Original Article

Effect of Prophylactic Vasopressin on Hemodynamic Parameters after Coronary Artery Bypass Graft Surgery

Alireza Jahangirifard[1], Majid Golestani Eraghi[1], Kamal Fani[2], Arash Tafrishinejad[2], Niloufar Dadashpour[3], Zargham Hossein Ahmadi[1], Shirin Salajegheh[4]

Abstract

Background: As common complications of coronary artery bypass grafting (CABG), low vascular resistance and hypotension could be life threatening. The aim of present study was to investigate the effect of low-dose vasopressin on hemodynamics in CABG patients.

Materials and Methods: In this randomized double-blinded clinical trial, 80 patients undergoing selective CABG were randomly divided into two equal case and control groups (n=40). Case group was received vasopressin 0.03 IU/min 30 minutes before the end of cardio-pulmonary bypass (CPB) until one hour after that. Control group was received normal saline in the same manner. Dopamine requirement, ICU stay, heart rate (HR), mean arterial blood pressure (MAP), central venues pressure (CVP) and atrial blood acidity (pH) were recorded and compared between groups in 5 phases (0,30,60,90,120 min) after separation of CPB.

Results: There was no significant difference between two groups in number of patients with severe hypotension (11 vs. 12 patients in case and control group respectively). CVP was corrected and then dopamine administration was compared in both groups. In vasopressin and the placebo group, 3 vs. 11 patients need to dopamine administration immediately after separation from CPB (p= 0.018) and 4 vs. 12 patients later in ICU (p=0.024), respectively. The mean needed dose of dopamine in vasopressin and placebo group immediately after separation from CPB were 7.63±3.42 vs. 9.21±2.08 µg/kg/min (p=0.031) and later in ICU were 7.42±2.02 vs. 8.66±4.08 µg/kg/min (p=0.045) respectively, which was significantly lower in vasopressin group in comparison with the placebo group.

Conclusion: Based on our results, low-dose vasopressin administration significantly reduced the mean needed dose of required dopamine, 24 hours urinary output, Duration of mechanical ventilation and patient's heart rate.

Keywords: Cardiac, surgical, procedure, Hemodynamics, Vasopressin

1. Tracheal Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Science, Tehran, Iran
2. Anesthesiology Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran
3. Department of Anesthesiology, Lorestanan University of Medical Sciences, Khoram Abad, Iran
4. Department of Anesthesiology, Kerman University of Medical Sciences, Kerman, Iran

Corresponding Author: Shirin Salajegheh, MD, Department of Anesthesiology, Kerman University of Medical Sciences, Kerman, Iran
Email: Shirin135353@gmail.com

Please cite this article as: Jahangirifard A, Golestani Eraghi M, Fani K, Tafrishinejad A, Dadashpour N, Ahmadi ZH, et al. Effect of prophylactic vasopressin on hemodynamic parameters after coronary artery bypass graft surgery. J Cell Mol Anesth. 2017;2(3):97-102.

Introduction

Postoperative vasoplegic syndrome (PVS) is one of the important complications of coronary artery bypass grafting (CABG) which is characterized by hemodynamic instability due to low systemic vascular resistance, normal or elevated cardiac output and poor response to volume administration (1). The incidence of such situation was reported about 8-26% in on-pump surgeries (2). Some different mechanisms have been associated with PVS, such as hypothermia and duration of cardiopulmonary bypass (CPB), total cardioplegic volume infused, preoperative medications, and systemic inflammatory response syndrome (SIRS) (3).

An advanced form of PVS is a life-threatening condition which is resistant to conventional treatment, fluid administration, inotropes, and catecholamines (4).

Comparable to septic shock, vasodilatory shock after cardiac surgery is characterized by poor response of vascular smooth muscles to circulating catecholamines (5). Recently the administration of low dose vasopressin has shown promising effect on improvement of left ventricular function (6), increasing cardiac output and coronary blood flow, which is effective in postoperative hypotension (7, 8).

Yimin and collages have been reported better hemodynamic stability by vasopressin in CABG (9). Elgebaly and his collages have shown similar results too. They concluded that infusion of low-dose vasopressin for patients with mild to moderate left ventricular systolic dysfunction during separation from CPB is beneficial for the postoperative hemodynamic profiles, reduces the catecholamine doses required and improves left ventricular systolic function (10).

Based on such reports, this study was conducted to investigate the effect of low dose vasopressin on the hemodynamics and inotrope requirement after on-pump CABG surgeries in patients that had mild to moderate LV systolic dysfunction.

Methods

In this randomized double-blinded clinical trial, 80 patients who were candidate for elective CABG, with ejection fraction (EF)=35-50% were enrolled in the study and received same anesthetic regimen and operated by the same surgical team. Patients were observed by transesophageal echocardiography (TEE) and EF was measured prior to and after cardio-pulmonary bypass (CBP). The protocol of the study was approved by Tehran University of Medical Sciences Ethics Committee and written informed consent forms were obtained from all patients.

Patients with EF>50% or EF<35%, history of renal or liver failure, epilepsy, patients who need emergent surgery or valvular surgery, and any history of allergic reaction to vasopressin were excluded.

The patients in this study were monitored with ECG, invasive blood pressure (IBP), SpO2, and cerebral oximetry after they entered the operating room. In all patients, premedication was administered 1mg oral Lorazepam and 0.1mg/kg intramuscular morphine was administered 2 hours and one hour before surgery. Induction of anesthesia was performed with midazolam 0.05 mg/kg, etomidate 0.3 mg/kg, atracurium 0.5 mg/kg, and fentanyl 5-10 µg/kg. Then central venous catheters were placed after anesthesia induction. Maintenance of anesthesia was performed with: Midazolam 0.05 mg/kg/h, atracurium 5-10µg/kg/min, and fentanyl 5µg/kg/min. If needed we used low doses of propofol.

The anesthesiologists, surgeons, nurses, and the statistician were blinded to the protocol. In operation room patients were randomly divided into two equal case and control groups (n=40). Case group was received vasopressin 0.03 IU/min. 30 minutes before the end of CPB until one hour after that. The control group was received normal saline in same manner.

Using crystaloids, colloids, inotropes, vasoactive drugs and red blood cells, CVP, MAP, HR and HCT were kept in the target range. Our target in this study was MAP; 50-70mmHg, and Hematocrit (HCT); 20-30% during CPB. Also, after CPB we managed to keep MAP≥ 70 mmHg, CVP; 6-12cmH2o; HR; 70-90 bpm and HCT≥27%.

Demographic and clinical information of all patients were recorded. Operation time, CPB time, 24 hours volume of blood loss and urinary output, the incidence of arrhythmia, dopamine requirement of

separation from CPB and in the ICU, mechanical ventilation duration and ICU stay were recorded and compared between groups. The heart rate (HR), mean arterial blood pressure (MAP), central venues pressure (CVP) and atrial blood acidity (pH) were recorded every 30 minutes after separation of CPB till 120 minutes after that.

All statistical analyses were performed with SPSS software 21 package and statistical significance was considered at $p \leq 0.05$.

Results

There was no significant difference between two groups in age, gender, weight, height, EF, hypertension, diabetes mellitus, CPB time, and blood loss volume. All patients were successfully separated from CPB in first attempt without any mortality. Postoperative urinary output during first 24 hours was significantly lower in vasopressin group (p=0.001). Moreover the blood loss in first 24 hours was insignificantly lower in vasopressin group in comparison to control group (p=0.214) (Table 1).

CVP was corrected in vasopressin and placebo group and then dopamine administration was compared in both groups. In vasopressin and placebo group, 3 and 11 patients need to dopamine administration immediately after separation from CPB (p= 0.018; using Fisher's Exact Test) and 4 and 12 patients in ICU (p=0.024; using Fisher's Exact Test) respectively. The mean needed dose of dopamine in vasopressin and placebo group immediately after separation from CPB were 7.63±3.42 and 9.21±2.08 µg/kg/min (p=0.031) and in ICU were 7.42±2.02 and 8.66±4.08 µg/kg/min (p=0.045), respectively which were significantly lower in vasopressin group in comparison to placebo group.

None of the patients have shown hypertensive crisis. Hemodynamic data of patients in both groups were reported in Table 2.

Severe hypotension was considered the hemodynamic state characterized by MAP of less than 70 mmHg (11). There was no significant difference in the number of patients with severe hypotension (11 vs. 12 patients in case and control groups respectively).

CVP was monitored as an index of preload. Metabolic acidosis was defined as pH<7.3, which was not reported in groups. There was no significant difference in CVP and PH between groups also (Table 2).

Despite similar CVP without significance difference between groups, heart rate in vasopressin group were significantly lower than control group in all five evaluations (p=0.000).

The number of patients using ACE inhibitors and angiotensin receptor blocker (ARB_S) were equal in both groups and there was no correlation between these medications and number of patients with severe hypotension in vasopressin and control group (p=0.934) or dose of dopamine needed for severe hypotension (p=0.975).

The number of patients with arrhythmia in vasopressin and control group were 6 and 7 patients respectively (p=0.983) that did not differ between groups.

Discussion

Severe and unresponsive hypotension are an abruption in hemodynamic stability in the first hours after open heart surgery due to either the inflammatory mediators produced by CPB or preoperative medications such as ACE inhibitors, angiotensin receptor blocker, and so on (4, 12). In our study there were no difference in two preoperative affective variables, ejection fraction and there was no correlation between these medications and number of patients with severe hypotension in vasopressin and control group or the dose of dopamine needed for severe hypotension. Argenziano showed that both low EF and the use of ACE inhibitors were independent risk factors for postoperative vasodilatory shock and severe hypotension (12).

As this study showed, prophylactic use of vasopressin did not increase MAP and prevent severe hypotension in comparison with the control group, this is opposite to Papadopoulos study that demonstrated low dose vasopressin can significantly reduce vasodilatory shock (4% vs. 20 % in vasopressin and control group respectively) (4). These different results may be due to different definition of postoperative vasodilatory shock and severe hypotension.

Postoperative urinary output during the first 24

Table 1: Demographic data, mean (SD), ratios and number (percentage) of patients.

	Vasopressin group (n=40)	Placebo group (n=40)	P value
Age (years)	58.35 (8.23)	58.35 (7.84)	1.000
Gender (M/F)	27/13	25/15	0.407
Weight (kg)	69.11(11.82)	68.82(11.03)	0.908
Height (cm)	166.80(7.20)	166.18(7.66)	0.708
Ejection fraction (%)	42.12(5.30)	44.21(7.75)	0.168
Hypertension (Y/N)	23/17	24/16	0.50
Diabetes mellitus (Y/N)	13/27	14/26	0.50
Angiotensin receptor blocker	7	11	0.607
Angiotensin-converting-enzyme inhibitor	18	20	0.412
Nitrates	34	36	0.369
Cardiopulmonary bypass (min)	90.45(29.57)	79.92(29.91)	0.118
24 hours Blood volume loss (ml)	505.00(293.28)	722.50(1057.56)	0.214
24 hours urinary output (ml)	4152.0(1198.01)	5011.2(1065.39)	0.001*
Duration of mechanical ventilation (hour)	12.025(10.12)	15.97(6.74)*	0.043*
Arrhythmia (Y/N)	6/34	7/33	0.983
ICU stay (day)	3.22(0.73)	3.22(0.69)	1.00

*statistically significant.

hours was significantly lower in vasopressin group. It can be due to the vasoconstrictive effect of vasopressin on renal arteries or its effect as antidiuretic hormone. Papadopoulos in his study concluded vasopressin administration was associated with a higher 24 hour diuresis (4).

Duration of mechanical ventilation was significantly lower in vasopressin group too. It can be because of less dopamine administration, and more stability of MAP and HR in this group.

Table 2: Hemodynamic data of patients in both study group.

group	parameter	At the end of CPB	30 min after the end of CPB	60 min after the end of CPB	90 min after the end of CPB	120 min after the end of CPB
	HR (beat/min)	84.3 (10.1)	82.5 (9.4)	81.4 (10.3)	82 (9.5)	84.2 (10.7)
Vasopressin	MAP (mmHg)	67.3 (12.8)	75.7 (11.4)	77.3 (11.6)	74.8 (14.0)	74.1 (15.8)
group(n=40)	CVP (cm H_2O)	8.2 (3.5)	7.7 (2.5)	8.7 (1.8)	8.4 (2.2)	9.4 (1.8)
	pH	7.44 (0.07)	7.42 (0.05)	7.44 (0.06)	7.43 (0.08)	7.38 (0.05)
	HR (beat/min)	91.1 (15.7)	92.9 (13.7)	94.1 (14.3)	94.3 (14.2)	94.7 (14.3)
Placebo	MAP (mmHg)	70.5 (12.3)	76.2 (11.6)	74.2 (12.14)	78.8 (11.8)	84.2 (15.7)
group(n=40)	CVP (cm H_2O)	7.7 (3.7)	7.4 (3.3)	8.4 (2.4)	9.1 (2.6)	9.1 (2.4)
	pH	7.42 (0.08)	7.39 (0.05)	7.40 (0.06)	7.40 (0.06)	7.40 (0.06)

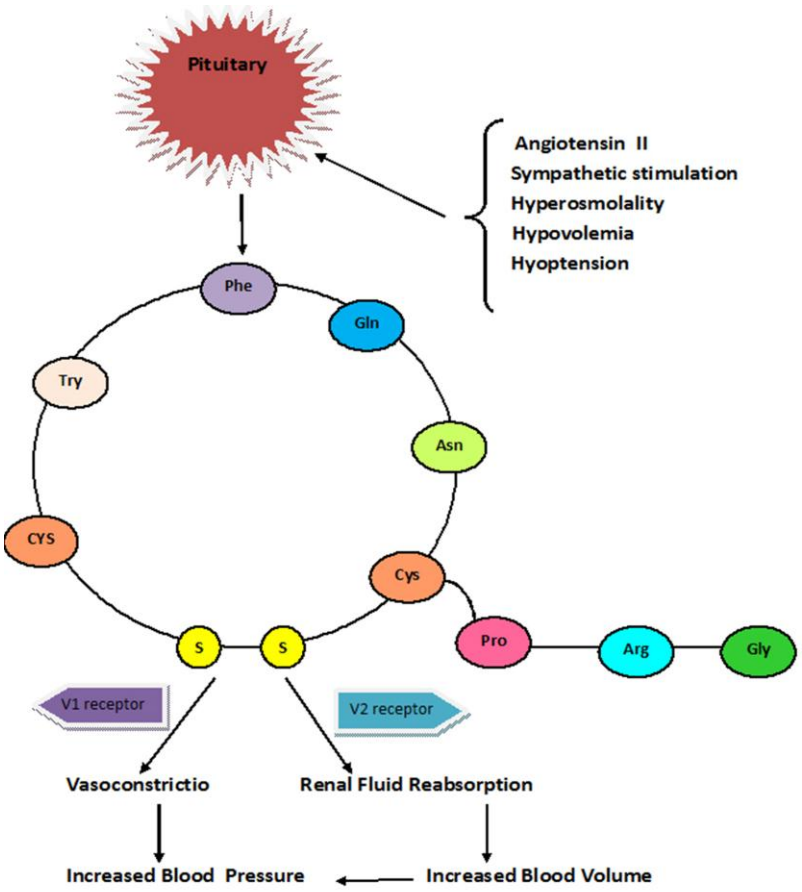

Figure 1. Mechanism of action of Vasopressin

There was not any sever complication and mortality in our study. Patel B, in his study, used low dose vasopressin (0.03 IU/min) and the study that was done by Suojaranta-Ylinen, used vasopressin in combination with norepinephrine and both study showed no increased mortality (13, 14). Our result is similar to both of these studies.

There is not enough knowledge about vasopressin effective and appropriate dose. Some investigators showed that vasopressin in dose of 2-6 U/h is effective in vasodilatory shock treatment (11, 15) but the appropriate dose for preventing the severe hypotension is not clear. In Papadopoulos G study showed 12.4±1.3 units of vasopressin may prevent vasodilatory shock and cause significant increase in MAP (4) which is different from our results.

It seems more investigations are needed to evaluate vasopressin effect on hemodynamic status after open heart surgery and CABG with different dosage.

Because of our limitation we could not measure cardiac output so we just measured MAP as only criteria for severe hypotension definition which is our strong study limitation. We were measured EF using TEE prior to and after CPB as an index of cardiac function and CVP as a preload indicator.

Conclusion

Based on our results, administration low-dose vasopressin (0.03 IU/min) significantly reduced the mean needed dose of required dopamine and patient's heart rate (30 minutes before the end of CPB until one hour after that). The number of patients with severe hypotension (MAP<70mmHg) was not different between groups. Vasopressin administration had no significant effect on ICU stay duration, mean arterial blood pressure, CVP, and arterial pH.

Acknowledgment

This article has been extracted from the thesis written by Dr Arash Tafrishinejad in school of medicine Shahid Beheshti University of Medical Sciences (Registration No:676).

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

1. Ozal E, Kuralay E, Yildirim V, Kilic S, Bolcal C, Kucukarslan N, Gunay C, Demirkilic U, Tatar H. Preoperative methylene blue administration inpatients at high risk for vasoplegic syndrome during cardiac surgery. Ann Thorac Surg. 2005;79:1615-9.

2. Sun X, Zhang L, Hill PC, Lowery R, Lee AT, Molyneaux RE, Corso PJ, and Boyce SW: Is incidence of postoperative vasoplegic syndrome different between off-pump and on-pump coronary artery bypass grafting surgery?

3. Noto A, Lentini S, Versaci A, Giardina M, Risitano DC, Messina R, David A: A retrospective analysis of terlipressin in bolus for the management of refractory vasoplegic hypotension after cardiac surgery. InteractCardioVascular and Thoracic Surgery. 2009;9:588-92.

4. Papadopoulos G, Sintou E, Siminelakis S, Koletsis E, Baikoussis NG, Apostolakis E. Perioperative infusion of low dose of vasopressin for prevention and management of vasodilatoryvasoplegic syndrome in patients undergoing coronary artery bypass grafting: A double-blind randomized study. J CardiothoracSurg 2010; 5:17.

5. Albright TN, Zimmerman MA, Selzman CH. Vasopressin in the cardiac surgery intensive care unit. Am J Crit Care. 2002;11:326–32.

6. Elgebaly AS, Sabry M: Infusion of low-dose vasopressin improves left ventricular function during separation from cardiopulmonary bypass: a double-blind randomized study. Ann Card Anaesth. 2012;15:128–33.

7. Mayr VD, Wenzel V, Müller T, Antretter H, Rheinberger K, Lindner KH, Strohmenger HU: Effects of vasopressin on left anterior descending coronary artery blood flow during extremely low cardiac output. Resuscitation 2004, 62:229–235.

8. Morales DL, Garrido MJ, Madigan JD, et al: A double-blind randomized trial: prophylactic vasopressin reduces hypotension after cardiopulmonary bypass [J]. Ann Thorac Surg. 2003;75:926–30.

9. Yimin H, Xiaoyo L, Yuping H, Weiyan L, Ning L. The effect of vasopressin on the hemodynamics in CABG patients. J Cardiothorac Surg. 2013;8:49.

10. Elgebaly AS, Sabry M. Infusion of low-dose vasopressin improves left ventricular function during separation from cardiopulmonary bypass: a double-blinded randomized study. Annals of Cardiac Anaesthesia. 2012;15(2):128-33.

11. Shanmugam G: Vasoplegic syndrome-the role of methylene blue. Eur J Cardio-thoracic Surg. 2005;28:705-10.

12. Argenziano M, Chen J, Choundhri A, Cullinane S, Garfein E, Weinberg AD, Smith CR Jr, Rose EA, Landry DW, Oz MC: Management of vasodilatory shock after cardiac surgery: identification of predisposing factors and use of a novel pressor agent. J Thorac Cardiovasc Surg. 1998;116:973-80.

13. Patel B, Chittock D, Russell J, Walley K: Beneficial effects of short-term vasopressin infusion during severe septic shock. Anesthesiology. 2002;96:576-82.

14. Suojaranta-Ylinen R, Vento R, Patila T, Kukkonen S: Vasopressin, when added to norepinephrine, was not associated with increased predicted mortality after cardiac surgery. Scand J Surg. 2007;96:314-8.

15. Morales D, Gregg D, Helman D, Williams MR, Naka Y, Landry DW, Oz MC: Arginine vasopressin in the treatment of fifty patients with postcardiotomyvasodilatory shock. Ann Thorac Surg. 2000;69:102-6.