

The influence of the perinatal environment on the heart: morphological, electrocardiographic, and multimodality imaging features

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From the womb to the adult

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Abstract

The purpose of this paper is to review the studies performed to evaluate the influence of perinatal environment on neonatal heart, detected by electrocardiography, echocardiography, and other imaging techniques. Prenatal conditions (such as intrauterine growth retardation and prematurity at birth) and some post-natal events (such as perinatal asphyxia and corticosteroids administration), may have early and late detrimental effects on the heart may predispose to a number of future cardiovascular adverse events. For example, subjects born preterm may be at potentially higher risk of developing malignant ventricular arrhythmias as well. Moreover, in individuals born with an extremely low birthweight atrial septal aneurysms are present in about one third of the subjects in the study. Thus, a long-life follow up is suggested in these subjects.

Keywords

Prematurity, intrauterine growth restriction, asphyxia, corticosteroids, arrhythmia, aneurism.

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Introduction

It is an undoubted finding that prenatal conditions such as intrauterine growth retardation and prematurity at birth may predispose to a number of future cardiovascular adverse events [1].

However, even some post-natal events, such as corticosteroids administration and perinatal asphyxia, may have early and late detrimental effects on the heart [2].

The purpose of this paper is to undertake a review about the studies conducted to assess the influence of the perinatal environment on the heart of newborns as it may be detected by means of electrocardiography, echocardiography, and other imaging techniques.

Influence of environmental factors: cardiovascular risk in preterm babies subjected to postnatal treatment with corticosteroids

In subjects born preterm the development of cardiac hypertrophy induced by corticosteroid administration is a well-known occurrence.

Corticosteroid administration was aimed at preventing and treating bronchopulmonary dysplasia in preterm subjects. Up until the early 1990s corticosteroids were widely used in neonatal intensive care units [3]. This practice was justified by the beneficial effects of corticosteroids in improving respiratory function, thus reducing the need for assisted mechanical ventilation and oxygen administration and resulting in a lower rate of perinatal mortality [4].

Taking into account the numerous side effects of corticosteroids, the American Academy of Pediatricians and the Canadian Society of Pediatrics have advised against using these drugs in the treatment of chronic lung disease in preterm babies, recommending that their administration is limited to extremely severe clinical situations [5].

This treatment however is not devoid of side effects at a cardiac level, because it often produces cardiac hypertrophy which generally regresses on withdrawal of treatment [6-9].

In a small number of cases corticosteroids are responsible for the onset of both an obstruction of left ventricular efflux and heart failure. These hemodynamic alterations require cardiac intervention to reduce preload, pulmonary congestion and decrease in cardiac output [10, 11].

In view of the potential, rapid and significant changes in the thickness of the left ventricular walls and in left ventricular efflux, a follow up by means of echocardiography is recommended [12].

The potential side effects produced by long-term corticosteroid treatment are however more severe and disturbing.

Recent studies have suggested that corticosteroids may indeed inhibit of mitosis in cardiomyocytes, thus determining a decrease in the number of cardiac muscle cells in adulthood [13]. These changes appear to induce the onset of an early diastolic dysfunction secondary to the development of dilated cardiomyopathy [14].

The above may result in a reduced life expectancy, as observed in laboratory guinea pigs treated during the neonatal period with corticosteroids [13].

Electrocardiographic alterations and risk of arrhythmia

Premature birth and retarded intrauterine growth are associated with the possible onset of supraventricular and ventricular arrhythmias.

In relation to supraventricular arrhythmias it has been recently demonstrated the association of low birthweight (in men) with an increased risk of onset of atrial fibrillation [15].

As pioneer in this field, our research group previously demonstrated that in subjects born with an extremely low birthweight the prevalence of atrial septal aneurysms – often associated with episodes atrial fibrillation – is approximately 30%, whilst prevalence of these events in the general population ranges from 0.2 to 3.2% [16, 17].

Other studies suggest that subjects born preterm may be at potentially higher risk of developing malignant ventricular arrhythmias as well.

The first observation in this field dates back several years, when a study reported how domperidone, a drug widely used in the past in the treatment of gastro-esophageal reflux in neonates, determined an increased prolongation of QT interval in preterm subjects [18].

Recently, a study conducted by Fouzas et al. immediately following delivery of neonates with retarded intrauterine growth, demonstrated how

dispersion of QT (QTd) – an electrocardiographic parameter that has proved to be of use in predicting the future onset of malignant ventricular arrhythmias – is increased in these subjects [19].

In another study, not only QTd, but also QTc were found to be at the upper limit of normal range. From a practical point of view, these findings underline a potential risk of developing ventricular arrhythmias when using drugs capable of prolonging QT interval [20, 21].

In addition, it has long been acknowledged that neonatal asphyxia, when complicated by the onset of myocardial ischemia, determines electrocardiographic alterations similar to those observed in angina pectoris and myocardial infarction (ST depression or elevation, T wave negativization, appearance of q waves) [22].

Cardiac enzymes and troponins

Neonatal asphyxia frequently results in myocardial ischemia [2]. In this case, cardiac enzymes and troponins display an increase similar to that observed in myocardial infarction in adults [22].

In the same way as adults, troponins administered to newborn infants also display a higher sensitivity in identifying even very small areas of myocardial necrosis compared to traditional cardiac enzymes [23].

To date however, the long-term clinical consequences of a form of ‘acute coronary syndrome’ or overt myocardial infarction in the newborn remain largely unknown.

Cardiovascular imaging in preterm subjects

Infants born preterm, although clinically stable, at echocardiography present with alterations of diastolic function whilst systolic function is normal.

In particular, infants born preterm display an increased atrial contribution to ventricular filling, with the condition persisting over time [24].

However, with regard to the right ventricle, in clinically stable preterm infants there is an alteration of both systolic and diastolic function, likely as a consequence of the increased hemodynamic load of right ventricular segments during fetal circulation [25].

Morpho-functional cardiac alterations in preterm infants include increased wall thickness and ventricular diameter [26]. These alterations appear to persist beyond the perinatal period.

In a previously published study, left ventricle changes have been evidenced in children born

preterm with fetal growth restriction, being the latter condition identified as the underlying trigger for this remodeling [27].

Furthermore, in a recent report it has been demonstrated that young adult subjects born preterm feature adverse structural alterations in their heart that may involve an increased risk of cardiac deficits. The study – conducted using cardiac magnetic resonance imaging – was the first of its kind to demonstrate that those born preterm had a significantly increased left ventricular mass, with greater prematurity associated with greater mass. Ejection fraction was preserved, but not the diastolic function [28].

As above stated, a pioneering study in the field was conducted by our research group by means of bi-dimensional echocardiography, demonstrating that in individuals born with an extremely low birthweight atrial septal aneurysms are present in about one third of the subjects in the study. This finding is probably related with respiratory distress and patency of the ductus arteriosus. In view of the association between atrial septal aneurysm and atrial fibrillation/stroke in young adults devoid of other cerebrovascular risk factors, this unexpected observation suggests that all former preterm subjects should undergo transthoracic or transesophageal echocardiographic examination with the aim of detecting this potentially emboligenic cardiac abnormality [16].

Conclusions

The reported findings suggest that events related with perinatal life may influence both the morphology and function of the heart, as detected by facilities routinely performed in clinical practice in cardiology. Based on these premises, a long-life follow up is suggested in these subjects.

Declaration of interest

The Authors declare that there is no conflict of interest.

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