SHORT COMMUNICATION

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Prognostic value of EEG in West syndrome

Prognostički značaj elektroencefalografskog nalaza u West-ovom sindromu

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Abstract

Background/Aim. West syndrome (WS) is an epileptic encephalopathy which is characterized by the trias: infantile spasms, psychomotor delay and specific electroencephalography (EEG) pattern. The aim of this study was to determine the prognostic value of EEG in the therapy of West syndrome. **Methods.** This study group comprised 68 patients (40 boys and 28 girls) with the diagnosis of WS. Criteria for inclusion of patients in this study were the disease onset in the first or the second year of life, specific seizure type and a characteristic EEG pattern. All patients were divided into 2 groups: symptomatic (37 patients) and cryptogenic (31 patients) WS. The outcome was assessed through the response to the therapy (seizure control and EEG findings). Follow-up was at 3, 6, 12 and 24 months after the diagnosis was established. **Results.** Three months after starting the treatment 80.6% of patients with improved EEG were seizure free ($p < 0.01$); 85.7% of patients with EEG improvement at 3 months check-up were seizure free after 6 months ($p < 0.01$); 82.8% of patients with better EEG findings after 3 months had no seizures after 12 months ($p < 0.05$). Also, the majority of patients with improvement in EEG at 6 month follow-up (95.8%) had no seizures at one year follow-up ($p < 0.01$). The presence of seizures during this period did not depend on EEG after 6 months of treatment ($p > 0.05$). Most of the patients with improved (89.7%) and unchanged (70.6%) EEG after 12 months had no seizures after two years, whereas the patients with worsened EEG were with seizures. **Conclusion.** Seizure control after 6, 12 and 24 months depended on EEG finding at 3 months follow up. Seizure control after 12 months correlated with EEG after 6 months. The correlation between EEG after 12 months and seizure control after 24 months was not clear. EEG at 6 months follow-up did not affect seizure control after 2 years.

Key words:
electroencephalography; prognosis; treatment outcome; spasm; infant, newborn; epilepsy.

Apstrakt

Uvod/Cilj. West-ov sindrom (WS) je epileptička encefalopatija koja se karakteriše trijasom: infantilni spazmi, zaostajanje u psihomotornom razvoju i karakterističan elektroencefalografski (EEG) nalaz (hipsaritmija). Cilj istraživanja bio je da se utvrdi prognostički značaj EEG nalaza u terapiji WS. **Metode.** Istraživanjem je obuhvaćeno 68 bolesnika (40 dečaka i 28 devojčica) sa dijagnozom WS. Kriterijumi za uključivanje u istraživanje bili su pojava simptoma u prvoj ili drugoj godini života, specifičan obrazac napada i karakterističan EEG zapis. Bolesnici su bili podeljeni u dve grupe: simptomatski (37 bolesnika) i kriptogeni (31 bolesnik) WS. Ishod je procenjivan kao odgovor na terapiju (kontrola napada i EEG nalaz). Bolesnici su praćeni u periodima 3, 6, 12 i 24 meseca od postavljanja dijagnoze. **Rezultati.** Posle tri meseca od početka terapije 80.6% bolesnika sa poboljšanjem u EEG nalazu bilo je bez napada ($p < 0,01$). Ukupno, 85,7% bolesnika sa poboljšanjem EEG nalaza posle tri meseca nije imalo napade ni posle šest meseci ($p < 0,01$). 82.8% bolesnika sa poboljšanjem EEG nalaza posle tri meseca nije imalo napade ni posle 12 meseci ($p < 0,05$). Takođe, najveći deo bolesnika koji su imali poboljšanje EEG nalaza posle šest meseci (95,8%) nije imao napade ni posle jedne godine ($p < 0,01$). Prisustvo napada u ovom periodu nije zavisilo od karakteristika EEG posle 6 meseci od početka lečenja ($p > 0,05$). Najveći deo bolesnika sa poboljšanjem (89,7%) ili nepromenjenim EEG (70,6%) posle 12 meseci nije imao napade ni posle dve godine, dok su bolesnici sa pogoršanjem u EEG nalazu imali napade. **Zaključak.** Kontrola napada posle 6, 12 i 24 meseca zavisila je od nalaza na EEG posle tri meseca. Kontrola napada posle 12 meseci bila je u korelaciji sa karakterom EEG posle šest meseci. Korelacija između EEG nalaza posle 12 meseci

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i kontrole napada posle 12 i 24 meseca nije bila jasna. Nalaz EEG-a posle šest meseci nije imao uticaj na kontrolu napada posle 24 meseca.

Ključne reči:
elektroencefalografija; prognoza; lečenje, ishod; spazam; novorođenče; epilepsija.

Introduction

West syndrome (WS) is an age-dependent epileptic encephalopathy characterized by a triad of symptoms: infantile spasms (IS), hypsarrhythmia and delay and/or regresion in psychomotor development (PMD). Although this is a well-defined syndrome, variations within all three components of the syndrome are well recognized. It is a multietiological disorder with special emphasis on perinatal factors due to their relative prevalence and opportunities for prevention. Etiologically, WS occurs in three forms: symptomatic, cryptogenic and idiopathic [1]. According to the latest International League Against Epilepsy (ILAE) proposed diagnostic scheme, WS is classified as: structural/metabolic, of unknown cause and genetic (or probably genetic) [2]. Although WS is considered to be one of the intractable epilepsies, the prognosis differs widely and depends primarily on the etiology and the degree of structural damage of the central nervous system (CNS) [3, 4].

The aim of this study was to determine the significance of electroencephalography (EEG) for long-term prognosis of WS in treated children.

Methods

Our study group comprised 68 patients (40 boys and 28 girls) with the diagnosis of WS, aged 2 to 17 months (mean 6.5 ± 2.7 months), who were examined and treated at the University Children's Hospital in Belgrade from 1987 to 2008.

Inclusion criteria for this study were the disease onset in the first or the second year of life, specific seizure type and a characteristic EEG pattern.

Bearing in mind the purpose of the research and for practical reasons, all patients were divided according to the old classification and terminology [5] into two groups: symptomatic (37 patients) and cryptogenic (31 patients) WS. Idiopathic forms of WS were excluded from our study group due to the small percentage of these patients as well as the fact that the prognosis for these children is generally better than for those with cryptogenic or symptomatic forms [6–11]. All patients underwent a standard EEG examination while awake and during sleep, where the existence of the characteristic EEG pattern – hypsarrhythmia was noted. After making the diagnosis of WS, therapy was introduced to all patients according to the current treatment protocols [12]. Control EEG examination was performed after 3, 6, 12 and 24 months and was defined as: improved (in the case of a better organization of the background activity and the partial or complete disappearance of specific graphoelements), unchanged or worsened.

The outcome was assessed through the response to therapy (seizure control and EEG findings) at each follow-up. The absence of seizures and improvement of EEG were considered as a good response to therapy, while the incomplete seizure control and unchanged EEG were regarded as partial response to therapy. Poor response to the treatment implied the continous presence of seizures and further aggravation of EEG. Response to therapy after two-years follow-up was considered equivalent to the outcome.

Statistical analysis was performed using Chi squared test and Spearman's rank correlation. All data were anlyzed using SPSS for Windows version 16.0 (SPSS Inc, Chicago, IL, USA).

Results

At 3 months follow-up, 34 (50%) patients were seizure-free, while 34 (50%) still presented with seizures. EEG improvement after 3 months was observed in 36 (52.9%) patients, the findings were unchanged in 25 (36.8%) while EEG deterioration was present in 7 (10.3%) patients.

Three months after starting the treatment 29 (80.6%) patients with improved EEG were seizure free, while seizure control was obtained in a small number of patients with unchanged (3, 12%) and worsened (2, 28.6%) EEG. Thus, there was a clear and statistically significant correlation between EEG findings and presence of seizures at 3 months follow-up ($p = 0.0001$, $p < 0.01$).

At 6 months follow-up, 20 (47.6%) patients were seizure free while 22 (52.4%) patients still had seizures. EEG showed improvement in 18 (42.9%) patients, 21 (50%) patients had unchanged EEG and worsened findings were recorded in only 3 (7.1%) patients.

Seizure control at 6 months follow-up clearly correlated with EEG findings at 3 months follow-up. Twelve (85.7%) patients with EEG improvement at 3 months check-up were seizure free after 6 months. On the other hand, the majority of patients with unchanged (13, 68.4%) and worsened (6, 85.7%) EEG continued to have seizures ($p = 0.0001$, $p < 0.01$) (Table 1).

Six months after starting the treatment, EEG was in correlation with the presence of seizures in the same period ($p = 0.0001$, $p < 0.01$). Sixteen (88.9%) patients with improved EEG had no seizures, while the majority of patients with unchanged (17, 81%) or worsened EEG (3, 100%) still had seizures.

Evaluation after 12 months showed that the large number of patients (40, 65.6%) was seizure free, while 21 (34.4%) patients continued to have seizures. EEG after 12 months in comparison to previous findings was improved in 34 (55.8%), unchanged in 21 (34.4%) and worsened in only 6 (9.8%) patients.

The presence of seizures 12 months after starting the treatment clearly depended on the EEG at 3 months evaluation, with 24 (82.8%) patients with better EEG findings after 3 months having no seizures after 12 months ($p = 0.019$, $p < 0.05$) (Table 1).

Table 1
Correlation between presence of seizures and electroencephalography (EEG) findings at 3, 6 and 12 months after starting the treatment follow-up period

EEG follow-up (findings)	Seizures		Total	*p*
	no	yes		
After 3 months				
	6 months			
improved	12 (85.7)	2 (14.3)	14	0.0001
unchanged	6 (31.6)	13 (68.4)	19	
worsened	1 (14.3)	6 (85.7)	7	
total	19	21	40	
	12 months			
improved	24 (82.8)	5 (17.2)	29	0.019
unchanged	10 (45.5)	12 (54.5)	22	
worsened	4 (57.1)	3 (42.9)	7	
total	38	20	58	
	24 months			
improved	31 (96.9)	1 (3.1)	32	0.0001
unchanged	10 (52.6)	9 (47.4)	19	
worsened	3 (100)	0	3	
total	44	10	54	
After 6 months				
	12 months			
improved	23 (95.8)	1 (4.2)	24	0.001
unchanged	10 (47.6)	11 (52.4)	21	
worsened	2 (50)	2 (50)	4	
total	35	14	49	
After 12 months				
	24 months			
improved	26 (89.7)	3 (10.3)	29	0.087
unchanged	12 (70.6)	5 (29.4)	17	
worsened	2 (50)	2 (50)	4	0.031*
total	40	10	50	

All data are given as number or (percentage) of patients.
***Spearman's rank correlation.**

Also, the majority of patients with improvement in EEG at 6 months follow-up (23, 95.8%) had no seizures at one year follow-up. This correlation was highly statistically significant ($p = 0.001$, $p < 0.01$) (Table 1).

There was no correlation between the one year evaluation EEG and the presence of seizures in the same period ($p = 0.323$, $p > 0.05$).

Two years after starting the treatment, epileptic seizures were still present in 10 (20.4%) patients, whereas 39 (79.6%) patients were seizure free. On the 24 months check-up, EEG improvement was recorded in 15 (30.6%), it was unchanged in 29 (59.2%), while it was worsened in 5 (10.2%) patients.

After a two-year period, the presence of seizures was clearly dependent on the EEG findings at 3 months follow-up ($p = 0.0001$, $p < 0.01$). Hence, the majority of patients who still had seizures 24 months after starting the treatment (10, 52.6%) had no change in EEG on the first evaluation while the majority of patients without seizures after two years (31, 96.9%) had improved EEG 3 months after initiation of the treatment (Table 1).

The presence of seizures during this period did not depend on EEG after 6 months of the treatment ($p = 0.331$, $p > 0.05$).

EEG findings after 12 months correlated with presence of seizures after two years: most of the patients with improved (26, 89.7%) and unchanged EEG (12, 70.6%) had no seizures after two years, whereas patients with worsened EEG were with and without seizures, 2 (50%) respectively. The χ^2 distribution was not statistically significant ($p = 0.087$, $p > 0.05$), but there was a positive Spearman's rank correlation ($p = 0.031$, $p < 0.05$) (Table 1).

There was a statistically significant correlation between EEG findings after 24 months and the presence of seizures in the same period ($p = 0.012$, $p < 0.05$). The absence of seizures was registered in all 15 (100%) patients with EEG improvement and in 22 (75.9%) patients without changes in EEG while the majority of patients with worsened EEG (3.6%) continued to have epileptic seizures.

Discussion

Great heterogeneity of WS, in terms of numerous etiological factors, considerable variability in clinical presentation and different neurophysiological findings, precludes giving the accurate prognosis. In order to provide more adequate diagnostic procedures, treatment and further follow-up, we

considered it would be useful to find out predictiveness of EEG during the course of the disease.

In our study group, there was a predominance of symptomatic and cryptogenic forms of WS. Idiopathic WS was rarely recorded and therefore excluded from our research. However, it should be taken into consideration that some of our patients were diagnosed more than 20 years ago and nowdays sophisticated functional and anatomic neuroimaging have resulted in a shift towards symptomatic WS.

Both seizure control and results of the control EEG 3 months after initiating treatment showed improvement which is certainly consistent with already known fact that EEG is an important indicator of the CNS maturation [6, 11, 13].

The trend of EEG improving under treatment continued after 6 months so that 88.9% of patients with improved EEG were seizure-free, while the majority of patients with no change or worsening of the EEG continued to have seizures which was in correlation with literature data [6, 12–15].

EEG improvement continued on the evaluation 12 months after initiating the treatment. This result correlates with the findings of Kotagal [13] who observed that chaotic hypsarrhythmic pattern in patients with WS gradually became better organized, fragmented and disappeared with time and, in clinical terms, disease may go into remission or evolve to the other form of epilepsy syndrome. However, clinical practice and various studies so far, have shown that the one year follow-up period is insufficient to make adequate conclusions and long-term prognosis [6, 16, 17].

At two-year follow-up, EEG was unchanged in most of our patients (59.2%), improvement was registered in 30.6%, whereas worsening was present in 10.2% of patients, which is consistent with the fact that WS generally has a poor prognosis [8, 10].

In our study, we tried to determine whether there were specific clinical and electrophysiological parameters based on which we could, in an early stage, provide parents with a certain prediction of seizure control, as an indicator of subsequent disease outcome.

In that way, we found that the EEG improvement after 3 months of the treatment was a good prognostic indicator in terms of seizure control after 6, 12 and 24 months of therapy. Similar observation was confirmed on 12 months follow-up, when a certain connection between EEG in this period and seizure control after 24 months of the treatment, which is consistent with the findings of Mackay et al. [18].

Response to therapy after 12 months depended on the EEG after 6 months of therapy, thus the majority of patients with better EEG in this period had a good outcome while the majority of patients with dysrrythmic EEG had partial or bad response after one year of treatment.

Our results suggest the existence of a clear correlation between the presence of seizures on two-year follow-up and EEG findings after one and two-year treatment. So, all of these parameters represent predictors of outcome after two years of treatment. That was in correlation with findings of Kotagal [13].

Conclusion

EEG improvement after 3 months was a predictor of better seizure control at 6, 12 and 24 months follow-up. EEG improvement after 6 months of treatment was associated with good seizure control and good response to therapy after one year. On the other hand, EEG after 6 months was not predictive of disease outcome after 2 years, while EEG improvement after 12 months of therapy correlated with good seizure control at two-year evaluation, but could not be used as a predictor.

REFERENCES

1. *Johnston M.* Generalized seizures. In: *Behrman RE, Kliegman R, Jenson J*, editors. Nelson textbook of pediatrics. Philadelphia: W. B. Saunders; 2007. p. 2462–4.
2. *Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross HJ, Emde BW,* et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010; 51(4): 676–85.
3. *Arzimanoglou A, Guerrini R, Aicardi J.* Aicardi's epilepsy in children. 3rd ed. USA: Philadephia: Lippincot Wiliams & Wilkins; 2004.
4. *Panayiotopoulos CP.* The Epilepsies. Seizures, Syndromes and Management. Oxfordshire (UK): Bladon Medical Publishing; 2005.
5. *Engel J Jr.* ILAE classification of epilepsy syndromes. Epilepsy Res 2006; 70 Suppl 1: S5–10.
6. *Dulac O, Plouin P, Jambaque I.* Predicting Favorable Outcome in Idiopathic West Syndrome. Epilepsia 1993; 34(4): 747–56.
7. *Cvitanović-Sojat L, Gjergja R, Sabol Z, Hajnzić TF, Sojat T.* Treatment of West syndrome. Acta Med Croatica 2005; 59(1): 19–29. (Croatian)
8. *Shields WD.* Infantile Spasms: Little Seizures, BIG Consequences. Epilepsy Curr 2006; 6(3): 63–9.
9. *Cohen-Sadan S, Kramer U, Ben-Zeev B, Lahat E, Sahar E, Nevo Y,* et al. Multicenter long-term follow-up of children with idiopathic West syndrome: ACTH versus vigabatrin. Eur J Neurol 2009; 16(4): 482–7.
10. *Fois A.* Infantile spasms: Review of the literature and personal experience. Italian J Pediatr 2010; 36: 1–10.
11. *Go CY, Mackay MT, Weiss SK, Stephens D, Adams-Webber T, Ashwal S*, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2012; 78(24): 1974–80.
12. *Hrachovy RA, Frost JD.* Severe Encephalopathic Epilepsy in Infants: Infantile Spasms (West Syndrome). In: *Pellock JM, Bourgeois B, Dodson WE*, editors. Pediatric Epilepsy - Diagnosis and treatment. 3rd ed. New York: Demos; 2008. p. 249–69.
13. *Kotagal P.* Multifocal independent Spike syndrome: Relationship to hypsarrhythmia and the slow spike-wave (Lennox-Gastaut) syndrome. Clin Electroencephalogr 1995; 26(1): 23–9.
14. *Riikonen R.* Infantile spasms: Modern practical aspects. Acta Paediatr Scand 1984; 73(1): 1–12.

15. *Vigevano F, Cilio MR*. Vigabatrin versus ACTH as first-line treatment for infantile spasms: A randomized, prospective study. Epilepsia 1997; 38(12): 1270−4.
16. *Jeavons PM*. West syndrome: Infantile spasms. In: *Roger J, Dravet C, Bureau M, Dreifuss FE, Wolf P*, editors. Epileptic syndromes in infancy, Childhood and Adolescence. London: John Libbey; 1985. p. 42−50.
17. *Riikonen R*. Infantile spasms: Therapy and outcome. J Child Neurol 2004; 19(6): 401−4.
18. *Mackay MT, Weiss SK, Adams-Webber T, Ashwal S, Stephens D, Ballaban-Gill K*, et al. Practice parameter: medical treatment of infantile spasms: report of the American Academy of Neurology and the Child Neurology Society. Neurology 2004; 62(10): 1668−81.

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