The Role of Amplitude Integrated Electroencephalography (a-EEG) in Neonates

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Abstract

Background: Amplitude-integrated electroencephalography (aEEG) is a method for continuous monitoring of brain activity that is increasingly used in the neonatal intensive care unit. In its simplest form, aEEG is a processed single-channel electroencephalogram that is filtered and time-compressed. It is useful to monitor cerebral background activity, diagnose and treat seizures and predict neurodevelopmental outcome.

Aim of the Work: Is to identify the role of a-EEG in neonates with different gestational ages, diseases, circumstances.

Patients and Methods: The study was carried out on 40 neonates (20 patients & 20 controls) admitted in International Tanta University Hospital NICU. Amplitude integrated EEG was done by Nicolet EEG v32. aEEG was recorded from 2 channels: F3-P4 & P3-P4.

Results: All controls had normal aEEG while 14 of 20 patients had normal aEEG and 6 had abnormal aEEG. The sensitivity of aEEG for detection of neurological abnormalities was 71.4% and specificity was 92.3%. There was significant difference between aEEG in preterm and full term as regards background activity and sleep wake cycling. Normal aEEG corresponded with normal EEG in 92.85% of the patients, and abnormal aEEG corresponded with abnormal EEG in 83.34% of the patients. 66.67% of patients with abnormal aEEG died and 33.33% had been discharged while 92.85% of patients with normal aEEG had been discharged and 7.15% died.

Conclusion: aEEG is a simple, inexpensive bedside modality that has a great role in monitoring brain function in neonates, predicting neurological outcome and demonstrating brain maturation.

Key Words: a-EEG – Neonatal brain function – Brain monitoring – Outcome.

Introduction

AMPLITUDE-integrated electroencephalography (aEEG) was first introduced in the 1960s by Maynard et al., as an instrument to study cerebral activity in resuscitated patients with suspected brain damage. Referred to as the cerebral function monitor (CFM), its application evolved over the next two decades to include neonates, both term and preterm [1].

Amplitude-integrated electroencephalography (aEEG) is a bedside brain monitoring tool that has gained widespread acceptance in neonatal intensive care units (NICUs) around the world [2]. aEEG uses a limited number of channels to record raw EEG signal that is then filtered, rectified, processed, and displayed on a semilogarithmic amplitude and time-compressed scaled, providing an overview of trends in cerebral background activity and the occurrence of seizures [3]. Continuous aEEG monitoring offers a possibility to directly monitor the functional state of the brain over hours and days [4].

Typically, leads are placed on a single pair of biparietal locations (P3 and P4) or modified to add an additional lead on each side (C3 and C4) according to International 10-20 system modified for neonates [5].

aEEG interpretation is to evaluate background pattern, seizure activity and sleep-wake cycles:

The background activity is the dominant pattern of electrical activity in the aEEG tracing. It is classified by the lower margin amplitude and upper margin amplitude of the activity band to Continuous (C), Discontinuous (DC), Burst Suppression (BS), Low voltage (LV) & Flat (FT) [6].
Seizures in aEEG appear as an abrupt rise in minimum and maximum amplitude, often followed by a postictal phase of decreased amplitude [7]. Sleep-wake cycling refers to cyclic fluctuation in the amplitude as the neonate enters various stages of sleep or wakefulness. On aEEG, this is reflected by the presence of smooth sinusoidal variation, mostly in the minimal amplitude [8].

**Aim of the work:** Is to identify the role of a-EEG in neonates with different gestational ages, diseases, circumstances.

**Patients and Methods**

This case control study was conducted on 40 neonates (20 patients & 20 controls) at the International Tanta University Hospital NICU from 1 March to 31 August 2016.

All patients were subjected to:
A- Full history taking and thorough clinical examination.

**B- Investigations:** Complete blood count, renal functions, liver functions, C reactive protein (CRP), capillary blood gases, serum electrolytes (Na, K, Ca, Mg), sepsis work up and neuroimaging when indicated.

C- Amplitude integrated EEG and conventional EEG were done by Nicolet EEG v32. Recording was done using caps including electrodes of 10-20 system modified for neonates. Recording was done for varying duration with minimum of 3 hours and maximum of 24 hours with speed of 30mm/sec, sensitivity 70µv/cm and impedance threshold 20 kohm. aEEG was recorded from 2 channels: F3-F4 & P3-P4.

**Results**

This study was carried out on 40 neonates (20 patients & 20 controls). All controls had normal aEEG while 14 of patients had normal aEEG and 6 had abnormal aEEG Table (1).

<table>
<thead>
<tr>
<th>Patients</th>
<th>Background</th>
<th>Seizures activity</th>
<th>Sleep wake cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male full term infant aged 3 days on MV with HIE grade 3 &amp; convulsions</td>
<td>Burst suppression</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Female full term infant aged 25 days with cyanotic congenital heart disease &amp; convulsions</td>
<td>Discontinuous</td>
<td>Yes</td>
<td>Developed</td>
</tr>
<tr>
<td>Female full term infant aged 40 days with disturbed consciousness due to traumatic intracranial hemorrhage</td>
<td>Continuous</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Male full term infant aged 3 days with disturbed consciousness due to inborn error of metabolism</td>
<td>Discontinuous</td>
<td>No</td>
<td>Immature</td>
</tr>
<tr>
<td>Male full term infant aged 5 days on MV with HIE grade 3 &amp; convulsions</td>
<td>Burst suppression</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Male full term infant aged 30 days with operated TOF &amp; sepsis</td>
<td>Discontinuous</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
There was significant difference between patients with normal and abnormal aEEG as regard the presence of abnormal neurological examination. The sensitivity of aEEG for detection of neurological abnormalities was 71.4% and specificity was 92.3%. There was significant difference between patients with seizures activity in aEEG as regards the presence of clinical seizures ($p$-value <0.05) as 75% of patients with seizures activity in aEEG had clinical seizures and 25% of them had no clinical seizures, while 100% of patients with no seizures activity in aEEG had no clinical seizures Table (2).

There was significant difference between aEEG in preterm and full term as regards background activity and sleep wake cycling, Figs. (1,2).

We performed aEEG and simultaneously recorded EEG and revealed that normal aEEG corresponded with normal EEG in 92.85% of the patients, and abnormal aEEG corresponded with abnormal EEG in 83.34% of the patients. aEEG sensitivity for detection of seizure activity in cEEG was 80% and the specificity was 100%. Table (3).

There was significant difference between patients with normal and abnormal aEEG as regard short term outcome ($p$-value <0.05) as 66.67% of patients with abnormal aEEG died and 33.33% had been discharged while 92.85% of patients with normal aEEG had been discharged and 7.15% died.

| Table (2): Seizures activity in aEEG and clinical seizures of the studied patients. |
|-----------------------------------------------|-----------------------------------------------|
| Clinical seizures | Seizures activity in aEEG | Chi-Square |
|                  | Yes (N) | % | No (N) | % | Total (N) | % | $X^2$ | $p$-value |
| No               | 1 | 25.00 | 16 | 100.00 | 17 | 85 | 8.848 | 0.003* |
| Yes             | 3 | 75.00 | 0 | 0.00 | 3 | 15 | | |
| Total           | 4 | 100.00 | 16 | 100.00 | 20 | 100.00 | | |

| Table (3): Comparison between conventional EEG and aEEG of the studied patients. |
|-----------------------------------------------|-----------------------------------------------|
| cEEG | Normal aEEG | Abnormal aEEG | Total | Chi-Square |
|      | N | % | N | % | N | % | $X^2$ | $p$-value |
| Normal | 13 | 92.85 | 1 | 16.66 | 14 | 70.00 | 15.522 | <0.00* |
| Abnormal | 1 | 7.15 | 5 | 83.34 | 6 | 30.00 | | |
| Total | 14 | 100.00 | 6 | 100.00 | 20 | 100.00 | | |

Fig. (1): Background activity in preterm and full term.

Fig. (2): Sleep wake cycling in preterm and full term neonates.
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Fig. (3): Abnormal aEEG of a female neonate with GA 38 weeks & CA 44 weeks with disturbed consciousness due to traumatic intracranial hemorrhage on mechanical ventilator showing seizures activity.

Fig. (4): Normal aEEG of a male neonate with GA 37 weeks & CA 39 weeks with Down syndrome on mechanical ventilator: continuous background, no epileptic activity, developed SWC. The two aEEG channels (p3-p4 & f3-f4) are shown.

Discussion

Our study revealed that there was significant difference between patients with normal and abnormal aEEG as regard neurological examination. The sensitivity of aEEG for detection of neurological abnormalities was 71.4% and specificity was 92.3%. This is very important as infants with severe respiratory distress can manifest decreased activity, poor tone, and sluggish response to stimuli. Assessment of consciousness level can be performed in very sick infants, but is often obscured by the sedative-hypnotic agents used in conjunction with respiratory support. The aEEG provides an attractive means to assess the integrity of the central nervous system of infants who are critically ill as proved by Toso et al., [9].

This study showed that there is a great role of aEEG in diagnosis and management of neonatal seizures as 75% of patients with seizures activity in aEEG had clinical seizures and 25% of them had no clinical seizures which is similar to results found by Shellhaas and Barks & Hellström-Westas et al., [10,11].

Shellhaas and Barks demonstrated that the introduction of aEEG did not change some aspects of clinical care, such as anticonvulsant drug treatment and the number of neuroimaging studies performed. However, they did find that fewer patients were diagnosed clinically with seizures, without electrographic confirmation, following the introduction of aEEG into NICU [10].

Hellström-Westas et al., also found that differentiating epileptic seizures from non-epileptic movements in severely ill newborns was possible with the use of aEEG [11].

In our study, aEEG sensitivity for detection of seizure activity in cEEG was 80% and the specificity was 100%. Similar to our findings, Bourrez-Swart et al. reported that even a single-channel aEEG may help identify most newborns with severe neonatal seizure patterns with the sensitivity of 92%, however, the use of multiple channels cEEG, results in identification of all patients with seizure patterns (sensitivity of 100%) [12].

Shah DK et al., also reported 76% accuracy of aEEG versus EEG in non-status epilepticus seizures. This sensitivity is adequate, and suggests aEEG could be used for detection of seizure activity, but aEEG is less accurate at detecting short, focal or low amplitude seizures [13].

In the present study, there was significant difference between aEEG in preterm and full term as regards background activity and sleep wake cycling. We found that in preterm the discontinuous background was most common (63.16%) while in full terms the continuous background dominated (85.71%). Developed sleep wake cycling was detected in 66.67% of full term neonates but in preterms, immature sleep wake cycling was detected in 52.63%, similar findings were reported by Griesmaier et al., and Ter Horst et al., [14,15].

In the present study, we performed aEEG and simultaneously recorded EEG and revealed that normal aEEG corresponded with normal EEG in 92.85% of the patients, and abnormal aEEG corresponded with abnormal EEG in 83.34% of the patients. This is similar to Toet et al., who found that a normal aEEG corresponded with a normal or a depressed EEG in 90% of the cases. The positive predictive value for a severely abnormal aEEG to correspond with a severely abnormal EEG was 100% [16].

The main limitation of our study is the small sample size and it did not follow-up the patients to predict long term outcome. Klebermass et al., reported that the presence of an abnormal aEEG-
pattern-score within the first 2 weeks of life was highly predictive for adverse long term outcome with a specificity of 94% and sensitivity of 81% [17].

Conclusion:
aEEG has a great role in monitoring brain functions in neonates and should be included in all NICUs.

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Conflicts of interest:
No conflicts of interest declared.

Authors’ contributions:
All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

References
دور رسم المخ في حديثي الولادة

رسم المخ هو تسجيل النشاط الكهربائي في الدماغ على مدى فترة من الزمن عن طريق أقطاب متعددة توضع على فروة الرأس. أما رسم المخ المتكامل يستخدم عدد محدد من الأقطاب لتسجيل رسم المخ التقليدي ثم يقوم بتصحيحه ومعالجته ووضعه في صورة رسم بياني لوحارتي.

يشير رسم المخ المتكامل أداء مهمة تقدير الجهاز العصبي في أطفال حديثي الولادة على الحالات الصحية المرتبطة حيث يمكن عمل رسم المخ المتكامل باستخدام للتدابير وظائف المخ خلال ساعات أو أيام.

الهدف من الدراسة: هو دراسة أهمية رسم المخ المتكامل في حديثي الولادة في مختلف الأعمار الجنينية والأمراض والظروف.

المرضى وطرق البحث: تم عمل هذه الدراسة على 40 من الأطفال حديثي الولادة (20 مريض - 20 أصهار) في حضانات مستشفى طنطا الجامعي العامي. تم عمل رسم المخ المتكامل عن طريق جهاز Nicolet EEG32.

النتائج: 14 من المرضى حصلوا على رسم المخ المتكامل طبيعي و 6 غير طبيعي بينما جميع الأطفال الأصحاء حصلوا على رسم المخ المتكامل طبيعي. يختلف الأطفال الغير مكتمل الدمو عن مكتمل الدمو في رسم المخ المتكامل من حيث الخلفية ودورة الدمو والنظرة. تبين أيضاً أن رسم المخ المتكامل يساعد في التنبؤ بصغر المرضى على مدى القريب حيث توفرت 34.7% من المرضى ذو الرسم غير الطبيعي بينما توفرت 57.1% من المرضى ذو الرسم الطبيعي.

الاستنتاج: رسم المخ المتكامل له دور مهم في الأطفال حديثي الولادة.

الوصولات: تحتوى في عمل رسم المخ المتكامل لجميع حالات حديثي الولادة في الحضانات كفحص روتيني لرصد التغيرات في نشاط المخ مبكرة كما تؤدي بتدريب طاقم التمريض المقابل على توصيات الجهاز وقراءة الرسم.