MY EXPERIENCE IN THE ANAESTHETIC MANAGEMENT OF CARDIAC TRANSPLANTATION IN RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI

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 INTRODUCTION

 Orthotopic Cardiac transplantation was successfully done on a twenty years old female patient from Chennai, who has been diagnosed with Dilated Cardiomyopathy with end stage cardiac failure manifestations, following the initial diagnosis of Hypertrophic Obstructive Cardiomyopathy, five years before ,at the Institute of Cardiology , RGGGH, Chennai. Donor heart was explanted from a Brain Dead Donor in a hospital in chennai and brought to the cardiac transplantation theatre in Cold Static heart preservation(Donor heart placed in a bag containing ice-cold saline and transported in an ice-filled cooler) and the procedure was completed within the stipulated Myocardial Cold Ischaemic Time of four hours.

Case History and Investigations:

 20 years old female patient. Height: 157 cms. Weight :71 Kgs:

Apparently normal patient five years back,developed breathlessness,orthopnea, chest pain, palpitations which were increasing in severity to symptoms persisting even at rest.

Patient had hypothyroid status which was treated with Tab. Eltroxin 25 microgm, and presently euthyroid and not on thyroxine replacement.

She is not a known case of Tuberculosis /Bronchial Asthma/epilepsy/ Diabetes Mellitus / Hypertension.

On Examination:

Patient conscious, oriented, Blood Pressure: 110/70 mmHg, Right Upper Limb in Sitting Position) , Pulse Rate : 78/mt, SpO2 in room air: 98%, CVS: S1, S2 Present, Muffled in nature. RS: Bilateral Air Entry: normal , No adventitious sounds. No pallor, icterus, cyanosis, clubbing, lymphadenopathy.

CVS Examination: Apical Impulse: 5th Intercostal space in the Anterior axillary line., No murmur.

Abdomen:Soft, No evidence of organomegaly.

Central Nervous System: No focal neurological deficit.

Airway: MMS II,TMD ,IID-adequate, No loose teeth, dentures.

Investigations :Hb: 13.4gms%, TC- 9,800/cmm, Platelet count: 2.18 lakhs

Blood group A positive. Random Blood Sugar-120 mgms%. Renal function – WNL.

LFT: WNL.

PT INR 1.42

APTT- 29.6
CXR PA view: cardiomegaly.

Serum Electrolytes: WNL.

ECG: LBBB

ECHOCARDIOGRAM: Non compaction of Left Ventricle., Grade I LV Diastolic Dysfunction, Global hypokinesia of LV, Severe systolic dysfunction, LA and LV dilated, No Pulmonary Embolism and Clot.

 PROCEDURE: ORTHOTOPIC CARDIAC TRANSPLANTATION- BICAVAL METHOD.

After obtaining High risk informed consent and ensuring the adequate supply of Blood and blood products, postoperative elective ventilator support, patient shifted into the operation theatre.

Monitors Used: 5 lead ECG, SpO2, NIBP initially. Baseline parameters recorded. Supplemental O2 was provided.with Venturi mask . 6litre/minute. Peripheral Intravenous line secured with 18G venous cannula in the dorsum of Right Hand.

Under Local Anaesthesia Left Radial artery cannulated with 18 G Venous Cannula., after ensuring the adequacy of collateral circulation with Allens Test.

Left Internal Jugular Vein cannulated with 7 Fr CVP catheter with modified Seldinger technique..

Baseline Activated Clotting Time. -175 Sec.

Baseline Arterial Blood Gas Analysis- Within Normal Limits.

In the meanwhile Cardiopulmonary Bypass machine is made ready,properly primed, heparinised, and circuits made ready taking care to eliminate air bubbles in the circuit.

Patient was preoxygenated with 100% oxygen for 6 minutes. Premedicated with Inj. Midazolam 1mg. Then Induced with Inj. Fentanyl increments upto 400 mic.gms. and Inj Thiopentone Sodium in small increments upto 100 mgms taking care to preserve the Mean Arterial Pressure .Intubated with7.5 mm Endotracheal tube after Inj Vecuronium Bromide 8.5 mg and Inj Xylocard 50 mg 90 secs before intubation. ETT position confirmed. Nasogastric tube and temperature Probe inserted. Antibiotic Prophylaxis given . Anaesthesia maintained with 50% O2 and 50% N2O , Inj Fentanyl and Inj Midazolam supplements.

After positioning, surgery proceeded with sternotomy.

Tab Mycophenolate Mofetil(30mg/kg) and Tab Cyclosporine 5mg/Kg given through the nasogastric tube.

Inj. Methylprednisolone 1gram given Intravenously as a low infusion so as to finish before the application of Aortic Cross Clamp.

Inj NTG was stopped at the time of initiation of aortic purse string sutures.Then Inj Heparin 300units/Kg body weight is administered I.V. to ensure a prolongation of Activated Clotting time upto 480 seconds and beyond.

Ascending Aorta is now cannulated and ensuring the absence of air bubbles connected to the arterial limb of Cardiopulmonary Bypass circuit.Then after obtaining right atrial purse string sutures, SVC and IVC cannulation done and connected to the venous limb of CPB machine

 With the table tilted to the Trendelenburg Position , arterial flow commenced through the aortic cannula and venous return ensured to the pump after gradually unclamping the venous cannulae one after the another. Gradually , starting from 0.5L/mt, full CPB pump outflow of 5.8L/mt flow was achieved.Ventilator putup in standby mode and peripheral infusions were also stopped.

Now cardiotomy vent is applied through a separate purse string suture in the Ascending Aorta proximal to the Aortic Cannula .Once full flow from the pump is ensured,patient was cooled to the level of moderate Hypothermia of 28-32º C .Mean Arterial Pressure maintained at 50-60 mmHg. Inj Nitroglycerine infusion started in the CPB.Aortic cross clamp applied and myocardial preservation done with cold cardioplegia solution.

Dissection proceeded and native diseased heart explanted.

In the meanwhile donor heart received the ice packed saline . After blunt dissection anastamosis started. Left atrial cuff with the intact native pulmonary veins is anastomosed to the donor left atrium. IVCs are anastomosed. The Aorta is anatomosed. Pulmonary artery is then anastomosed.SVCs anastomosed at the end.

ACT maintained >480 secs with hourly heparin supplements throughout the pump time. ABGA done and maintained at normalcy throughout the pump flow period with a haematocrit of around 20% on pump.

Rewarming started after the anastomotic procedure. Aortic Cross Clamp released after a cross clamp period of one hr and 30 minutes.

 When the temperature reached 34 °Celcius cardiac contractile activity commenced in the transplanted heart. Slowly it matured into the sinus rhythm with the intravenous supports of Inj.Isoprenaline.02mic gm/kg/mt, Inj. Dobutamine 2 mic gm/ Kg/mt. and Inj Nitroglycerine was continued at a slow infusion rate of 0.3mg/kg/mt.When pt reached a temperature of 37 deg celcius in a sinus rhythm without the support of the artificial cardiac pacemaker with normal arterial blood gas parameters , pt was gradually weaned from the cardiopulmonary bypass pump with above mentioned haemodynamic support with drugs. Gradually patient’s vascular volume was filled taking care to prevent overfilling and distension.Then after achieving proper surgical haemostasis ,venous cannulae were removed,effect of heparin was reversed with Inj. Protamine Sulphate at the ratio of 1.3 mg of protamine per every 100 units of heparin used.When no untoward effect of protamine Aortic cannula was removed . Fresh Frozen Plasma and platelet units were transfused.Intercostal drains applied , Sternotomy wound closed followed by skin closure.

 Postoperative parameters: ACT -121 secs

BP 106/60 mmHg.

PR- 122/mt

SpO2 – 99%

CVS – S1S2 present.

RS – BAE Equal and adequate.

Supports :

Noradrenaline- 0.5µg/kg/mt

Adrenaline - 0.01µg/kg/mt

NTG - 0.05µg/kg./mt

Dobutamine- - 8µg/kg/mt

Patient shifted to Elective Post Operative Ventilatory Support with the hemodynamic support infusions.After 24 hours of elective ventilation patient gradually weaned from ventilator.

 Arterial Blood Gas Analysis

 Preop values On CPB Post CPB

pH 7.39 7.37 7.34

pCO2 35.4 37.6 42.6

pO2 503 638 470

HCO3 21.9 21.3 22.5

 Na+ 145 144 152

 K+ 3.75 3.85 4.92

 Ca+ 4.84 5.30 4.90

Post Transplant ECHO:

 No RWMA

 Mild Concentric Left Ventricular Hypertrophy.

 LV ID: 3.5/1.8/65%

 No PE/Clot.Mild RV Dysfunction.

 Normal LV Systolic Function.

Post operative care.

Ist POD: inotropic support continued .at a lesser titration doses .

 ABG abnormalities corrected

FiO2 brought down to 60%

Inj Meropenem 1gm Iv tid

 Intake /outout monitored

 Haematology, coagulation, LFT,RFT, watched.

 Inj methyprednisolone 500 mg tid I.V. in slow small volume saline infusion.

 Thro’ ryles’ tube:tab prednisolone 20 mg od, tab cyclosporine 150 mg bd, tab MMF 500mg tid.

POD 2:

 Inotropes : dobutamine , Noradrenaline, NTG weaned further .

 Tab prednisolone , cyclosporine and MMF continued as before.

 Oral and skin care given

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POD 3

 Inotropes ; negligible rate of infusion.

 Blood investigations repeated.and found to be in normal range.

 ECHO showed normal biventricular function.

 Steroid continued IV and orally .

Oral immunosuppessants continued in the same dose

POD 4:

 Inotropes weaned fully

 Steroid – oral and I.V.

 Oral immunosuppressants

 Same antibiotic

 Investigations - NAD

POD 5 :

 Steroid and immunosuppressants - Oral .

 Same antibiotic.

 Investigations –NAD.

 POD 6

 Antibiotic stopped.

 Oral steroid and immunosuppressants in the same dose.

 POD7 :

 Normal oral diet allowed

 Oral steroid and oral immunosuppressants

 DISCUSSION:

Cardiac transplantation is an established treatment option for End stage heart diasease. First human cardiac transplant was performed by Dr Christian Barnard in 1967, on December 3rd in Cape Town, South Africa.

1. Patients with End Stage Heart Disease with NYHA class III or IV symptoms not relieved despite maximal therapy with a life expectancy of less than 1 year, with atleast one of the following:

1. Requiring continuous mechanical or inotropic support
2. PeakVO2 (max) i.e. peak oxygen consumption ≤14ml/kg/mt or less than 50% of predicted for age and gender during anaerobic exercise are the pts who will benefit best from this surgery.
3. LV Ejection Fraction <20%

2. Severe symptomatic hypertrophic / restrictive cardiomyopathy.

3. congenital heart disease for which no conventional therapy exists or that conventional therapy has failed.

4. severe inoperable angina, refractory ventricular arrhythmias or unresectable cardiac tumors confined to myocardium without the evidence of metastases.

5. All these indications with a Pulmonary vascular resistance < 2 wood units and age less than 70 years.

 Contraindications

Absolute:

 Severe irreversible pulmonary hyoertension

 Pulmonary vascular resistance: > 6 wood units/m², TransPulmonary Gradient >12 mmHg.

 Irreversible , severe hepatic, renal/pulmonary disease

 Active infection

 HIV positive serology (CD4 count <200)

 SLE /sarcoid with multisystem involvement

 Relative:

 Recent malignancy

 COPD

 Severe cerebral/Peripheral Vascular disease

 Insulin Dependent Diabetes Mellitus with end organ damage

 Unresolved pulmonary infarction with pulmonary embolism

 Morbid Obesity

 Major Psychiatric disorder

 Active peptic ulcer disease

 Severe osteoporosis

 Alcohol or IV drug abuse

 Current / recent diverticulosis

Recent Prioritization for cardiac transplant

 STATUS I A

 Inpatient with atleast one of the following:

 Assisted mechanical circulatory support for acute haemodynamic decompensation with one or more of the following:

 IABP,ECMO, total artificial heart, VAD.

 Assisted mechanical circulatory support for more than 30 days with significant device- related complication

 Mechanical ventilation

 Continuous infusion of single high dose inotrope/multiple inotropes, in addition to continuous haemodynamic monitoring of LV filling pressures.

 Life expectancy without transplantation < 7 days.

STATUS IB

 Assisted mechanical circulatory support for > 30 days with continuous infusion of IV inotropes .

STATUS 2.

 A patient of any age who does not meet the criteria for status IA or 1B

PATHOPHYSIOLOGY OF END STAGE HEART FAILURE

 Irreversible severe ventricular dysfunction

low cardiac output

activation of neurohumoral pathways.

Poor end organ perfusion

Initial phase of ventricular failure

 ↓

SV maintained by ↑LVEDV and ↑Myocardial fibre length.

 ↓

 Cardiac dilation, ↑pulmonary venous and LV pressures and PHT.

 ↓

 Cardiomegaly, severe dyspnea, peripheral edema.

 ↓

 Elevated venous pressures and decreases in end organ perfusion in liver and kidneys

 ↓

 Sympathetic nervous system activation with persistent elevation in circulating catecholamines to restore C.O. and end organ perfusion

 ↓

 Activation of Renin angiotensin aldosterone system

 ↓

 Increased sodium and water retention

With progression of cardiac failure SV becomes “fixed” and unresponsive to preload.

 Increase in afterload are poorly tolerated.

 ẞ1 receptor downregulation due to persistent catecholamine elevations making the heart less responsive to positive inotropic therapy.

Medical management of end stage heart disease

 Goals – to increase c.o., reduce myocardial afterload, decrease sodium and water retention and prevent thromboembolism.

1. Inotropes – digitalis, sympathetic amines, and phosphodiesterase III inhibitors.
2. Diuretics- -reduce intravascular volume and so decrease pulmonary and peripheral venous pressures
3. Vasodilators-ACE inhibitors –both venous and arteriole dilators

 Nitrates –NTG and SNP

1. ẞ -adrenergic receptor blockade-standard trt for End stage cardiac disease.
2. Anticoagulants- warfarin- may cause increased periop bleeding.

Mechanical circulatory assist devices

 IABP or VAD as a bridge to cardiac transplantation.

 Implantable VADs approved by U.S. FDA are : the NOVACOR N 100and HEARTMATE ventricular assist systems.

Anaesthetic management of donor during organ harvest.

 Monitor volume status, systemic arterial and central venous pressures

 FiO2 of 1 unless lungs are to be harvested

 Nondepolarising muscle relaxants- to inhibit spinal reflex mediated muscle movement in response to noxious stimuli.

 Organ harvest technique- after full heparinisation,perfusion sensitive organs like liver and kidneys are removed before cardiectomy.

 Median sternotomy done, pericardial attachments are dissected, SVC and IVC ligated , aorta cross clamped and cold cardioplegia administered

 Aorta and pulmonary arteries are transected, and at the end pulmonary veins are transected individually

 Hypothermia is the principal means of heart preservation –donor heart is placed in a plastic bag containing Ice-cold saline and transported in an ice filled cooler.

 Surgical techniques for cardiac transplantation

 Orthotopic cardiac transplantation

 98% of cases

 Recipient is placed on standard CPB

 PA catheter is withdrawn into the SVC.

 Aortic and bicaval cannulae are placed with snares

 Aorta and pulmonary arteries are clamped and divided.

 Either both native atria or a single left atrial cuff containing the pulmonary veins is preserved. Native atrial appendages are discarded because of the risk of postoperative thrombus formation.

 Donor heart is first examined and of PFO is present it is surgically closed. The donor and recipient left atria are anastomosed first followed by the right atria, or cavae when a bicaval anastamosis is done.then the donor and recipient aortas are joined and the aortic cross clamp removed with the pt in the trendelenburg position to decrease air embolism. After completion of the PA anastomosis and placement of temporary epicardial pacing wires , the heart is de-aired and the patient weaned from CPB.

 Biatrial implantation

 Portions of the recipient’s native atria preserved.

 Bicaval implantation

 Bicaval and left atrial anastomoses are performed.

 Potential advantages are:

 - Decreased distortion of the tricuspid valve annulus

 - Decreased incidence and severity of tricuspid valve regurgitation

 - preserved synchronous atrial contraction

 - improved right heart function

 - lowered risk of thromboembolism

Heterotopic cardiac transplantation

 Recipient’heart is not excised.instead the donor heart is placed within the right anterior thorax and anastomosed to the recipient’s native heart such that a parallel circulation is established. Recipient and donor atria are anastomosed, followed by the aortas. An artificial conduit usually joins the pulmonary arteries, with the native and donor RVs ejecting into the native PA. similarly the donor and native LVs eject into the native aorta.Thus the recipient’s RV anf the healthy donor LV will make the major contribution to the respective ventricular output . Done in :

 Recipients with severe pulmonary HTN

 Small donor to recipient size ratio

 Prolonged donor heart ischemic time.

 Disadvantages of heterotopic cardiac transplantation include the following:

 High operative mortality rate

 Requirement for continued medical treatment for the failing native heart

 Potential for the native heart to be a thromboembolism source

 Compromised pulmonary function due to the placement of donor heart in the right chest.

Preoperative management of the cardiac transplant patient

1. Personnel timing and coordination

To prevent prolonged donor heart ischemic times close communication between the transplant center and the organ retrieval team must be maintained CPB must be commenced immediately upon the donor heart arrival.

1. Preop evaluation of the cardiac transplant patient

Recipient will be under the care of a medical team managing the End stage heart failure and the pt’s condition must be optimized.

Limited time is available

Thorough history, physical examination, review of the pt’s medical record

 Evaluation done.

 ECG, ECHO, CXR, cardiac catheterization,haematologic, renal, liver function tests noted.

Make an idea about the concomitant organ dysfunction-LFT and RFT-mild elevation of hepatic enzymes , bilirubin and prolongation of PTT common.BUN is elevated in these pts due to chronic hypoperfusion and use of diuretics.

Continue inotropic support throughout the pre-CPB period . Apart from the effect of diuretics and digoxin ,warfarin effect, previous exposure to antifibrinolytics like aprotinin should be kept in mind.

 Preop monitoring and circulatory support continued and pt transported with the circulatory support devices to the operation theatre.

 Anaesthetic management of the cardiac transplant recipient

 Pt is preload dependant . sedation may lead to haemodynamic decompensation-carefully titrate premedication,.

 Aseptic technique is very important

 Monitoring: Noninvasive monitoring-standard 5 lead ECG,NIBP, Pulse oximetry, capnography, nasopharyngeal temperature, urine output.

 Invasive monitoring – Large bore central venous access , IBP, .

 TEE -, PA catheter – helpful. – C.O., systemic vascular resistance and PVR.

 These indices are useful for treatingPost CPB pulmonary HTN and RV dysfunction.

 Catheterization of Right IJV is avoided to preserve this route for multiple postoperative endomyocardial biopsies routinely performed to screen for myocardial rejection.

 Considerations for repeat sternotomy : these pt should have external defibrillation pads placed, cross-matched, irradiated, packed RBCs must be available in the OR before anaesthetic induction . Potential for a prolonged surgical dissection time must be kept in

 mind. Femoral or axillary CPB cannulation done considering the potential for increased periop bleeding.

Anaesthetic induction :

1. Haemodynamic goals –

Recipients have hypokinetic , non compliant ventricles sensitive to alteration in preload and afterload . continue inotropic support to maintain HR, contractility, Preload, afterload and PVR.

1. Aspiration precautions

Consider “full stomach”.-short notice to surgery,preop oral immunosuppressants

Use sodium/ IV metoclopramide

Rapid sequence induction

1. Anaesthetic agents

 Slow circulation time.- induction must be careful.

 Agents for induction - etomidate – 0.2mg/kg in combination with fentanyl 5-10µg/kg or sufentanil 5-8 µg/kg.

 High dose narcotic regimens.- but bradycardia treated promptly as failing heart is HR dependent.

 Small dose of Midaz, ketamine, scopolamine –for amnesia.-synergistically lower SVR.

Anaesthetic maintenance:

Goal – haemodynamic stability/end organ perfusion.

 Narcotic based regimes

 Supplement inhalational agents and benzodiazepines.-for ↓awareness

 Anaesthetic depth difficult to assess as sympathetic response to light planes is blunted.

Aprotinin, tranexamic acid,EACA administered.

Aprotinin – anaphylaxis caution.

Cardiopulmonary Bypass

 Femoral venous and arterial cannulation sites for repeat sternotomy.

 Moderate hypothermia

 Haemofiltration and / or mannitol administration

 Methylprednisolone before ACC to reduce the chances of hyperacute rejection.

Termination from CPB and post coronary bypass period.

TEE- for deairing

 Normothermia

 Normal ABGA

 Inotropic agents-HR 90-100 beats/mt,mean SBP > 65 mmHg,

 CVP-12-16 mmHg, PCWP- 14-18mmHg.

 Cardiovascular support and prevention of infection and immunosuppression

 Triple immunosuppressive regimen –in the immediate postop period.

 Inotropic support may be needed for several days .

 Pt extubated in 24 hrs.

 Discharged from ICU in the 3rd POD.

Clinical consideration in the immediate postoperative period :

 Autonomic denervation of the transplanted heart:

 In orthotopic cardiac transplantation, cardiac autonomic plexus is transected, leaving the heart without autonomic innervations.

 Newly denervated heart does not respond to drugs that act indirectly through the ANS( atropine)., or to direct ANS stimulation.

 But responds to direct acting catecholamines.

 As slow nodal rhythms common after ACC release, Isoprenaline is used to maintain HR of 90-100 beats/mt.

 Dopamine, dobutamine, epinephrine are also effective.

 If not responsive to drugs – temporary epicardial pacing.

 Requirement for permanent pacemaker-5-10% of cases.

 RV Dysfunction:

 Significant cause of morbidity and mortality – accounts for 20% of early deaths.

 Etiology: preexistent pulmonary HTN, transient pulmonary vasospasm, TR, Pulmonary Regurgitation.,prolonged donor heart ischemic time, inadequate myocardial protection, surgical manipulation of the heart.-

 TEE –RV dilation and hypokinesis

Findings in RV failure: elevated CVP, PA pressure, transpulmonary gradient>15 mmHg).

 Goals to treat RV dysfunction:

 PVR< 6 woods units

 Transpulmonary gradient< 5-10mmHg.

 Increased Fio2 correction

 Correct AB abnormalities

 Hypereventilation (PaCO2 25-30 mmHg).

 Treatment: Inotropic support and pulmonary vasodilation.

 Nitrates,prostacyclin,PGE2 Phosphodiesterase III inhibitors, inhaled

 NO.(20-80 ppm.

 RV failure refractory to treat: insertion of VAD.

 LV Dysfunction :

 Cause – prolonged donor heart ischemic time, inadequate myocardial perfusion, intracoronary embolization of intracavitary air, surgical manipulation.

 Trt : Dobutamine, epinephrine, norepinephrine.

Coagulation

 Coagulopathy treated aggressively.

 Etiology- hepatic dysfunction, preop anticoagulation, platelet dysfunction, hypothermia, haemodilution of clotting factors.

 Control surgical bleeding

 Administer blood products and platelets.

 Blood products must be CMV negative, irradiated or leucocyte depleted .

 RBCs and platelets administered thro’leukocyte filters.

Renal dysfunction

 Etiology: preexisting renal impairment, cyclosporine associated toxicity, periop hypotension and CPB.

 Optimize C.O. , avoid nephrotoxic drugs, maintain systemic BP>

Pulmonary dysfunction reduced by PEEP ventilation, regular endobronchial suctioning, chest physiotherapy.

Hyperacute allograft rejection

 Caused by preformed antihuman leukocyte antigen antibodies in the recipient.

 Results in severe cardiac dysfunction and death within hrs of surgery.

 Assisted mechanical circulatory support until cardiac transplantation is the only option.

 Role of Intraoperative TEE

 Pre-CPB period- identify intracavitary thrombus,recipient PA pressures , evaluate aortic cannulation and cross clamp sites for the presence of atherosclerotic disease.

 Post bypass period:-to evaluate de-airing, cardiac function, surgical anastomosis.

Cardiac transplantation survival :

 1-3 yr survival rates- 86% and 80% respectively.

 After 1st year- annual mortality is 4%.

Complications

 Infection

 Acute allograft rejection

 Systemic hypertension

 Allograft CAD

 Immunosuppressive drug side effects