INOTROPIC SUPPORT IN CARDIOGENIC SHOCK

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CARDIOGENIC SHOCK

• Cardiogenic shock occurs when adequate oxygen and nutrient delivery to the organs and tissues of the body is compromised as a direct result of myocardial dysfunction

“Failure of the heart to effectively pump blood”

• 3rd most common shock in pediatrics (1st septic shock, 2nd hypovolemic shock)
CARDIOGENIC SHOCK

• 5-13% of diagnosed cases of shock

• Most advanced stage of heart failure

• In hospitalized children lethal in 5-10% of cases

• Extracardiac co morbidities eg sepsis, AKI and liver failure lead to 5 fold increase in mortality
MORTALITY

• Directly related to underlying disease:
  - CHD 4.7%
  - Rhythm disorder 23%
  - Acquired heart disease 8.7%
  - Cardiomyopathies 25%

• Management differ from normal heart and CHD

• In CHD need to refer to the pediatric cardiologist
ALGORITHM FOR DECOMPENSATED SHOCK

Initial insult

Triggers shock

Decreased perfusion

Body's compensatory mechanism

Compensated shock

Decompensated shock

Tissue damage

Multisystem organ failure

Death
DEFINITIONS OF CARDIOGENIC SHOCK

- Sustained hypotension (SBP <2SD for age for at least 30 min)

- Reduced cardiac index <2.2 L/min/m²) in the presence of elevated pulmonary capillary occlusion pressure (>15 mmHg)

<table>
<thead>
<tr>
<th>AGE</th>
<th>SYSTOLIC BLOOD PRESSURE (mmHg)</th>
</tr>
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<tbody>
<tr>
<td>0 – 28 days</td>
<td>&lt;60</td>
</tr>
<tr>
<td>1 month – 12 months</td>
<td>&lt;70</td>
</tr>
<tr>
<td>1 – 10 years</td>
<td>&lt;70 + (2x age in years)</td>
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<tr>
<td>&gt;10 years</td>
<td>&lt;90</td>
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</table>
PHYSIOLOGIC DETERMINANTS

• DO2 is amount oxygen delivered to tissues /min

Equation 1: DO2 = CaO2X CO

Equation 2: CaO2 = Hb XSaO2X1.34+(0.003XPaO2)

Equation 3: CO = SVXHR

Equation 4:BP = COXSVR
a - Cardiac performance increase as preload increase
b - LV systolic dysfunction
c - Increase in LVEDP results in pulmonary congestion
ETIOLOGIES

- Primary or secondary cardiomyopathy
- Acute or fulminant myocarditis enterovirus, adenovirus, influenza, EBV, CMV, Herpes simplex
- Toxic-sulfonamides, penicillin's and anthracyclines
- Autoimmune/connective tissue-SLE/Juvenile RA/Kawasaki/Acute rheumatic fever
- Neuromuscular disorders-Duchenne Muscular Dystrophy
ETIOLOGIES

• Dysrhythmias
  - Prolonged SVT
  - Brady arrhythmia
  - Complete heart block
  - Ventricular arrhythmia

• Obstructive lesions
  - Cardiac tamponade
  - Acute pulmonary embolism

• Others
  - Acute valvular valve regurgitation secondary to infective endocarditis
  - Sepsis induced myocardial failure, pneumothorax
CONGENITAL HEART DISEASE

• Left ventricular outlet tract obstruction (LVOTO);
  - Hypoplastic left heart syndrome
  - Critical AS
  - COA
  - HOCM

• Large L-R shunt with physiologic/pathologic pulmonary steal e.g. in ASD/VSD/AVSD/PDA
SIGNS & SYMPTOMS

Sign and symptoms cardiogenic shock :-

- Tachycardia
- Oliguria
- Changes in skin temperature
- Impaired mental status → may indicate shock is irreversible
- Skin mottled, cool and clammy
- Tachypnea, S3 gallop
- Wheezing
- Dyspnea and cough
- Cyanosis, Diaphoresis
- Hepatomegaly
DIAGNOSTIC EVALUATION

- CXR
- ECG
- ECHO
- ABG
- Lactate
- Mixed venous oxygen saturation
- Cardiac enzyme
- Electrolytes
- BNP – is high in patient with ventricular dysfunction
MANAGEMENT OF CARDIOGENIC SHOCK

• Goal-directed therapy to optimize cardiac output and oxygen delivery to vital organs;
  - Mixed venous oxygen content
  - Lactate level
  - ABG
• Drugs;
  - Inotropes
  - Chronotropes
  - Vasoconstrictor
  - Vasodilators
  - Newer cardiotonic and vasoactive agents (levosimendan)
Cardiogenic shock

Preload

Heart rate and rhythm

Blood pressure

Fluid restrict
Diuretic
Venodilator

Fluid challenge 5-10 ml/kg colloid, blood if Hct <0.4
Reassess and repeat
Beware of bleeding

12-lead ECG
Determine rhythm
Consider:
- Anticholinergic
- Pacing
- Isoproterenol (0.05-2µg/kg/min)

Volume status adequate?
Sedation/ analgesia OK?
Obtain 12-lead ECG and determine rhythm
Consider:
- Antiarrhythmic
- Cooling
- Overdrive pacing
- DC cardioversion

High or normal

Vasodilator

Low

Inotrope

Adrenalin 0.01-0.1µg/kg/min
Dobutamine 5-15µg/kg/min
(Dopamine 3-10µg/kg/min)

Adrenalin 0.1-0.2µg/kg/min
+ vaso/ inolidator

Noradrenalin 0.05-0.2µg/kg/min
Consider vasopressin for severe hypotension, especially in sepsis

Low

No response

Vasodilator

Nitroglycerine 1-5µg/kg/min
Nitroprusside 1-4µg/kg/min

Inodilator

Milrinone
Load +0.25-0.75 µg/kg/min

Mechanical circulatory support (ECMO/ VAD)

Aiming for recovery of native heart or bridging to cardiac transplantation

High

No response
THE PRESSURE-VOLUME RELATIONSHIP

- Normal

Pressure-Volume Loop

Diagram showing the pressure-volume relationship with various annotations and labels.
i. Preload Recruitment

- LV Pressure vs. LV Volume
  - SV_A
  - SV_B
  - SV_C
  - SV_D

- Stroke Volume vs. LA Pressure
  - Edema Formation
  - Pleural Effusions
ii. Improve Diastolic Function (Positive Lusitropy)
THE PRESSURE-VOLUME RELATIONSHIP

iv. Afterload Reduction

![Graph](image-url)
MILRINONE

- Inodilators and exerts a positive inotropic effect by inhibiting phosphodiesterase III.

- Increase in cyclic AMP in cardiac myocytes improves systolic and diastolic function

- Peripheral and coronary vasodilation (effective in reducing SVR)

- Increase CO and oxygen delivery without increasing myocardial work and demand
PHOSPHODIESTERASE (PDE) INHIBITORS

• Effective for CHF, PHT and impaired RV function

• Serum half-life 0.8 hours in patients with congestive heart failure patients

• Primarily excreted in the kidney - dose adjustment in AKI

• Recommended dose 0.25-0.75 mcg/kg/min

• 227 pediatric patient undergoing open heart surgery those that received higher infusion 0.75 mcg/kg/min reduced incidence of LCOS by 55%.
LEVOSIMENDAN

• It is a positive inotrope and vasodilator
• It act by increasing the sensitivity of contractile apparatus (especially troponin-T) to intracellular calcium.
• Pro arrhythmic activity less common.
• Induce peripheral, pulmonary and coronary vasodilatation, via ATP-sensitive potassium channels
• Dose : is 6 to 12 µg/kg loading dose over 10 minutes followed by 0.05 to 0.2 µg/kg/min as a continuous infusion
• In 15 children with acute heart failure levo increased the EF
• and weaning dobutamine infusion.
LEVOSIMENDAN

- Augments myocardial contractility by ↑ sensitivity to calcium

- Single 24 hours infusion produce clinical effect 7-9 days via the active metabolites.

- Beneficial in improving cardiac

- Performance by reducing LV afterload
iii. Increase Contractility (Positive Inotropy)
ADRENALIN

• Hormone secreted by the adrenal glands

• Potent α- and β-adrenoceptor agonist.

• A powerful vasoconstrictor, a positive inotrope, and a positive chronotrope.

• At lower dose (<0.05mcg/kg/min) increase SBP due to increase in ventricular contraction

• Higher dose more prominent vasoconstriction via alpha receptor and reduced renal blood flow. May induce atrial/ventricular arrhythmias
ADRENALIN

• Short acting and half-life is after a few minutes

• During CPR-is the drug of choice has a profound alpha stimulation that maintain the coronary and cerebral perfusion

• Increase dose – ↑ afterload and myocardial work maybe detrimental in single ventricle

• Recommended dose is 0.02-0.2mcg/kg/min

• Prolonged high dose >0.2mcg/kg/min for several hours cause myocardial necrosis esp in neonates and infants
DOBUTAMINE

• Primary action on β-1 receptor, less effect on β-2 and α-1

• Had positive inotropic and chronotrophy. Increase CO. Perihereral vasodilator

• As established dobutamine as a first line therapeutic choice in patients with cardiogenic shock

• Dose : 5-15µg/kg/min

• Higher doses result in tachyarrythmias
DOPAMINE

• An endogenous catecholamine

• Stimulates both adrenergic and dopaminergic (D1 and D2) receptors.

• Low-dose infusion (<5 µg/kg/min) – activate DA 1 receptor in renal coronary and mesenteric vessel

• Intermediate doses (5-10 µg/kg/min) B1 receptor has inotropy and chronotrophic effect

• Higher doses (>10 µg/kg/min) activate alpha 1 receptor leading to peripheral vasoconstriction increase SVR
CASE BABY M

• 6 months old baby
• History of interrupted feeding and sweating during feedings since age of 4 months
• He presented at ED with history of low grade fever,
• Severe respiratory distress and chesty cough.
• He was given nebulizer and volume 20ml/kg on admission after which he collapsed and required intubation
• IV Dopamine 15mcg/kg/min
• IV Dobutamine 15 mcg/kg/min
• IV Noradrenalin 0.2mcg/kg/min
- CXR showed cardiomegaly with congested lungs
• ECG showed sinus tachycardia with Q wave most prominent in leads 1 and AVL.
• Echo showed poor LV function with EF 16 %
USEFULLNESS OF FLUID RESUSCITATION

- Indicated after clinical assessment and advised to use ECHO as a guide

- Use of colloids and crystalloids should not be used on patients with cardiogenic shock
INOTROPES

• Dobutamine-gold standard for cardiogenic shock

• Milrinone

• Levosimendan

• Adrenalin instead of noradrenalin

• Dopamine not advisable
PROGRESS

• Post operative complicated by low cardiac output syndrome, poor LV function, and the sternal wound was closed later on post operative day 1 due to severely dilated LV.

• Patient was supported by mechanical ventilation and inotropes in form of adrenaline, milrinone, nitroglycerine.

• Eventually patient recovered slowly and weaned off inotropes and ventilation.

• Echocardiography showed improving LF function with EF 34 %
CONCLUSION

• Common cause of cardiogenic shock is CHD and infections of the heart
• Dobutamine gold standard inotrope for cardiogenic shock
• Milrinone in RV failure/PHT
• Levosimendan to be considered in non-responder
• In CHD the understanding of physiology will help in choosing the right inotropes to stabilize patients
ANY QUESTION
THANK YOU
Low cardiac output

Fluid restrict
Diuretic
Venodilator

Preload

Optimal

Very high
Heart rate and rhythm
Normal for age

High or normal
Blood pressure

Vasodilator

Inotrope

Nitroglycerine 1–5 μg/kg/min
Nitroprusside 1–8 μg/kg/min

Inodilator
Milrinone Load +0.25–0.75 μg/kg/min

Epinephrine 0.01–0.05 μg/kg/min
Dobutamine 5–15 μg/kg/min
(Dopamine 3–10 μg/kg/min)

Epinephrine 0.06–0.5 μg/kg/min
± vaso/inodilator

No response

Norepinephrine 0.05–1 μg/kg/min
Consider vasopressin for severe hypotension, especially in sepsis

Fluid challenge 5–10 ml/kg colloid, blood if Hct <0.4
Reassess and repeat
Beware of bleeding

Volume status adequate?
Sedation/anaesthesia OK?
Obtain 12-lead ECG and determine rhythm
Consider:
- Antiarrhythmics
- Cooling
- Overdrive pacing
- DC cardioversion

12-lead ECG
Determine rhythm
Consider:
Anticholinergics
Pacing
Isoproterenol
(0.05–2 μg/kg/min)

Mechanical circulatory support (ECMO/VAD)
Aiming for recovery of native heart or bridging to cardiac transplantation
INOTROPE IN ICU

INOTROPE USED in ICU
2008 - 2015

- 5101, 71%
- 2080, 29%

**Inotrope days**

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Days</th>
</tr>
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<tbody>
<tr>
<td>Mean</td>
<td>3.14</td>
</tr>
<tr>
<td>Median</td>
<td>2.00</td>
</tr>
<tr>
<td>Mode</td>
<td>1</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>3.723</td>
</tr>
<tr>
<td>Minimum</td>
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</tr>
<tr>
<td>Maximum</td>
<td>55</td>
</tr>
<tr>
<td>Percentiles</td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>2.00</td>
</tr>
<tr>
<td>Q3</td>
<td>4.00</td>
</tr>
</tbody>
</table>
CASE

• 6 months/ 5.8kg/ boy, presented with HF

• Diagnosis is ALCAPA at age of 4 months

• Preoperative;
  - Patient was ventilated with moderate setting
  - On antifailure, IVI dopamine, IVI adrenaline, IVI milrinone
  - Echocardiography showed poor LV function EF is 20 %
NORADRENALIN

• Principal neurotransmitters in the sympathetic nervous system

• Potent α - adrenoceptor agonist \(\rightarrow\) strong asoconstrictor

• Norepinephrine stimulates \(\beta_1\)-adrenoceptors, \(\rightarrow\) increases both heart rate and contractility.

• Dose : 0.05\(\mu\)g/kg/min – 0.5\(\mu\)g/kg/min
NORADRENALIN

- Noadrenalin does not affect β2-adrenoceptors.

- Dose: (0.05-0.5 µg/kg/min)

- Use from vasodilatory inflammatory response to CPB

- Improve coronary flow in patient diastolic run off after Blalock Taussig shunt

- May improve pulmonary after Fontan operation
NORADRENALIN

- Noadrenalin does not affect β2-adrenoceptors.

- Use from vasodilatory inflammatory response to CPB

- Improve coronary flow in patient diastolic run off after Blalock Taussig shunt

- May improve pulmonary circulation and cardiac output after Fontan operation
SIGN OF CARDIOGENIC SHOCK

• Signs of cardiogenic shock;
  - Tachycardia
  - Dyspnea
  - Jugular vein distention
  - Hepatomegaly

• Respiratory effort is often the distinguishing characteristic that sets cardiogenic shock apart from the forms of shock

• Irritability

• Sweating
CLASSIFICATION OF INOTROPIC AGENTS

- **cAMP dependent agents**
  - Adrenergic agonists
  - Dopaminergic agonists
  - Phosphodiesterase III isoenzyme inhibitors

- **cAMP independent inotropic agents**
  - Na+-K+-ATPase inhibitors
  - Potassium channels inhibitors
  - Agonists of β-adrenergic receptors
  - Calcium
  - Phenylephrine

- **Other new agents**
  - Calcium sensitizers
  - Vasopressin
  - Natriuretic brain peptide
ADVANCED THERAPEUTIC MEASURES

• Minimize oxygen demand ➔ intubate and ventilate
• Normothermia (anti-pyretics and cooling blanket)
• Sedate and paralysed
  - Eliminates movement of skeletal muscles as a source of oxygen consumption
• Maximizing myocardial performance
• Correct dysrhythmia
• Optimized preload
• Current metabolic derangements, adequate serum ionized calcium, inotropic support
ADVANCED THERAPEUTIC MEASURES

• After load reduction by providing sedation and pain by use of pharmacologic agents

• E.g. Nitroprusside $\rightarrow$ arteriola and venodilator

• Milrinone $\rightarrow$ inotropics and inodilator