Renal, Splanchnic and Systemic Hemodynamic Changes in Children with Congenital Cyanotic Heart Disease

Thesis

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بسم الله الرحمن الرحيم

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عنوان الرسالة

تغيرات حركية الدم فى الكلى و الأمعاء فى الأطفال المصابين بعيوب خلقية إزرقاقية بالقلب

ملخص الرسالة:

نقص أكسجة الدم فى الأطفال المصابين بعيوب خلقية إزرقاقية بالقلب يحث على حدوث إزدياد تعويضى فى كرات الدم الحمراء مما يزيد لزوجة الدم. و لقد درسنا تغييرات حركية الدم فى الشرايين الكلوية والفخذية و المساريقى العلوى بواسطة الدوبلر الملون فى 40 طفل مصاب بعيوب خلقية إزرقاقية بالقلب وكذلك فى 20 طفل من الأصحاء متوافقين فى العمر و الجنس كمجموعة ضابطة. و قد وجد أن دلالات الدوبلر كانت اعلى فى الحالات عن مجموعة السيطرة و لكن بدون فارق احصائى هام. و مع ذلك وجدت علاقة ذات أهمية إحصائية بين دلالات الدوبلر فى الشرايين الكلوية و الفخذية و بين كلا من فترة الأزرقاق و سرعة ضربات القلب. و من هذة النتائج يمكن أن نستنتج أن أضطرابات تصاعدية فى حركية الدم يمكن أن تحدث فى الشرايين الكلوية و الفخذية فى الأطفال ذوى العيوب الخلقية الأزرقاقية بالقلب و أن استعمال الوبلر الملون قد يساعد فى التشخيص المبكر لاصابات الكلى فى هؤلاء الأطفال.

و ترى اللجنة قبول البحث

أ.د./ مجد أحمد قطب

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Abstract

Keywords: congenital cyanotic heart disease – Doppler ultrasonography – renal – femoral – superior mesenteric.

Chronic hypoxia in CCHD results in erythrocytosis causing blood hyperviscosity. We studied hemodynamic changes in 40 CCHD patients by Doppler US on renal, femoral & superior mesenteric arteries. We demonstrated progressive increase in resistance & pulsatility indices in renal & femoral arteries but it was statistically non significant increase. This increase was correlated to the duration of cyanosis. No changes in superior mesenteric artery hemodynamics. Finally, we recommend doing Doppler examination for assessment of renal condition in CCHD.

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List of Abbreviations

ASD	**Atrial septal defect**
AVC	**Atrio-ventricular canal**
AVSD	**Atrio-ventricular septal defect**
CCHD	**Congenital cyanotic heart disease**
CDI	**Color Doppler imaging**
CHD	**Congenital heart disease**
CWD	**Continuous wave Doppler**
DORV	**Double outlet right ventricle**
ECG	**Electrocardiogram**
EDV	**End diastolic velocity**
GFR	**Glomerular filtration rate**
Hb	**Hemoglobin**
HOA	**Hypertrophic osteoarthropathy**
IGF-1	**Insulin like growth factor-1**
Ig M	**Immunoglobulin M**
MRI	**Magnetic resonance imaging**
NMI	**Non-occlusive mesenteric ischemia**
PDA	**Patent ductus arteriosus**
PI	**Pulsatility index**
PSV	**Peak systolic velocity**
PWD	**Pulsed wave Doppler**
RBCs	**Red blood cells**
RI	**Resistance index**
RPF	**Renal plasma flow**
SMA	**Superior mesenteric artery**
TEE	**Trans-esophageal echocardiography**
TGA	**Transposition of the great arteries**
TOF	**Tetralogy of Fallot**
US	**Ultrasound**
VEC MR	**Velocity encoded cine magnetic resonance**

Introduction and Aim of work

Nephropathy is known to occur in patients with long-standing congenital cyanotic heart disease (CCHD). Glomerular filtration rates were below normal in half of these patients with glomerular-type and tubular-type proteinuria occur. An elevated hematocrit and duration of cyanosis were identified as the main risk factors for the development of glomerulopathy. The risk of developing glomerular lesions rises sharply during the second decade of life ***(Dittrich et al., 1998).***

The actual mechanism of cyanotic nephropathy is not known ***(Berry & Belsha, 1998)***; the suggested pathophysiologic explanation of these findings is that the blood hyperviscosity seen in patients with CCHD causes an overall increase in renal vascular resistance with a rise in intraglomerular blood pressure. Despite a sluggish flow of blood in the glomerular capillary bed, the effective filtration pressure was adjusted to conserve the glomerular filtration rate ***(Burlet et al., 1999).***

Color coded Doppler ultrasound has the potential to become a useful screening test for patients at risk of renovascular hypertension and a tool for follow-up of patients who undergo revascularization procedures ***(Lencioni et al., 1999).*** Duplex ultrasound (US) is established as having a major role in the assessment of both extracranial carotid disease and lower limb graft surveillance ***(Phillips, 2000).***

The aim of this study was to assess renal, splanchnic and systemic hemodynamic changes in children having CCHD using Doppler

ultrasonography. The relation of Doppler findings to clinical, laboratory and echocardiographic parameters were evaluated as well.

Embryology of the heart

For centuries scientists have wondered how hearts become malformed. This desire to understand the formation of abnormal hearts has motivated the study of normal cardiac embryology ***(Colvin, 1998).***

The processes of cardiac development have been grouped into two stages. The first stage, early cardiogenesis, or the premorphologic stage, starts at the fertilization process and ends at the formation of the two lateral endothelial heart tubes. The second stage, the morphologic stage, starts at the straight or primitive heart tubes and ends at the mature heart stage ***(Valdes-Cruz & Cayre, 1999).***

☒ Early Cardiogenesis, or Premorphologic Stage:

Initially, after fertilization, the zygote is unicellular, but then it undergoes a series of cleavages that results in an increase in the number of the cells. During the second week of development, the embryoblast differentiates into two layers, the endodermal germ layer and the ectodermal germ layer. At the end of third week, an intermediate cell layer appears the intraembryonic mesoderm ***(Colvin, 1998; Valdes-Cruz & Cayre, 1999; and Needlman, 2004).***

Figure (1): *Schematic drawing of right lateral view of a sagittal cut of an embryo, showing the location of cardiogenic areas and the rotation over its transverse axis.* ***A:*** *Presomite embryo.* ***B:*** *Embryo of 14 paired somites* ***(Valdes-Cruz & Cayre, 1999).***

☒ Late Cardiogenesis, or Morphologic Stage:

Formation of the cardiac tube:

Cardiac precursor cells form a bilaterally symmetric cardiogenic field, parallel cardiac primordia. Further migration of the mesodermal cells takes place in a cephalic direction to meet anteriorly where they form the cardiogenic plate and finally fuse at the midline to form the primitive straight cardiac tube, Fig. (1) ***(Colvin, 1998; Srivastava & Baldwin, 2001; and Hill, 2006).***

The straight heart tube has four regions, called primitive cardiac cavities, separated by three pairs of ectodermal grooves and their corresponding endodermal crests, Fig. (2), ***(Valdes-Cruz & Cayre, 1999***).

Figure (2): *Schematic drawing of the primitive cardiac cavities in the preloop stage, AB=aortic bulb; BC=bulbus cordis; PV=primitive ventricle; RA=right atrium; LA=left atrium; 1=right and left interbulbar groove; 2=right and left bulboventricular groove; 3= rigt and left interventricular groove* ***(Valdes-Cruz & Cayre, 1999).***

Formation of the heart loop:

The heart tube continues to elongate and the cephalic portion of the tube bends in ventrocaudal directions and to the right, while the caudal atrial portion shifts in dorsocranial direction and to the left. This bending

creates the cardiac loop, Fig. (3), ***(Sadler, 2007).*** In normal hearts, the looping is anterior and to the right and it is termed as D (dextro) loop. This usually results in the right ventricle being to the right, and the aorta is posterior and to the right of the pulmonary artery ***(Kidd & Neill, 1995)***. Although the looping of the heart is associated with an increase in length, this is not the only cause of looping as is sometimes suggested. If the heart is removed from the pericardial cavity at a time, it is still straight and placed in culture; it will loop on schedule ***(Mc Lachlan, 1994).***

Figure (3): *formation of the cardiac loop.* ***A:*** *At 8 somites.* ***B:*** *AT 11 somites.* ***C:*** *At 16 somites. Broken line indicates pericardium. Note how the atrium gradually assumes an intrapericardial position* ***(Sadler, 1993).***

Septation of the heart:

When looping is complete the heart has an external appearance similar to that of adult heart. The internal structure still consists of a single convoluted tube with several local expansions ***(Colvin, 1998).***

At the end of the forth week a sickle shaped crest grows from the roof of the common atrium [the septum primum] ***(Sadler, 2007)***. The free border of the septum primum and the free border of the endocardial cushions delineate an orifice, the ostium primum. Before foramen primum closes, another orifice appears in dorsocephalic portion of

septum primum, the ostium secundum, which stays open until birth ***(Valdes-Cruz & Cayre, 1999***). As the ostium secundum forms, a second septum also begins to form along the roof of the atrium. The inferior rim of this septum is an arc which never closes but forms an oval rim, the limbus of foramen ovale ***(Colvin, 1998).***

The endocardial cushions are a central feature of cardiac septation. Septation of the A-V canal begins with the appearance of opposing endocardial cushions at the superior and inferior borders. Smaller lateral masses, the right and left lateral atrioventricular cushions appear. These regional swellings of extracellular matrix provide valve like function in the primitive heart, form the anlagen of the semilunar and AV valves, and contribute to the definitive valve leaflets ***(Garson et al, 1990; and Srivastava & Baldwin, 2001).***

Septation of the ventricles begins with protrusions of the endocardium in both the inlet (primitive ventricle) and outlet (bulbus cordis) segments of the heart. The inlet protrusions fuse into the bulboventricular septum and extend posteriorly toward the inferior endocardial cushion, giving rise to the inlet and trabecular portions of the interventricular septum. The outlet or conotruncal septum develops from ridges of cardiac jelly, similar to the atrioventricular cushions. These ridges fuse to form a spiral septum, bringing the future pulmonary artery into communication with the anterior and rightward right ventricle, and the future aorta into communication with the posterior leftward left ventricle, Fig. (4) & (5) ***(Bernstein, 2004; and Sadler, 2007).***

Figure (4): *Schematic drawing showing the start of cardiac septation in the early postloop stage.* ***A:*** *View from the right side of a sagittal cut of the heart.* ***B:*** *Transverse cut of the heart.* *PRA = primitive right atrium; PLA = primitive left atrium; IEC = inferior endocardial cushions; SEC = superior endocardial cushions; LLEC = left lateral endocardial cushions; RLEC = right lateral endocardial cushions; LAVO = left atrioventricular orifice; RAVO = right atrioventricular orifice; 1=foramen primum; 2=primary interventricular foramen* ***(Valdes-Cruz & Cayre, 1999).***

Figure (5): *Schematic drawing of the formation of the interatrial and interventricular septa.* ***A:*** *Transverse cut of the heart.* ***B-D:*** *The right and left atrial septal surfaces.* *The arrow indicates the direction of blood flow across the formen ovale. RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle; 1=orifice of the proximal portion of the left ventricular outflow tract (primary interventricular foramen); 2=secondary interventricular foramen* ***(Valdes-Cruz & Cayre, 1999).***