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Electroencephalography Findings in Children with Congential Heart Disease

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Abstract

Background: Children with Congenital Heart Disease (CHD) as well as survivors of cardiac surgeries are at risk for brain injury and neurodevelopmental deficits.

The Aim of this Work: Is to evaluate the Electroencephalography (EEG) findings as an indicator for cerebral function in children with congenital heart disease and to correlate these findings to the oxygen saturation.

Patients and Methods: This is a cross-sectional study included 30 patients (17 males and 13 females) with CHD (20 with cyanotic and 10 with acyanotic CHD) with age range 4-9 years. Compared with 30 age and sex matched healthy children as controls. All children underwent; digital EEG recording for detection of background slowing and epileptic changes and measurement of oxygen saturation using pulse oximeter.

Results: EEG findings were present in 17 (30%) patients (16 patients with cyanotic and 1 with acyanotic CHD). Detected EEG changes were: Epileptic activity in 6 (20%) patients (all had cyanotic CHD), background activity slowing in 16 (53.3%) patients (1 with acyanotic and 15 with cyanotic CHD), while both epileptic changes & back ground activity slowing were detected in 5 (16.7%) patients (all with cyanotic CHD). The cut off value of O_2 saturation below which background activity slowing are liable to occur was 87%, with a sensitivity and specificity of 81.2% and 71.4% respectively.

Conclusion: Children with cyanotic CHD had significantly higher EEG changes than those with acyanotic CHD.

Recommendation: The digital EEG should be performed routinely in patients with CHD (particularly cyanotic) to detect abnormalities in the cerebral function.

Key Words: *Congenital heart disease – Cyanotic – Electroencephalography – Oxygen saturation.*

Introduction

CHILDREN with severe Congenital Heart Defects (CHD) requiring open heart surgeries (especially in the first year of life) are at high risk for developing neurological and psychomotor abnormalities. Depending on the type and severity of the CHD, between 15 and over 50% of these children have deficits, which are usually confined to distinct domains of development, although formal intelligence tends to be normal. Children with mild CHD, who comprise the majority of congenital heart defects, have a far better developmental prognosis than those with complex CHD [1]. Children with cyanotic lesions will show a greater degree of cognitive impairment than those with acyanotic lesions [2], as the duration and severity of hypoxia contributes to the cognitive deficits in those children [3].

These neurodevelopmental abnormalities are clinically underappreciated [4]. Identification of such significant deficits as early as possible, allows for appropriate therapies and education to enhance later academic, behavioral, psychosocial, and adaptive functioning [5].

An accurate tool to monitor brain function is digital EEG. It is increasingly used in neonatal intensive care units to record both background patterns and electrographic seizure activity & can be used to evaluate the brain function prior to cardiac surgery, and in follow-up after surgery [6].

Patients and Methods

This is a cross sectional study including 30 children with CHD aged from 4-9 years, as well as 30 age and sex matched healthy children as controls. Patients were recruited from the pediatric cardiology clinic & inpatient Pediatric Cardiology Unit at Cairo University Children's Hospital, during the period of January 2014 to January 2015.

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Exclusion criteria were: Acquired heart diseases, prior history of convulsions, patients with family history of epilepsy and patients with other systemic diseases (i.e.; liver or renal failure and nervous system affection).

All patients were subjected to: Full history taking (with special attention to cardiac symptoms), cardiac examination & echocardiographic diagnoses were documented. All children were evaluated for respiratory and heart rates with measurement of oxygen saturation using the pulse oximeter.

Digital awake Electro-Encephalo-Gram (EEG) and brain mapping was performed for all children (patients and controls) at the Clinical Neurophysiology Unit, Cairo University Hospital, using: "EbNeuro Galileo" machine. Electrodes were placed according to the 10-20 international system of electrode placement using a cap to which the electrodes are adherent. Monopolar and bipolar montages with 21 channels were recorded for 30-40 minutes of recording. Provocative techniques like hyperventilation couldn't be done at most of patients due to their heart conditions.

The EEG machine parameters were adjusted before the recording as follows:

- *Time constant:* 0.3sec. for EEG.
- *Drawing speed:* 3.0cm/sec.
- *Filter:* 75Hz for EEG
- *Gain:* 70v/cm.

The EEG tracings were analyzed digitally and then reviewed manually as regards frequency, amplitude and symmetry of the background activity, as well as the presence of any epileptic charges.

The background slowing was defined as; if the posterior dominant background rhythm is reactive but the frequency is too slow for age. At age of 3 years; 82% of normal (full term) children show a mean occipital alpha rhythm of 8Hz mixed with theta, by 5-6 years; background become all of alpha rhythm (8-9Hz), and at 8 years; if not 8Hz so its definite abnormal [7].

The epileptic abnormalities were defined as: Spike; which is a pointed peak with 20-<70msec duration, sharp waves; pointed peak with 70-200 msec duration, polyspikes or spike and wave complexes. These abnormalities could be: Focal, generalized or focal with secondary generalization. Epileptiform activity was considered lateralized if more than 80% of the discharges originated from one side.

Spectral analysis:

Artifact free recordings were selected. Ten epochs of 10 seconds each were analyzed by applying Fast Fourier Transfor-Spectral EEG and the mean absolute power spectrum are calculated for the frequencies of delta (1-4c/s), theta (5-7c/s), alpha (8-12c/s), beta (>13c/s) waves.

Normal reference patterns for, EEG were established from the evaluation of cerebral function in healthy subjects matched for age and sex. The patient's parents attended during the recording sessions for reassurance of the patients and to report any abnormal events, this criterion can increase the diagnostic accuracy of this tool, oral informed consent was obtained from all parents.

Statistical analysis:

Data were statistically described in terms of mean ± standard deviation (± SD), or frequencies (number of cases) and percentages when appropriate (the data was normalized if not, by using square root). Comparison of numerical variables between the study groups was done using student *t*-test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed.

Accuracy was represented using the terms sensitivity, and specificity. Receiver Operator Characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. Pearson correlation coefficient (*r*) was used to measure correlation between quantitative variables. (*p*-value) less than 0.05 was considered statistically significant and less than 0.01 was considered statistically highly significant.

All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 20 for Microsoft Windows (2010).

Results

Patients' characteristics:

The study included 30 patients with CHD (17 males and 13 females), their ages ranged from 4 to 9 years with a mean of (5.84±1.54 years). Compared to 30 healthy children with matched sex and age (14 males and 16 females), as controls, their mean ages were (5.89±1.31 years) with (p<0.05).

The mean weight among the patients and controls was (16.33±4.27 and 19.9±3.16kg) respectively, while their mean height was (105.34±16.8 cm) for patients and (1 13.07±10.54cm) for controls. The patients had significantly lower anthropometric

values (weight, height) than control group with (p<0.05) (Table 1).

On comparing the mean values of oxygen saturation, heart rate and respiratory rate between patients and controls we found highly significant difference between both groups (p<0.01).

In 9 (30%) patients there was history of prior cardiac surgery, either open in 5 (16.7%) patients or closed heart surgeries in 4 (13.3%) patients.

Patients were classified into two groups according to the type of the cardiac lesion and their oxygen saturation, namely:

A- Patients with acyanotic heart diseases which included 10 (33.3%) patients.

B- Patients with cyanotic heart diseases including 20 (66.7%) patients.

EEG finding among patients with congenital heart diseases:

Abnormal EEG findings were present in 17 (56.7%) patients while none of the control group showed abnormal EEG changes.

EEG abnormalities detected were in the form of:

A- Epileptic changes were found in 6 (20%) patients.

B- Background activity slowing detected in 16 (53.3%) patients.

C- Both epileptic changes & back ground activity slowing were found in 5 (16.7%) patients.

On comparing the EEG findings between patients with cyanotic & acyanotic heart diseases, cyanotic patients had background slowing in 15 patients, compared to 1 acyanotic patient. While epileptic changes were found in 6 patients in comparison to 0 patients with acyanotic heart diseases. Both epileptic changes and background activity slowing were found in 5 cyanotic patients compared to 0 acyanotic patients. And this was statistically highly significant (p-value <0.001) (Table 2). Also, 5/9 patients with cardiac surgery had abnormal EEG findings; 1 patient had background slowing, 1 had epileptic changes and 3 patients had both slowing and epileptic changes.

Correlations:

On correlating the EEG findings with the other parameters we found; highly significant correlation between background slowing and presence of cyanosis, and significant negative correlation between slowing and oxygen saturation. Epileptic changes were significantly correlated with the presence of previous operation. High significant correlation between oxygen saturation and cyanosis was present, (Table 3).

When performing the receiver-operator characteristic (ROC) curve analysis to determine the cutoff values of oxygen saturation below which background slowing are liable to occur was (0.87), which gives a sensitivity of 81.2% and 71.4% specificity (Table 4). When performing the (ROC) curve analysis for the epileptic changes, no cut off value could be obtained.

Table (1): Demographic data comparison between patients and control.

Variable	Patients (n=30) Mean ± SD	Control (n=30) Mean ± SD	p-value
Age (in years)	5.84±1.54	5.89±1.31	0.886
Weight (in Kg)	16.33±4.27	19.9±3.16	0.001**
Height (in cm)	105.34±16.8	113.07±10.54	0.032*

SD: Standard Deviation.
p-value <0.05: Significant*.
p-value <0.01: Highly significant**.

Table (2): Showed EEG findings among the patients.

Variable	Cyanotic CHD (n=20) (%)	Acyanotic CHD (n=10) (%)	Total numbers (n=30) (%)	p-value
• Background slowing only	10 (50)	1 (10)	11 (36.7)	<0.001**
• Epileptic changes only	1 (5)	0 (0)	1 (5)	
• Both	5 (25)	0 (0)	5 (16.7)	

p-value <0.01: Highly significant**.

Table (3): Correlations between different parameters in the patient group.

	Oxygen saturation	Background slowing	Epileptic changes	Cyanosis	Cardiac operation
Oxygen saturation:					
(r)		–0.367	–0.161	–0.798	–0.222
p-value		0.046*	0.395	0.000**	0.237
Background slowing:					
(r)	–0.367		0.301	0.614	–0.117
p-value	0.046*		0.106	0.000**	0.539
Epileptic changes:					
(r)	–0.161	0.301		0.354	0.400
p-value	0.395	0.106		0.055	0.028*
Cyanosis:					
(r)	–0.798	0.614	0.354		0.154
p-value	0.000**	0.000**	0.055		0.416
Cardiac operation:					
(r)	–0.222	–0.117	0.400	0.154	
p-value	0.237	0.539	0.028*	0.416	

(r): Correlation coefficient.
p-value <0.05: Significant*.
p-value <0.01: Highly significant**

Table (4): ROC curve analysis of oxygen saturation to detect background slowing.

Area under the curve	82%
Standard error	0.088
95% confidence interval	0.653–0.999
p-value	0.002*
Cutoff value	>0.87
Sensitivity	81.2%
Specificity	71.4%

p-value<0.05: Significant*

Discussion

In our study, patients with CHD showed significantly lower mean weight & height than the control group. The study done by Cheung et al., had similar results as they found that more than 50% of their patients fall below the 16 th centile for weight and height [8]. Weintraub and Menahem also found that 25-30% of their patients fall below the 3 rd centile for both parameters in their previous study [9]. Failure of growth is common in patients with congenital cardiac malformations, and may be related to congestive heart failure and/or hypoxia as repair of simple lesions appears to reverse the retardation in growth. This growth failure could have many explanations, as hemodynamic disturbances, higher basal metabolic rates and decreased caloric intake, also the degree of growth impairment did not always correlate with the severity of the cardiac lesion [9].

Our study showed that (56.7%) of the patients had EEG abnormalities. EEG changes were in the form of: Epileptic activity in (20%), background activity slowing in (53.3%) or both in (16.7%). Similarly, Horst et al., demonstrated in their study, that (60%) of the infants with CHD had mild to severe abnormal EEG background pattern at some point during the recording period [6]. Epileptic activity appeared in (19%) of the infants which was also comparable with data reported by Limperopoulos et al., and El-Nagger et al., [10,11].

Another study performed by Aberastury et al. to detect abnormal cerebral function in neonates with congenital heart disease, revealed that (70%) of patients had EEG abnormalities with (35%) of them had moderate abnormalities with focal epileptiform activity [12], while Clancy et al., reported EEG changes in the absence of obvious clinical seizure in (11.5%) of neonates with CHD in their study [13].

In our study, EEG changes were more frequent in cyanotic CHD than those with acyanotic heart disease (53.3% and 3.3% respectively). Epileptic changes and background slowing were found in (20% and 50% respectively) of cyanotic while only one acyanotic patient had background slowing. Both epileptic changes and background slowing were found in (16.7%) of cyanotic patients compared to (0%) of acyanotic patients. This goes in line with many previous studies, which reported more common neurological abnormalities in cyanotic infants [4,10,14,15]. Although, the results obtained by Horst et al., Limperopoulos et al., and Rosenblatt, revealed that background patterns emerged equally often in infants with acyanotic and infants with cyanotic CHD and surprisingly, epileptic activity was more frequent in infants with acyanotic CHD [6,14,16]. This discrepancy between our results and their results may be due to the difference in the study design as they included infants with previous history of convulsions, while we excluded such patients from our study. Also Horst et al., used amplitude integrated EEG which records only one channel [6], while conventional EEG (used in our study) always will provide more detailed information, but recordings are often shorter [17].

EEG abnormalities may be explained by many factors including associated genetic syndromes, potential risk of hypoxia, acidosis, and hypotension, all of which may increase the risk of neurodevelopmental delay [4,14,18,19]. Contributing factors include, associated congenital brain anomalies, coexisting genetic disorders that result in brain dysfunction, cerebrovascular complications, and complications of therapy. In addition to the developmental lesions previously mentioned, acquired lesions may be detectable in babies with CHD [20].

In the current work, we found that 5/9 (55.6%) patients with previous cardiac surgery had an abnormal EEG findings, also 3/5 patients with both epileptic changes and background slowing, showed history of previous cardiac operation, however we lack the early post-operative data and also the number of patients was too small. Post-operative EEG abnormalities were also reported in many studies where the incidence of post-operative seizure detected by continuous EEG monitoring was 12-20% of patients in the 48 hours following surgery [13,17,21,22]. And could be recorded in up to 56% of patients after the first week of surgery [15]. Many factors during the cardiac surgery could affect the brain development, longer ventilation duration and longer intensive care stay were associated with a greater risk for an abnormal post-operative background pattern abnormality and epileptic activity [17].

In our study we estimated that the cut off value of O_2 saturation below which background activity

slowing are liable to occur was 87%. To the best of our knowledge, only few papers were concerned with noninvasive O_2 saturation monitoring and its relation to EEG abnormalities as Donofrio and Massaro who reported that cyanotic infants with an oxygen saturation <85% had a higher incidence of abnormalities in the form of background activity disturbance and epileptiform activity **[20]**.

In our result we found negative significant correlation between oxygen saturation and background slowing in EEG. Reduction in oxygen delivery initiates the shift to anaerobic metabolism which results in rapid depletion of energy reserves, accumulation of lactic acid, and the inability to maintain cellular functions. This energy failure will eventually cause neuronal cell death in the developing brain **[6]**.

As the mortality rate for all congenital heart surgeries decreasing to be 1-2% in many large experienced centers, attention has increasingly turned to other morbidities affecting quality of life especially neurological outcome. Many non-invasive monitors for cerebral oxygenation, blood flow and EEG can improve the outcome and most importantly the quality of life of our patients **[23]**.

Limitations:

Our study had some limitations, first the small number of patients with many heterogeneous characteristics (cyanotic and acyanotic, pre-operative and post-operative). Another limitation of our study is that we do not have early post-operative data and long-term follow-up. Third, the intra-operative management strategies were not standardized.

Conclusion:

The early & sustained exposure to hypoxia in patients with CHD results in significant cerebral function changes in the form of background slowing, epileptic changes or both.

References

1- HERBERG U. and HÖVELS-GÜRICH H.: Neurological and psychomotor development of fetuses and children with CHD-causes and prevalence of disorders and longterm prognosis. Z Gegurtshilfe Neonatal, 216: 132-40, 2012.

2- WRAY J. and SENSKY T.: CHD and cardiac surgery in childhood: Effects on cognitive function and academic ability, Heart, 85: 687-91, 2001.

3- REYES D.L.E. and ROACH S.E.: Chapter 5 Neurologic complications of congenital heart disease and its treatment. In: Handbook of Clinical Neurology. Neurologic Aspects of Systemic Disease Part I. 1 st edition, Jose Biller and Jose M. Ferro, (Editors). Elsevier B.V.: 49-59, 2014.

4- LIMPEROPOULOS C., MAJNEMER A., SHEVELL M.I., ROSENBLATT B., ROHLICEK C. and TCHERVENKOV C.: Neurodevelopmental status of newborns and infants with congenital heart defects before and after open heart surgery. J. Pediatr., 137: 638-45, 2000.

5- MARINO B.S., LIPKIN P.H., NEWBURGER J.W., PEACOCK G., GERDES J. and GAYNOR W.: Neurodevelopmental outcomes in children with CHD: Evaluation and management. Circulation, 126: 1143-72, 2012.

6- HORST H.J., MUD M., ROOFTHOOFT M.T.R. and BOS A.F. : Amplitude integrated electroencephalographic activity in infants with congenital heart disease before surgery. Early Human Development, 86: 759-64, 2010.

7- LUDERS H. and NOACHTAR S.: Atlas and Classification of Electroencephalography. 2 nd Edition, Saunders WB., (Editor), Philadelphia: 300-20, 2000.

8- CHEUNG M.M., DAVIS A.M., WILKINSON J.L. and WEINTRAUB R.G.: Longterm somatic growth after repair of tetralogy of Fallot: Evidence for restoration of genetic growth potential. Heart, 89 (11): 1340-3, 2003.

9- WEINTRAUB R.G. and MENAHEM S.: Early surgical closure Of a large ventricular septal defect: Influence on long-term growth. J. Am. Coll. Cardiol., 18: 552-8, 1991.

10- LIMPEROPOULOS C., MAJNEMER A. , ROSENBLATT B., SHEVELL M.I., ROHLIECK C. and TCHERVENKOV C.: Association between electroencephalographic findings and neurologic status in infants with congenital heart defects. J. Child. Neurol., 16: 471-6, 2001.

11- EL-NAGGER W.I., KEYZERS M. and MC-NAMARA: Role of amplitude-integrated electroencephalography in neonates with cardiovascular compromise. J. Crit. Care, 25: 317-21, 2010.

12- ABERASTURY M., AGOSTA G.E., PUGA C., VACCAREZZA M.M., MAXIT C. and SILVA W.H.: Neurological Outcomes in Newborns with Congenital Heart Disease and Seizures. JICNA., 15: 103, 2015.

13- CLANCY R.R., SHARIF U., ICHORD R., SPRAY T.L., NICOLSON S. and TABBUTT S.: Electrographic neonatal seizures after infant heart surgery. Epilepsia, 46 (1): 84-90, 2005.

14- LIMPEROPOULOS C., MAJENEMER A., SHEVELL M.I., ROSENBLATT B., ROHLICEK C. and TCHERVENKOV C.: Neurologic status of newborns with congenital heart defects before open heart surgery. Pediatrics, 103: 402-8, 1999.

15- CHOCK V.Y., REDDY V.M., BERNSTEIN D. and MADAN A.: Neurologic events in neonates treated surgically for congenital heart disease. J. Perinatol., 26: 237-42, 2006.

16- ROSENBLATT B.: Monitoring the central nervous system in children with congenital heart defects: Clinical neurophysiological techniques. Semin. Pediatr. Neurol., 6: 27-31, 1999.

17- GUNN J.K. and HUNT R.W.: Amplitude-integrated Electroencephalography following infant cardiac surgery: A window to the brain or a crystal ball. Available at: www.Jpeds.com, 2016.

18- GAYNOR J.W., WERNOVSKY G., JARVIK G.P., BERNBAUM J., GERDES M., ZACKAI E., NORD A.S., CLANCY R.R., NICOLSON S.C. and SPRAY T.L.: Patient characteristics are important determinants of neurodevelopmental outcome at one year of age after neonatal

and infant cardiac surgery. Thorac. cardiovasc. Surg., 133: 1344-53, 2007.

19- ZELTSER I., JARVIK G.P. and BERNBAUM J.: Genetic factors are important determinants of neurodevelopmental outcome after repair of tetralogy of Fallot. J. Thorac. Cardiovasc. Surg., 135: 91-7, 2008.

20- DONOFRIO M.T. and MASSARO A.N.: Impact of congenital heart disease on brain development and neurodevelopmental outcome. Int. J. Pediatr., 2010: 1-13, 2010.

21- GAYNOR J.W. and JARVIK G.P.: "The relationship of postoperative electrographic seizures to neurodevelopmental outcome at 1 year of age after neonatal and infant cardiac surgery," Journal of Thoracic and Cardiovascular Surgery, 131: 181-9, 2006.

22- CLANCY R.R. and MC-GAURN S.A.: "Risk of seizures in survivors of newborn heart surgery using deep hypothermic circulatory arrest," Pediatrics, 111: 592-601, 2003.

23- STAYREC S.A., RUSSELL I.A. and MOSSAD E.B.: Neurologic monitoring during cardiac surgery. In Anaesthesia for congenital heart disease. 2 nd edition. Andropoulos D.B. (editor), Blackwell Publishing Ltd. Hobokin: 2060-6, 2011.

نتائج رسم المخ الكهربائى فى الأطفال المصابين بأمراض القلب الخلقية

هذا البحث يهدف إلى دراسة التغيرات الدماغية التى تحدث فى الأطفال المصابين بأمراض القلب الخلقية بعد تشخيصهم (بإستخدام تخطيط صدى القلب) فى صورة تغييرات فى رسم المخ الديچيتال، تضمنت الدراسة ٦٠ طفل (٣٠ طفل تم تشخيصهم بأمراض القلب الخلقية و٣٠ طفل طبيعى). تم تقسيم الأطفال المصابين إلى مجموعتين (مجموعة مصابة بأمراض القلب الخلقية المسببة للزرقة وبها ٢٠ طفل ومجموعة بها ١٠ أطفال مصابين بالمرض بدون زرقة). وقد أوضحت الدراسة وجود تغيرات دماغية بنسبة أكبر فى الأطفال ذوى أمراض القلب الخلقية المسببة للزرقة فى صورة بطء فى رسم المخ الديچيتال بنسبة ٥٠٪ وفى صورة صرع بنسبة ٥٪ وفى صورة صرع وبطء فى رسم المخ الديچيتال بنسبة ٢٥٪، أما فى الأطفال ذوى أمراض القلب الخلقية الغير المسببة للزرقة فكانت التغيرات الدماغية فى صورة بطء فى رسم المخ الديچيتال بنسبة ١٠٪، وبالتالى فإن التعرض المبكر والمستمر لنسبة منخفضة من الأكسچين تؤدى إلى تغيرات فى الوظائف الدماغية فى صورة تغييرات فى رسم المخ لذلك يوصى بعمل رسم المخ الديچيتال لجميع الأطفال المصابين بأمراض القلب الخلقية وأيضاً يوصى بالتدخل المبكر لرفع نسبة الأكسچين لدى الأطفال ذوى أمراض القلب الخلقية المسببة للزرقة وذلك للحد من تأثير الزرقة ونقص الأكسچين على الوظائف الدماغية.