Early Human Development 88 (2012) 287–290

Contents lists available at SciVerse ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Best practice guidelines

Rationale for and current status of prenatal cardiac intervention

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ARTICLE INFO

Keywords:
Heart defects
Congenital
Aortic stenosis
Pulmonary atresia
Balloon dilatation

ABSTRACT

The idea of prenatal intervention in congenital heart defects was put forward over 20 years ago, arising from the observation that some forms of cardiac malformation progressed in severity as pregnancy advanced. The simultaneous development of minimally invasive catheter techniques in children, led to the concept of treating the foetal heart directly, in an attempt to prevent the changes which had been observed.

Early efforts at prenatal valvuloplasty were largely set aside after poor results and the coincidental development of alternative, increasingly successful, postnatal surgical strategies. However, in the last 10 years or so, some centres have revived and extended the interventional techniques, with some success.

The application of these techniques is limited to very few conditions, and suitable cases are relatively uncommon. Exploration of these procedures, therefore, should be limited to very few centres and the results should be closely scrutinised before this becomes an accepted management option.

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1. Introduction and historical perspective

The ability to define the structure of the foetal heart by two-dimensional echocardiography became possible in the early 1980s. This allowed researchers the opportunity to observe cardiac structure and function, in both the normal and abnormally formed heart, from a fairly early stage in gestation until delivery. Most major congenital heart defects (CHD) involve an incorrect arrangement of cardiac structure, which arises at the time of cardiac development before 8 completed weeks of gestation – as in transposition of the great arteries, for example – and the malformation is fixed in nature from this time. There is therefore no feasible prenatal intervention applicable to the majority of CHD. But using the new echocardiographic techniques, it was noticed that some forms of CHD, particularly obstructive valve disease, changed in nature as gestation advanced [1]. Although many paediatric cardiologists found this surprising, it was in fact consistent with the experience of arterial valve defects after birth. In postnatal life, a bicuspid aortic or pulmonary valve can be associated with no stenosis or flow disturbance, even until late adult life, or, alternatively, can progress to an important degree of obstruction during growth in childhood. The actual arterial valve malformation – a bicuspid instead of a tricuspid valve – is present from the initial time of formation of the valve cusps, but the degree of obstruction to blood flow which the malformed valve produces is widely varied. In similar fashion to the child, aortic or pulmonary stenosis can progress with growth of the foetus, from a mildly obstructed valve to a severely obstructed or even completely atretic valve, while still in utero.

If either arterial valve presents an important degree of obstruction to flow in foetal life, there are consequences with respect to the related ventricle. In the face of a severely obstructed aortic valve, for example, the left ventricle can begin to fail to overcome the obstruction. It then

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doi:10.1016/j.earlhumdev.2012.02.012

dilates and contracts poorly. The high pressure within the left ventricle restricts filling of the chamber through the mitral valve. This in turn leads, over time, to a relatively small left ventricle, as the rest of the heart (and foetus) grows and the left ventricle does not, resulting in a ventricle which is too small to support the systemic circulation after birth. Therefore, what is first seen to be aortic stenosis, can evolve into a typical picture of a hypoplastic left heart by the end of pregnancy. In some cases, possibly where failure to overcome the obstruction occurs rather later in gestation, the ventricle remains larger than normal but becomes lined by thickened endocardium (endocardial fibroelastosis). This results in a ventricle which is significantly impaired in terms of function after birth. These sequential findings can also be seen on the right side of the heart, although it is much less common. It is important to understand that this sequence of events – ventricular dysfunction followed by growth failure – is only possible in the foetus, where there is an alternative circulatory pump working in parallel to the other ventricle, but not possible in the infant or child, where the ventricles work in sequence independently of each other. In postnatal life, poor left (or right) ventricular function quickly results in severe symptoms or even death.

Coincident with the observation of increasing valve stenosis occurring in utero, balloon catheter techniques to stretch a stenotic arterial valve became more widely and successfully used to treat the child or neonate with arterial (semilunar) valve stenosis. Thus, the idea was proposed to try to open the aortic valve in foetal life, using minimally invasive catheter techniques, in an attempt to prevent the growth failure and/or the left ventricular myocardial damage which is the usual consequence of a severely obstructed valve [2]. At this time (in the late 1980s), there was no established postnatal surgical strategy available for a neonate with effectively no systemic pump, so a critically obstructed aortic valve was usually a fatal condition in infants.

Five procedures were undertaken in 4 patients in the period 1989–1992 in our centre. All procedures were performed percutaneously under local anaesthetic. The apex of the left ventricle was punctured directly and a guide wire passed through the aortic valve. A balloon catheter was then passed over the wire and inflated when it was correctly positioned across the aortic valve (Fig. 1). Two procedures were technically unsuccessful. There was one long-term survivor (who is still alive and well at 19 years of age), one intrauterine death and two postnatal deaths, despite successful dilatation of the valve. At that time, it was difficult to obtain balloon catheters which were small enough for the foetal aorta (1.5–2.5 mm in diameter) and which could be safely retracted into the introducing needle. In two cases (including our survivor), a small portion of catheter remained embedded in the myocardium as the apparatus was withdrawn from the heart. The limited success, the technical difficulties with the equipment and the advent of an alternative postnatal surgical approach for this condition by converting the heart to a one ventricle repair (the Norwood procedure), led to suspension of the project. A few investigators subsequently tried the procedure in small numbers world-wide [3], but suitable cases are rare and success was limited.

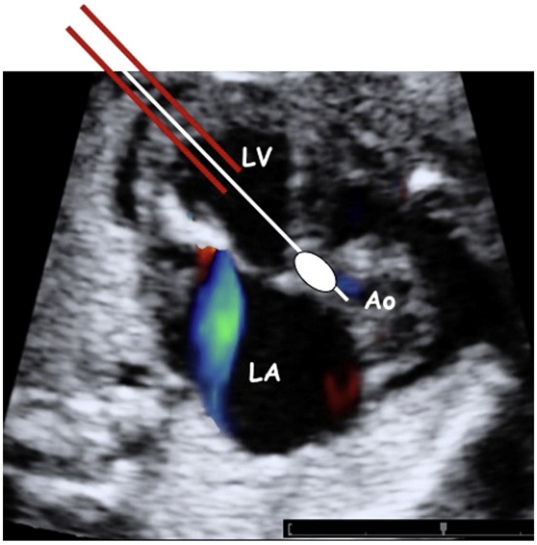

Fig. 1. The heart is imaged in the left ventricular outflow tract view. The needle punctures the left ventricular (LV) apex. A guide wire is passed into the aorta (Ao). A balloon catheter passed over the wire is positioned across the aortic valve and inflated to stretch the valve. LA = left atrium.

The concept of prenatal intervention was revisited in the early years of this century. By this time, catheter technology and experience with innovative catheter techniques had advanced considerably. Also, there was some disillusionment amongst cardiologists with the long-term results of the Norwood approach, which involves a three-stage surgical strategy to convert the right ventricle into the systemic pump. The longer such patients are followed into adult life, the more complications of a one ventricle circulation become evident. These include arrhythmias, thrombosis, protein-losing enteropathy and increasing exercise intolerance leading to failure of the one ventricle circuit after 15–30 years [4]. Once the one ventricle (or Fontan) circulation fails, transplantation is the only option currently available. However, these patients make poor candidates for transplant, as they are debilitated by long-term disability and have had multiple thoracic surgeries. There is already an increasing shortage of donors for transplant and these children will have to compete for transplant organs with candidates at lower risk for organ replacement.

2. Aortic valve intervention

The group at Boston Children's Hospital started a programme for prenatal intervention in 2000 [5]. The main focus has been the treatment of critical aortic stenosis, but they have also attempted procedures on the pulmonary valve and the atrial septum. Procedures have been undertaken under general anaesthesia. There have been technical difficulties in terms of good visualisation and a suitable line of approach, resulting in a high proportion of mothers being subjected to laparotomy. The group have been able to document growth of the aorta and mitral valve orifice after a successful procedure, but not significant growth of the left ventricle [6]. Overall, the results have been rather disappointing. Of 70 patients with aortic stenosis treated, there was technical success in 74%, but with only 17/70 (24%) able to reach a biventricular repair [7]. No details of the quality of life and ongoing morbidity in those achieving a biventricular repair are available. What has been useful is that, based on their results, they have learnt how to modify their techniques to improve the outcome [8] and to refine the criteria for selection of suitable patients [9]. In contrast to postnatal balloon techniques, they use a balloon which is slightly larger than the size of the aorta, and aim to produce some aortic regurgitation. The optimum gestational age for intervention appears to be between 24 and 30 weeks. An ideal subject for treatment would have a left to right shunt across the atrial septum, a monophasic short duration of mitral inflow, severe left ventricular dysfunction but an apex-forming left ventricle, some forward flow across the aortic valve at modestly increased velocity (about 2 m/s) and reverse flow in the aortic arch (Fig. 2). On the other hand, a foetus with aortic stenosis with a high velocity, good ventricular function and forward flow in the arch could safely wait for postnatal treatment. Alternatively, if the ventricle is already small, a prenatal procedure is not likely to be effective in avoiding one ventricle palliation. However, if strict selection criteria are enforced, this limits the number of eligible patients for the procedure in an already rare condition. Starting in 2002, a group [10] in Linz, Austria have performed 24 procedures in 23 foetuses with aortic stenosis, of which 16 (67%) were technically