RECENT ADVANCES

New developments in the treatment of cardiac failure

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The prognosis for severe heart failure in children (in the absence of a correctable congenital lesion) is poor. Recently, there have been advances in treatment in both medical and surgical fields.

Medical

Diuretics are still used to produce rapid symptom relief; however, there has recently been a trend to use a combined lower dose regimen of loop and thiazide diuretic,[1] which has some therapeutic advantage, although pre-prepared combination drugs are limited in children by the high doses available. Digoxin use remains controversial, although it is now accepted to be an orally active inotrope its use in adults does not improve survival.[2] Angiotensin converting enzyme (ACE) inhibitors are now considered the cornerstone of heart failure treatment. In adults they have been shown to reduce mortality.[3 4] There is no equivalent published data on such large series in children, but most paediatric cardiologists agree on the effectiveness of these drugs. A paediatric suspension of captopril has become available in the UK this year, a suspension of crushed tablets was used in infants before this. Careful introduction of captopril in a hospital environment is essential because of first dose hypotension and exacerbation of occult renovascular disease. β Blockers have been shown to improve outcome in adults with heart failure by reducing the pathologically increased sympathetic drive.[5] The new third generation β blockers such as carvedilol also have vasodilatory properties and therefore (like ACE inhibitors) will also offer benefit by lowering afterload.[6] There are few data on β blockers in children with heart failure; we have recently introduced metoprolol into our management without any early adverse effects. Oral phosphodiesterase inhibitors are theoretically both inotropes and vasodilators, but they have disappointed in adult studies[7 8] and they are not widely used in children.

Growth hormone acting in its own right or via insulin related growth factor 1 has been increasingly considered as a theoretical treatment in cardiac failure. A small study[9] showed beneficial effect of subcutaneous growth hormone as an adjunct to conventional treatment. Echocardiographic indices and exercise capacity increased, and myocardial oxygen consumption declined on treatment. We have used growth hormone in three children as a bridge to transplantation; two were successfully transplanted.

Surgery

CIRCULATORY SUPPORT

Until recently cardiac transplantation was the only surgical option for a child presenting in cardiogenic shock, but because of the shortage of donors many did not survive to transplantation. The aortic balloon pump or extracorporeal membrane oxygenation are unlikely to provide prolonged support in this setting. External left ventricular support devices are now available for children of all sizes (fig 1) although their use is restricted to a small number of centres.[10] Second generation implantable devices are now in development and prototypes have been used clinically in young patients with myocarditis. In patients with acute left ventricular failure and low pulmonary vascular resistance a left ventricular assist device (LVAD) alone may provide sufficient cardiac output and reverse multiorgan failure. If right ventricular dysfunction is severe, then biventricular support with an external pulsatile system is used. Currently LVADs are not routinely available in the UK as a mechanical bridge to transplantation for children. We have nevertheless demonstrated their efficacy in a 10 year old transplanted patient whose dilated

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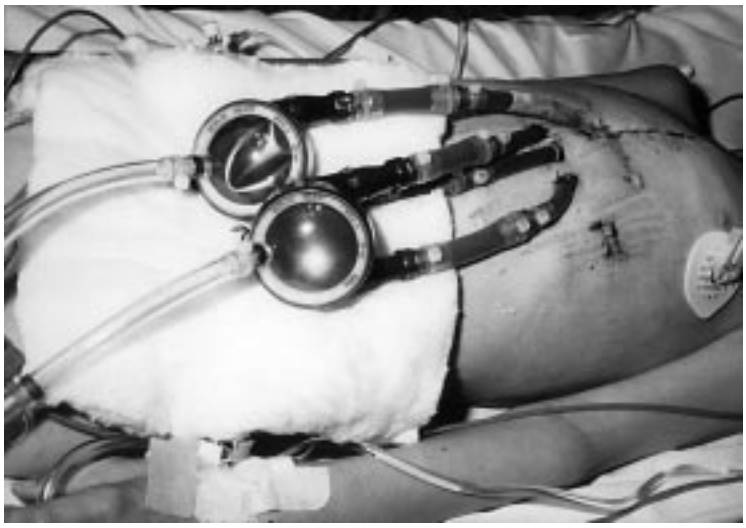

Figure 1 Berlin heart in situ in a child. Both the right and left heart are supported.

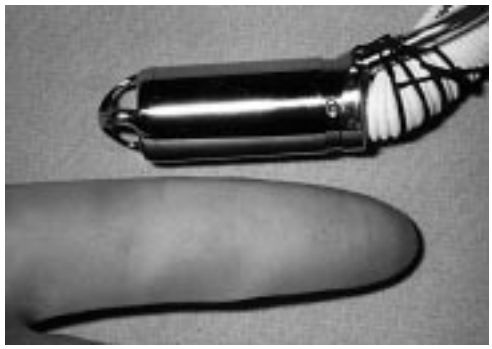

Figure 2 Jarvik 2000 impeller pump, compared to index finger.

cardiomyopathy masqueraded as acute myocarditis.

The second emerging treatment option is mechanical bridge to myocardial recovery.[11–13] This "keep your own heart" strategy is aimed principally at patients with cardiogenic shock from acute fulminant myocarditis, a problem that affects previously normal hearts. These patients can be salvaged and returned to virtually normal myocardial function by a period of left ventricular or biventricular support.[11] We and others have used this method to treat young patients who required external cardiac massage and urgent cardiopulmonary bypass to sustain life. Duration of circulatory assistance has ranged from five to 70 days (median 11). These successful outcomes suggest that a period of circulatory support and attempted weaning is preferable to early transplantation for this problem.

None of the existing LVADs are suitable for long term support in children with chronic heart failure, although recent reports suggest that left ventricular recovery is possible in off-loaded patients with dilated cardiomyopathy.[12 13] The LVAD normalises left ventricular pressure–volume relations, increases myocardial and systemic perfusion, and reverses the neurohormonal changes and cytokine release in heart failure. Current developments in axial flow impeller pump technology are producing much smaller blood pumps suitable for children. In particular the Jarvik 2000 Heart (fig 2) has been miniaturised to less than the size of the fifth finger with a flow of 3 litres/min.[14] Such devices may enable long term mechanical support as either a bridge to transplant or recovery.

BATISTA OPERATION

Some interest has been expressed in the paediatric use of the Batista operation, where partial left ventriculectomy and mitral valve repair or replacement is performed. This surgery has mainly been applied in cases of dilated cardiomyopathy, where it is thought that restoration of normal left ventricular dimensions will improve myocardial performance. Early experience in the USA, which was limited to adult patients with end stage dilated cardiomyopathy, demonstrated a two year survival of 55%, with most of the patients showing an improvement in their New York Heart Association functional class.[15] We have successful experience of the Batista operation in two infants.

Potential medical advances

A considerable amount of effort is now directed towards preventing apoptosis in the failing human heart. A better understanding of how apoptosis is regulated will provide new treatment opportunities such as gene therapy to influence cardiac and vascular remodelling. Obvious targets are the caspase enzymes and the antiapoptotic bcl-2 family, which are central regulators of apoptosis under most circumstances.[16]

Conclusion

In future, medical treatment for heart failure may be combined with long term mechanical circulatory support to promote myocyte and myocardial recovery. Carefully combined medical and surgical treatments may then transform the bleak outlook for infants and children in end stage heart failure.

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