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Treatment of heart failure in children

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Summary Heart failure in children is usually of a very different aetiology to that in the adult population. Accurate diagnosis, particularly of structural defects, is essential to direct treatment. There are no agreed guidelines for the treatment of heart failure in children and limited specific research. Treatment is therefore largely driven by the extrapolation of adult data. Diuretics and angiotensin-converting enzyme (ACE) inhibition are the first lines of therapy, with beta-blockade being used less than in adults. Newer drugs, such as angiotensin receptor blockers are used on an anecdotal basis. Because of the usual relative physiological health of other organ systems in children and potential for longevity, heart transplantation has a higher prominence in end-stage cardiac failure in children. ABO mismatch transplantation and mechanical devices that may offer a bridge to transplant are a focus of on-going research. Research into further drug therapies is largely focussed on neurohormonal modulation.

Introduction

Heart failure occurs when the heart cannot pump enough blood to supply the demands of the body and/or there is pulmonary or systemic venous congestion. The aetiology of heart failure in children is very different to that in the adult population, where 60–70% is caused by coronary artery disease[1] (rarely seen in children). Many aspects of the treatment of heart failure in children are extrapolated from adult medicine and research because of the lack of evidence in children. However, the strong association with congenital structural heart lesions and the usual relative physiological health of other organ systems seen in children means that different focuses are required in the management. There are now well-established guidelines for the management of heart failure in adults[1,2] but no equivalent consensus for children. This article offers an overview of current approaches to the treatment of paediatric heart failure, in the context of its aetiology, pathophysiology and underlying diagnosis. Established therapies will be reviewed, along with newer drug treatments, novel treatments, and future directions that research is taking.

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Aetiology

The incidence in the UK of congenital heart disease is seven per 1000 live births, and it is the most common cause of heart failure in the first few months of life. The closure of the ductus arteriosus (DA) in the first few days may precipitate failure in congenital heart disease, although persistence of the DA may itself lead to heart failure in subsequent weeks and months. Older children may have residual structural lesions after previous heart surgery or have unrepaired structural lesions (including valvular heart disease).

Mason et al.[3] found evidence of myocarditis in 10% of adults with new-onset heart failure, but no coronary heart disease, and it is likely that this figure is much higher in children without structural heart disease.[4] Viruses, such as adenovirus and coxsackie species, account for most cases.[5] Both fulminant and non-fulminant cases are seen, with fulminant myocarditis offering a much better prognosis if support is provided through the initial illness.[6]

Cardiomyopathies, usually dilated, account for most of the remaining cases. A wide variety of aetiologies are seen, including idiopathic and inherited, infective [e.g., human immunodeficiency virus (HIV)], infiltrative (e.g., inborn errors of metabolism), associated with generalised muscle disease (e.g., Duchenne muscular dystrophy), mitochondrial disorders, nutritional (e.g., Beri-Beri), iatrogenic or toxic (e.g., anthracyclines, radiation, illicit substance misuse), and ischaemia (e.g., Kawasaki disease). Heart failure secondary to arrhythmia is also well recognised.

Non-cardiac causes of heart failure are frequently seen in the paediatric intensive care unit (PICU). For example, the increased oxygen demand, cytokine release and mitochondrial dysfunction of sepsis, profound anaemia (with a reduced ability of the blood to deliver oxygen), and altered preload (increased in volume overload and reduced severe haemorrhage or septic shock).[7] Shunt syndromes (such as that sometimes seen in large arteriovenous malformations) are uncommon but important non-cardiac causes of heart failure.

Physiology/pathophysiology

The cardiac output (CO) is determined by the product of heart rate (HR) and stroke volume (SV), and is equivalent to

mean arterial pressure (MAP)−central venous pressure (CVP)/systemic vascular resistance (SVR).[8]

In normal physiology, both HR and SV are varied to modulate the CO. An increase in HR is achieved by reducing vagal and then increasing sympathetic tone, or by circulating chronotropes such as catecholamines from the adrenal glands. To double their HR an adult must move from 60 to 120 beats/min, but a neonate would have to sustain a change from 130 to 260. Thus children have less scope for rate increases than adults.[9] Increasing SV is more complex. In health an increase in the volume of blood filling the ventricle during diastolic relaxation follows the Starling curve and increases the inherent contractility of the ventricles. Renal water conservation and constriction of venous capacitance increases preload into the right atrium. Ventricular contractility is also increased via the autonomic innervation of the heart and by circulating catecholamines.

If the body is unable to adequately regulate CO via the above mechanisms the heart will fail. Preload continues to increase to the right side of the Starling curve and the ventricles no longer contract effectively. Maximal stimulation of adrenoceptors limits the effects of further increases in circulating catecholamines. Several pathological factors contribute to this process:

- An increased afterload may be due to high SVR, local obstruction (e.g., valve stenosis, coarctation) or fluid overload (e.g., acute renal failure). The increased ventricular work to maintain SV will eventually lead to systolic heart failure.
- Failure of contractility is seen when muscle fibres are diseased (e.g., myocarditis), poorly function because of low oxygen delivery or when contractility is disordered (e.g., arrhythmias).
- Diastolic function is often overlooked. A stiff and non-compliant heart cannot fill adequately during its relaxation phase, and a higher preload is necessary to maintain SV (e.g., tamponade, restrictive cardiomyopathy).
- Even a healthy heart can reach a point where the demands of the body are too great leading to high output cardiac failure. The two most commonly seen occurrences are the low SVR associated with septic shock and severe anaemia, where the blood itself is failing to deliver adequate oxygen for the body's requirements.

Beyond the mechanics

In recent years there has been greater appreciation of the role of neuroendocrine and genetic factors in