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RESEARCH ARTICLE

COMPARATIVE STUDY OF LEVOSIMENDAN VERSUS DOBUTAMINE IN VIEW DIFFERENCE IN MEAN HEART RATE , SBP & DBP BETWEEN TWO GROUPS IN PATIENTS OPERATED FOR CARDIACSURGERY PATIENTS IN TERTIARY CARE HOSPITAL.

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Abstract

Introduction:-
Cardiopulmonary bypass is associated with clinically asymptomatic to clinically symptomatic myocardial injury . Oxygen & ATP deprivation and/or reperfusion injury following cross clamp removal are associated with myocardial insult. Levosimendan has also been used in this context but only in a small number of patients so the clinical-experience is very limited. So we studied a comparison between levosemendan and dobutamine in on-pump surgery patients.

Methods:- 60 patients posted for CABG in cardiac on pump surgeries. They were allocated randomly to two equal groups (Group L - inj. levosimendan 12µg/kg over 10 minutes after cross clamp removal and 0.1µg/kg/min started after that andinj.Dobutamine 5 µg/kg/min infusion at the time of weaning from cardiopulmonary bypass) from feb 2014 to july 2015 at dheeraj general hospital piparia Vadodara..

Results:- In our study we found there was statistically significant difference in mean heart rate between two groups ($p<0.001$).Heart rate increased more in the levosimendan group than in the dobutamine group. there is no statistically significant difference in systolic and diastolic blood pressure in both groups($p>0.05$).

Conclusion:-Levosemendan is better than dobutamine in maintaining hemodynamic stability during intraoperative and postoperative period of patients coronary artery bypass graft going for on-pump surgery

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Introduction:-

Cardiopulmonary bypass is associated with clinically asymptomatic to clinically symptomatic myocardial injury . Oxygen & ATP deprivation and/or reperfusion injury following cross clamp removal are associated with myocardial insult. Levosimendan has also been used in this context but only in a small number of patients so the clinical-experience is very limited. So we studied a comparison between levosemendan and dobutamine in on-pump surgery patients.

Aims and objectives of study:-

Aim:-

1.To study the Ionotropic action of Levosimendan and Dobutamine.
2.To study the side effects of both drugs.

Objectives:-

1.To compare action of Levosimendan and DobutamineIonotropic action in the form of hemodynamics .
2.Tocompare Intraoperative and post-operative outcome of both drugs.

Material and methodology:-

In a prospective randomized study 60 patients will be scheduled for Cardiac Surgery at "Matsama" Heart Centre, Dhiraj General Hospital. Clearance from institutional ethics committee will be obtained. They will be randomly allocated to two groups of 30 each. Patients will be subjected to pre-anesthetic checkup and informed consent will be obtained from all the patientsfrom feb 2014 to july 2015 at dheeraj general hospital piparia Vadodara..

Inclusion criteria:-

- Adult patients posted for cardiac surgery using cardiopulmonary bypass .
- Probable cardiopulmonary bypass time 60 to 90 minutes.

Exclusion criteria:-

- History of allergic reaction to any of the drug under study.
- Patients with renal and hepatic disease.
- Pre-operative poor cardiac function ,EF< 40%.
- History of arrhythmia

Pre operative preparation:-

Tab. Alprazolam 0.25 mg was given on the night prior to surgery. Patients were nil by mouth at least eight hours before operation. The patients were reassured; the procedure of anesthesia explained and a written informed consent was obtained from them.

On the day of operation, multipara monitors were applied and base line respiratory rate, pulse rate, non-invasive blood pressure, SpO2 and ECG was recorded. Intravenous line was secured with 18G IV line and the patients were started I.V. fluids. Premedication of Inj. Glycopyrrolate 0.2 mg, Inj. Ondensatron 4 mg and Inj. Ranitidine 50 mg iv given. All invasive preanesthesia procedure were done under strict aseptic precaution under local anesthesia. O2 by face mask given at 4lit./min. Radial cannulation was done and baseline ABG was taken. Then all other invasive (femoral, PA/CVP) cannulation was done. Arterial pressure monitoring and CVP/PA was started.

Patients were induced with Inj. Fentanyl 5-10 µg/kg, Midazolam 0.05 to 0.1 mg/kg, Vecuronium 0.2 mg/kg i.v. as per body weight and Isoflurane, IPPV with 100% oxygenation on mask and circuit and intubated by direct laryngoscopy. Tube was fixed after bilateral air entry check & maintained on Air on oxygen, Isoflurane, Muscle relaxants (top-ups) with fentanyl-midazolam combination.

Throughout the surgery heart rate,bloodpressure,PAP/CVP,SPO2,urine output will be monitored.

inj.levosimendan with inj.dopamine will be started in group L and inj.dobutamine with inj.dopamine will be started in group D patients while coming of cardio pulmonary bypassGroup L (n=30) will receive inj. levosimendan12µg/kg over 10 minutes after cross clamp removal and 0.1µg/kg/min started after that. Group D (n=30) will receive inj. Dobutamine 5 µg/kg/min infusion at the time of weaning from cardiopulmonary bypass. Both the group received inj.dopamine 5-8 µg/kg/min from beginning of ionotrope. Inj.noradrenaline 0.1µg/kg/min added as rescue drug if there is persistent hypotension due to low SVR.. Both the group will be monitored for the parameters mentioned above as well as any side effect/ complications related with the drug.Both the group will be monitored for the fluid requirement also.Need for other ionotropic agents /any other drug will be taken into account.

Patient will be shifted to the surgical intensive care unit and monitored 48hrs for required parameters and extubated once stability achived.Ionotropic support will be removed gradually as for condition of heart.Both the drugs compared for haemodynamics, respiratory parameters, urine output monitoring and also for routine laboratory investigations (including LFT ,RFT) postoperatively.Time taken for extubation after shifting the patient to SICU also taken in to account.Both the groups would be compared for side effects and need of additional ionotropic support ,antiarrhythmic drug or other medication-interventionrequiremen

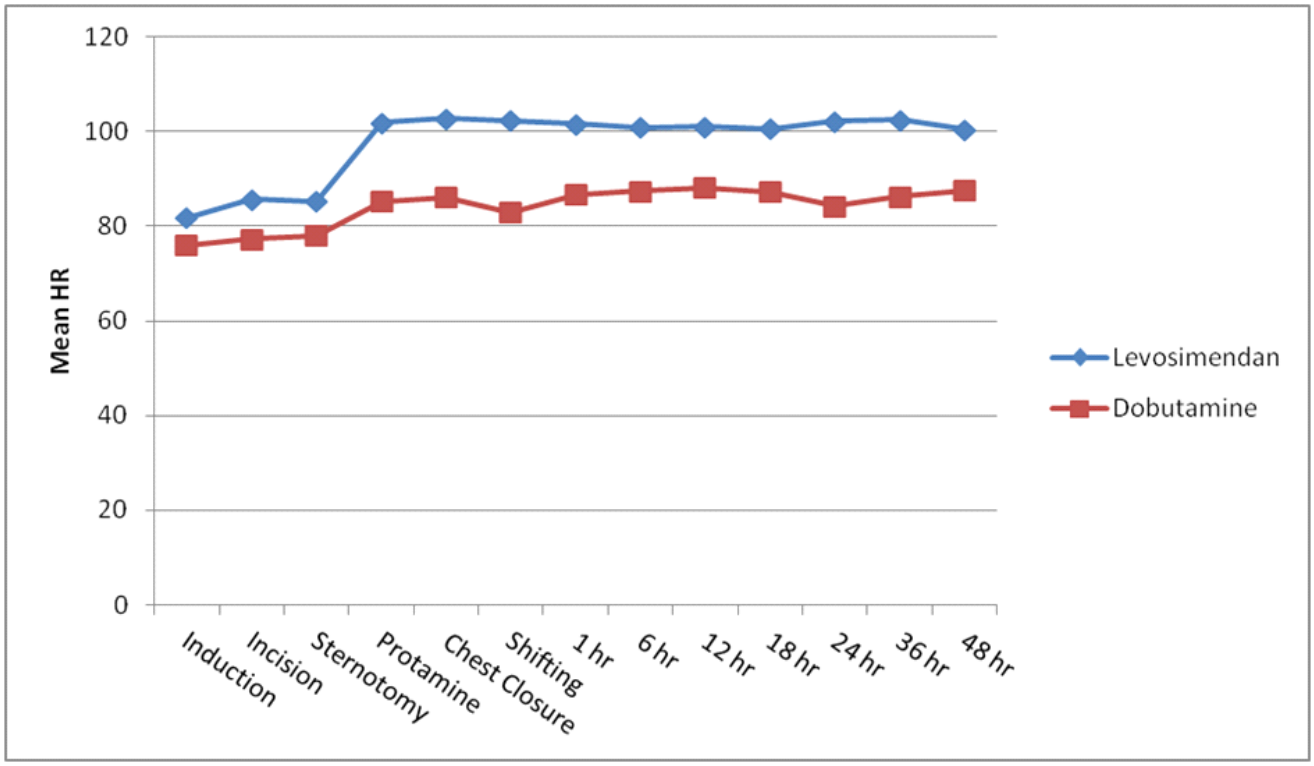
Observation and results:-

60 patientsposted for CABG between the ages of 40 yrs.- 70 yrs. of both sexes under ASA I and II were taken for study in cardiac on pump surgeries. They were allocated randomly to two equal groups. (Group L - inj. levosimendan 12µg/kg over 10 minutes after cross clamp removal and 0.1µg/kg/min started after that) and(inj.Dobutamine 5 µg/kg/min infusion at the time of weaning from cardiopulmonary bypass)

The various observations were summarized as follows :-

Heart rate changes between two groups.

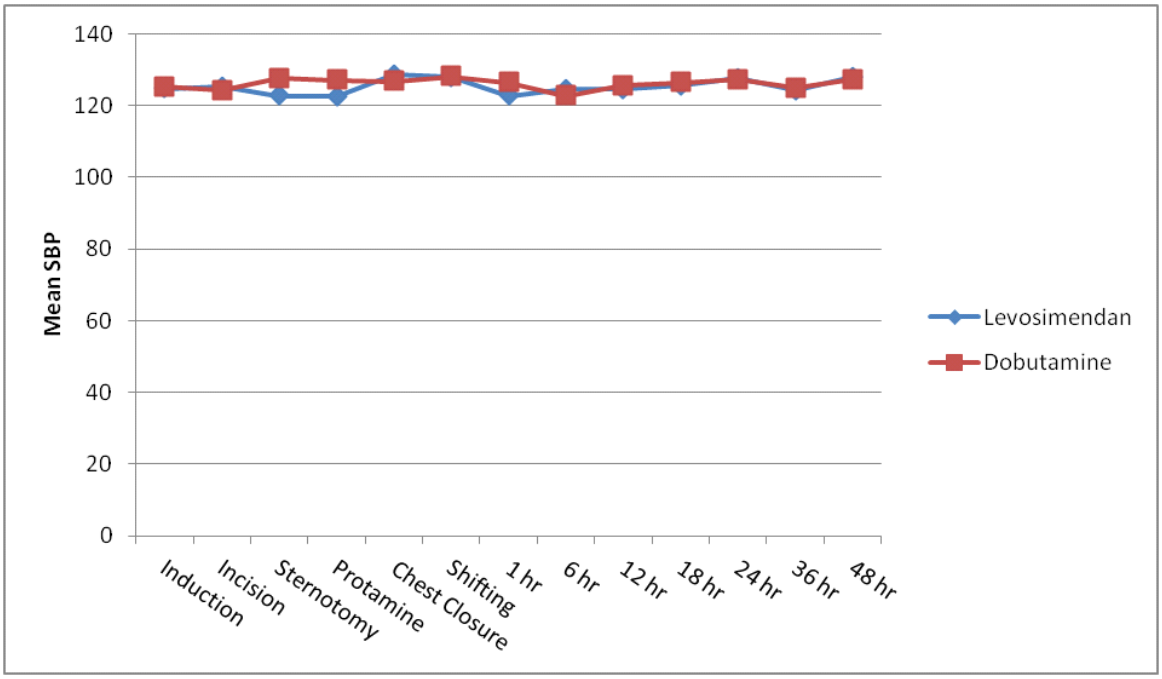
HR	Levosimendan	Dobutamine	p-value
Induction	81.77±9.626	76.03±10.2	0.029
Incision	85.73±9.244	77.33±9.312	0.001
Sternotomy	85.2±8.13	78±9.127	0.002
Protamine	101.9±7.827	85.2±10.087	<0.001
Chest Closure	102.73±6.422	86.07±9.734	<0.001
Shifting	102.33±7.048	83.0±8.481	<0.001
1 hr	101.6±7.152	86.73±8.296	<0.001
6 hr	100.93±6.575	87.47±8.772	<0.001
12 hr	101±7.625	88.07±7.656	<0.001
18 hr	100.53±5.964	87.27±5.836	<0.001
24 hr	102.13±5.482	84.2±5.641	<0.001
36 hr	102.47±5.722	86.2±6.02	<0.001
48 hr	100.47±7.785	87.6±6.157	<0.001



As shown in table and graph from induction to sternotomy there was no statistically significant difference in mean heart rate between two groups ($p>0.05$). From administration of both drugs to 48hours post operatively there was statistically significant difference in mean heart rate between two groups ($p<0.001$). Heart rate increased more in the levosimendan group than in the dobutamine group.

Mean systolic blood pressure at different intervals in both the groups.

SBP	Levosimendan	Dobutamine	p-value
Induction	124.7±8.972	125.33±8.919	0.785
Incision	125.33±7.053	124.27±8.546	0.600
Sternotomy	122.73±23.22	127.6±6.089	0.271
Protamine	128.53±6.252	127.07±5.03	<0.656
Chest Closure	128.6±7.668	126.8±3.263	0.242
Shifting	127.9±6.645	128.07±5.212	0.914
1 hr	122.73±8.379	126.4±6.112	0.058
6 hr	124.6±6.626	122.67±6.567	0.261
12 hr	124.47±9.258	125.67±8.001	0.593
18 hr	125.53±7.06	126.47±7.496	0.621
24 hr	127.67±5.898	127.27±8.781	0.837
36 hr	124.2±5.738	124.8±9.182	0.763
48 hr	128±6.808	127.2±7.019	0.656



As shown in table and graph there is no statistically significant difference in systolic blood pressure in both groups(p>0.05). .

Mean diastolic blood pressure at different time intervals in both the groups.

DBP	Levosimendan	Dobutamine	p-value
Induction	76.8±9.463	74.67±7.397	0.335
Incision	76.03±8.122	75.07±8.383	0.801
Sternotomy	76.53±7.123	76.73±4.996	0.900
Protamine	77.33±8.376	77.87±6.078	0.900
Chest Closure	73.2±5.623	77.27±5.105	0.005
Shifting	75.27±5.471	78.2±4.852	0.032
1 hr	75.4±8.885	77.33±4.708	0.297
6 hr	77.6±6.836	77.33±5.542	0.869
12 hr	78.13±5.704	79.33±4.992	0.389
18 hr	80.27±5.426	77.47±5.251	0.047
24 hr	75.27±5.471	78.2±4.852	0.032
36 hr	75.4±8.885	77.33±4.708	0.297
48 hr	77.6±6.836	77.33±5.542	0.869

From induction to 48hours postoperative periode there was no statistically significant difference in diastolic blood pressure between two groups. (p>0.05).

Discussion:-

Post-operative low cardiac output syndrome due to transitory ventricular dysfunction after surgery involving extracorporeal circulation(ECC) is characterized by an improvement in ventricular function during the first hour after ECC is terminated, followed by a deterioration that reaches a maximum at 4-5 h after surgery. A gradual recovery then usually begins, with full recovery at 24 h.

Transitory myocardial dysfunction induced by ischemia through clamping of the aorta followed by reperfusion is the cause of post-operative myocardial stunning. This condition involves depletion of high energy phosphates, intracellular calcium overload, generation of free radicals, and impairment of the coronary microcirculation. Patients with this condition respond to positive ionotropic agents, the treatment of choice in post-operative low cardiac output syndrome.

Beta-adrenergic agonists and inhibitors of phosphodiesterase III/IV induce good early hemodynamic values, but favor myocardial ischemia and arrhythmias and are associated with high mid-term mortality in non-surgically treated patients with heart failure. However, they are habitually used in patients who undergo heart surgery since other agents--vasodilators and beta-blockers--may be contraindicated given the hemodynamic instability commonly seen in the immediate postoperative period .Myocardial stunning, anesthetic agents, vasodilation, and hyperthermia caused by the inflammatory response associated with ECC all contribute to this instability.

In a prospective randomized study, 60 patients aging 40-70 years posted for on pump surgery. were randomly divided into two groups such as group Levosemendan and group Dobutamine after obtaining informed written consent.

Follath F et.al.in 2002 conducted a study Levosimendan Infusion versus Dobutamine.

Patients were infused, an initial loading dose of levosimendan of 24 µg/kg was infused over 10 min, followed by a continuous infusion of 0.1µg/kg/min for 24 h. Dobutamine was infused for 24 h at an initial dose of 5µg/kg/min without a loading dose..

Alvarez J et.al (2005) conducted a study The hemodynamic effect of levosimendan was compared to that of dobutamine. Levosimendan in a single dose of 18µg/kg followed in 15 to 20 minutes by start of infusion at a rate of 0.2 µg/kg/min for 24 hours (levosimendan group). Another 15 randomized patients received dobutamine infused at a rate of 7.5µg/kg/min . Hemodynamic parameters were measured before starting infusion of the drug and after 24 hours of treatment.

Labriola C et al.[15](2004) conducted a similar study in which each patient was given levosimendan as a loading dose of 12 µg/kg over 10 minutes, followed by a continuous infusion of 0.1 µg/kg/min for 12 hours. Within 3 h after the start of levosimendan infusion.Dobutamine was infused for 12 h at an initial dose of 5µg/kg/min without a loading dose.

Gandham R et.al.in 2013 in there study Group-L patients received levosimendan 0.1 µg/kg/min and Group-D patients received dobutamine 5 µg/kg/min while weaning off CPB.

In view of the above mentioned studiesFollath F et.aL and Alvarez J et.al found hypotension just after giving the loading dose whereas no hypotention was observed in the dose used by Labriola C. et al hence we took similar dose for our study i.e 12 µg/kg, Few studies on the use of levosimendan in the immediate post heart surgery period have been undertaken. The loading and maintenance doses used in the present study are within the therapeutic margins recommended by the European Society of Cardiology. A perfusion rate of 0.1 µ g/kg/min.

Dobutamine was chosen as the inotropic control drug since its effects on low cardiac output syndrome following surgery involving ECC have been described in detail. The dose used was lower than that administered by Nieminen MS et al, Feneck RO et al, Dupuis JY et al(5 µ g/kg/min) in there similar studies (and within the range recommended by the European Society of Cardiology), and higher than that used in other studies. The dose of 5 µ g/kg/min was chosen because this was previously administered in a large study that compared the hemodynamic effects of levosimendan and dobutamine.

In our study from induction to sternotomy there was no statistically significant difference in mean heart rate between two groups ($p>0.05$). From administration of drugsto 48hours post operatively there was statistically significant difference in mean heart rate between two groups ($p<0.001$). Heart rate increased more in the levosimendan group than in the dobutamine group.

There was no statistically significant difference in systolic and diastolic blood pressure in both groups ($p>0.05$).

F Follathet. Al in 2002 in there study found no statistically significant difference in systolic and blood pressure in both groups($p>0.05$).

J Álvarez et Al in their study observedno statistically significant difference in mean arterial blood pressure between in L group and in D group no statistically significant difference ($p>0.05$).

MebazaaAlexandre et al in 2007 in his studtynoted no statistically significant difference in systolic and blood pressure in both groups($p>0.05$)

Summary:-

The aim of the present study is to compare intra operative and post-operative effects between Levosemendan and dobutamine in the patients operated for coronary artery bypass graft on pump surgery..

60 patients posted for Coronary artery bypass graft surgery were selected. They were randomly allocated into two groups of 30 each.It was observed that heart rate was found to be better with use of levosemendan thandobutamine. Systolic and diastolic blood pressure was found to be No statistically difference between two groups.

Conclusion:-

Levosemendan is better than dobutamine in maintaining hemodynamic stability during intraoperative and postoperative period of patients coronary artery bypass graft going for onpump surgery.

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