Glasgow Coma Scale, Brain Computerized Tomography and Neurophysiological Methods as Prognostic Factors of Pediatric Coma

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Abstract

Background and objectives: Coma is characterized by the total absence of both arousal and awareness. The outcome of coma depends on the etiology, depth and duration of impaired consciousness.

It is likely that brain electrical function monitoring will play an increasingly important role in evaluating prognosis of coma in children.

Aim: To compare the predictive values of clinical examinations combined with the recordings of Electroencephalography (EEG) and Brainstem Auditory-Evoked Potentials (BAEP) and computed tomography (CT) of the brain in the evaluation of coma outcome in children.

Methods: Twenty children with coma aged 3-14 years were included in the study and subjected to: full history, clinical, neurological and ophthalmological examination. Medical investigations for coma, EEG, CT brain and auditory brainstem evoked potential (BAEP) measurements were performed for all patients. They were subdivided into 2 groups: group 1 included 8 patients with surgical causes of coma, group 2 include 12 patients with medical causes of coma.

Results: There was younger age, lower Glasgow Coma Scale (GCS) and more significant incidence of unfavourable outcome (death, disability) in patients of surgical coma (group 1). A significant difference between both groups was observed regarding the presence of brain edema and intracranial hemorrhage (100% in group 1) while normally visualized basal cisterns were significantly more in group (2) (p=0.02). Favorable outcome was strongly related to normally visualize basal cisterns in CT brain (p=0.002), normal/borderline EEG activity (p=0.03) and normal BAEP waves (p=0.009). Disability was significantly related to slow activity waves (p=0.015) and diffuse high voltage EEG discharges (0.009). While mortality was significantly related to the presence of intracranial bleeding in CT brain (p=0.02), silence EEG waves (p=0.005) and absent BAEP waves (0.012).

Conclusion: EEG and Auditory brainstorm response are valuable as prognostic predictors of pediatric coma either due to medical or surgical causes. The Glasgow Coma Scale (GCS) has several important limitations as a predictor of survival in the general critically ill population while CT brain is mostly important for diagnostic rather than prognostic factor in comatosed children.

Introduction

Coma and other states of impaired consciousness represent a medical emergency in pediatric Intensive Care Unit (ICU). The potential causes are numerous, and the critical window for diagnosis and effective intervention is often short. The common causes of non-traumatic coma include central nervous system infections, metabolic encephalopathy (hepatic, uremic, diabetic ketoacidosis, etc…), intracranial hemorrhage, and stroke and status epilepticus [1].

The incidence of non-traumatic coma is about 30/100,000 children per yr, and that of traumatic brain injury is about 670/100,000 [2].

The Glasgow Coma Scale (GCS) is a powerful predictor of survival and neurologic outcomes after head trauma, non-traumatic coma, ischemic stroke, subarachnoid hemorrhage, intracerebral hemorrhage, and meningitis. The GCS is also an independent predictor of survival in the general critically ill population and has been incorporated into a number of widely used prognostic intensive care scoring systems [3,4].

Computed Tomography (CT) of the brain is warranted in virtually all patients with an acute onset of unexplained coma. CT will readily identify intracranial hemorrhage, hydrocephalus, brain edema, and compartmental shift and may suggest stroke, abscess, or tumor. CT brain has an unrevealing value in most instances of hypoxic ischemic or toxic-metabolic coma [5].

Neurophysiological methods [Electro-encephalogram (EEG) and Evoked Potentials (EPs)] provide functional assessment of the Central Nervous System (CNS). EEG is a dynamic physiologic process when it is important to evaluate events of time and space in neuronal network, so called time-space biodynamic of neuronal activity. The EEG reflects cortical neuronal activity modulated by both physiological and pathological diencephalic and brainstem influences and possibly affected by metabolic and/or toxic factors [6].

Evoked Potentials (EPs) remain a unique tool to demonstrate brainstem dysfunction interfering with Brainstem Auditory Evoked Potentials (BAEPs) and/or Somatosensory Evoked Potentials (SEPs). In some instances, BAEPs can demonstrate unexpected brainstem lesions in patients who were initially considered as post-anoxic, in which case heart failure or respiratory arrest are likely to be the consequence of primary brainstem damage rather than the primary cause of coma. Auditory Brainstem Response (ABR) represents the far field synchronous activity produced by neuronal fiber tracts of eighth
cranial nerve and auditory brain stem pathway. The defect in BAEPs waves morphology and interpeak latency or interural difference of wave latencies represents the most common disorders for neuro-otologic evaluation [7].

BAEP is used with expectation to evaluate disturbances of sensorineural pathways, identify the lesion of the brain tissue that is invisible in clinical evaluation or Computer Tomography (CT). The use of auditory evoked potentials (AEPs) offered greater precision than EEG parameters in evaluating neurological function because responses to stimulation of specific populations, or groups, of neurones could be identified. In contrast, EEG parameters, because of their simplified yet increasingly quantitative nature, permit electrical activity of the brain to be observed at any given moment [8].

The aim of the study was to compare the predictive values of clinical examinations combined with the recordings of Electroencephalography (EEG), Brainstem Auditory-Evoked Potentials (BAEP) and Computed Tomography (CT) of the brain in evaluation of coma outcome in children.

Methods

This was a prospective observational study conducted at ICU of Pediatric, Anaesthesia and Otorhinolaryngological departments, Zagazig University Hospitals on 20 comatose patients including 11 males and 9 females with coma. They were subdivided into 2 groups: surgical and medical coma. Their mean age ranged between 3 to 14 years, treated and observed during the period between December 2009 to June 2011.

Coma was defined as state of unresponsiveness without evidence of awareness of self or environment from which the patient cannot be aroused by vocal or sensory stimuli. A score of 8 or less on Glasgow Coma Scale (pediatric adaptation) was mandatory [9].

Eight patients of surgical coma were included in this study: 4 with traumatic intracranial hemorrhage, 4 subarachnoid hemorrhage. While 12 children of medical causes of coma included: 1 patient with brain abscess, 1 brain tumour, 3 meningocencephalitis, 2 diabetic ketoacidosis (DKA), 2 uremia, 2 respiratory failure and 1 hypertensive encephalopathy.

All patients were subjected to:

• Full history taking.
• Thorough physical examination: including daily recording of the Glasgow Coma Scale (GCS)
• Routine laboratory investigations: including
  1. Complete blood picture, ESR, liver function tests and thyroid function were assessed
  2. Blood glucose, urea and serum creatinine.
  3. Serum electrolytes and arterial blood gases (ABG).
• Routine coma care of children in ICU: both medical and surgical.
• Complete ear examination and tympanometric evaluation to exclude any external and/or middle ear pathology as it may affect results of Auditory Brainstem Response (ABR).
• CT brain was done on admission and on routine follow up.

In the present study, the first EEG was performed within the first 24 hours after admission as recommended by Synek [10]. EEG was recorded using an on-line 16-channel.

EEG system (Siemens-Elema system, Sweden). Sixteen scalp electrodes were applied according to international EEG 10-20 system. EEG data were collected using both referential linked ears; low frequency filter was set at 0.3 Hz and the high frequency filter at 30 Hz.

Visual analysis of the raw EEG was performed by independent neurophysiologist and identified as different patterns of activity by dominant frequency, amplitude and stability.

BAEP testing was performed with recording electrodes placed as one active electrode placed on ipsilateral mastoid, one reference electrode placed at forehead, and ground electrode placed on the contralateral mastoid. The impedance level was to be kept below 5 Kohm; hearing threshold was detected for both ears separately. Mononeural activity stimuli consisting of refraction clicks of 0.1 msec. Square wave pulses were delivered through the ear phones at a rate of 1/ second. The intensity clicks were adjusted to be 90 dBnHL. Recording filters were 100-3000 Hz and 2000 stimuli were delivered.

The response picked up by recording electrodes BAEP, summed and averaged, and displayed on the screen. The results were graded as:

1. Normal response.
2. Unilateral or bilateral prolonged interpeak latencies between I and III, and III and V waves beyond 2 standard deviations of the mean value of control group.
3. Abnormal left-right ear differences beyond 2 standard deviations of the mean value of control group.
4. Absent waves [12].

The prognostic implications of single BAEPs were studied in two different sets of responses and recorded respectively during the first 48 hours of coma and at the beginning of the second week (day 6-7 of coma). These two sets of responses were respectively labeled “early” and “late” BAEPs; they were investigated separately to assess whether the moment at which recordings were made could influence their prognostic value.

BAEP modifications related to body temperature changes or observed under blood levels of anaesthetic drugs known to alter BAEPs were excluded [13,14].

CT brain

CT scan of the brain was performed in radiology department (GE, high speed system), the patient was lying supine with the head in comfortable position, cuts were taken from the foramen magnum to the skull vault, thin cuts (3 mm) were taken in the posterior fossa, thicker cuts (7 mm) were taken at the higher levels. No contrast was taken in our study except in 2 cases where focal mass was noted and further examination with contrast administration was performed using iodinated contrast medium (after an intravenous bolus injection of 1 mL Urografin /kg body weight). The data were collected and the images were analyzed.

Statistical analysis

Data were collected, entered and analysed by using SPSS, version 15. Data were expressed as number and percentage for qualitative variables, mean ± standard deviation (SD) for quantitative variables. Chi squared test (χ²), student t-test and F test (ANNOVA) were used.
for comparison between studied groups. P value < 0.05 was considered significant.

Results

Table 1 shows the demographic data of studied patients: there was younger age, lower Glasgow Coma Scale and more significant unfavourable outcome (death, disability) in patients with surgical coma (group 1) compared to patients with medical, (group 2).

Table 2 shows CT findings among studied subjects: there was a significant difference between both groups regarding the presence of brain edema and intracranial hemorrhage (100% in group 1) while normally visualized basal cisterns were significantly more in group 2 (p=0.02).

Table 3 shows EEG findings among studied subjects, Table 4 shows BAEP findings among studied subjects; there was no significant difference between both groups of patients regarding both EEG and BAEP findings.

Table 5 shows the relation of outcome of comatose children to both BAEP, CT, EEG findings and GCS: Favourable outcome was significantly related to normally visualize basal cisterns in CT brain (p=0.002), normal borderline EEG activity (p=0.03) and normal BAEP waves (p=0.009). Disability was significantly related to slow activity waves (p=0.015) and diffuse high voltage EEG discharges (p=0.009), moreover, 4 patients representing 100% of patients with disability had BAEP waves. While mortality was significantly related to the presence of intracranial bleeding in CT brain (p=0.02), silence EEG waves (p=0.005) and absent BAEP waves (p=0.012).

Figure 1 and 2 demonstrated ABR traces showing normal and prolonged I-III and I-V interpeak latencies. Figure 3 demonstrated ABR showing absent ABR waves.

Discussion

Coma is a medical emergency and may constitute a diagnostic and a therapeutic challenge for the intensivist. The Glasgow coma scale remains the “gold standard” for routine assessment of consciousness, but relies exclusively on behavioural responses. The degree of coma is commonly determined by the Glasgow scale, being that the score 3 in the scale corresponds to deep coma [15,16,17].

In the present study, we noticed that younger age, lower Glasgow Coma Scale and more significant incidence of unfavourable outcome (death, disability) were present in patients with surgical coma than those of medical coma.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Surgical (n=8)</th>
<th>Medical (n=12)</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial bleeding</td>
<td>No 100%</td>
<td>No 0%</td>
<td>16.05</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>No 100%</td>
<td>No 4%</td>
<td>33.3</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>2 25%</td>
<td>1 8.3%</td>
<td>0.15</td>
<td>0.7</td>
</tr>
<tr>
<td>Focal mass</td>
<td>0 0%</td>
<td>2 16.7%</td>
<td>0.21</td>
<td>0.6</td>
</tr>
<tr>
<td>Normal visualization of basal cisterns</td>
<td>0 0%</td>
<td>7 58.3%</td>
<td>4.84</td>
<td>0.02*</td>
</tr>
<tr>
<td>P &lt;0.05 significant,&lt; 0.001 highly significant,&gt; 0.05 non significant.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: CT findings in studied patients.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Surgical (n=8)</th>
<th>Medical (n=12)</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/borderline</td>
<td>No 0%</td>
<td>No 3%</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>I- Slow activity</td>
<td>2 25%</td>
<td>3 25%</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>II- Generalized low voltage</td>
<td>2 25%</td>
<td>5 41.7%</td>
<td>0.08</td>
<td>0.8</td>
</tr>
<tr>
<td>III- Silence</td>
<td>4 50%</td>
<td>2 16.7%</td>
<td>1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>IV- Diffuse high voltage</td>
<td>4 50%</td>
<td>3 25%</td>
<td>0.45</td>
<td>0.5</td>
</tr>
<tr>
<td>Discharges focal</td>
<td>2 25%</td>
<td>2 16.7%</td>
<td>0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>P &lt;0.05 significant,&lt; 0.001 highly significant,&gt; 0.05 non significant.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: EEG findings in studied patients.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Surgical (n=8)</th>
<th>Medical (n=12)</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal bilateral BAEP</td>
<td>0 0%</td>
<td>4 33.3%</td>
<td>1.58</td>
<td>0.2</td>
</tr>
<tr>
<td>Delayed BAEP</td>
<td>6 75%</td>
<td>5 41.7%</td>
<td>1.02</td>
<td>0.3</td>
</tr>
<tr>
<td>Absent BAEP</td>
<td>2 25%</td>
<td>3 25%</td>
<td>0.28</td>
<td>0.6</td>
</tr>
<tr>
<td>P &lt;0.05 significant,&lt; 0.001 highly significant,&gt; 0.05 non significant.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4: BAEP findings in studied patients.

The GCS has several important limitations. Subtle alterations in wakefulness and brainstem findings may not be captured by the GCS. A full GCS cannot be obtained in patients who are endotracheally intubated, are sedated, or have craniofacial trauma or in patients with dominant hemisphere lesions and aphasia. Mid range scores may result in different combinations of the three components yielding equivalent total scores that do not reflect the same degree of unconsciousness. Finally, differences in the higher GCS range correlate poorly with outcome and neuroimaging findings [18,19].

Electroencephalogram (EEG) is useful in evaluation of patients with altered sensorium. Diffuse theta and delta activity, absence of faster frequencies, and intermittent rhythmic delta activity are characteristic of severe encephalopathies. Specific abnormalities may include epileptiform activity consistent with absence or complex partial status; triphasic waves indicating hepatic or uremic encephalopathy; and periodic lateralizing epileptiform discharges, suggesting herpes encephalitis [20].

Five grades of EEG abnormality in coma are internationally accepted: alpha rhythm, dominant theta, diffuse dominant delta, burst suppression and iso electric. At 48 hours, these grades provide prediction with an accuracy of about 88%. The main advantage of the EEG is that it provides on-line assessment of the cerebral cortex, contrary to the EPs, which summarize the functional status of the tested CNS structures over the time needed for averaging [21].

Our results showed that there was no significant difference between patients of surgical and medical coma regarding EEG findings. Moreover, favourable outcome was significantly related to normal/
In a study performed by Singhi et al. [25], CT findings were useful in a very large number of patients. In addition to providing useful information on the extent of injury, valuable prognostic information could also be obtained from the CT scan.

In patients with newly diagnosed type I diabetes mellitus, the first episode of DKA may not be recognized clinically. This results in a large accumulation of osmolytes which cause intracellular edema. On CT examination, cerebral edema is recognized as a loss of the gray-white matter interface, effacement of the sulci, and decrease in ventricular size [26].

Fetal cerebral oedema with herniation as a complication of diabetic keto-acidosis appears to be more common in childhood than in adults. More than half the recorded cases occurred in newly diagnosed diabetics during their first episode of ketoacidosis [27].

The present study showed that there was no significant difference between studied groups regarding BAEP findings.

Our results showed that favorable outcome was significantly related to normal BAEP waves (p=0.009) while mortality was significantly related to absent BAEP waves (p=0.012). Moreover, 4 patients (100%) with disabilities had delayed BAEP findings and these disabilities were observed later after discharge in the form of neurological deficits or recurrence of coma.

The value of evoked potentials for assessment of functional impairment of afferent pathways has been documented in a large number of studies in patients suffering from non-traumatic cerebral disease. Two main advantages of EPs, when compared to the EEG, are their relative insensitivity to the environmental noise (owing to the averaging process) and, before all, the fact that they provide straightforward brainstem assessment [28].

The interpeak latency of BAEPs has been reported as being almost constantly normal when recorded during the first six hours of traumatic coma. This suggests that most abnormalities encountered later are secondary to hemisphere lesions, and reflect an ongoing process of rostrocaudal deterioration of the brainstem. Discrete brainstem lesions

### Table 5: Relation between BAEP, CT, EEG and GCS findings and the outcome in studied patients.

<table>
<thead>
<tr>
<th>BAEP findings</th>
<th>Death N=9</th>
<th>Disable N=4</th>
<th>Good N=7</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal bilateral</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>57.1</td>
<td>9.29</td>
</tr>
<tr>
<td>Delayed</td>
<td>4</td>
<td>44.4</td>
<td>4</td>
<td>100</td>
<td>3</td>
</tr>
<tr>
<td>Absent</td>
<td>5</td>
<td>55.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CT findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>6</td>
<td>66.7</td>
<td>2</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>Cerebral edema</td>
<td>7</td>
<td>77.8</td>
<td>2</td>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>2</td>
<td>22.2</td>
<td>1</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Focal mass</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>Normal visualization of basal cisterns</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>EEG findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I- Normal/borderline</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>II- Slow activity</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>75</td>
<td>2</td>
</tr>
<tr>
<td>III-Generalized low voltage</td>
<td>4</td>
<td>44.4</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>IV- Silence</td>
<td>6</td>
<td>66.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>V-Diffuse high voltage</td>
<td>2</td>
<td>22.2</td>
<td>4</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>VI Discharges focal</td>
<td>2</td>
<td>22.2</td>
<td>1</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.86 ± 0.9</td>
<td>4.2 ± 0.5</td>
<td>5.6 ± 1</td>
<td>4-6</td>
<td>4-5</td>
</tr>
</tbody>
</table>

P <0.05 significant, <0.001 highly significant, >0.05 non significant.

may, however, also induce severe BAEP abnormalities (like complete absence of waves) if they involve the central auditory pathways [29,30].

Balogh et al. [31] proved that BAEPs testing provides relevant prognostic information, since improvement of graded BAEPs. Moreover, Chiappa [32] said that BAEP provided a sufficient safety margin to be used in comatose patients and remain an indicator of a preserved brain-stem function in difficult clinical situations. Unlike the cortical auditory brain potentials (late evoked potentials) in patients with severe cerebral lesions, BAEPs have much greater information value. Their waveforms are more stable and they are less influenced by various exogenous and endogenous factors.


