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Paediatric cardiogenic shock

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Abstract

Shock is a state of acute circulatory failure characterised by tissue perfusion inadequate to meet the needs of the body. It rapidly leads to multi-organ failure and death if not recognised and treated early. In its simplest form, cardiogenic shock is considered "pump failure" with structural heart disease, arrhythmias and myocarditis recognised causes in children. Maximizing myocardial performance by optimising the preload, contractility and minimising afterload and enhancing systemic oxygen delivery are essential in the treatment of this high mortality condition.

Key words: shock; cardiogenic; paediatric

SHOCK - DEFINITION AND CLASSIFICATION

Our understanding of the complex phenomena that is shock is constantly evolving. Defined as an acute state of circulatory failure characterised by tissue perfusion inadequate to meet the needs of the body, it rapidly leads to multi-organ failure and death if prolonged. The recognition of shock and early initiation of treatment is therefore essential. However, this can be very difficult in paediatric practice. The presence of multiple paediatric clinical shock definitions (e.g. WHO, FEAST criteria, APLS) or those based on SIRS criteria and age based parameters, coupled with the large amount of inter-observer variability during clinical assessment make diagnosis of paediatric shock problematic. The shock definition in adults is less subjective, defined as it is by the presence of hypotension and a lactate rise.

The complexity of recognising a "pre-shocked" state and the known increased mortality with fluid bolus therapy mean diagnosing and treating shock in a child, especially in a resource limited setting, is challenging.

Many conditions can ultimately lead to a state of shock. It can be broadly classified by pathophysiology (table 1). Certain conditions, such as sepsis, can lead to more than one type of shock.

SHOCK PHYSIOLOGY

Understanding the physiology of shock enables a greater appreciation of treatment options and the ability to explain the clinical features seen. At its core, is an unbalancing of the relationship of oxygen consumption (VO2) to that of oxygen delivery (DO2).

$$VO2 = DO2 \times O2\ ER$$

- VO2 = Oxygen consumption is the total amount of oxygen removed from the blood due to tissue oxidative metabolism per minute. The value cannot be measured directly but can be assessed by measuring the amount of oxygen delivered on the arterial side compared to the amount on the venous side. Oxygen consumption Index (VO2I) calculated using cardiac index rather than cardiac output
- DO2 = Global oxygen delivery is the total amount of oxygen delivered to the tissues per minute, irrespective of the distribution of blood flow
- O2 ER is the oxygen extraction ratio (ratio of VO2 to DO2)

At rest, DO2 is more than adequate to meet VO2 and ensure that aerobic metabolism is maintained. Paediatric DO2 range from 160 to 804ml/min^2 and oxygen consumption index values range from 120 to 200ml/m^2. O2ER is 25% and varies for different organs. Oxygen that is not extracted returns to the mixed venous circulation. A Scv02 (central venous oxygenation saturation) of 70% indicates oxygen delivery is adequate.

As VO2 increases or DO2 decreases, O2ER rises to maintain aerobic metabolism and oxygen consumption remains independent of oxygen delivery. At 'critical DO2' however, the maximum O2ER is reached. Beyond this point, any further increase in VO2 or decline in DO2 leads to tissue hypoxia and anaerobic

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Table 1: Causes of shock

Cardiogenic shock	Obstructive shock	Hypovolaemic shock	Distributive shock
Impaired contractility - Myocardial ischaemia and complications, including congenital heart disease - Myocarditis - Septic shock - Poisoning or toxic exposure - End stage cardiomyopathy	*Within the circulatory system* - Massive pulmonary embolus	Haemorrhage *Fluid loss* - GI losses (vomiting, diarrhoea, short gut, etc) - Excessive diuresis (diabetes insipidus, diuretics) - Excessive diaphoresis (heat-related illness) - Diabetic ketoacidosis/Burns/ Third spacing (pancreatitis, severe sepsis, anaphylaxis)	Neurogenic shock Liver failure Adrenal insufficiency Anaphylaxis Septic shock Post-bypass vasoplegia *Drugs and toxic exposures* - e.g. calcium hannel blockers, epidural anaesthesia
Dysrhythmia - Tachycardias/Bradycardias	*External to the circulatory system* - Cardiac tamponade - Abdominal compartment syndrome - Tension pneumothorax		
Valvular dysfunction			
Left ventricular outflow tract obstruction - Hypertrophic cardiomyopathy			

metabolism. Cellular metabolism becomes much less efficient in a stressed state, resulting in the accumulation of lactic acid. This will eventually lead to cell dysfunction, acidosis and cell death.

Oxygen delivery (DO2) is the product of cardiac output (CO) and arterial oxygen content.

$$DO2 = CO \times CaO2$$

$$CO = HR \times SV$$

$$CaO2 = (Hb \times SaO2 \times 1.34) + (0.003 \times PaO2)$$

- D02 depends on the cardiac output, and the arterial content of blood (Ca02)
- Cardiac output is dependent upon heart rate (HR) and Stroke Volume (SV)
- The CaO_2 depends on how much oxygen carrying capacity is available, which is primarily a function of the haemoglobin (Hb) level and the arterial oxygen saturation (Sa02). Pa02 is the partial pressure of oxygen in arterial blood. A small, usually insignificant amount of oxygen is directly dissolved in the blood rather than bound to Hb.
- 1.34 is the amount of O_2 that can combine with 1 gram of haemoglobin (Oxygen carrying capacity has been referenced between 1.34-1.39). Called Hüfner's constant.
- 0.003: Dissolved oxygen in plasma is determined by the solubility coefficient of oxygen at body temperature and the PaO_2 (mmHg)

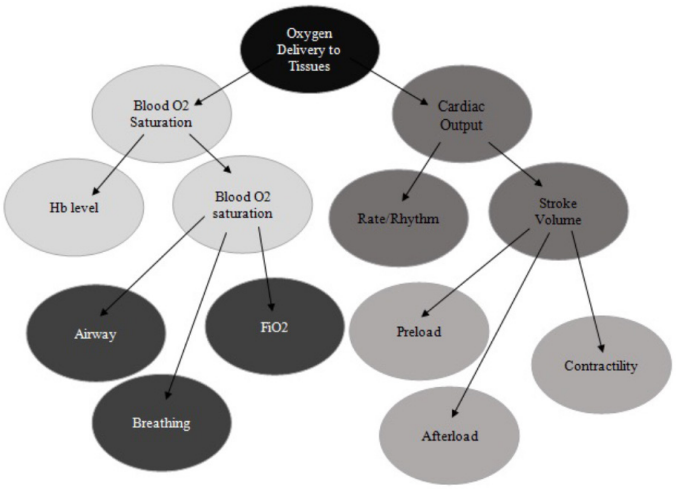

Figure 1: Determinants of oxygen delivery

Causes of reduced oxygen delivery

- Hypoxia, anaemia, poor contractility, shock, abnormal heart rate or rhythm

Causes of increased oxygen consumption

- Fever and inflammatory states eg sepsis, burns, trauma, increased metabolic rate, increased muscular activity, increased respiratory effort

Causes of impairment of the extraction or utilization of oxygen by cells

- Sepsis, cyanide poisoning

Table 2: Causes of cardiogenic shock

Heart rate abnormalities	Congenital heart defects	Cardiomyopathy
• Supraventricular tachycardias • Ventricular dysrhythmias • Bradycardia	• Lesions with ductal dependent systemic blood flow in neonates (Coarctation of Aorta, Critical Aortic Stenosis, Interrupted Aortic Arch, Hypoplastic Left Heart Syndrome) – neonatal presentation usually • Lesions with increased pulmonary blood flow – Atrial Septal Defect, Ventricular Septal Defect, Patent Ductus Arteriorus, Atrioventricular Septal Defect • Lesions with reduced pulmonary blood flow – Tetralogy of Fallot • Ischaemic cardiomyopathies (e.g. Anomalous Left Coronary Artery from Pulmonary Artery) • Congenital heart defects that present with shock are those that have obstruction to flow from the left ventricular tract and occasionally those with large left to right shunts.	• Hypoxic ischaemic events • Infectious • Metabolic e.g. hypothyroid, acidosis, hypocalcaemia • Connective tissue disorders e.g. • Rheumatic fever, • Neuromuscular disorders e.g. Duchenne Muscular Dystrophy • Toxic reactions e.g. chemotherapy • Other - Familial or idiopathic dilated

The overall goal in the treatment of shock is to maximise oxygen delivery to the cells and minimise oxygen consumption (Figure 1).

- Stroke Volume (SV) is a function of preload, afterload, contractility and diastolic relaxation. Therefore optimising heart rate (HR), contractility, diastolic relaxation, preload and afterloa improves cardiac output (CO).
- Oxygen carrying capacity can be increased by raising haemoglobin and optimising its saturation with oxygen.
- Systemic oxygen delivery can be improved by manipulation of all these factors.
- A reduction in oxygen consumption can be achieved in a number of ways, including intubation and ventilation, sedation and temperature control.

CARDIOGENIC SHOCK

In simple terms, cardiogenic shock is considered "pump failure". Myocardial dysfunction, usually systolic, is responsible for the failure of the cardiovascular system to meet the metabolic demands of the body. Occasionally diastolic dysfunction can cause cardiogenic shock, including post operatively or during ischaemia from certain cardiac lesions. It is the most advanced stage of heart failure and is lethal in 5 – 10% of cases. Outcomes are highly variable and dependent upon the extent and nature of the underlying myocardial insult, co-morbidities and promptness of myocardial support.

The numerous causes of cardiogenic shock can be classified into three broad categories (table 2).

PATHOPHYSIOLOGY

Cardiogenic shock can lead to a progressive fall in myocardial function if not identified and corrected early (figure 2). Reduced myocardial contractility leads to a rightward shift of the left ventricular end-systolic pressure volume curve and a fall in stroke volume. A metabolic acidosis can develop which may impair

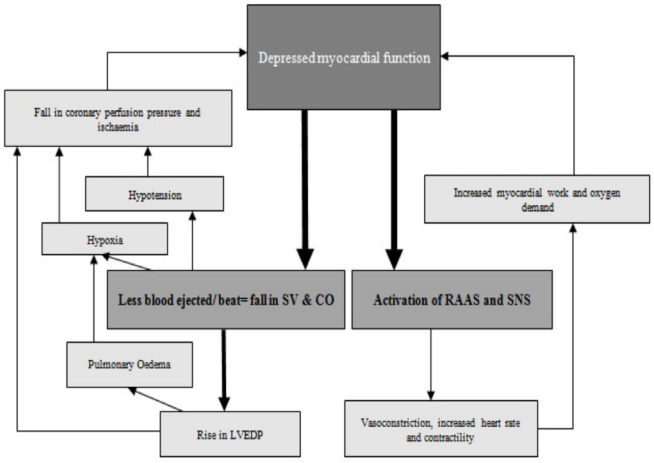

Figure 2: Pathophysiology of cardiogenic shock

contractility further. Hypotension may ensue, prompting a fall in coronary perfusion pressure and subsequent myocardial ischaemia. A rise in left ventricular end diastolic pressure (LVEDP) from diastolic dysfunction causes decreased myocardial perfusion pressure and pulmonary oedema, contributing to hypoxemia and myocardial ischaemia. A downward spiral of failing myocardium and worsening myocardial ischaemia can be difficult to break and reverse. Significant arterial oxygen desaturation often occurs in cardiogenic shock as a result of a decrease in mixed venous oxygen saturation (SVO2) and intrapulmonary shunting. SVO2 decrease occurs as a result of increased tissue oxygen extraction because of the low CO.

In addition as systemic perfusion falls, compensatory neurohumeral mechanisms are activated. An increase in systemic vascular resistance via the renin-angiotensin-aldosterone system (RAAS) and sympathetic stimulation causes an increase in heart rate and contractility. This can be counterproductive, increasing the afterload

on the heart and a rise in myocardial oxygen demand. As a result, blood flow is redistributed from nonessential vascular beds such as the skin and skeletal muscles, to the brain, heart and lungs. Blood pressure is therefore a poor indicator of cardiovascular status in paediatric patients due to this prolonged compensatory regulation of vascular tone.

CLINICAL FEATURES

Clinical findings depend upon the aetiology, presence of co-morbidities, degree of shock, and the patient's age. Tachycardia is the main compensatory mechanism to maintain the CO and systemic perfusion. Nonspecific signs of shock suggestive of poor perfusion include oliguria, cyanosis, cold extremities, weak distal pulses, lethargy or altered mentation and hypotension. Signs of heart failure may give a hint to the cause being cardiogenic shock. These include irregular pulse, narrow pulse pressure, hepatomegaly, distended jugular vein, heart murmur, gallop rhythm, distant heart sounds and pulmonary crackles. Infants may present with difficulty feeding, while older children may complain of difficulty breathing and chest pain.

INVESTIGATIONS

Cardiogenic shock is an emergency. Simultaneous history and examination with rapid clinical diagnosis and initiation of treatment is essential. Investigations should not delay management (table 3). They however should be undertaken if available and are necessary for a number of reasons. Investigations can determine the cause and severity of disease, assess the functional status of the myocardium, direct the treatment and assess its therapeutic response.

MANAGEMENT

The goals of management of a patient in cardiogenic shock are three-fold:

1. Minimise oxygen demand/consumption
2. Maximise myocardial performance and systemic oxygen delivery
3. Treat underlying cause

Early recognition and immediate administration of resuscitation therapies are the primary aims of initial management to prevent worsening organ dysfunction by restoring adequate oxygen delivery to peripheral tissues. Resuscitation should commence even whilst investigation is ongoing to identify and rapidly treat reversible causes. Management of cardiogenic shock in certain congenital heart diseases is discussed elsewhere and involves balancing the pulmonary and systemic circulations.

A simplified approach using the Airway, Breathing, Circulation technique is best utilised in the management of a patient with cardiogenic shock. Optimisation of all components in figure 1 is vital. The goal is to maximise oxygen delivery whilst reducing oxygen consumption and myocardial work load.

- *Airway*
  - If able to maintain – give O2 with positive end expiratory pressure (PEEP) aim >92%
    - PEEP has both advantages and disadvantages in cardiogenic shock. Not only can it increase airway pressure and improve oxygenation and alveolar ecruitment, but also decrease left ventricular afterload due to decreased LV transmural pressure. However, PEEP can lead to decreased cardiac output through its effects on the right heart (decreased RV preload and increased RV afterload), especially if co-existent hypovolaemia.
    - Can be given via T piece or self-inflating bag with peep valve
  - If apnoeic or unstable airway – plan early intubation using ketamine and rocuronium
  - If patient requires intubation, this is a very high-risk situation
    - Avoid use of induction medications that adversely affect myocardial contractility as much as possible. Caution should also be taken in the use of positive pressure ventilation due to its effects on the right heart with possible reduction of preload and increased afterload. Efforts to avoid apnoea are very important as it exacerbates the coexistent acidemia
    - Consider commencing peripheral inotropes (such as adrenaline) prior to induction to improve myocardial contractility and use small aliquots of luid boluses.
    - Ketamine proves to be the ideal first choice for induction for it is the least cardio-depressant agent widely available. Should be used with caution in those with chronic heart failure.
    - Prepare for a possible cardiac arrest – allocating team members and ensure resuscitation dose adrenaline is prepared.
- *Breathing*
  - Use of non-invasive or invasive ventilation may be required to augment cardiac function and reduce oxygen consumption, diverting oxygen delivery to areas that need it most. Positive pressure ventilation can be beneficial through improvement of blood gas tension, reduction of work of breathing and afterload reduction to the left heart.
  - Supplement ventilation with assisted breaths and addition of positive end expiratory pressure
  - Monitor oxygen saturations, ensure >92%
- *Circulation*
  Goal is to optimise preload, afterload and contractility
  - Obtain IV access.
  - Assessment of fluid status – optimise preload
    - If evidence of dehydration
- Used of volume expansion with small fluid boluses (5-10mL/kg)
    - If evidence of fluid overload

Table 3: Investigations for cardiogenic shock

Investigation	Findings
Chest X-ray	• Perhaps the most readily accessible imaging required in the management of cardiogenic shock in resource limited settings. • Can diagnose air leak syndromes (pneumothorax, pneumomediastinum), assess lung parenchyma and vessels and exclude other causes of shock or chest pain. • Signs of pulmonary oedema of cardiogenic origin (perihilar fluffy opacities with butterfly/bat wing patterns) can be detected and cardiomegaly may give a clue towards the underlying aetiology. • ericardial effusion, with its characteristic water bottle sign along with typical clinical findings, can be easily detected. • A boot-shaped heart suggests right ventricular dilatation.
Electrocardiography (ECG)	• Can elude to certain structural diseases, such as the anomalous origin of the left coronary artery arising from the pulmonary artery (ALCAPA), or acute conditions (e.g., pericarditis, myocarditis) • Detect rhythm disorders resulting in cardiogenic shock.
Echocardiography	• Essential to diagnose anatomic abnormalities, ascertain functional status, and for follow-up assessment of response to therapy. • Goal-directed echocardiography (GDE) aims to rapidly help assess cardiac anatomy and function in the patient with haemodynamic failure to guide subsequent therapy. Five views including the parasternal long-axis, parasternal short-axis, apical four-chamber, substernal, and inferior vena cava (IVC) views are performed. In addition, color Doppler analysis of the mitral and aortic valves may also be considered.
Blood gas and electrolytes	• Can help differentiate acute from chronic congestive heart failure (CHF). Metabolic acidosis and lactic academia are usually present in patients with acute CHF with low cardiac output, while pH is usually normal and partial pressure of carbon dioxide (PaCO2) low in case of chronic CHF. • It is recommended to repeatedly obtain arterial pH and blood lactate levels to assess the course of shock and evaluate the efficacy of therapy. • A decrease in tissue perfusion can lead to hypokalemia and lactic acidemia • Mixed venous oxygenation (SVO2) and its serial measurements can give an indication of cardiac output. • Patients on diuretic therapy should be regularly monitored for hyponatremia and hypochloremia through electrolyte analysis.
Other laboratory tests	• Renal and liver function tests help to determine the adequacy of end-organ perfusion. • Complete blood count will reveal anemia; low haemoglobin can increase left to right shunt by reducing the pulmonary vascular resistance, and hence worsen the clinical picture of failure. • Essential to rule out hypoglycemia and hypocalcemia in neonates with left ventricle failure, • Creatine phosphokinase- MB (CPK-MB) and troponin I levels can help to diagnose myocardial ischaemia. • The determination of B-type natriuretic protein (BNP) is widely used to assess the severity of cardiac involvement, particularly in patients with preexisting cardiomyopathy, in the diagnosis of congenital heart disease and heart failure and monitoring postoperative hemodynamics in cardiac surgery patients. • Anti-dsDNA and antinuclear antibody (ANA) assays can rule out autoimmune disorders. • Abnormalities of lactate, glucose and carnitine can inform the diagnosis of a mitochondrial cardiomyopathies. • Urine analysis may reveal albuminuria, increase in urine specific gravity, and microscopic hematuria. The presence of methylglutamic aciduria implies a metabolic cause of failure.
Cardiac catheterization	• Provides functional data of the failing myocardium and identifies structural abnormalities and/or microbial causes of cardiogenic shock.

- *Diuretics and maintenance fluid restriction (50mls/kg/day)*
    - Cautious fluid administration in those with malnutrition. See WHO ETAT guidelines
    - Constant clinical reassessment of fluid status
  - Ensure adequate haemoglobin
    - Red cell transfusion may improve preload and oxygen delivery
  - Ensure normal heart rhythm
    - Cardioversion or cautious administration of anti arrhythmics may be required
  - Vasoactive Agents – optimise afterload and contractility
    - Vasopressors
    - Inotropes
    - Vasodilators
  - Resuscitation dose of Adrenaline
    - 10mcg/kg (0.1ml/kg of 1 in 10,000 solution)
- *Additional*
  - Prostaglandin (PGE1) therapy
    - Used to maintain ductal patency in newborns and young infants with shock secondary to duct dependent congenital heart defects.
    - Maintains systemic circulation through the patent ductus arteriosus
    - Infusion dose is 0.05-0.1mcg/kg/min. Hypotension and apnea are important side effects.
  - Normothermia
    - Avoid hypothermia and fever.
  - Nutrition
    - If the acute phase and resuscitation are passed, nutrition should be optimized to maintain daily calorie and protein intake. The calorie requirement in infants can be up to 130-170 cal/kg/day
  - Frequent weights are important to assess fluid balance status
  - Review investigations and treat underlying cause

Although fluid resuscitation to correct hypovolemia and hypotension is often one of the most important initial steps, it is indispensable to highlight that goal-directed therapy should be based on continuous clinical, laboratory and echocardiographic assessment. The increased mortality with fluid bolus therapy in children from Sub-Saharan African (FEAST trial) highlights that this can no longer be considered a benign therapy, especially in settings lacking critical care expertise and facilities.

Continuous monitoring of patients is essential. Placement of an arterial catheter for monitoring of blood pressure and blood sampling, plus a central venous catheter for the infusion of fluids and vasoactive agents is desirable.

Diuretics are indicated when ventricular dysfunction is associated with fluid overload to relieve systemic and pulmonary vascular congestion. Common classes used include loop diuretics, thiazide, and aldosterone antagonists. Furosemide, a loop diuretic drug with rapid onset of action of 2-5 minutes and duration of action of 3 hours, is by far the widely used drug. It can be administered as a bolus or as a continuous infusion with the latter option being associated with less hemodynamic instability and electrolyte imbalances. Adverse effects of furosemide include hypokalemia, metabolic alkalosis, hypocalcemia and hyponatremia.

Vasoactive agents

Many vasoactive drugs have both vasopressor and inotropic actions (table 4). The choice is guided by matching the therapeutic goals with the mechanism of action of different agents. Catecholamines comprise the mainstay for inotropic and/or vasopressor support in the setting of cardiogenic shock, where their inotropic effect promotes increased cardiac output by improving myocardial contractility through engaging ß1receptors. The understanding of underlying pathophysiologic mechanisms and the mode of action of available agents are essential for a goal-directed therapy. Dopamine may be the first option to treat mild to moderate cardiogenic shock. Milrinone or dobutamine is the first choice to treat acute severe cardiac failure in the absence of hypotension. If cardiogenic shock is complicated by severe hypotension, epinephrine or norepinephrine is preferred depending upon the haemodynamics and myocardial function.

Digoxin

- An inotrope and exerts its effects by binding to and inhibiting sodium-potassium ATPase. This inhibition results in an increase in intracellular calcium, hence enhanced myocardial inotropic state and a slowing of the heart rate.
- Has a narrow therapeutic window, long half-life and multiple side effects and this toxicity rather limits its use in certain circumstances.

Vasodilators

This category includes nitrated derivatives, angiotensin-converting enzyme (ACE) inhibitors (captopril, enalapril) and angiotensin II receptor blockers (ARBs) and hydralazine. Vasodilators can improve the cardiac function by favorably altering afterload and preload but they are not generally advisable for use to treat acute cardiogenic shock.

Mechanical Circulatory Support (MCS)

Extracorporeal life support (ECLS) and ventricular assist devices (VADs) are the two forms of mechanical circulatory support currently available in certain centres to infants and children with cardiogenic shock not amenable to conventional therapy.

Table 4: Pharmacology and relative potency of inotropes and vasopressors commonly used in shock

Drug	Dose	Effect					Additional Notes
		Cardiac ((ß1)		Peripheral vasculature		Dopaminergic	
		HR	contractility	Vasoconstriction (α1)	Vasodilation (ß2)		
Dopamine (short)	1-5mcg.kg^{-1}.min^{-1}	1+	1+	0	1+	4+ (located in the brain and in vascular beds in the kidney, mesentery, and coronary arteries)	
	6-10mcg.kg^{-1}.min^{-1}	2+	2+	1+	0	2+	
	11-20mcg. kg^{-1}.min^{-1}	2+	3+	3+	0	2+	
Dobutamine	1–20mcg. kg^{-1}.min^{-1}	2+	3-4+	0	2+	0	Causes mild vasodilatation, increases the CO, and reduces the SVR, with minimal alteration of BP and HR and does not alter or impair renal flow
Epinephrine	0.01-1mcg.kg^{-1}.min^{-1}	4+	4+	4+	3+	0	Higher concentrations are detrimental to myocardial function with increased oxygen consumption out of proportion to the increase in force of contraction
Norepinephrine	0.01-1mcg.kg^{-1}.min^{-1}	1+	2+	4+	0	0	
Phenylephrine	0.1-0.5mcg.kg^{-1}.min^{-1}	0	0	3+	0	0	
Milrinone (PDE-I)*	0.1-1mcg.kg^{-1}.min^{-1}	1+	3+	0	2+	0	Selectively inhibits phosphodiesterase III. Used as both inotrope and vasodilator to reduce preload and afterload. Possible adverse effects include hypotension especially in patients with a relative depletion of intravascular volume and those with renal dysfunction in whom drug clearance is reduced.

* Milrinone is a phosphodiesterase inhibitor (PDE). Its effects (inotropy and vasodilation) are independent of α or ß- receptors.

CONCLUSION

Cardiogenic shock is an uncommon, but important cause of paediatric shock. It has a high mortality and early recognition is essential. Interventions to maximise oxygen delivery whilst reducing oxygen consumption form the basis of critical care management.

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