PAEDIATRIC CARDIAC ICU: WHERE ARE WE IN 2011 AND WHAT DRUGS ARE WE DOING?

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INTRODUCTION

DEVELOPMENTAL CARDIAC PHYSIOLOGY

PATHOPHYSIOLOGIES/PATHOLOGIES

THERAPEUTIC STRATEGIES
  • BASIC SUPPORTIVE MEASURES
  • NEW TECHNOLOGIES
  • SMART SURGICAL APPROACHES
  • DEM’ DRUGS MAN!!!!!

SUMMARY AND TAKE HOME POINTS

CONCLUSION
GOOD MORNING
DUMELANG
NDI MATSHELOLENI
SANIBONANI
MOLWENI
TAAMENG
MANGWANANI
JAMBO!
GOEIE MORE
AVUSHENI
KHOTSO!
HI!
BUENOS DIAS
ALOHA
A’SALLAM ALEIKUM
WAZZUP MY PEEPS!
YA MAHN!

TO ALL HUMANS, ALIENS, ELVIS AND INTER-GALACTIC BEINGS
ENGAGE WARP SPEED!!!
FLIGHT to where we’ve never been; Captain: CHAOS
INTRODUCTION

• Topic: title and approach a bit different
  • Remiss not to address basics before we do drugs

• Paediatric Cardiac Critical Care
  – Rapidly evolving field
  – Complex cardiovascular diseases – challenging
  – Evolution enabled by Multidisciplinary approach
  – Collaborative studies have also contributed to the evolution of Paediatric Cardiac ICU
    » PEDIATRIC HEART NETWORK
    » MILRINONE AFTER CARDIAC OPERATION IN PEDIATRICS
    » SINGLE VENTRICLE AND THYROID SUPPLEMENTATION STUDY
DEVELOPMENTAL PHYSIOLOGY

• MYOCYTE
  – Number of myocytes
  – Expression of myocardial protein composition

• MUSCLE CONTRACTION
  – Paucity of sarcoplasmic reticulum
  – Calcium channels

• RECEPTOR PHYSIOLOGY
  – G-protein coupled receptors
  – Adrenergic beta 1 : 2 ratio
  – Decreased total number of receptors
  – Functionally desensitised

• VENTRICULAR INTERDEPENDENCE
  – High R-sided pressures – impairment of LV ejection
PATHOPHYSIOLOGY/PATHOLOGY

- **COMPROMISED DO$_2$**
- **CONGENITAL/AQUIRED HEART DISEASE WITH ABNORMAL CVS PHYSIOLOGY**
  - LOW CO; RHYTHM DISTURBANCES; increased pulmonary vascular resistance etc
- **SIRS: THROUGH STIMULATION OF THE INFLAMMATORY CASCADE**
  - Pre op condition
  - Sepsis/ shock
  - CPB
  - SURGERY INDUCED
  - EXPOSURE TO NON ENDOTHELIALIZED MEMBRANES/SURFACES
  - MYOCARDIAL REPERFUSION INJURY

![Diagram of Infection and SIRS with categories: sepsis, trauma, pancreatitis, burns, other]
PATHOPHYSIOLOGY OF SIRS

Infection
→
Microbial Products
(endotoxin/Peptidoglycans)

Cellular Responses

- Thromboxanes
- Leukotrienes/PAF
- Oxidases
- sPLA2
- Kinins
- Complement
- Cytokines
  - TNF, IL1, IL6, IL8

Inflammation/Vascular Injury
Inflammation/Vascular Injury

Mediators (e.g. TNF)
Endothelial Injury

Tissue Factors
Coagulation Sys. Activation

Consume Protein C

Apoptosis
Uncontrolled Inflammation

Impaired Fibrinolysis
Coagulation / DIC

MOSF
Shock
Death
EFFECTS OF CYTOKINES

• Hypotension- Fluid refractory
  – Up regulation of Inducible NO (iNO)
  – NO + O2, super oxide - free radicals

• Cardiac dysfunction
  – -systolic & diastolic
  – Reperfusion Injury

• Coagulopathy: Micro vascular thrombosis and inflammation
  – Protein C pathway
  – TNFα
  □ Other cytokines and chemical molecules

• Organ Dysfuntion – Death!
THERAPEUTIC STRATEGIES

• RECOGNISING COMPROMISE
  – Close monitoring
  – Deviation from physiologic limits
  – Assessment and Accurate Determination of Decreased DO2
    » Often discordance between actual measurement and clinical estimation: BP; CVP may be misleading

• GENERAL PRINCIPLES
  – Rx underlying cause
  – Correct metabolic profile: Ca++; pH; Hypoxia etc
  – Optimise CO: Rate; Rhythm; Preload; Afterload
  – Optimise Contractility
  – OPTIMIZE OXYGEN DELIVERY
THERAPEUTIC STRATEGIES

• NEW SURGICAL TECHNIQUES
  – Minimally invasive techniques: videoscopic surgery
  – Neuroplegia to avoid sequelae
  – Use of fibrin seals

• NEWER TECHNOLOGY
  – Different biocompatible membranes during CPB
  – Improved and miniaturized devices for catheterization
  – Tissue bioengineering: creation of cardiac valves from autologous tissue
  – Blockade of selectins after vascular injury
ORGAN SYSTEM DYSFUNCTION

- **RESPIRATORY DYSFUNCTION**
  - Diminished respiratory reserve
  - Increased lung water
  - Impaired surfactant function
  - V/Q issues
  - Increased Pulmonary Vascular Resistance
  - Decreased lung compliance

- **CARDIOVASCULAR DYSFUNCTION**
  MYOCARDIAL SYSTOLIC AND DIASTOLIC DYSFUNCTION, PHT, ARRHYTHMIAS
  - Need to improve CO
  - Optimize Ventricular loading conditions
  - Optimize myocardial conduction and ventricular performance

- **Neurologic sequelae**
  - Monitor Cerebral oxygenation

- **Protect other organ systems**
IT AIN'T ONLY ABOUT DRUGS MY PEEPS!!!!!

RESPIRATORY DYSFUNCTION

Smart approach to ventilatory support
Lung protective strategies; HFOV; PLV, NPV
Surfactant REPLACEMENT
iNO
CO2 inhalation in excessive pulmonary blood flow
Go easy on fluids! Diurese if necessary
Watch out for precedent RSV infection in CHD
CARDIOVASCULAR DYSFUNCTION

- DIASTOLIC DYSFUNCTION: VASOACTIVE SUPPORT
  - Reduced ventricular compliance so we need lusitropic support
  - INOTROPIC AND AFTERLOAD-REDUCING AGENTS NOT OF GREAT BENEFIT
  - NITROGLYCERIN; NITROPRUSSIDE; NATRIURETIC PEPTIDES AND MILRINONE PROVIDE GOOD DIASTOLIC RELAXATION BUT.......
  - ........VENODILATION AND INCREASE IN VENOUS CAPACITANCE, SO PRELOAD AND VENTRICULAR FILLING MAY DECREASE
  - SO, WE NEED VOLUME REPLACEMENT, BUT........AT EXPENSE OF INCREASE IN PVR, LUNG WATER etc
  - SO, WTF DO WE DO?
  - RECOMMENDATION: GO WITH MILRINONE, OR DOBUTAMINE
  - WATCH YOUR POSITIVE PRESSURE VENTILATION AND AVOID ADVERSE CARDIOPULMONARY INTERACTIONS

SYSTOLIC DYSFUNCTION: OPTIMIZE VENTRICULAR LOADING CONDITIONS

- POSITIVE PRESSURE VENTILATION REDUCES SYSTEMIC VENTRICULAR AFTERLOAD
- LOW DOSE NITROGLYCERINE <3mics/kg/min INCREASES VENOUS CAPACITANCE WITHOUT COMPROMISING ARTERIAL RESISTANCE: DECREASE IN VENTRICULAR FILLING AND CO
- NATRIURETIC PEPTIDES: COUNTER REGULATE RENINANGIOTENSINALDOSTERONE. PRODUCED BY MYOCARDIUM IN RESPONSE TO WALL STRESS: STIMULATION OF THEIR RECEPTORS LEADS TO A DOSE DEPENDENT NATRIURESIS/DIURESIS AND VASODILATION(AFTERLOAD)
- NESIRITIDE IS AVAILABLE (Human Recombinant B-Type Natriuretic Peptide)
- NESIRITIDE GIVES FAVOURABLE RESULTS WHEN USED FOR CARDIAC FAILURE
- CATECHOLAMINES: EPINEPHRINE; DOBUTAMINE; DOPAMINE
OTHER DRUGS!!!(PHARMACOLOGY) Systolic dysfunction

• Phosphodiesterase III Inhibitors
  – Milrinone; Amrinone
  – Inotropy; NOT chronotropy; NOT arrhythmogenic
  – lowers SVR
  – Hoffman et al: Efficacy and safety of prophylactic milrinone in paed patients undergoing CPB – High Dose 75mics/kg/min prevented Low CO states post op

• Levosimendan
  – Calcium sensitizer
  – Inotropy without increased myocardial Oxygen consumption
  – Long half life 3-4 days
  – Nmachivayam et al: levosimendan in catecholamine dependent kids....favourable results
• PULMONARY HYPERTENSION
  • Common in patients with cardiac disease and CPB
  • Initial approach: correct pH; Alveolar hypoxia by titrating PEEP to achieve normal FRC; FIO2; RV inotropy
  • Reduce Pulmonary vascular resistance: non selective vasodilators not good
  • iNO : SAY YES!!!!
DRUGS: there are other options!!

- ARRHYTHMIAS
  - EPICARDIAL PACING
  - CARDIAC RESYNCHRONIZATION THERAPY
  - Zimmerman et al: Improvement in haemodynamics and CO using multisite ventricular pacing
  - JET: DEXMETOMIDINE; amiodarone,
OTHER STRATEGIES TO IMPROVE CIRCULATORY FUNCTION

- **Arginine Vasopressin**
  - Physiological levels necessary for vascular tone
  - Defense of Arterial Blood Pressure
  - Rationale for use: Neurohypophyseal stores may be depleted in Critical illness
    - Rosenweig et al: 11 kids post cardiac op, with refractory hypotension: significant improvement in BP and inotrope score on vasopressin

- **Glucocorticoids**: Rationale - relative adrenal insuff

- **Thyroid Hormone**: Serum thyroid hormone decreased after bypass
OTHER STRATEGIES TO IMPROVE CARDIOVASCULAR FUNCTION

• Mechanical Circulatory Support
  – ECMO
  – CENTRIFUGAL VENTRICULAR ASSIST DEVICE
## INOTROPIC AGENTS: Catecholamines

<table>
<thead>
<tr>
<th>Agent</th>
<th>Beta</th>
<th>Alpha</th>
<th>Dopa</th>
<th>Effect</th>
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<tr>
<td>Dobutamine</td>
<td>1&amp;2</td>
<td>weak</td>
<td>0</td>
<td>inotrope</td>
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<td></td>
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<td></td>
<td>vasodilator</td>
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<td>Tachyarrhythmias</td>
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<td>Lowers PVR</td>
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<tr>
<td>Dopamine</td>
<td>1&amp;2</td>
<td>+++</td>
<td>++</td>
<td>Renal vasodilator</td>
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<td>Vasopressor</td>
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<td>Increased PVR</td>
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<td>1&amp;2</td>
<td>++++</td>
<td>0</td>
<td>Inotrope</td>
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<td>Tachycardia</td>
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<td></td>
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<td>MVO2</td>
</tr>
<tr>
<td>Noradrenaline</td>
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<td>++++++</td>
<td>0</td>
<td>Inotrope</td>
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<td>Profound constrictor</td>
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<td>MVO2; SVR</td>
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<tr>
<td>Isoprenaline</td>
<td>1&amp;2</td>
<td>0</td>
<td>0</td>
<td>Inotrope; MVO2</td>
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<td>Vasodilator</td>
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<td>Medication</td>
<td>Dosage Range</td>
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<tr>
<td>Adrenalin</td>
<td>0.05 - 2 ug/kg/min</td>
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<tr>
<td>Noradrenaline</td>
<td>0.05 - 2 ug/kg/min</td>
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<td>Dopamine</td>
<td>5 - 20 ug/kg/min</td>
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<tr>
<td>Dobutamine</td>
<td>10 – 20 ug/kg/min</td>
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<td>Milrinone</td>
<td>0.25 - 1 ug/kg/min</td>
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<td>Isoprenaline</td>
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<td>Nitroprusside</td>
<td>0.5 – 10 ug/kg/min</td>
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<td>Nitroglycerin</td>
<td>1 – 20 ug/kg/min</td>
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<tr>
<td>PGE1</td>
<td>0.05 –0.2 ug/kg/min</td>
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</table>
CLINICAL TIPS

• INOTROPES DO NOT WORK:
  - Acidotic environment
  - Best Diluted with NS
  - If the tank is not full
# PULSE RATE AT REST

<table>
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<tr>
<th>Age</th>
<th>Lower limit</th>
<th>Average</th>
<th>Upper limit</th>
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<tbody>
<tr>
<td>Newborn</td>
<td>70/min</td>
<td>125/min</td>
<td>190/min</td>
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<tr>
<td>1-11months</td>
<td>80</td>
<td>120</td>
<td>160</td>
</tr>
<tr>
<td>2yrs</td>
<td>80</td>
<td>110</td>
<td>130</td>
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<tr>
<td>4yrs</td>
<td>80</td>
<td>100</td>
<td>120</td>
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<tr>
<td>6yrs</td>
<td>75</td>
<td>100</td>
<td>115</td>
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<tr>
<td>8yrs</td>
<td>70</td>
<td>90</td>
<td>110</td>
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<tr>
<td>10yrs</td>
<td>70</td>
<td>90</td>
<td>110</td>
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<tr>
<td>12yrs</td>
<td><strong>Boys</strong> 65</td>
<td><strong>Girls</strong> 70</td>
<td><strong>Boys</strong> 85</td>
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<tr>
<td>14yrs</td>
<td><strong>Boys</strong> 60</td>
<td><strong>Girls</strong> 65</td>
<td><strong>Boys</strong> 80</td>
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<tr>
<td>16yrs</td>
<td><strong>Boys</strong> 55</td>
<td><strong>Girls</strong> 60</td>
<td><strong>Boys</strong> 75</td>
</tr>
<tr>
<td>18yrs</td>
<td><strong>Boys</strong> 50</td>
<td><strong>Girls</strong> 55</td>
<td><strong>Boys</strong> 70</td>
</tr>
<tr>
<td>Age</td>
<td>Mean Systolic</td>
<td>Mean Diastolic</td>
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<tr>
<td>Newborn</td>
<td>75</td>
<td>40</td>
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<tr>
<td>6 months- 1 year</td>
<td>89</td>
<td>60</td>
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<tr>
<td>2 years</td>
<td>99</td>
<td>64</td>
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<tr>
<td>4 years</td>
<td>99</td>
<td>65</td>
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<tr>
<td>5- 6 years</td>
<td>94</td>
<td>55</td>
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<tr>
<td>7- 8 years</td>
<td>102</td>
<td>56</td>
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<tr>
<td>9 – 10 years</td>
<td>107</td>
<td>57</td>
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<tr>
<td>11 – 12 years</td>
<td>113</td>
<td>59</td>
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</tr>
<tr>
<td>13 – 14 years</td>
<td>118</td>
<td>60</td>
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</table>
MONITORING THERAPY

- PATHOPHYSIOLOGY DIRECTED THERAPY
  - Hypothesis testing
  - Best guess

- CONTINUOUS ASSESSMENT
  - Clinical Evaluation: End Organ function
  - CVS monitoring: HR, ECG, BP, Perfusion, Urine output

- INVASIVE MONITORING
  - Cardiac Output studies
  - CathETERIZATION

- NON-INVASIVE MEASURES
  - Echocardiography
  - Noninvasive CO monitoring

- LABORATORY
  - ABG’s; Serum lactate; Mixed venous saturations; jugular venous sats
TAKE HOME POINTS

• Paediatric Cardiac Intensive Care has evolved considerably with exciting advances being made in perioperative care
• This is an exciting and demanding discipline that is evolving
• Requires a multidisciplinary approach
• YOU are still the best machine there is in assessing your patient
• Do not forget the BASICS: ABC’s, General supportive therapy, Pathophysiology directed therapy
• And yes, you do not have most of the stuff mentioned in this talk
• More depressing, we ain’t got the resources
• But, do not despair......your ship will come in
• Keep pushing the boundaries

2 IMPORTANT REFERENCES:
“Pediatric cardiac Intensive Care: current state of the art and beyond the millennium” Current Opinion in Pediatrics 2000,12:238-246
CONCLUSION

• Critical cardiac illnesses in children is common
• Cardiovascular compromise
• Pediatric specific developmental factors
• Early diagnosis & Intervention
• Use pathophysiology specific agents
• Don’t max-out on one agent before adding another one.
• Consider non conventional approaches if stuck
TODA!!!