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Hemodynamic and hydroelectrolitic changes secondary to the heparin administration in patients undergoing coronary revascularization

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SUMMARY

Objective: Evaluate if there is a direct relationship between the way of administration of heparin and the presence of hemodynamic and hydroelectrolitic changes in patients who underwent revascularization surgery in the Instituto Nacional de Cardiología «Ignacio Chávez». **Methods:** 26 patients were included in this study underwent revascularization surgery with extracorporeal circulation. Group BD we give 300 U/kg of heparin in bolus through the central catheter. Group FD we give 300 U/kg of fractionated heparin in three equivalent doses with an interval of one minute through of central catheter. Measurement of CO, CI, SVR, PVR, MPP, HR, MAP, potassium and seric calcium by five minutes before administrating the doses and three minutes after, and of activated coagulation time before and after heparin were made. **Results:** It was not found significant difference between both groups in gender, age, weight, height, body mass index, superficial corporeal area, LVEF and CARE scale. A decrease of the SVR and MAP was found posterior to the administration in bolus of the dose of heparin p = 0.04, p = 0.002, an increase of serum potassium after the administration in bolus of heparin was found p = 0.005. **Conclusions:** The administration in bolus of heparin in high doses has important vasodilating properties.

Key words: Heparin, hypotension, hyperkalemia.

RESUMEN

Objetivo: *Evaluar si existe una relación directa entre la forma de administración de heparina y la presencia de cambios hemodinámicos e hidroelectrolíticos en pacientes sometidos a cirugía de revascularización coronaria en el Instituto Nacional de Cardiología «Ignacio Chávez».* ***Métodos:*** *Se incluyeron 26 pacientes sometidos a cirugía de revascularización coronaria con circulación extracorpórea: grupo DB: 300 U/kg de heparina en bolo por el catéter central, grupo DF: 300 U/kg de heparina fraccionada en tres dosis iguales con intervalo de 1 minuto por el catéter central. Se realizó medición de GC, IC, RVS, RVP, PPM, FC, PAM, potasio y calcio sérico 5 minutos antes de administrar la dosis y 3 minutos después en ambos grupos y de tiempo de coagulación activado pre y posheparina.* ***Resultados:*** *No hubo diferencia significativa en sexo, edad, peso, talla, índice de masa corporal, área de superficie corporal, fracción de eyección del ventrículo izquierdo y escala CARE. Disminución de RVS y PAM posterior a la administración de la dosis en bolo de heparina p = 0.04, p = 0.002, aumento del potasio sérico posterior a la administración de la dosis en bolo de heparina p = 0.005.* ***Conclusiones:*** *La administración intravenosa en bolo de heparina a dosis altas tiene propiedades vasodilatadoras importantes.*

Palabras clave: *Heparina, hipotensión, hipercaliemia.*

INTRODUCTION

Heparin has been used almost exclusively as an anticoagulant for cardiopulmonary bypass for over 50 years[1]. The acute intravenous administration of heparin for cardiopulmonary bypass has been associated with hypotension, which is believed to be caused by a reduction in the systemic vascular resistance[2]. While most clinicians are aware of the heparin induced thrombocytopenia, the association of heparin and hyperkalemia is less recognized[3]. Hemodynamic changes have been observed after intravenous heparin administration in single dose for total anticoagulation such as hypotension, bradycardia and increase in the serum potassium requiring intensive treatment[4]. Intravenous heparin has become a standard therapy for patients with acute coronary syndrome. Clinical observations suggest that heparin provides more than its anticoagulant effect to those patients. Some patients with unstable angina report immediate relieve of the chest pain when heparin is administrated. Heparin may act as a vasodilator in those patients[5]. The objective of this study was to evaluate if there is a direct relation between the type of heparin administration and the presence of hemodynamic and hydroelectrolitic changes in patients who underwent coronary revascularization surgery with extracorporeal circulation in the National Institute of Cardiology «Ignacio Chávez».

MATERIAL AND METHODS

Prior authorization from the Institutional Ethics Committee, a prospective, comparative and transversal study involving 26 patients who underwent an elective coronary revascularization surgery with extracorporeal circulation was made; they were divided in two groups: (Bolus dose) BD group n=13 and (fractionated dose) FD group n =13. Patients who underwent a coronary revascularization surgery with extracorporeal circulation in the National Institute of Cardiology were included. Patients who underwent emergency surgery or revascularization surgery without extracorporeal circulation, hemodynamically unstable patients, patients with previous use of inotropic and/or vasodilator agents and preoperative heparin infusion were excluded. Patients with hypotension for reasons not related to the heparin administration and patients who presented a surgical and/or anesthesic complication previous to the heparin administration were excluded.

An invasive monitoring was placed in the operation room: DII and V5 continuous electrocardiogram, peripheral oxygen saturation, radial arterial line, end-expiratory CO_2 concentration, vesical catheter, central catheter and Swan-Ganz catheter. Induction of anesthesia was performed with fentanyl 3-5 mg/kg, diazepam or etomidate and pancuronium 100 mg/kg and the anesthesia was maintained with inhaled sevoflurane 0.5-2.0 vol%, air, oxygen, and fentanyl in infusion at 5 mg/kg/h. Volume-controlled mechanical ventilation was maintained to maintain an $ETCO_2$ in 35 mmHg. The hemodynamic profile was measured by thermodilution (cardiac output, cardiac index, systemic vascular resistance, pulmonary vascular resistance, mean pulmonary pressure, heart rate, mean arterial pressure), similarly serum potassium and calcium were measured by blood gasometry 5 minutes before administration of the dose and three minutes after it in both groups, and finally pre- and post- heparin activated coagulation time was measured. Data obtained from the clinical records were: age, weight, height, body mass index, body surface area, left ventricular ejection fraction and CARE (Cardiac Anesthesia Risk Evaluation) scale.

A hemodynamic parameter was taken with three samples using thermodilution with 10 mL of 0.9% saline solution five minutes before the administration of heparin, as well as the blood gases for the measurement of electrolytes. At the time of heparinization, the surgeon avoided the manipulation of the heart, aorta and internal mammary artery. In the BD group, 300 U/kg of heparin were administered in bolus through the central catheter, and in the FD group 300 U/kg of heparin were administered divided in three equal fractionated doses at 1 minute interval between each dose through the central catheter. Hemodynamic parameters was measured with three samples by using thermodilution with 10 mL of 0.9% saline solution three minutes after the last heparin dose, as well as blood gases to measure the electrolytes.

Statistical analysis was performed by Microsoft Excel 2003 for Windows, descriptive statistics and Student t test were used for comparison of the two groups. A $p < 0.05$ value was considered statistically significant.

RESULTS

There was no significant difference between both groups in gender, age, weight, height, body mass index, body surface area, left ventricular ejection fraction and CARE scale (Table I). A decrease in SVR after administration of bolus dose of heparin ($p = 0.04$) was found, but not after the administration of fractionated dose $p = 0.77$ (Figure 1) was found; decrease in MAP after bolus dose of heparin $p = 0.002$ was observed, but not after the administration of fractionated dose $p = 0.62$ (Figure 2) was observed; increase in serum potassium after administration of bolus dose of heparin ($p = 0.005$) was observed, but not after administration of fractionated dose $p = 0.63$ (Figure 3) was observed.

Table I. General information.

Total of patients	26				
Bolus doses	13		Fractionated doses		13
Men		9		7	
Women		4		6	
	Average	SD ±	Average	SD ±	p value
Age (years)	58.77	10.44	59.69	9.30	0.81
Weight (kg)	72.54	14.05	68.92	12.09	0.49
Height (cm)	161.50	9.71	162.50	9.97	0.80
BMI (kg/m^2)	27.31	4.09	25.38	2.75	0.17
BSA (m^2)	1.80	0.19	1.76	0.17	0.52
LVEF(%)	54.80	8.21	56.30	7.06	0.63
CARE	3.00		3.00		1.00

BSA = Body surface area
CARE = Cardiac anesthesia risk evaluation
BMI = Body mass index
LVEF = Left ventricular ejection fraction

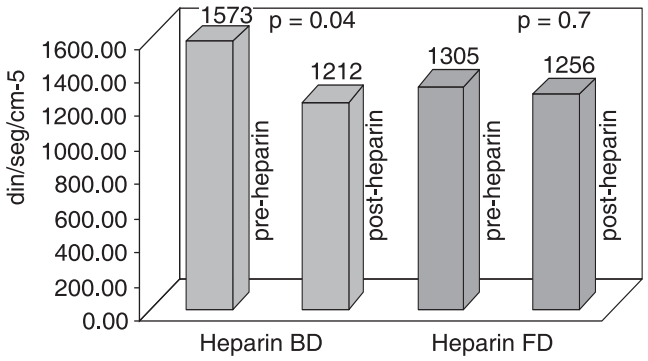

Figure 1. Changes in SVR.

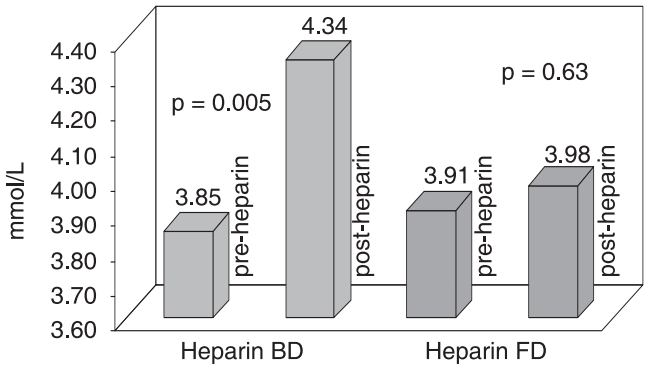

Figure 3. Changes in serum potassium.

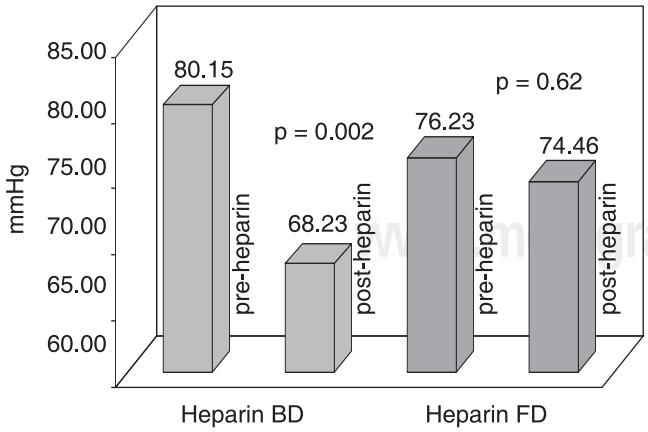

Figure 2. Changes in MBP.

There was no significant difference in basal serum calcium, ACT, CO, CI, PVR, MPP, and HR, and after administration of heparin in both groups.

DISCUSSION

In a study by Jack et al, intravenous administration of heparin for cardiopulmonary bypass was associated with a 12.5% reduction in mean arterial pressure, and a 28% decrease in systemic vascular resistance, indicating that heparin has significant vasodilator properties. Cardiac index increased by only 7% which was lower than that required to maintain mean arterial pressure, increasing the possibility of myocardial depression[6]. Our study is consistent with study by Jacka et al in regard to changes in mean arterial pressure and systemic vascular resistances. In a prospective study, Urban

et al reported hypotension in 17 of 20 patients in response to intravenous administration of 300 U/kg heparin, and a 13% decrease in mean arterial pressure at 76 ± 26 seconds of heparin administration. The authors showed that administration of 125 mg calcium chloride before intravenous administration of heparin was increasing serum ionized calcium and preventing the hypotensive response, furthermore they recommend slow bolus administration of heparin[7]. Casthely et al demonstrated an association between heparin-mediated hypotension and release of histamine. In his study, the H_1-receptor blockade significantly attenuated the hypotensive response to heparin[8]. Slaughter et al recommends the administration of calcium chloride or a vasopressor in cases of exaggerated or prolonged hypotension. Also he recommends that patients with a history of hypotensive response to heparin clinically significant, the preoperative administration of an H_1-receptor blocker would be prudent[9]. Jacka et al have noted hypotension (mean arterial pressure <60 mmHg) and/or bradycardia (heart rate <40 bpm) early after administration of intravenous heparin for cardiopulmonary bypass in some patients. They observed in their study early cardiovascular instability after administration of intravenous heparin for cardiopulmonary bypass in 16 of 256 patients (6.25%) and increased serum potassium 1.94 mmol/L in these patients, while only is increased 0.50 mmol/L in patients without cardiovascular instability[4]. Our study showed an increase in serum potassium after administration of heparin-bolus dose, and not after administration of fractionated dose. In a study, Edes et al noted hyperkalemia could occur within 7 days after starting therapy with low doses of heparin and that patients with diabetes mellitus or chronic kidney failure were especially prone to this complication[3]. Although it has been reported hyperkalemia associated with heparin in normal patients, it occurs more frequently in patients with a pre-existing defect in the potassium homeostasis (8-19%)[10]. There is evidence that heparin is suppressor of aldosterone and natriuresis. Therefore, heparin may increase serum potassium levels precipitating hyperkalemia and, less frequently, hyponatremia or metabolic acidosis[11-15].

CONCLUSIONS

The intravenous bolus administration of heparin at high doses has significant vasodilator properties, unlike from fractionated administration. It is important to take this into account in patients undergoing cardiopulmonary bypass dependent on systemic vascular resistances and high serum potassium concentrations.

REFERENCES

1. Kaplan J, Reich D, Lake C, Konstadt S. Kaplan's cardiac anesthesia. Transfusion medicine and coagulation disorders. Fifth edition. United States of America. Elsevier Saunders. 2006: 948-57.
2. Seltzer JL, Gerson JI. Decrease in arterial pressure following heparin injection prior to cardiopulmonary bypass. Acta Anaesthesiol Scand 1979;23:575-8.
3. Edes TE, Sunderrajan EV. Heparin-induced hyperkalemia. Arch of Int Med 1985;145:1070-72.
4. Jacka M, Clark A. Cardiovascular instability requiring treatment after intravenous heparin for cardiopulmonary bypass. Anesth Analg 2000;90:42-4.
5. Hawari F, Shykoff B, Izzo J. Heparin attenuates norepinephrine-induced venoconstriction. Vascular Medicine 1998;3:95-100.
6. Jacka M, Clark A. Intravenous heparin for cardiopulmonary bypass is an acute vasodilator. J Clin Anesth 2002;14:179-182.
7. Urban P, Scheidegger D, Buchmann B, Skarvan K. The hemodynamic effects of heparin and their relation to ionized calcium levels. J Thorac Cardiovasc Surg 1986;91:303-6.
8. Casthely PA, Yoganathan D, Karyanis B. Histamine blockade and cardiovascular changes following heparin administration during cardiac surgery. J Cardiothorac Anesth 1990;4:711-14.
9. Slaughter T, Mark J. Heparin-mediated hypotension associated with cardiac surgery. Anesth Analg 2000;91:766-67.
10. Osther JR, Singer I, Fishman LM. Heparin-induced aldosterone suppression and hyperkalemia. Am J Med 1995;98:575-86.
11. Kageyama Y, Susuki H, Saruta T. Effects of routine heparin therapy on plasma aldosterone concentration. Acta Endocrinol 1991;124:267-70.
12. Siebels M, Andrassy K, Vecsei P. Dose-dependent suppression of mineralocorticoid metabolism by different heparin fractions. Thromb Res 1992;66:467-73.
13. Aull L, Chao H, Coy K. Heparin-induced hyperkalemia. DICP 1990;24:244-46.
14. Durand D, Ader JL, Rey JP. Inducing hyperkalemia by converting enzyme inhibitors and heparin. Kidney Int Suppl 1988;25: S196-S197.
15. Day J, Landis R, Taylor K. Heparin is much more than just an anticoagulant. J Cardioth Vasc Anesth 2004;18:93-100.