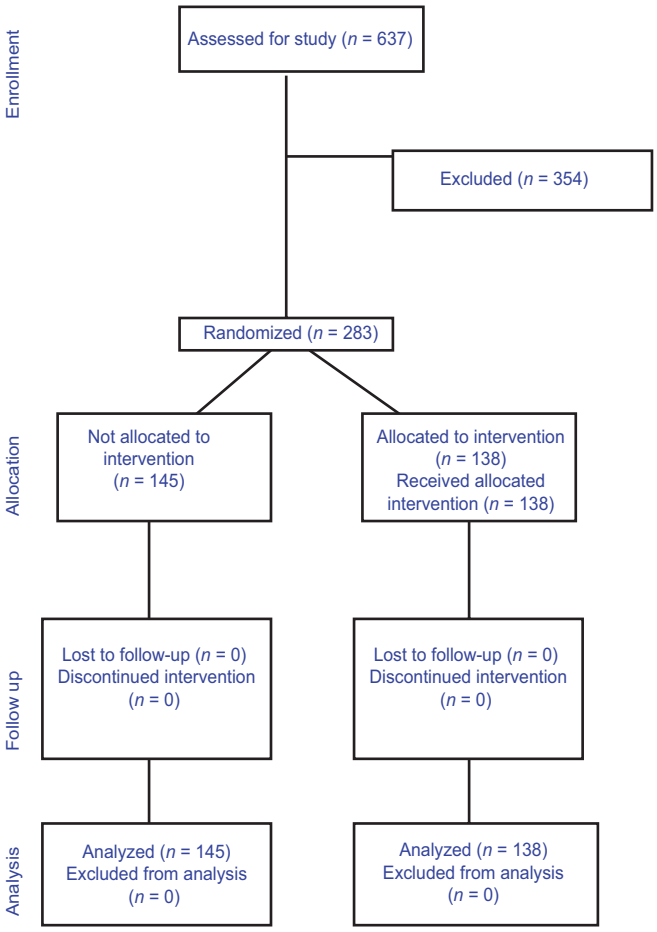

Figure 1: Consort flow diagram of adult patients undergoing cardiac surgery and participating in the study

Table 1: Preoperative data of patients

Items	Group H (*n*=138)	Group C (*n*=145)	*P*
Age (year)	59.66±11.57	59.75±12.10	0.949
Weight (kg)	81.60±7.12	80.37±6.67	0.812
Gender (female:male)	73:72	77:61	0.358
DM (number of patients)	83	91	0.651
Hypertension (number of patients)	102	98	0.242
IHD (number of patients)	108	105	0.547
Ejection fraction (%)	55.35±16.40	56.51±15.88	0.145
Euroscore	12.31±2.41	12.00±2.52	0.557

Data are presented as mean±SD, *n* (%). DM: Diabetes mellitus, IHD: Ischemic heart disease, SD: Standard deviation

Table 2: Intraoperative data of patients

Items	Group H (*n*=138)	Group C (*n*=145)	*P*
Heart rate (bpm)	80.17±7.20	80.37±6.78	0.151
MAP (mmHg)	93.02±6.12	92.77±7.15	0.751
CVP (mmHg)	12.68±1.76	12.50±1.83	0.399
SPO_2 (%)	99.30±0.80	99.27±0.65	0.730
Temperature (°C)	36.76±0.11	36.72±0.33	0.102
CABG (number of patients)	73	68	0.857
CABG + valvular surgery (number of patients)	35	39	0.430
Valvular surgery (number of patients)	37	31	0.547
CPB time (min)	115.34±17.21	114.32±17.63	0.625
Cross clamping (min)	99.36±13.79	99.31±13.30	0.971
Duration of cooling (min)	79.40±11.78	77.16±9.35	0.850
Duration of rewarming (min)	25.55±4.10	26:00±4.01	0.961
Dopamine			
Number of patients	96	123	0.001
Dose (μg/kg/min)	5.23±1.63	7.95±197	0.001
Epinephrine			
Number of patients	42	40	0.001
Dose (μg/kg/min)	0.08±0.02	0.12±0.05	0.001
Norepinephrine			
Number of patients	16	33	0.001
Dose (μg/kg/min)	0.03±0.02	0.05±0.03	0.008
IABP (number of patients)	17	38	0.015
Packed red blood cells (units)	1.55±0.28	2.78±0.78	0.005
Urine (L)	1.49±0.28	3.62±0.46	0.001
Fluid removal (L)	2.56±0.22	-	0.001

Data are presented as mean±SD, number. MAP: Mean arterial blood pressure, SPO_2: Arterial oxygen saturation, CVP: Central venous pressure, CABG: Coronary artery bypass grafting, IABP: Intra-aortic balloon pump, CPB: Cardiopulmonary bypass, SD: Standard deviation

in the ICU ($P > 0.05$) [Table 3], but during CPB, the HCT was higher in patients of Group H than Group C ($P = 0.003$) [Table 3].

DISCUSSION

The indication of hemofiltration during CPB is an excessive oxygenator volume with decreased HCT. Hemofiltration removes plasma water and results in increased HCT, plasma albumin concentration, increased plasma colloidal osmotic pressure,[13-16] decreased plasma and extracellular volumes.[17,18]

In the present study, the hemofiltration during CPB lead to hemoconcentration, increased HCT, decreased blood transfusion and resulted in hypotension due to hypovolemia during CPB, impaired tissue perfusion, decreased oxygen supply and the result was an elevation of serum lactate level. On the other side, Group C patients without hemofiltration during CPB, there was hemodilution that improved tissue perfusion, oxygenation and decreased level of serum lactate. The central VO_2 and urine output decreased greatly in patients with hemofiltration. The type of prime solutions was the same in both groups and was mainly Ringer's lactate. There was one study showed that infusion of Ringer's lactate does not affect the accuracy of lactate measurement,[19] and other study showed the occurrence of metabolic alkalosis due to metabolism of lactate to bicarbonate and the lactate act as a base and cannot cause acidosis.[20,21]

In the present study, there was hypotension during hemofiltration and the perfusionist had to give phenylephrine to maintain the mean arterial blood pressure in Group H as a result of hypovolemia during hemofiltration and these findings were documented by other studies.[22-24]

The phenylephrine induces vasoconstriction of microcirculation, decreases tissue blood flow, decreases oxygen supply, potentiating the anaerobic metabolism and more production of lactic acid, and many studies support these findings and documented that the using of phenylephrine during CPB resulted in an impairment of microcirculatory blood flow, peripheral arteriovenous shunting, deterioration in microvascular flow pattern of erythrocytes within capillaries, potentiating the anaerobic metabolism, more production of lactic acid and a rise in lactate levels in spite of an apparently adequate oxygen supply,[25-29] and the same result was confirmed by another study that showed the using of catecholamines is responsible for splanchnic vasoconstriction thereby reducing perfusion to the gastrointestinal tract during and after surgery and leads to elevated lactate level.[30] Therefore, some authors recommend to add crystalloids to the circuit and increasing the pump flow to maintain adequate circulating volume, oxygen supply and demand better than to give phenylephrine but may counteract the favorable hemofiltration effect on hemodilution.[31,32]

Keshaviah *et al*.[11] and Naka and Bellomo[33] have reported the use of hemofiltration may result in a mild metabolic acidemia and the pathophysiology of this acidemia has been suggested to be a depletion of plasma bicarbonate due to preferential movement of the anion into the hemofiltrate and this movement was thought to be related to the Gibbs–Donnan phenomenon as a result of hemofiltration induced increase in plasma protein

Table 3: Laboratory data of patients

Items	T0	T1	T2	T3	T4	T5	T6
Lactate level (mmol/L)							
Group H	1.17±0.49	3.05±0.60	5.07±1.00	6.31±1.20	7.33±1.05	5.33±1.25	2.10±0.90
Group C	1.09±0.51	2.87±0.36	3.03±0.65	3.20±0.80	2.28±0.62	2.10±1.15	1.92±0.73
P	0.251	0.003	0.003	0.001	0.001	0.004	0.060
VO_2 (%)							
Group H	70.78±2.26	60.07±5.30	51.83±5.15	56.42±4.31	61.55±4.39	66.44±3.73	72.23±2.94
Group C	71.00±3.44	63.00±4.75	58.50±4.43	61.30±5.59	67.43±4.50	69.70±2.25	71.84±2.70
P	0.07	0.001	0.001	0.001	0.001	0001	0.245
Blood sugar (mmol/L)							
Group H	7.90±0.70	8.42±1.19	8.15±0.83	8.40±1.98	8.20±1.65	8.73±1,30	8.45±1.40
Group C	8.19±1.24	8.24±1.37	7.93±1.86	7.99±1.59	8.12±1.50	8.23±1.50	8.31±1.61
P	0.127	0.225	0.312	0.055	0.669	0.267	0.436
pH							
Group H	7.37±0.02	7.30±0.03	7.31±0.03	7.30±0.04	7.31±0.03	7.33±0.04	7.36±0.02
Group C	7.38±0.02	7.36±0.02	7.36±0.01	7.34±0.03	7.36±0.03	7.37±0.03	7.36±0.04
P	0.168	0.023	0.031	0.021	0.025	0.041	1.000
$PaCO_2$ (mmHg)							
Group H	35.62±1.51	35.35±1.74	34.64±1.51	35.12±1.35	35.50±1.21	36.40±1.10	35.76±1.42
Group C	35.36±2.31	35.03±1.58	34.23±1.68	34.84±1.60	35.33±1.34	36.74±1.35	35.54±1.51
P	0.263	0.259	0.116	0.113	0.264	0.237	0.208
Hematocrit value (%)							
Group H	38.69±3.04	29.86±3.25	31.57±2.62	32.43±2.33	33.25±2.50	34.62±2.40	35.29±2.32
Group C	39.30±3.20	26.42±2.73	31.88±2.74	31.98±2.67	32.87±2.81	33.81±2.73	35.44±2.45
P	0.104	0.003	0.334	0.133	0.231	0.263	0.597

Data are presented as mean±SD, percentage. Group H: Hemofiltration group, Group C: Control group, T0: Values before cardiopulmonary bypass, T1: Values before weaning of cardiopulmonary bypass, T2: Values after cardiopulmonary bypass, T3: Values on ICU admission, T4: Values 6 hours after ICU admission, T5: Values 12 h after ICU admission, T6: Values 24 h after ICU admission, VO_2: Central venous oxygen saturation, $PaCO_2$: Arterial partial pressure of carbon dioxide, SD: Standard deviation

concentration and also reported that lactic acidosis due to excessive hemofiltration cannot be excluded[12,33] and they recommended frequent blood gas monitoring during bypass to detect any possible academia.[34]

Levraut *et al*.[35] investigated the effects of continuous hemofiltration on lactate clearance and concluded that hemofiltration removed only 3% of lactate production, and the hemofiltration is associated with lactic acidosis.

Another possible cause of increased lactate levels may be due to hypothermia.

The hypothermia induces peripheral vasoconstriction,[36] and this may decrease the tissue blood flow, but during CPB the tissues are protected by two factors: The first is decreasing the metabolism in response to hypothermia,[37,38] and the second is an increase in the blood flow due to hemodilution, but as a result to hemoconcentration, this factor is lost in Group H.

Also with hemofiltration, there is an elevated plasma oncotic pressure,[39,40] and this lead to absorption of interstitial fluids,[12] and intracellular fluid leading to dehydration of cells,[41-43] and building up anaerobic metabolism.

Another study documented that the relationship of hypoperfusion and increased lactate level is the delay in the tissue washout of lactate and increased lactate plasma levels only after rewarming, with a consequent increase in tissue perfusion after CPB.[44]

The patients in Group C (without hemofiltration) did not show hypotension during CPB, and there was a decreased need for phenylephrine. Also, there was hemodilution during CPB and this led to improved tissue perfusion and decreased elevation in the serum lactate and this is supported by some studies that showed that hemodilution led to reduced blood viscosity and improved microcirculatory flow and tissue perfusion.[45-47]

Presently, as the impact of hemofiltration on the number of transfusions is unclear, the routine use of hemofiltration during or immediately after CPB is

considered not helpful for blood conservation in adult cardiac operations (Class III, level of evidence B).[5]

Limitations

There are some limitations of the present study. It was done in a single center, limited number of patients, and limited researches talking about the same topics as the present study to discuss these findings in details.

CONCLUSION

Hemofiltration during the CPB leads to hemoconcentration, an increase in serum lactate level and inotropic support and there are some recommendations for hemofiltration during CPB. First, it should be limited to patients with impaired renal function, excessive and positive fluid balance, reduced response to diuretics or prolonged bypass time more than 2 h.

Second, administration of minimal amount of fluids to maintain adequate cardiac output and the reduction of priming volumes is preferable to maintain controlled hemodilution (HCT >23%). Third, it should be done before weaning of CPB or after CPB and not during the whole time of CPB.

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Conflicts of interest

There are no conflicts of interest.

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