

Search for clinical and neurophysiological prognostic patterns of brain coma outcomes in children

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Key words: severe brain trauma; early prognosis of brain coma outcome; electroencephalography; brainstem auditory evoked-potentials.

Summary. *Objective.* The aim of the study was to evaluate the possible predictive values of clinical examinations combined with the recordings of electroencephalography and brainstem auditory-evoked potentials in traumatic coma of pediatric patients.

Material and methods. A total of 43 children in coma with severe acute head trauma were included in the study. They were investigated and treated in pediatric intensive care unit using standard evaluation and treatment protocol. Evaluation of coma was performed using Glasgow Coma Scale. Electroencephalography for 35 patients and brainstem auditory-evoked potentials for 24 patients were recorded.

Results. Glasgow coma scale statistic pool median was equal to 4 points as measured in presence of brain edema, meanwhile it was 6 as measured in absence of edema. In case of supratentorial damage, median duration of consciousness recovery was 10 days. In absence of above-mentioned supratentorial damage, recovery of the consciousness was earlier – median was 5 days. Determined duration of artificial lung ventilation was statistically significantly shorter for those who had edema ($P=0.048$). In 20 patients (57% of all cases), constant or alternating slow wave activity was observed during the first electroencephalographic recording. In other cases, “alpha coma” or low amplitude of arrhythmic activity and local slowing activity corresponding to brain damage seen on computerized tomography were recorded. For 24 patients, brainstem auditory-evoked potentials were recorded. In 9 cases, they were abnormal; in these cases, the consciousness of the patients recovered after 44 days or did not recover.

Conclusions. Glasgow coma scale results alone may have limited prognostic value in absence of other objective neurophysiologic investigation data concerning the coma outcome in children. Prognosis may be worse if pathological brainstem auditory-evoked potentials correlate with pathological dynamic changes in electroencephalography and brain lesions, diagnosed during computerized tomography scan.

Introduction

Trauma is the main cause of death for young people and children. World Health Organization (WHO) notes that “young people die early frequently and they also live longer with disability” (1). Most of children death cases in Lithuania in year 2005 were related to traffic accidents – 78 cases (41 out of them were teenagers, aged 15–17 years, 28 boys and 13 girls). During the year 2006, 156 children died due to trauma (103 boys and 53 girls); out of this number, 71 teenagers died after injuries acquired in traffic accidents (2). Traumas and other accidents require direct and indirect state resources, increasing spending of state budget, budget of mandatory health insurance

and budget of social insurance. WHO prognosis says that in 2020, traumatism in traffic accidents will be in the third place among the main health care problems worldwide (1). Timely help after traumatic injury and correct means of early detection may improve the outcome after traumatic brain injury, decrease the level of disability in further life.

Functional investigations of central nervous system (CNS) in acute trauma period are one of the most important indicators to evaluate consciousness recovery possibilities after traumatic injury. Functional processes of central nervous system and their changes reflect in bioelectrical activity of the brain (3). Registration of brain bioelectric activity (electroencephalography –

EEG) may be informative method to evaluate degree of brain injury and prognosis of recovery. Evoked potentials (EP) are the methods to investigate conductive capacity of brain neuronal network. These parameters can show conditions of sensorial neuronal paths, level and degree of their injury (4). Brainstem auditory-evoked potentials (BAEP) are the responses of brainstem structures to sound. They allow evaluating the level and location of injury within the brainstem – location for vital centers. BAEP is used with expectation to evaluate disturbances of sensorial pathways, identify the lesion of the brain tissue that are invisible in computer tomography (CT), neither visible during clinical investigation. Thus, above-mentioned parameters are giving a value to make prognosis for recovery from trauma (5). Local brain cortex and brainstem damage as well diffuse neuronal axonal junction damages are often apparent in traumatic brain coma cases (5). Hypoxic injury gives complication to the outcomes. Even relatively small traumatic brain injury that is unmanageable recognized using visualized recognition methods may outcome in long lasting coma status. Possibly, this is determined by neuronal cell activity and instability of functional mode (5). 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 (3). One can get better understanding of brain injury correlation with clinical picture and outcome prognosis while evaluating dynamic of functional brain processes. Investigations of visual and neurophysiologic neuronal system are widely used to estimate the severity of children traumatic injury with coma status. Scientific literature (1995–2007) describes valuable parameters, showing coma outcome (33 research works), and they show that it is worth to evaluate patient's clinical status during acute coma with following criteria: pupil reaction, corneal reflexes, eye movement, to use assessment scales of clinical coma, to perform investigations of brain bioelectrical activity, evaluate EEG, specific visualizations of brain bioelectric activity that show functional status of neuronal tissue (6–12) and status of brainstem conductive system while performing brainstem evoked potential investigations. We used the complex of all of the above-described investigations to evaluate prognosis of investigated children after brain injury during acute coma status and during the first week (early recovery period) and follow-up after one month.

Patients and methods

Group of 43 investigated patients (17 girls and 26 boys) consisted of 1 to 18-year-old children (mean

age, 10.88 years) with severe traumatic brain injury, who were treated in Kaunas University of Medicine Hospital during the period January 2005 and May 2007. They were treated according to the standard severe traumatic brain injury protocol: benzodiazepines in dosages used for adequate sedation, relaxation, opiate analgesia, artificial pulmonary ventilation, prophylaxis of convulse activity, infusion therapy to ensure circulating fluid volume control and correction of electrolyte balance, normal temperature or cooling according to the clinical indications of cooling protocol. Severe traumatic brain trauma diagnosis was confirmed during clinical investigations, via objective investigation and evaluation of consciousness status using Glasgow Coma Scale (GCS). It was done during primary investigation after injury when GCS score was ≤ 8 points.

For 35 patients, electroencephalography (EEG) was recorded twice – during early posttraumatic period (24–72 hours) and during early recovery period (after >72 hours), in most cases then standard protocol was done. As Gevins and Remond indicate in Handbook of EEG and Clinical Neurophysiology (1987) and as it is stated in scientific papers, level of sedation in experimental surrounding and during clinical investigation does not change BAEP data, and brain conductive system is not affected by benzodiazepine or barbiturates that are used for sedation. Pressler 2001 and Theilen 2000 mention that during EEG investigation in traumatic brain injury and sedation, barbiturates, benzodiazepines, or phentanyl are used for diminishing artefacts that are created by motion and muscle activation. Authors conclude that effect of sedation is general and it does not change output of bioactivity in localized injury. The more important effect on EEG visual and spectral analysis depends on coma depth as authors state. Literature states usage of standard EEG patterns for evaluation and description of coma state: delta coma, alpha coma, spindle coma and burst-suppression pattern as deterioration symptom or isoelectric line as sign of brain death.

EEG was recorded using an on-line 16-channel EEG system (Siemens-Eléma 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. Brainstem auditory-evoked potentials were investigated in 24 patients during early recovery period. Bio-Logic (USA) evoked potentials

system was used for that purpose. Monaural clicks 23.1/s were applied through standard headphones. One channel recordings were registered – ipsilateral earlobes referred to Cz. Filters were set at 150–3000 Hz. Analysis time was 10–15 ms.

Brain computed tomography (CT) was performed and evaluated by radiologist. Intracranial pressure (ICP) was monitored together with brain perfusion pressure (BPP) and evaluated in this research. Timeliness of decompressive craniectomies was evaluated in absence of conservative measures to control brain edema progression. Several other measures were also analyzed; they are as follows: tactics of further on treatment modalities, such as duration of application of severe traumatic brain injury treatment protocol, demand of vasoactive substances, and duration of artificial lung ventilation (ALV). Status of consciousness was evaluated using GCS score after expiration of severe traumatic brain injury treatment protocol. Dynamics of the consciousness recovery was evaluated in three observations: during primary investigation after injury, after the end of the treatment in pediatric intensive care unit (at the moment of the patient's transfer for further treatment to the department of neurosurgery), and 1 month after trauma. We have also collected the information on which day after trauma the patient's consciousness had recovered.

Statistical methods were applied for the evaluation of the obtained results: description statistics (explorer tables), group comparison (Npar, Mann-Whitney tests tables), test of two attribute independence (crosstabs tables). The main index that was used for the analyzed data was median (explorer table) and 25th and 75th percentiles (percentiles table). Fisher accurate criterion was applied for the evaluation of the statistical significance.

Results

During brain computed tomography investigation, it was disclosed that the most frequent site of damage was supratentorial (84% of all cases). Intraventricular, parenchymal, subarachnoidal hemorrhages were noticed in 72% of patients, brain edema in 91% of cases. GCS score statistic pool median (Md) on admission was equal to 4 points (25 percentiles 3.5 points, 75 percentiles 4.5 points) was measured in presence of brain edema, meanwhile GCS score Md 6 (25 percentiles 5, 75 percentiles 9) was measured in absence of edema. Mann-Whitney test was used to test if localization of damage and clinical evaluation using GCS had a statistically significant relationship. In case of supratentorial damage, median duration of consciousness recovery by days was 10 days (25 per-

centiles 6.5 days, 75 percentiles 14.5 days). In absence of above-mentioned damage, recovery of the consciousness was shorter – median was 5 days (25 percentiles – 4 days, 75 percentiles – 8 days). Most of the investigated and treated patients survived (35 patients). Eight patients died, and in most of the cases, death occurred within the first 24 hours after incurred traumatic injury. One-third (33%) of investigated were children with level of consciousness at score 3 using GCS. Most frequently death occurred (38.5% of cases) when GCS was scored 3 during the first evaluation of consciousness. Protocol of severe traumatic brain injury treatment was applied in 79% of cases (full sedation, relaxation, analgesia, artificial lung ventilation), for this group EEG and BAEP registrations were applied. Determined duration of artificial lung ventilation was statistically significantly shorter for those who had edema ($P=0.048$, exact Fisher criteria); statistical Md in hours of artificial lung ventilation was 179 (25 percentiles 113.5 hours, 75 percentiles 222 hours). We might presume that such results were received as a consequence of aggressive severe brain trauma treatment protocol in presence of brain edema and low GCS score, *i.e.* in presence of coma. Intracranial pressure was monitored for 31 children (72% of cases). Decompressive craniotomy was performed for 21 patients (49% of cases) when brain edema was progressing and perfusion brain pressure was insufficient.

In EEG, constant (Fig. 1) or alternating (Fig. 2) slow wave brain activity (delta coma pattern) (57% of all cases) was noticed while monitoring brain bioelectric activity in coma. In addition, alpha coma (Fig. 3) or low amplitude arrhythmic and locally slow activity waves were noticed which corresponded to brain injury localization, established by CT scan. Extinct bioelectric activity and brain death was registered in one case.

Investigation of brainstem auditory-evoked potential was performed for 24 patients. In 9 cases, pathologic outcome was registered (Table) (Fig. 4) due to impaired conductivity of the auditory pathway at the brainstem level. Among those patients, recovery of consciousness was registered as following – in 5 cases during 10 days, in 2 cases after 41 and 44 days; 2 patients remained in coma until the end of hospitalization. In 15 cases (62.5% of all registered BAEP), no malfunction of the auditory pathway from the cochlear to the midbrain was registered; nevertheless, the consciousness recovery was registered only from 19 to 24 days.

Analysis of the traumatic coma outcome was performed one month after trauma. Clinically conscious-

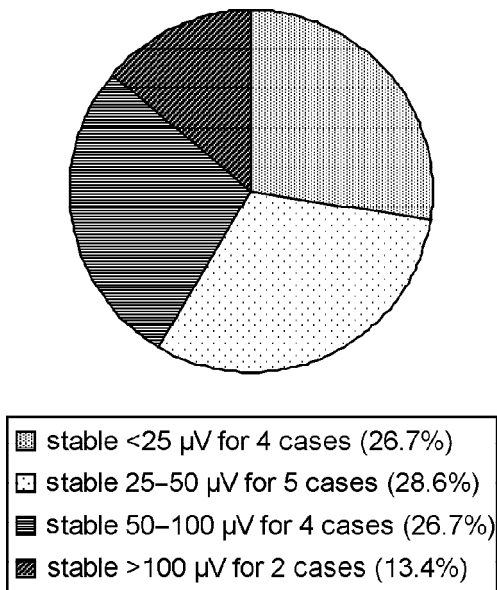


Fig. 1. Distribution of EEG amplitude in patients with constant activity

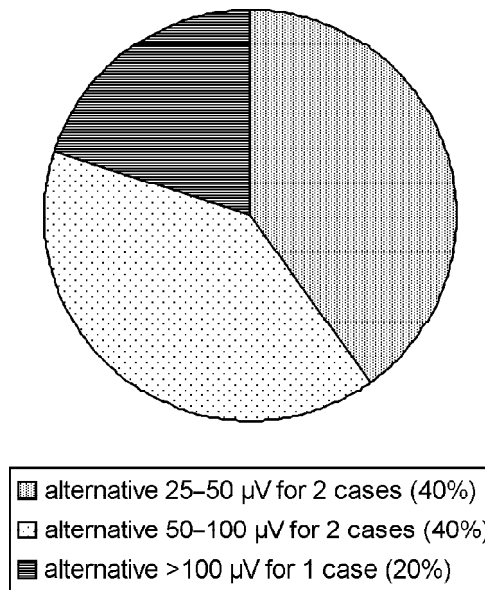


Fig. 2. Distribution of EEG amplitude in patients with alternating activity

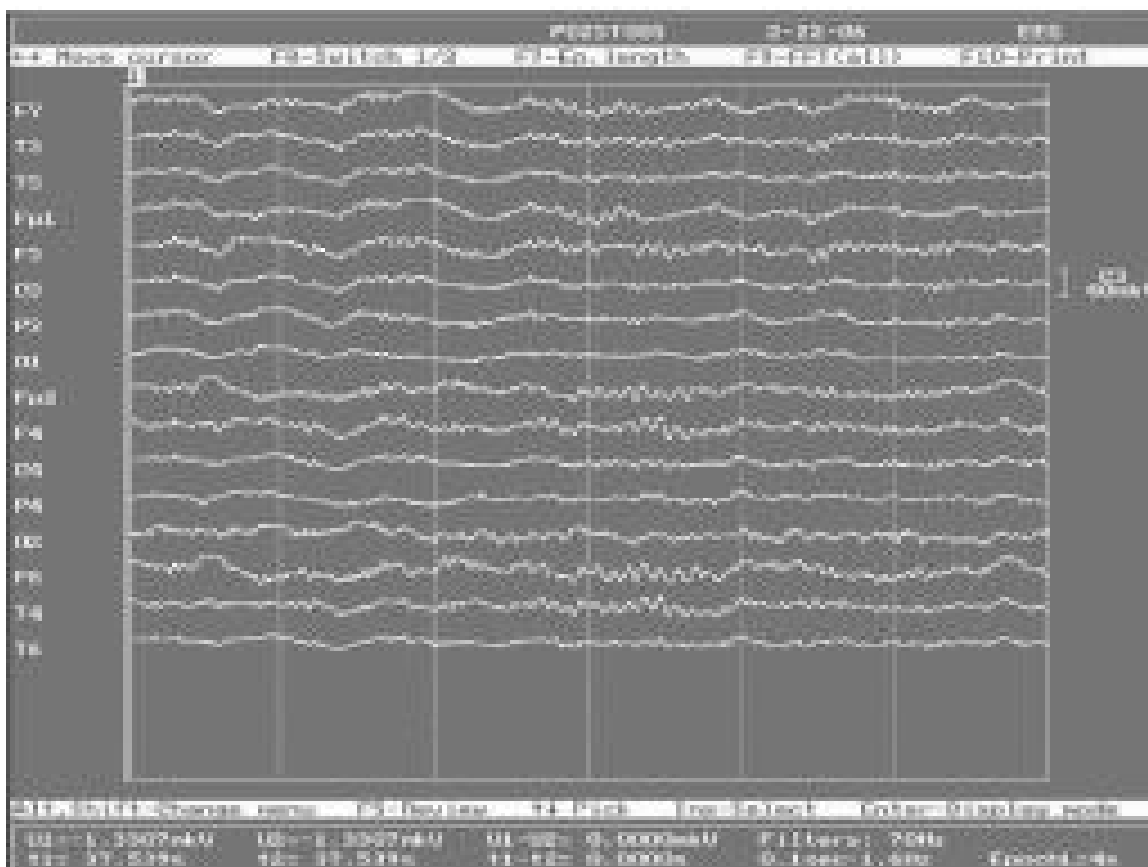


Fig. 3. Example of EEG pattern in “alpha coma,” the background activity is in alpha frequency with amplitude up to 40 μV

Table. Measurements of various brains function parameters in cases of pathologic BAEP results

No.	Patient	GCS*	CT	EEG	BAEP	Day when consciousness recovered
1	S. J.	7	Supratentorial right hemisphere injury, intraventricular hemorrhages	Alternating delta activity, 100 μ V to 68%	Increased IPL I-III, I-V on the left	4
2	O. Z.	7	Supratentorial left and right hemisphere injury, intraparenchymal and subarachnoidal hemorrhages	Stable delta activity, >100 μ V to 70%	Absence of the waves on the right, absence of III waves and increased IPL I-V on the left	44
3	K. B.	3	Supratentorial left and right hemisphere injury, epidural hemorrhages	Stable delta/alfa activity to 55% delta frequency	Increased IPL I-III and I-V on the right	41
4	M. K.	3	Supratentorial left and right hemisphere injury, intraventricular hemorrhages	Stable delta activity, 70 mV amplitude, delta activity to 78% frequency	Increased IPL I-V on the left	10
5	Z. S.	5	Subtentorial, right hemisphere injury, subdural hematoma	Alternating delta activity and burst-suppression	Absence of V waves on the right, increased IPL III-V, I-V on the left	Remained in coma until the end of hospitalization >75
6	V. P.	5	Subtentorial and supratentorial left hemisphere injury subarachnoidal hemorrhages	Delta/alfa activity, low 30 μ V amplitude, delta activity to 65%	Increased IPL I-III, I-V on the left	Remained in coma until the end of hospitalization >70
7	G. T.	6	Supratentorial injury, contusion zone in left temporal lobes	Alfa activity, 40 μ V amplitude	Increased IPL I-III, I-V on the left	9
8	A. N.	3	Supratentorial injury, contusion zone in left temporal lobes, subdural and epidural hemorrhages in left hemisphere	Stable delta activity, 100 μ V to 67%	Increased IPL I-III on the left	6
9	E. B.	7	Subtentorial left hemisphere injury, intraparenchymal hemorrhages	Stable delta activity, 40 μ V to 70%	Increased IPL I-V on the left	7

*Glasgow coma scale score during primary investigation after severe brain injury.

ness recovered for 29 children; 6 patients remained in coma during all period of their hospitalization in children intensive care unit, and 6 children (14% of investigated) come with no consciousness continued for longer than one month.

Discussion

There are no prospective studies done up to now to make prognosis of outcomes and recovery of children after severe brain trauma. This dynamic process requires new attitude as intangible part of treatment, evaluating consciousness recovery possibilities while performing noninvasive investigations of brain bioelectric activity, which improves monitor-

ing of clinical picture. Literature reviews show multiple sources to prove necessity of even uninterrupted EEG monitoring while following after brain functional status during brain injury and especially in perturbation of consciousness (13, 14). Technically available frequency EEG analysis may help to discover brain function disturbances during all the recovery period and improve prognosis and therapeutic possibilities for brain function recovery (15, 16). In worldwide literature, most of investigators recommend to evaluate neurophysiologic parameters in dynamics together with clinical parameters that show how deep coma is (5). Above-mentioned methodology was also respected in our research. In absence of brainstem ref-

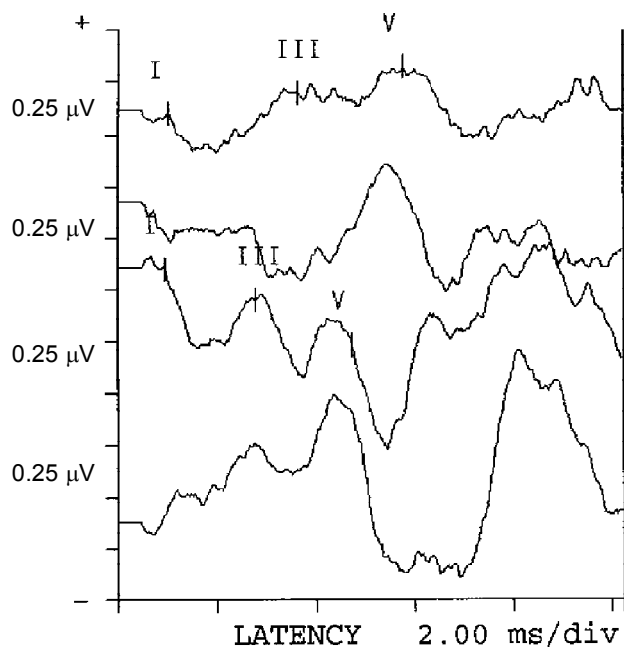


Fig. 4. Example of pathologic BAEP (increased interpeak latencies I-III, I-V on the left) in case of brain trauma

Two above curves are the recordings of the left ear, two below – right ear.

lexes and when coma severity in GCS comes to score 4–5 within the first 24 hours after injury without sedative medication, prognosis of recovery is minimal (17). Evaluation of neurophysiologic parameter correlation is important while monitoring brain activity dynamics during coma as Guerit (2005) thinks (18) and evaluating brain activity recovery prognosis for patients in vegetative status (19). When changes correlate with extremely expressed (outstandingly bad) EEG changes (“burst-suppression” pattern), prognosis is bad (14, 20). We have described poor

coma outcomes in our results, such as no recovery of consciousness during all period of hospitalization (>2 months), and it matches well with bad prognostic clinical signs and electrophysiological investigations (EEG and evoked potentials) pathologic data, described in published studies. Prognosis of the outcome and establishment of prognostic criteria and their value for patients in case of life-threatening situation is continuous work in children intensive care unit. We do continue this research through the expansion of neurophysiologic research database, expansion of wider group of cases, performing analysis of correlation between brainstem auditory evoked potentials and EEG spectral frequency and amplitude dynamics in outcome period from coma.

Conclusions

Glasgow coma scale results alone may have limited prognostic value in absence of other objective neurophysiological investigation data concerning the coma outcome in children. Lesions found in computed tomography and changes of background activity in electroencephalography do not necessarily mean poor outcome. Prognosis may be worse if pathological brainstem auditory-evoked potentials correlate with pathological dynamic changes in electroencephalography and brain lesions, diagnosed during computed tomography scan. After evaluation of these data and overview of literature, conclusion can be done that evaluation of early prognosis in children’s severe brain trauma is possible with adjustment of encephalographic and brainstem auditory-evoked potential recordings. Neurophysiologic brain function investigations are suitable, noninvasive, and practical methods for prognosis of severe brain trauma early outcome.

Klinikinių ir neurofiziologinių rodiklių paieška prognozuojant vaikų galvos smegenų traumos sukeltos komos baigtis

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Raktažodžiai: sunki galvos smegenų trauma, ankstyva traumos baigčių prognozė, elektroencefalografija, galvos smegenų kamieno klausos sukeltų potencialų tyrimas.

Santrauka. *Tyrimo tikslas.* Įvertinti, kurie klinikiniai bei neurofiziologiniai tyrimai galėtų padėti spręsti apie sąmonės atsikūrimo prognozę sunkių galvos smegenų sužalojimą patyrusių vaikų, ištiktų komos.

Tyrimo medžiaga ir metodai. Tiriamųjų grupę sudarė sunkią galvos smegenų traumą patyrę vaikai, ištikti komos, kurie buvo tirti bei gydyti pagal sunkios galvos smegenų traumos tyrimo bei gydymo protokolą. Kliniškai sąmonės būklė buvo vertinama remiantis Glazgo komų skale. Tiriamiesiems atlikti galvos kompiuterinės tomografijos, elektroencefalografijos ir smegenų kamieno klausos sukeltų potencialų tyrimai.

Rezultatai. Ištirti 43 vaikai komos būklės, patyrę sunkią galvos smegenų traumą. Esant smegenų edemai, remiantis radiologiniais kriterijais bei intrakranijinės hipertenzijos požymiais, galvos kompiuterine tomografija, Glazgo komų skalės balų statistinė imties mediana buvo 4 balai, nesant smegenų edemos – 6 balai. Nustatyta, kad dirbtinės plaučių ventilacijos trukmė buvo statistiškai reikšmingai trumpesnė tiems pacientams, kuriems buvo smegenų edema ($p=0,048$), jų ventilacijos trukmės statistinė imties mediana buvo 179 valandos. Elektroencefalogramose komos metu užfiksuotas pastovus ar kintamas lėtųjų bangų aktyvumas, žemos amplitudės aritminės bei lokaliai sulėtėjusio aktyvumo bangos, atitinkančios galvos smegenų pažeidimo lokalizaciją, nustatytą kompiuterinės tomografijos tyrimu. Smegenų kamieno klausos sukeltų potencialų tyrimo metu užregistruoti klausos laido pralaidumo sutrikimai buvo susiję su ilgesne sąmonės atsikūrimo trukme.

Išvados. Kai nėra kitų objektyvių duomenų, vien Glazgo komų skalės rezultatai gali turėti ribotą praktinę prognozinę vertę. Galvos smegenų traumos sąlygotos komos baigčių prognozė gali būti blogesnė, jei smegenų kamieno klausos sukeltų potencialų tyrimo metu nustatomi klausos laido pralaidumo sutrikimai susiję su elektroencefalografijos metu registruojamais pokyčiais bei kompiuterinės tomografijos tyrimo metu nustatytu galvos smegenų pažeidimu.

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References

1. Dėl valstybinės traumatizmo profilaktikos 2000–2010 metų programos įgyvendinimo nutarimas. (Decision on implementation of 2000–2010 governmental trauma prophylactic program on traumatism.) 2007 m. kovo 22 d. Nr. N-2, Vilnius. Available from: URL: http://www3.lrs.lt/pls/inter/w5_show?p_r=698&p_d=23390&p_k=1
2. Statistikos departamentas prie Lietuvos Respublikos Vyriausybės. Lietuvos vaikai. (Statistic department of Government of Lithuanian Republic. Children of Lithuania.) Vilnius: Statistikos departamentas; 2007.
3. Liesienė V, Bertašius K, Jurkevičienė G. Smegenų bioelektrinis aktyvumas: kilmė, registracija, įvertinimas. (Brain bioelectrical activity: genesis, registration, and evaluation.) Neurologijos seminarai, Neurologinės diagnostikos metodai 1998;2(4):62-72.
4. Ulozienė I, Šeštakauskas K. Sukeltųjų potencialų naudojimas klinikoje. (Evoked potential usage clinical practice.) Neurologijos seminarai, Neurologinės diagnostikos metodai 1998; 2(4):80-7.
5. Liesienė R, Ulozienė I, Kėvalas R, Grinkevičiūtė DE. Vaikų funkcinės smegenų būklės įvertinimas ištikus smegenų komai. (Evaluation of the functional brain state in comatose children.) Medicina (Kaunas) 2006;42(5):355-61.
6. Biagioni E, Mercuri E, Rutherford M, Cowan F, Azzopardi D, Frisone MF, et al. Combined use of electroencephalogram and magnetic resonance imaging in full term neonates with acute encephalopathy. Pediatrics 2001;107(3):461-8.
7. Gire C, Nicoise C, Roussel M, Soula F, Girard N, Somma-Mauvais H, et al. Hypoxic ischemic encephalopathy in the term newborn: contribution of the electroencephalographic and magnetic resonance imaging or computed tomography to the prognostic assessment. A review of 26 cases. Neurophysiol Clin 2000;30(2):97-107.
8. Toet MC, Meij W, Vries LS, Uitervaal CS, Huffelen KC. Comparison between simultaneously recorded amplitude integrated electroencephalogram (cerebral function monitoring) and standard electroencephalogram. Pediatrics 2002; 109(5):772-9.
9. Sánchez-Chávez JJ, Barroso E, Cubero L, González-González J, Farach M. The evaluation of patients with ischemic cerebral lesions by CT, SPECT, and qEEG in acute, subacute and chronic phases. Rev Neurol 1988;27(156):213-23.
10. Kane NM, Moss TH, Curry SH, Butler SR. Quantitative electroencephalographic evaluation of non-fatal and fatal traumatic coma. Electroenceph Clin Neurophysiol 1998; 106(6):244-50.
11. Yamakami I, Nakamura M, Karasudani H, Suda S, Ono J, Isobe K. Prognostic value of spectral analysis of electroencephalogram in patients with severe head injury. Jap Shinkei Geka 1991;19(10):939-44.
12. Shalak LF, Laptook AR, Velaphi SC, Perlman JM. Amplitude-integrated electroencephalography coupled with early neurologic examination enhances prediction of term infants at risk for persistent encephalopathy. Pediatrics 2003;111(2):351-7.
13. Grinkevičiūtė D, Kėvalas R, Tamašauskas A, Matukevičius A, Gurskis V, Liesienė R. Sunki vaikų galvos smegenų trauma. Ar yra optimalus gydymo būdas? (Severe pediatric head injury: is there any optimal solution?) Medicina (Kaunas) 2006;42(4): 278-87.
14. Jordan KG. Continuous EEG monitoring in the neuroscience intensive care unit and emergency departments. J Clin Neurophysiol 199;16:14-39.
15. van Putten MJ, Tavy DL. Continuous quantitative EEG monitoring in hemispheric stroke patients using the brain symmetry index. Stroke 2004;35:2489-92.
16. Scheuer ML. Continuous EEG monitoring in the intensive care unit. Epilepsia 2002;43:114-27.
17. Ong L, Selladurai BM, Dhillon KM, Atan M, Lye MS. The prognosis value of the Glasgow coma scale, hypoxia and computerized tomography in outcome prediction of pediatric head injury. Pediatric Neurosurg 1996;24:285-91.
18. Guerit JM. Evoked potentials in severe brain injury. Progress Brain Res 2005;150:415-25.
19. Gire C, Nicoise C, Roussel M, Soula F, Girard N, Somma-Mauvais H, et al. Hypoxic ischemic encephalopathy in the term newborn: contribution of the electroencephalographic and magnetic resonance imaging or computed tomography to the prognosis assessment. A review of 26 cases. Neurophysiol Clin 2000;30(2):97-107.
20. van Putten MJ. Nearest neighbor phase synchronization (NNPS) as a measure to detect epileptic seizures from scalp EEG recordings. J Clin Neurophysiol 2003;20:320-5.

Received 3 March 2008, accepted 18 April 2008
Straipsnis gautas 2008 03 03, priimtas 2008 04 18