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THE EFFECT OF DOPAMINE ON SERUM LACTATE LEVEL IN OPEN HEART SURGERY IN PATIENTS WITH EF ≤35%

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All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: To evaluate the efficacy of dopamine on hyperlactatemia in patient's candidate for elective open heart surgery with EF≤35%.

Methodology: In this randomized double blind clinical trial we evaluated 101 patients age between 18-75 candidate for elective open heart surgery with EF≤35% undergone CPB in Rajaie Cardiovascular center. Patients were randomized and allocated in to two groups. One group received normal saline (NS or group A, 51 patients) and the other received low dose of dopamine (2μgr/kg/min) (dopamine or B group 50 patients).

Results: Patients in the study population had more diabetes mellitus (29% vs 16%, p< 0.001), hypertension (61% vs 51%, p <0.001), hypercholesterolemia (66% vs 54%, p <0.001), and family history of coronary artery disease (57% vs 50%, p < 0.01) Of the study population (29%) had a history of diabetes mellitus. PMI occurred in 5% of the study population. PMI occurred in five patients, 1 with 3 stents, 2 with 2 stents and 1 with 3 stents.

Conclusion: Low dose of dopamine did not affect the lactate serum levels in patients with EF≤35% undergoing open heart surgery.

Keywords: Dopamine, Serum lactate level, Cardiac surgery.

INTRODUCTION

Elevated blood lactate concentration above the accepted normal reference range Hyperlactatemia (HL) in cardiac surgery is common. 1-3 In normal conditions the blood lactate concentrations are low because there is a continuous cycle of lactate production and metabolism, [4] but higher blood lactate concentrations occur when lactate production exceeds clearance, when clearance capacity is decreased or more frequently when both occur concurrently. [5]

Previous reports indicated that the prevalence of HL in adult patients was 10% to 20% during cardiac surgery with cardiopulmonary bypass that remarkably increased mortality and morbidity in these patients.[6]

The exact cause of HL is not clear and previous studies have provided conflicting evidences about the cause of HL during and after cardiac operations but these studies signified that tissue hypoxia is a leading cause of HL during cardiac surgeries. [7, 8] The most important procedure among the patients with severe heart disease is cardiac surgery and it is well-recognized that Hyperlactatemia (HL) is a marker of circulatory failure, and its severity has been associated with increased hospital stay and mortality in different clinical conditions.[9] Moreover, it has been postulated that hyperlactatemia is potentially sensitive and specific marker for adverse outcome on admission to the cardiac intensive care unit (CICU). [10]

Dopamine in intermediate dosages (5-10 μg/kg/min) have a positive inotropic and chronotropic effect through increased ß1 receptor activation, so, dopamine is used in patients with shock or heart failure to increase cardiac output and blood pressure and with low dose dopamine (2μg/kg/min) improve renal and mesenteric blood flow.[11] The outcome of cardiac surgeries is determined by preoperative patient's characteristics, intra operative factors such as surgical technique, myocardial protection, CPB and immediately post operation care. Moreover the findings of previous studies expand our understanding of lactate as a clinical biomarker in the patients under cardiac surgery. Previous reports indicated that HL increased the risk of death and is a common phenomenon in ill patients and in patients under cardiac surgeries. [12,13]

However, the effect of dopamine on serum lactate level is not clear, so we steered this controlled study to shed light on the efficacy of dopamine on hyperlactatemia in open cardiac surgery patients with EF≤35% under cardiopulmonary bypass.

METHODOLOGY

In this randomized double blind clinical trial we evaluated 101patients. Sample size calculated on WHO calculator. Patients having age between 18 to75 candidate for elective open heart surgery with EF≤35% undergone CPB in Rajaie cardiovascular center were included.The study protocol was approved by ethical committee of Shahid Rajaie Cardiovascular Medical and Research Center, Tehran University of Medical Science, furthermore the study procedure was explained for all patients and written informed consents were given. The criteria for enrolment were elective open heart surgery with CPB. The exclusion criteria were; emergency and hepatic disease, renal failure, metabolic disease, alcohol consumption, metformin intake before operation. All surgeries were performed by the same anesthesia, surgery and perfusion team. Patients were randomized and allocated in to two groups. Patients were randomized based on numerical order. In our study, every odd number of patients received normal saline (normal saline or A group), while every even number patients received low dose of dopamine (2μg/kg/min)(dopamine or B group). Both participants and study staff (site investigators and trial coordinating center staff) were masked to treatment allocation. Finally we allocated 51 patients in control group (group A) and 50 patients in dopamine group or group B. All patients were premeditated with lorazepom 1mg orally two hours and morphine 0.1 mg/kg intramuscularly 30-45 minutes prior to induction of anesthesia.

Anesthesia was induced with intravenous midazolam (0.1 mg/kg) ,sufentanil (0.6-0.8 μg.kg-1), Endotracheal intubation was facilitated with cisatracurum (0.15mg/kg). Anesthesia was maintained with oxygen in air (50%), isoflurane and infusion of intravenous sufentanil, midazolam and cisatracurum. The lungs were mechanically ventilated to maintain a pH of 7.35-7.45 and normocapnia.Volume replacement was done with Ringer Lactate. After systemic heparinisation with intravenous heparin 300 IU kg^{-}, to achieve an activated clotting time (ACT) of >480 sec, aortic and atrial cannulations were done. CPB and surgical techniques were standardized and did not change during the study period. All patients underwent cardiac surgery with a standard CPB protocol under moderate hypothermia at 30-32°C. Pump flow rates and perfusion pressures were maintained at 2.2-2.6 L/min/m2 and 50-80 mm Hg, respectively. Heart rate, blood pressure, Hemoglobin (Hb) , hematocrit (HCT), BS, temperature, blood gas, lactate level, pH , HCO3 and potassium were recorded before induction(1)following anesthetic induction (2), pre-pump (3), during pump(4)and immediate post-pump (5). Statistical analysis was performed using SPSS version-20 software. Data were checked for normality before statistical analysis. Continuous variables were expressed as mean± SD or median (range) according to normality, and categorical variables were presented as either absolute numbers or percentage. Normally distributed continuous variables were compared using the unpaired Student's t-

test,. Categorical variables were analyzed using ×2 test. Statistical significance was set at P-value < 0.05

RESULTS

In this trial we evaluated 101 patients (69 male,67.6%, 32 female 31.4%) with mean age 53.41±18.56. In dopamine group 50 patients (31 male,62%,19female 38%) and in control group 51 patients (38 male 73%,13 female 25%) were evaluated. The difference between dopamine and control groups regarding demographic data was not significant (p>0.5)(Table1). Moreover the difference between two groups regarding lactate ,pH .pump time ,clamp time and operation time was not

Table 1: Demographic characteristics of patients in two groups

Varible	Groups	Mean	SD
Age	A	53.8200	18.56559
	B	53.0900	18.67818
HTN	A	0.3654	0.48624
	B	0.3800	0.49031
DM	A	0.1923	0.39796
	B	0.2600	0.44309
EF	A	42.4038	10.50165
	B	42.5000	9.75464
B_Bloker	A	0.5769	0.49887
	B	0.4200	0.49857
ACE_I	A	0.1923	0.39796
	B	0.2600	0.44309
Metformin	A	0.962	0.29768
	B	0.5769	0.49887
Transformin	A	1.6346	0.86385
	B	1.0400	0.78142
Operation Time	A	233.3654	46.91169
	B	251.4800	74.85585

Table 2:The mean and standard deviation of two groups

Varible	Groups	Mean	SD
Lactat_1	A	1.2615	0.76444
	B	1.1580	0.84975
Lactat_2	A	1.3058	0.83535
	B	1.4440	1.03946
Lactat_3	A	2.4327	1.46712
	B	6.6660	27.43667
Lactat_4	A	2.5596	1.35245
	B	2.9084	1.43582
Lactat_5	A	3.0519	1.63641
	B	3.0626	1.53957

Table 3: The Pump and Clamp Time in two groups

Variable	Groups	Mean	SD
Pump Time	A	94.7885	34.29991
	B	106.5000	60.21026
Clamp Time	A	54.4615	27.14844
	B	55.8600	22.28664

significant($p>0.5$)(Table2&3) . Considering heart rate and blood pressure, the difference between systolic blood pressure (SBP 3,4,5) , diastolic blood pressure (DBP 2,4,5) , mean arterial pressure (MAP 1,3) and heart rate (HR 1,2,3,4,5) in dopamine and control was significant ($p<0.05$).

DISCUSSION

Toramanet al.in a study signified that serum lactate levelplaysa critical role on the prediction of mortality risk. They discovered that the serum lactate level of patients who died revealed an early increase when compared with those who survived. [12] Furthermore, another study by Basaran etal.spesifiedthat a peak serum lactate level of 4.8 mmol/L or more during the early postoperative period is related to an increased risk of perioperative morbidity and mortality (13).So, we steered this controlled study to evaluate the dopamine effect on HL on patients under cardiac with EF≤35% surgery.Dopamine is a simple organic chemical of the catecholamine family that increased the cardiac output and blood pressure. [11] In agreement to this fact, blood pressure during operation in dopamine group was significantly more than NS group. while the difference between dopamine and control groups regarding lactate ,pH ,pump time ,clamp time and operation time was not significant($P>0.05$). Literatures about the dopamine effect on HL are low and available previous studies have prepared conflicting information about the effect of dopamine on serum lactate level. [14,15] The reason for such a discrepancy might be related to the heterogeneity in patient samples, dosage of medication, trial design and the fact that several factors may have influenced HL levels and affected the study findings.

In current study the difference between two groups regarding sex, age, underline disease and alcohol consumption was not significant. These findings showed that we properly matched dopamine and control groups. However considering heart rate and blood pressure, the difference between systolic blood, diastolic blood pressure, mean arterial pressure and heart rate in dopamine and control group was significant.

As mentioned in preceding sections we did not find a study about the dopamine effect on HL in patients under cardiac surgery, however, in a survey by Thorén et al. has shown that dopamine, dopexamine, and dobutamine raised jejunal mucosal perfusion .Furthermore they showed that the increase in jejunal mucosal perfusion by dopamine and dopexamine were significantly more noticeable compared with dobutamine, while there was no difference between dopamine and dopexamine. Additionally, in line with our results, this study indicated splanchnic lactate extraction did not change for any of the drugs. [16] Another study by Levy et al. compared the effect of norepinephrine and dobutamine to epinephrine on serum lactate level; they showed epinephrine increases lactate level after 6 hours, moreover they indicated that norepinephrine and dobutamine increase the serum lactate level, but it return to base line after 24 hours. [17]

The results of investigations in this field are inconsistence; moreover, another problem inherent in the literature is that few studies take into account the effect of dopamine on lactate level.

Hence, further studies are needed to evaluate the dopamine effect on lactate levels and identification of high blood lactate levels should prompt further evaluation of all potential factors that may modify the dopamine efficacy.

CONCLUSION

We specified that dopamine did not affect the lactate serum levels in patients under open heart with EF≤35% surgery. However dopamine has impact on heart rate and blood pressure.

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