



Hemodynamic Effects of Prophylactic Administration of Vasopressin in Patients Undergoing Off Pump Coronary Artery Bypass Graft Surgery: A Randomized Control Double Blind Interventional Study

Indu Verma^{1*}, Priyanka Beelwal¹, Chandan Verma², Chand Kishan Vyas¹

¹Department of Anaesthesia, SMS Medical College and Hospital, Jaipur, India.

²Department of Pharmacology, SMS Medical College and Hospital, Jaipur, India.

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ABSTRACT

Background: Off-pump coronary artery bypass grafting (OPCABG) is associated with hemodynamic fluctuations which usually require the use of various vasoactive drugs like norepinephrine and phenylephrine. The aim of this study was to evaluate the effect of low dose vasopressin on hemodynamics in patients undergoing Off-pump Coronary Artery Bypass Graft Surgery (OPCABG).

Methods: Sixty patients undergoing elective Off pump coronary artery bypass grafting (CABG) having triple vessel coronary artery disease (CAD) were randomly divided into two groups: group A (n=30), patients received Vasopressin 0.03 IU/min via infusion pump (diluted in 50 ml syringe) during the LIMA extraction and continued till the end of surgery; group B (n=30), patients received normal saline infusion pump during the LIMA extraction and continued till the end of surgery. The anesthetic technique was the same in both the groups. Hemodynamic parameters were recorded at various time intervals during the surgery.

Results: HR, CO and CI were lower and MAP, SVR and SVRI were higher in vasopressin group. CVP was stable with no significant difference in SV and SVV.

Conclusion: To achieve better intra operative hemodynamic stability during the triple vascular coronary anastomosis and to cope up with post-operative vasodilatory shock, low dose vasopressin infusion is a safe option.

Off-pump coronary artery bypass grafting (OPCABG) is achieving rapid increase in developing countries [1]. But it is associated with hemodynamic fluctuations which usually require the use of various vasoactive drugs like norepinephrine and phenylephrine. Vasoplegic syndrome in off pump CABG can be due to repeated episodes of hypotension because of mobilization and displacement of heart, surgical stress, use of devices, neutralization of heparin with protamine, transfusion of blood products, hypothermia or pre-operative use of ACEI [2-8]. Infusion of catecholamines during surgery often leads to cardiovascular destabilization because of arrhythmias [9-10].

Lot of studies have used a non-catecholamine drug like vasopressin to correct the hemodynamic disturbances during this period. Vasopressin can improve the left ventricular function by elevating the ejection fraction and it causes an increase in coronary perfusion pressure by increasing the cardiac output and the coronary blood flow [10]. Vasopressin also does not elevate the pulmonary vascular resistance and mean arterial pressure which may be attributed to the vasodilatory effects on the pulmonary vasculature [11-12].

Low dose vasopressin may decrease the dose requirement and duration of catecholamine administration. The vasoconstrictor action of this drug persists for up to 2

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*Corresponding author.

E-mail address: dr.induverma@gmail.com



hours in patients having hypotension and not responding to high doses of nor-epinephrine, dopamine and fluid administration [13-14].

Prophylactic administration of vasopressin is less well established although studies have shown their utility in preventing vasoplegia. At doses 0.03-0.1U/min, exogenous administration of vasopressin has proven to be safe and effective. Early identification and anticipation of post-operative vasoplegia can lead to improved hemodynamics with less post-operative complications. The combination of vasopressin with traditional catecholamines limits the need for increased doses of catecholamines and can lead to improve heart rate and myocardial oxygen demand and lower rates of cardiac arrhythmias. The patient hemodynamics are dependent on the preload, afterload, and contractility of the heart and other than low dose infusion of vasopressin the fluid and inotropic management was done with the help of Flo-Trac monitor of EV 1000 Edwards.

The present study was done to investigate the effect of low dose vasopressin on hemodynamics in patients undergoing Off-pump Coronary Artery Bypass Graft Surgery with the primary objective of Hemodynamic monitoring- including HR, SVV, SVR, SVRI, CO, C.I. MAP, CVP and SV and secondary objective including adverse effects if any the Troponin level, Lactate level, Urine output and renal function tests.

Methods

The study was conducted in the Department of Anesthesia with due permission from the institutional ethical committee and review board and with written informed patient consent. It is a hospital based, Prospective, Randomized, Double blind Interventional study conducted at a tertiary level hospital in patients undergoing elective Off-pump CABG surgery for triple vessel disease.

Sample Size

Sample size was calculated to be 29 cases in each group at alpha error 0.05 and study power 80% to verify a minimum difference of 10.4 ± 13.7 in heart rate (as per reference article). Hence for study purpose sample size was rounded off to 30 cases in each group

Eligible cases were randomly allocated in two different groups using sealed envelope method.

Each group was randomly allocated 30 patients (n=30/group)

GROUP A: Received vasopressin 0.03 IU/min infusion during the LIMA extraction in patient of OFF-pump CABG continued till the end of surgery with other inotropes prepared and kept standby.

GROUP B: Received normal saline infusion with Noradrenaline infusion and other inotropes as standby for any hemodynamic instability during the LIMA extraction in patient of OFF-pump CABG continued till the end of surgery

Patients of both genders were included in the study with age range of 30-70 years. All the patients were of ASA III grade weighing between 40-70 kilograms undergoing off-pump CABG surgery. Patients who were not willing to give written informed consent, with LVEF < 30%, who needed emergent surgery or valvular surgery, on pump CABG, diabetes mellitus, liver or renal impairment and history of allergic reaction to vasopressin were excluded from the study.

In all the 60 patient's internal jugular and femoral artery cannulation was done under local anesthesia. Baseline data in the form of Heart rate (HR), Mean arterial pressure (MAP), Central venous pressure (CVP), Cardiac index (CI), Systemic Vascular Resistance Index (SVRI), Lactate level was recorded. Cardiac output and its derived parameters were measured with EV1000 Flo-Trac system monitor having a flow track sensor.

Anesthesia

Patients were oxygenated with 100% oxygen for 5 minutes. Patients were induced with Midazolam (0.15mg/kg), Fentanyl (5µg/kg), Etomidate (0.3mg/kg) and Rocuronium(0.9mg/kg) intravenously. Patient were intubated with appropriate size ET tube. Anesthesia was maintained with oxygen, Vecuronium, Midazolam, Fentanyl and inhalational agent sevoflurane.

The infusion of drugs was started via syringe pumps diluted in 50 ml syringe at the rate of 0.03 IU/min. Heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), stroke volume (SV), stroke volume variation (SVV), cardiac output (CO), cardiac index (C.I.), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI) and lactate levels were measured in both groups A and B at baseline, after induction of anesthesia, 5 min after surgical incision, 5 min after sternotomy, during left anterior descending artery (LAD) grafting, during left circumflex artery/obtuse marginal (LCx/OM) grafting, during posterior descending artery (PDA) grafting, and at the end of surgery . CPK-MB level, Serum urea, Serum creatinine and 24 hr urine output were also measured at baseline, 24 hours after surgery and 48 hours after surgery.

Statistical analysis

Was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05.

Results

The two groups were comparable in terms of age, sex, body weight, baseline LVEF, baseline serum creatinine, serum urea, diabetes and hypertension as shown in (Table 1).

Heart rate (HR) showed no significant difference from baseline and till 5 minutes after sternotomy between both group A and B. Group A showed a decrease in HR during LAD grafting till the end of surgery as compared to Group B, p value <0.05 (Table 2).

Mean arterial pressure (MAP), systemic vascular resistance (SVR) and systemic vascular resistance index (SVRI) were statistically not different at baseline and did not differ till 5 minutes after sternotomy in both group but as the infusion (vasopressin/saline) was started during extraction of LIMA, MAP, SVR and SVRI were found to be significantly higher in vasopressin group during grafting and the effect persisted till the end of surgery with statistical significance p value <0.05 (Table 2).

Central venous pressure (CVP) was maintained at 8-12 mm of Hg. In both groups at all the time points we studied difference in CVP, which was statistically not different including before and after infusion (vasopressin / saline) except after surgical incision, at which point CVP was found to be lower in vasopressin group p value <0.05 [Table 3].

Stroke volume (SV) was found to be higher in control group before starting infusion which was statistically significant. However, it was similar after starting infusion (vasopressin/saline) (Table 3). Stroke volume variation (SVV) was found to be higher in control group both before and after starting infusion (p value <0.05).

Cardiac output (CO) decreased in both the groups from baseline but the decrease was more in the Group A as compared to Group B p value < 0.05 (Table 3).

Blood urea and serum creatinine levels were lower in Group A as compared to Group B on post-operative day 1 and 2, These were statistically not significant (p value >0.05) (Table 4)

CPK-MB level was also measured in this study which was 17.63 ± 2.19 in group A on post-operative day 1 while in group B it was 19.05 ± 3.45 ($p = 0.061$). On post-operative day 2, it was 17.57 ± 2.17 in group A while in group B it was 19.05 ± 3.39 ($p = 0.049$). Values calculated on both days were statistically significant (Table 4).

Serum lactate level on post-operative day 1 was 1.41 ± 0.65 in vasopressin group while in control group it was 1.87 ± 0.58 ($p = 0.005$). On post-operative day 2 it was 1.22 ± 0.72 in vasopressin group while in control group it was 2.13 ± 0.65 ($p = 0.001$). On both day's the difference was statistically significant (Table 4).

Urine output was more in Group A as compared to Group B but was statistically insignificant (p value >0.05) on post-operative day 1 and 2 (Table 4).

Inotropic requirement

In group B the inotropic requirement was more as compared to patients in group A. 44 patients required inotropes in the form of dobutamine (p value <0.01), noradrenaline (p value = 0.02), epinephrine (p value = 0.06) and milrinone (p value = 0.27) and nitroglycerine (p value = 0.02) While only 35 patients required inotropic support in group A.

Table 1- Baseline characteristics

	Vasopressin group mean \pm SD		Control group mean \pm SD		P value
Age	55.4 \pm 8.60		57.2 \pm 9.93		0.456
Sex	M= 24; F = 6		M= 26; F=4		0.729
Weight	61.3 \pm 6.2		59.6 \pm 4.6		0.224
LVEF	46.93 \pm 8.76		47.93 \pm 8.96		0.663
DM	6		6		0.295
HTN	10		15		1.000
S.urea	29.55 \pm 9.5		30.01 \pm 6.6		0.428
S.creatinine	1.08 \pm 0.22		1.13 \pm 0.27		0.831

Table 2- Heart rate, mean arterial pressure, systemic vascular resistance measurements

	Heart Rate					Mean Arterial Pressure					Systemic Vascular Resistance				
	Group A		Group B		P value	Group A		Group B		P value	Group A		Group B		P value
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Baseline	97.30	19.46	99.63	17.43	0.626	103.43	16.07	107.17	10.37	0.289	1328.77	351.22	1452.83	323.64	0.160
After induction of anesthesia	100.57	14.56	97.47	13.82	0.401	96.30	15.31	92.27	9.79	0.229	1253.30	337.64	1395.83	395.43	0.138
5 min after surgical incision	95.93	14.75	98.37	14.61	0.523	92.93	14.34	95.90	6.81	0.310	1404.47	413.53	1517.53	402.08	0.287
5 min after sternotomy	94.30	13.50	99.33	13.87	0.159	92.03	12.76	90.37	16.96	0.668	1362.90	379.98	1493.87	348.15	0.169
During LAD grafting	92.63	13.04	99.70	13.05	0.040*	92.53	9.03	86.57	9.42	0.015*	1451.87	408.58	1274.10	250.17	0.046*
DURING LCx/OM GRAFTING	91.87	14.03	99.57	12.65	0.029*	92.60	11.07	86.87	10.26	0.041*	1463.07	354.39	1293.23	288.54	0.045*

During PDA grafting	91.53	15.93	98.53	8.35	0.037*	93.87	9.98	87.33	9.26	0.010*	1496.00	536.24	1274.00	231.53	0.041*
At the end of surgery	92.30	13.80	99.00	11.61	0.048*	95.53	7.69	90.50	9.45	0.027*	1502.30	284.99	1296.77	237.90	0.003*

Table 3- Central venous pressure, stroke volume and cardiac output measurements

	Central Venous Pressure					Stroke Volume					Cardiac Output				
	Group A Mean	Group A SD	Group B Mean	Group B SD	P value	Group A Mean	Group A SD	Group B Mean	Group B SD	P value	Group A Mean	Group A SD	Group B Mean	Group B SD	P value
Baseline	10.50	4.85	10.30	2.61	0.843	56.90	21.71	61.87	11.59	0.273	6.53	7.22	5.40	1.07	0.401
After induction of anesthesia	10.30	5.47	9.33	1.42	0.352	51.17	14.13	57.40	9.10	0.046*	4.58	1.14	4.54	0.83	0.887
5 min after surgical incision	9.03	2.98	11.13	2.03	0.002*	52.03	15.71	61.57	11.08	0.008*	4.52	1.18	4.83	0.93	0.262
5 min after sternotomy	10.00	3.83	11.20	1.94	0.131	55.20	16.45	63.67	9.46	0.017*	4.62	1.20	4.94	0.83	0.229
During LAD grafting	10.30	6.61	10.00	1.51	0.809	55.13	14.42	60.87	9.40	0.073	4.61	1.03	5.05	0.99	0.102
During LCx/OM GRAFTING	9.37	3.15	9.30	1.29	0.914	56.40	14.90	59.63	7.85	0.297	4.71	1.34	5.03	1.00	0.303
During PDA grafting	8.20	3.07	8.23	1.57	0.957	54.33	15.73	57.07	8.98	0.411	4.50	1.47	4.91	0.90	0.200
At the end of surgery	9.37	3.76	10.17	0.95	0.262	55.47	13.91	61.13	8.86	0.064	4.48	1.28	5.06	0.82	0.040

Table 4- CPK-MB level, serum urea, serum creatinine, lactate level and 24 hour urine output on post-operative day 1 and post-operative day 2

		Group A		Group B		P value
		Mean	SD	Mean	SD	
CPK-MB level	Post-Operative Day 1	17.63	2.19	19.05	3.45	0.061
	Post-Operative Day 2	17.57	2.17	19.05	3.39	0.049*
Lactate level	Post-Operative Day 1	1.41	0.65	1.87	0.58	0.005*
	Post-Operative Day 2	1.22	0.72	2.13	0.65	p<0.001*
Serum urea	Post-Operative Day 1	29.22	7.99	29.84	5.40	0.726
	Post-Operative Day 2	28.59	7.75	30.79	6.34	0.232
Serum creatinine	Post-Operative Day 1	1.07	0.22	1.23	0.30	0.023*
	Post-Operative Day 2	1.02	0.23	1.37	0.37	p<0.001*
24 hour urine output	Post-Operative Day 1	1612.33	211.64	1522.23	182.17	0.082
	Post-Operative Day 2	1593.47	160.46	1545.33	208.45	0.320

Discussion

In OPCABG to expose coronary artery and for its grafting mobilization and displacement of heart takes place which results in intermittent episodes of hypotension throughout the procedure. This type of insults might result in vasoplegic syndrome (vs).

After volume resuscitation catecholamines are considered to be the cornerstone of VS treatment. This therapeutic class includes dopamine, epinephrine, norepinephrine, and phenylephrine which increase mean arterial pressure (MAP) by stimulating the α 1 adrenergic receptor. It is of limited use because of evident resistance and toxicity [15].

Another therapeutic agent is methylene blue (MB), used as prophylactic as well as adjuvant treatment option. But it is responsible for greenish-blue discoloration of skin, mucosa and body fluids and it might interfere with pulse oximeter and cerebral oximeter readings. It is

remarkable that the risks are taking into more consideration than the lifesaving benefits. So, although MB have obvious MAP-increasing and catecholamine-sparing effects but has no enough convincing evidence on outcomes for treating vasodilatory shocks. In selected high-risk circumstances, it might be considered as additional off-label therapy [15].

Vasopressin is an endogenous peptide hormone, released by the posterior pituitary gland in response to hyperosmolar plasma, systemic hypo-perfusion and other stress stimuli. It produces vasoconstriction through stimulation of V1 receptors in vascular smooth muscle. As in cardiogenic and hemorrhagic shock states, distributive (vasodilatory) shock state is also characterized by a relative vasopressin deficit in plasma. So, exogenous low dose vasopressin is beneficial in vasodilatory shock like in cardiac surgeries with preservation of urine output [16].

In this study we used vasopressin in low dose (0.03 IU/min), which was given prophylactically in one group

and compared the hemodynamic changes with control group who had given normal saline as volume expander with Nor-adrenaline infusion as standby if the mean arterial pressure fell below 70mm Hg.

There was no statistically significant difference in the baseline characteristics in both groups including mean age, sex, weight and ejection fraction.

There was significantly lower heart rate in vasopressin group in comparison to control group. Low heart rate during CABG surgery reduces myocardial oxygen consumption and facilitates the surgical procedure. Our study was supported by Alireza Jahangirifard et al [17] who found heart rate in vasopressin group was significantly lower than control group. In other studies, conducted by Yimin et al [18], Elgebaly et al [19] and Papadopoulos et al [5], it was observed to be stable.

We observed higher mean arterial pressure (MAP) in vasopressin group in comparison with control group. Various studies conducted by Yimin et al [18], Papadopoulos et al [5], Yunsheok jeon et al [20], and Eissa et al [21] also had similar results and concluded that low dose infusion of vasopressin causes higher MAP. Elgebaly et al [19] observed no significant difference in MAP in their study.

In this study SVR and SVRI were found to be significantly higher in vasopressin group. Similarly, significant higher value of SVR was recorded in the patients of vasopressin group in studies of Yimin et al [18], Papadopoulos et al [5], Yunsheok jeon et al [20], Eissa et al [21], Luckner et al [9] and Masetti et al [13]. Regarding high value of SVRI our results were similar with the results reported by Elgebaly et al [19], Papadopoulos et al [5] and Eissa et al [21]. Increased SVR is the result of vasopressin-induced systemic vasoconstriction in patients with shock. This change is usually not observed in normotensive subjects [22].

In our study, CVP was stable in both groups but Yimin et al [18] and Papadopoulos et al [5] noted CVP to be significantly higher. Cardiac output (CO) was lower in vasopressin group in this study. Elgebaly et al [19] found CO to be higher in vasopressin group. Our result doesn't concur with this. Cardiac index (C.I.) was lower in vasopressin group. Similar result was noted in study of Yimin et al [18]. and Masetti et al. [13]. Whereas, Papadopoulos et al [5] concluded no significant difference in C.I. and Elgebaly et al [19] found C.I. to be higher in vasopressin group.

In this study SV and SVV showed no significant difference after vasopressin infusion. To the best of our knowledge no previous literatures mentioned the effect on these parameters.

In this study we found that post-operative serum lactate level, CPK-MB, urea and creatinine was significantly lower when measured at 24 and 48 hours after surgery in vasopressin group compared to control group. Lactate level is an established indicator of systemic perfusion. As

explained by Yunseok Jeon et al [20] study that vasopressin significantly reduces PVR/SVR ratio which reflects better systemic perfusion. As PVR measurement is not routine in CABG surgery we measured lactate level which in our study concluded a better systemic perfusion in vasopressin group.

In our study we found that CPK-MB which is selective marker of myocardial damage was significantly lower 17.63 ± 2.19 in vasopressin group as compared to 19.05 ± 3.45 in control group on post-operative day 1 with p value of 0.06 and on post-operative day 2 it was 17.57 ± 2.17 vs 19.05 ± 3.39 with p value of 0.049 which is suggestive of cardioprotective action of low dose of vasopressin.

There is high prevalence of acute kidney injury in shock. The mainstays of prevention and treatment include avoidance of nephrotoxins and ensuring adequate renal perfusion. In addition to its potent vasoconstrictor effects, vasopressin also has specific beneficial effects on renal function secondary to its binding to a family of vasopressin receptors. In several studies of vasodilatory shock, vasopressin increased glomerular filtration rate, urine output and creatinine clearance [9,13,23,25]. Masetti et al [13] also noted increased urine output after vasopressin infusion.

If vasopressin has been used in low doses it has little or no influence on blood pressure of the normotensive patients, while the same doses in patients in vasodilatory shock produce an effective constrictive vessel action [24]. Thus, we found vasopressin is a good agent to maintain hemodynamics in patients undergoing off pump CABG with cardioprotective as well as nephroprotective action without any significant adverse effects.

However, clinical and experimental studies certainly support the beneficial effects of low-dose vasopressin infusion in vasodilatory shock. But still they are not quite enough, so there is requirement of more studies to evident its beneficial aspects. Here in this study we tried to shed light on cardioprotective role of vasopressin in patients who underwent off pump coronary artery bypass grafting surgery.

Vasopressin group required less inotropic support as compared to the control group.

Conclusion

From this study we conclude that prophylactic "low" dose vasopressin infusion in off pump coronary artery bypass grafting surgery is safe. It is cardio-protective as well as nephroprotective also. It significantly obtained a better hemodynamic profile, and lower blood loss. Its use seems to be preventive for the incidence of post-surgery vasodilatory shock. Finally, it decreases the inotropic requirement. Therefore, Vasopressin in low doses may be an alternative agent to deal with hypotension during cardiac surgeries.

References

- [1] Lee YK, Na SW, Kwak YL, Nam SB. Effect of pre-operative angiotensin converting enzyme inhibitors on hemodynamic parameters and vasoconstrictor requirements in patients undergoing off-pump coronary artery bypass surgery. *J Int Med Res.* 2005; 33(6):693-702.
- [2] Gomes WJ, Erlichman MR, Batista-Filho ML, Knobel M, Almeida DR, Carvalho AC, et al. Vasoplegic syndrome after off-pump coronary artery bypass surgery. *Eur J Cardiothorac Surg.* 2003; 23(2):165-9.
- [3] Argenziano M, Chen JM, Choudhri AF, Cullinane S, Garfein E, Weinberg AD, et al. Management of vasodilatory shock after cardiac surgery: identification of predisposing factors and use of a novel pressor agent. *J Thorac Cardiovasc Surg.* 1998; 116(6):973-80.
- [4] Levin RL, Degrange MA, Bruno GF, Del Mazo CD, Taborda DJ, Griotti JJ, et al. Methylene blue reduces mortality and morbidity in vasoplegic patients after cardiac surgery. *Ann Thorac Surg.* 2004; 77(2):496-9.
- [5] Papadopoulos G, Sinton E, Siminelakis S, Koletsis E, Baikoussis NG, Apostolakis E. Perioperative infusion of low dose vasopressin for prevention and management of vasodilatory vasoplegic syndrome in patients undergoing coronary artery bypass grafting-A double-blind randomized study. *J Cardiothorac Surg.* 2010; 5:17-28.
- [6] Gomes WJ, Carvalho AC, Palma JH, Teles CA, Branco JN, Silas MG, et al. Vasoplegic syndrome after open heart surgery. *J Cardiovasc Surg (Torino).* 1998; 39(5):619-23.
- [7] Mekonto-Dessap A, Huel R, Soustelle C, Kirsch M, Thebert D, Loisançe DY. Risk factors for post cardiopulmonary bypass vasoplegia in patients with preserved left ventricular function. *Ann Thorac Surg.* 2001; 71(5):1428-32.
- [8] Ohri SK, Becket J, Brannan J, Keogh BE, Taylor KM. Effects of cardiopulmonary bypass on gut blood flow, oxygen utilization and intra-mucosal pH. *Ann Thorac Surg.* 1994; 57(5):1193-9.
- [9] Luckner G, Dünser MW, Jochberger S, Mayr VD, Wenzel V, Ulmer H, et al. Arginine vasopressin in 316 patients with advanced vasodilatory shock. *Crit Care Med.* 2005; 33(11):2659-66.
- [10] Dunser MW, Wenzel V, Mayr AJ, Hasibeder WR. Management of vasodilatory shock: defining the role of arginine vasopressin. *Drugs.* 2003; 63(3):237-56.
- [11] Dunser MW, Mayr AJ, Ulmer H, Knotzer H, Sumann G, Pajk W, et al. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized, controlled study. *Circulation.* 2003; 107(18):2313-9.
- [12] Mc Graw C, Scarlett M, Irvine R, Ramphal P. Vasopressin for refractory hypotension during cardiopulmonary bypass. *West Indian Med J.* 2007; 56:550-4.
- [13] Masetti P, Murphy SF, Kouchoukos NT. Vasopressin therapy for vasoplegic syndrome following cardiopulmonary bypass. *J Card surg* 2002;17: 485-9.
- [14] Argenziano M, Chen JM, Choudhri AF, Cullinane S, Garfein E, Weinberg AD, et al. 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.
- [15] Fischer GW, Levin MA. Vasoplegia during cardiac surgery: current concepts and management. *Semin Thorac Cardiovasc Surg.* 2010; 22(2):140-4.
- [16] Park KS, Yoo KY. Role of vasopressin in current anesthetic practice. *Korean J Anesthesiol.* 2017; 70(3):245.
- [17] Jahangirifard A, Golestani Eraghi M, Fani K, Tafreshinejad 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.
- [18] 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.
- [19] 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.
- [20] Jeon Y, Ryu JH, Lim YJ, Kim CS, Bahk JH, Yoon SZ, et al. Comparative hemodynamic effects of vasopressin and norepinephrine after milrinone-induced hypotension in off-pump coronary artery bypass surgical patients. *Eur J Cardiothorac Surg.* 2006; 29(6):952-6.
- [21] Eissa MI. Prophylactic vasopressin versus norepinephrine in patients receiving the angiotensin-converting enzyme inhibitor undergoing coronary artery bypass graft surgery. *Aamj.* 2014; 12(4).
- [22] Tayama E, Ueda T, Shojima T, Akasu K, Oda T, Fukunaga S, et al. Arginine vasopressin is an ideal drug after cardiac surgery for the management of low systemic vascular resistant hypotension concomitant with pulmonary hypertension. *Interact Cardiovasc Thorac Surg.* 2007; 6(6):715-9.
- [23] Barrett LK, Singer M, Clapp LH. Vasopressin: mechanisms of action on the vasculature in health and in septic shock. *Crit Care Med.* 2007; 35(1):33-40.
- [24] Landry DW, Levin HR, Gallant EM, Seo S, D'Alessandro D, Oz MC, et al. Vasopressin pressor hypersensitivity in vasodilatory septic shock. *Crit Care Med.* 1997; 25(8):1279-82.
- [25] Mitra JK, Roy J, Sengupta S. Vasopressin: Its current role in anesthetic practice. *Indian J Crit Care Med.* 2011; 15(2):71-7.