ECOCARDIOGRAFIA E VARIE

C11

CARDIOVASCULAR ABNORMALITIES IN PEDIATRIC PATIENTS WITH OSTEOGENESIS IMPERFECTA

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BACKGROUND
Osteogensis Imperfecta (OI) is a heterogeneous hereditary connective tissue disorder caused by genetic defects in type I collagen synthesis. The collagen type I is the main protein of connective tissue in human beings, with an important function of mechanical support: it accounts for approximately 75% of total collagen in the myocardium and contributes to aortic wall strength and stiffness. The literature describes cardiovascular involvement in adults with OI, but the prevalence and the type of cardiovascular abnormalities in children is currently unknown.
The aim of this study was to investigate for the first time cardiovascular abnormalities in a large pediatric population of patients with OI.
MATERIALS AND METHODS
Between January 2008 and May 2012, 69 pediatric patients with OI have been evaluated at our Institution. The OI group consisted of 31 females (44,9%) and 38 males (55,1%), with a mean age of 9,27±4,3 years (range 1,5 - 18 years). Patients had not yet started treatment with bisphosphonates at the time of the study. The OI group was classified according to Sillence criteria into three clinical types: I, III, IV. Fifty-three healthy subjects (32 females), matched for age and sex, without history of congenital or acquired heart disease, served as controls. Left ventricular (LV) size (left ventricular internal dimension in diastole – LVIDd; left ventricular internal dimension in systole – LVIDs) and aortic diameters (aortic annulus, aortic root, sino-tubular junction and ascending aorta) were measured by standard echocardiography and indexed by body surface area (BSA). Pulsed-wave Doppler analysis of mitral valve inflow velocities and Tissue Doppler Imaging (TDI) were used to assess LV systolic and diastolic function.
RESULTS
The LVIDd and LVIDs were significantly larger in the OI group compared with controls (LVIDd/m2 4±1 cm/m2 vs 3,6±1 cm/m2, p< 0,05; LVIDs/m2 2,7±0,7 cm/m2 vs 2,3±0,7 cm/m2, p<0,05). Moreover, LV dimensions and dilation of aorta in type III OI patients were significantly greater compared with types I and IV (see Table 1). <FILE IMAGE='695_20130625124131.jpg'>Mitral Valve Deceleration time appeared shortened in patients with OI (148 msec ±28,3) compared with controls (159,5 msec ± 25,1, p<0,05). TDI evaluation showed a reduction of e' (peak velocity during early ventricular diastole) and e'/a' ratio, and an increase of E/e' ratio (early diastolic velocity ratio) in the OI group. LV systolic function was normal in both groups.
CONCLUSIONS
Our study shows that the same cardiovascular abnormalities present in adult patients with OI are already present in pediatric patients. Moreover, this early LV abnormal function and the dilation of the aorta in type III OI patients are more pronounced compared with types I and IV. It is noteworthy that our patients have been evaluated before starting a therapy with bisphosphonates and in the future, a revaluation will permit to assess possible improvement of cardiac abnormalities after therapy.

C12

USE OF SILDENAFIL IN PULMONARY HYPERTENSION ASSOCIATED WITH BRONCHOPULMONARY DYSPLASIA IN PREMATURE INFANTS. SINGLE CENTER EXPERIENCE

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Pulmonary hypertension (PH) is an emerging potentially lethal complication of bronchopulmonary dysplasia (BPD) of prematurity(O2 dependency at 36 weeks GA) , Its incidence is unknown and treatment is not yet standardized. We present retrospectively the experience with sildenafil (S) in a single large Center

We analyzed all very low birth weight (VLBW) infants admitted at our Neonatal Intensive Care Unit (NICU) between 01/2007 and 12/2011 who developed BPD and PH and were treated with S for PH defined as systolic PA pressure (PAP) above 40 mmHg by Echo (mean >25 mmHg). S was discontinued when PAP was normal at 2 subsequent evaluations. Safety was assessed by adverse events while on S and the discontinuation of treatment for reasons other than improvement . Data were analyzed with SPSSv 18. Continuous variables are expressed as mean ± standard deviation and dichotomic variables as number (percentage).

Between 2007 and 2011, 649 VLBW infants were admitted to our center. Mean gestational age (GA) and birth weight were 29 ± 2.8 weeks and 1136 ± 274 grams respectively. 45 patients (pts) died before 36 weeks GA, Of the 604 survivors, 87 (14,2%) developed BPD, severe in 51 (8,4%). PH was detected in 14/51 (27%) pts with severe BPD (14 % of all BPD), and they were treated with S (2.5 ± 1.25 mg/kg/day) Mean GA at diagnosis was 46 ± 9.7 weeks and mean systolic PAP 53 ± 16 mmHg. Three pts (21%) died before discharge because of chronic respiratory failure and PH. Three patients (14.3%) recovered for PH during hospital stay and discontinued S before discharge. Eight patients (57%) were discharged on S and O2 therapy and monitored as outpatients. Sildenafil was successfully weaned by 5.2 ± 4.7 months of corrected age in 5 patients. Three patients are still under treatment age 18, 22 and 39 months.

There were no adverse effects related to S treatment PH is emerging as a serious common problem in pts with severe BPD of prematurity Chronic use of S seems to be safe in these pts, although larger series will be needed to establish this firmly.

C13

ECHOCARDIOGRAPHIC NOMOGRAMS FOR VENTRICULAR, VALVULAR AND ARTERIAL DIMENSIONS IN NEONATES AND CHILDREN: PRELIMINARY RESULTS

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Background: A quantitative assessment is essential during the performance of a paediatric echocardiography. Despite this actual nomograms are limited and heterogeneous, particualrly in noenates and infants.
Aim of the present study is to establish reliable echocardiographic nomograms in a population of healthy neonates, infants and children. Special attention will be given to neonates, since most critical management decisions for patients with congenital heart disease occur during the first few weeks of life.
Methods. Two-dimensional and M-mode measurements were made of 22 individual cardiac structures in 420 healthy subjects (mean age 4,98 Sd 8,47 months; 211 F, 208 M) with a BSA <0,6 m2 ranging in age from 1 day to 2 years (Table 1). Models using linear (y = a + b*x), logarithmic (y = a + b*ln[x]), exponential (ln[y] = a + b*ln[x]), and square root (sqare y=a + b*x1/2) relationships were tested. The presence or absence of heteroscedasticity was then tested by observing the graphical analysis of standardized residuals (if the distribution of standardized residuals is normal, 95% of the values must be between -1,96 and +1,96). The assumption of independence of residuals was tested by calculating the coefficient of Durbin-Watson. Age, weight, height and body surface area (BSA) (calculated using the formulas by Du Bois and Du Bois and by Haycock) were used as the independent variables in four different linear regression analyses to predict the mean values of each echocardiographic measurement. It was also evaluated the presence of confounding factors such as sex, cesarean section, prematurity.
Results:
The use of body surface area calculated by Du Bois formula provided the best results, and these are presented in Table 1. According to these data, different equations should be employed for various parameters. For each measurement was chosen the model that best fitted the data. Were chosen models exponential (ln[y] = a + b*ln[x]) and square root (y = a + b*x) because satisfied the assumption of homoscedasticity and normality of residuals and shows the highest R2 score. Predicted values and Z scores boundaries for all measurement are presented In Table 1.
We found no significant effects in the most of measurements, gender and the type of delivery that were not included in the final models.
Intra and inter-observer variability was within the 95% tolerance limit.
Conclusions: We present preliminary data on the widest population of healthy neonates and infants reported so far. Our data will allow for a more reliable calculation of cardiac z scores for some essential cardiac and vessels dimensions in neonates and infants. In particular this work overcome some of the methodological and numerical limitations affecting previous works offering the adjunctive advantage to cover a very important age group (neonates and infants) and some essential cardiac structures measurements (aortic arch, pulmonary arteries) that have been scarcely investigated in previous works. Further studies however are required to reinforce these data, as well to evaluate other parameters.

Table 1: Coefficients for regression equations relating echocardiographic measurements and body surface area, the Standard Error of the Estimate, the determination coefficient. Normality test: Shapiro-Wilk and Lilliefors (Kolmogorov-Smirnov).of DuBois.
Ao= aorta; Asc Ao=ascending aorta; IA = innominate artery; IVC=inferior vena cava; IVSd=interventricular septal diastolic thickness LVED=left ventricular end diastolic diameter; LCA=left carotid artery; LSA=left subclavian artery; LPA=left pulmonary artery; LVES=left ventricular end systolic diameter; LVPWd= left ventricular wall diastolic thickness; MPA=main pulmonary artery; RPA=right pulmonary artery.
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C14

RISK OF ISCHEMIC STROKE IN TOTAL CAVOPULMONARY CONNECTION

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Objective: The objective of this study was to evaluate the incidence of cerebral stroke in patients with total cavopulmonary connection (TCPC).
Background. Thrombotic events have been reported as a major cause of morbidity after TCPC . However there is no consensus concerning postoperative mode and duration of anticoagulation prophylaxis.
Methods: This is a retrospective study concerning 60 patients (26 female, median age 6,85 years old) having had TCPC from January 1988 to January 2013 at the Pediatric Hospital Regina Margherita, Turin.. Mean follow-up was 9,55 years ± 4,77. (median e range). The anticoagulation strategy in our center includes warfarin for 6 months after TCPC, followed by acid acetysalycilic life-long. 21 patients had a percutaneous closure of the fenestration during the follow up. Cerebral ischemic events were documented with MRI or TC. Thromboembolic events in the immediate post-operation period (1 month) were not included in this series.
Results: 4 patients (6,66%) had documented ischemic cerebral stroke after TCPC. Mean age at the time of cerebral event was 10,5 years, and mean interval from TCPC 5,0 years. All events occurred under acetylsalycilic treatment. 2 out of 4 patients had an opened fenestration. Echographic imaging did not show any vascular or intracardiac thrombus. In one patient MHTFR heterozygosity was reported.
Conclusions: Although patients after TCPC have a high incidence of thromboembolic complications, anticoagulant therapy is not handled uniformly.
This small retrospective study shows the high risk of cerebral stroke suggesting the In our series ASA does not protect aging cerebral events. A particular attention FU has to be done to these patients.

C15

SOME REMARKS ABOUT 30 YEARS OF FETAL ECHOCARDIOGRAPHY ACTIVITY

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First examinations of fetal echocardiography, in our pediatric cardiology service, were performed exactly 30 years ago. Since then, many things have changed in prenatal diagnosis of congenital heart diseases (CHD). We have studied and followed more than 10,000 pregnancies and diagnosed about 1000 congenital heart diseases (in the last year we studied 1040 pregnancies and we diagnosed 74 (7%) CHD: 28 VSD, 6 VCSS, 4 CAV, 4 HLHS, 4 situs anomalies, 4 AOB, 3 TGA, 2 APSI, 2 DORV, 2 Cardiac Tumor, 2 Tricuspid Dysplasia, 2 Right Aortic Arch, 1 ToF. 1 Truncus, 1 UH, 1 AT, 1 CoAO, 1 Ebstein, 5 other anomalies and 5 pulmonary diseases with heart involvement) and as many heart rhythm disorders (in the last year we mainly monitored PR interval in pregnants with anti Ro antibodies).
The directions, the approach and the use of the method, however, are greatly changed over time.
In the past years prenatal diagnosis of CHD was directed almost exclusively to improve the outcome of fetuses with severe cardiac malformations, but the surgical results on complex heart diseases were not excellent; nowadays about 80% of parents with fetuses with severe cardiac malformations decides to the IVG, even if the surgical results are now excellent.
Moreover once only pregnancies selected for classical risk factors for CHD were studied in our center, but now obstetricians require fetal echocardiography for all pregnancies and this method is part of obstetrician screening; this practice lengthens waiting lists.
At the present time the obstetricians require the fetal echocardiography not only for morphology diagnosis of CHD, but also for a functional study of the heart in pregnancy pathologies (f.e. IURG, twin pregnancy, placental disfunction, etc) and in extra cardiac pathologies and new techniques (TDI, strain rate etc.) are specifically targeted at the study of cardiac function.
The diagnostic accuracy is increased significantly with the new equipment and the new knowledge, but is not yet predictable, with absolute certainty, the morphological evolution of the anatomy of some pathologies, which leads to a different therapeutic approach and consequently a different quality of life (f.e. complex aortic coartaction vs Shone syndrome vs HLHS).
The fragile psychology of parental couple increases and requires the figure of the psychologist in the counseling time, that it should not be reduced to a simple communication of the disease and its follow-up, but it is also extended to the management of the new life with the “heart disease”.
The medico-legal issues are becoming more frequent because the parents require perfection in prenatal diagnosis and so defensive medicine is widely used by obstetricians and consequently by fetal echocardiographers, especially during the counseling.
In this congress, the our entire series will be shown, examples for each of the above points will be discussed and new guidelines proposed for a more comprehensive approach to fetal echocardiography and to reconsider the use of this method.

C16

STUDIO DEL SISTEMA NERVOSO AUTONOMO MEDIANTE HEART RATE VARIABILITY IN BAMBINI CON EPISODI DI APPARENT LIFE-THREATENING EVENTS IDIOPATICI

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Scopo della ricerca
Per Apparent life-threatening events (ALTE) si intendono episodi acuti, che occorrono durante il primo anno di vita, caratterizzati da apnea, cambiamento del colorito cutaneo e del tono muscolare, apparente soffocamento. Sono percepiti dall'osservatore come minacciosi per la vita, con impatto emotivo elevato. L'incidenza è intorno a 0,58 e 2,46 ‰ nati vivi. Un percorso diagnostico sia pure rigoroso permette una diagnosi eziologica nel 50-70% dei casi; i rimanenti, anche in forma grave, restano senza causa riconoscibile (ALTE idiopatiche o IALTE). Un'ipotesi avanzata già in molti studi è che le IALTE possano avere origine da un'alterazione del Sistema nervoso Autonomo (SNA). Una modalità di valutazione del SNA é lo studio delle oscillazioni degli intervalli tra battiti consecutivi, per un tempo variabile (HRV). Scopo del nostro studio è la ricerca di alterazioni del SNA in bambini con IALTE, utilizzando l'analisi di HRV mediante esecuzione di Elettrocardiogramma dinamico secondo Holter (ECG-D).
Metodi
Presso il Centro per lo Studio dei Disturbi respiratori nel Sonno e la SSD di Cardiologia Pediatrica sono stati arruolati 26 pazienti (età media 11 mesi; 11 F, 15 M), nati a termine, con diagnosi di IALTE dopo screening diagnostico completo (esami clinico-laboratoristici, ECG, ecocardiogramma, polisonnografia e pH-metria). Tutti i bambini sono stati sottoposti a monitoraggio cardiopolmonare domiciliare (per 9,16 ± 7,4 mesi) ed ECG-D 24 ore (Sistema Synescope Ela Medical, 5 elettrodi). E' stata eseguita analisi di HRV mediante software dedicato sia nel dominio del tempo (RMSSD, SDNN), sia nel dominio delle frequenze (HF, LF, VLF e LF/HF). I dati ottenuti sono stati confrontati con i valori di riferimento disponibili in letteratura (1) ed è stato considerato significativo un valore di $p< 0,05$.
Risultati
In tutti i bambini è stato possibile ottenere una registrazione ECG-D correttamente valutabile. 26/26 pazienti hanno presentato SDNN al di sopra dell'intervallo di confidenza al 95% dei controlli riscontrati in letteratura, mentre RMSSD è risultata al di sopra in 25 pazienti (96,2%). In 15 bambini (60%) il rapporto LF/HF è risultato compreso tra 0,81 e 2,39, più basso del valore medio di riferimento (2,43). La variazione di LF/HF è dovuta all'aumento di HF come espressione di maggiore attività vagale. Si è inoltre evidenziato che tra i pazienti con LF/HF alterato, 5 (35,7%) avevano presentato alla polisonnografia un quadro di gravità moderata e 2 (14,3%) di gravità severa. Tra i pazienti con LF/HF normale solo 3 (27,3%) avevano un quadro di gravità moderata, mentre gli altri di gravità lieve. Dai dati relativi al follow up tra i pazienti con rapporto LF/HF alterato è stato riscontrato che 13 bambini (93%) hanno necessitato di un monitoraggio cardiorespiratorio domiciliare superiore ai 6 mesi.
Conclusioni
I dati ottenuti permettono di concludere che i bambini con storia di IALTE possono avere un'alterazione del SNA ed in particolare una prevalenza del tono vagale; in questo gruppo gli episodi clinici sono più gravi e richiedono un follow-up più prolungato. ECG-D secondo Holter con analisi HRV si è confermato un esame di semplice esecuzione ed utile per lo studio del SNA in corso di IALTE.
(1) Edner, Katz-Salamon et al. "Heart Rate variability in infant with Apparent Life Threatening Events", Acta Paediatrica 2000; 89: 1326-1329).