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PREDICTORS OF DISABILITY IN PRETERM INFANTS DURING EARLY CHILDHOOD

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Summary. *There is impossible to give clear recommendations on the trajectory of the further development of a premature baby for a practical doctor. Despite the rich accumulated experience of the risks of developmental disorders in premature infants, the search for its predictors is continuing.*

The aim was to assess the developmental evaluation of preterm infants during early childhood and predict of disability. Materials and methods. The data of 172 children were processed. Perinatal period, electroencephalographic patterns and developmental assessment by KID-RCDI-2000 was performed. Multivariate statistical logistic regression analysis was used to determine the predictors of disability in young children. Results. Predictive factors of disability (from 38 clinical and instrumental characteristics) were following: bronchopulmonary dysplasia, electroencephalographic's patterns as delta- and teta-rhythm, and developmental delay by developmental scale till 12 month corrected age. Conclusion. The tool for predicting the development delay and disability in children born prematurely was established by multiple logistic regressions. The basis predictors are clinical, instrumental (standard EEG), and developmental scale results. This allows of a practicing doctor to focus on the development of the child and to apply of children with developmental delays to early intervention or rehabilitative services.

Key words: *Preterm Infant; Disability; Predictors; Early Childhood.*

Introduction

Premature infants are at increased risk of health problems and disability, and many studies conducted on the definition of development and quality of life of these children at the population level at different ages [1, 2, 3, 4]. Early age of any child is characterized by a completely unique processes that occur in the acquisition of many child psychomotor skills: a combination of determination and verticalization and stability, the formation of abstract thinking (search for hidden objects), associations (comparison of animal object painted with a book), game activities and social contact (a reflection of the relationship of the child with adults "friend or foe") and so on due to the high neuroplasticity of brain [5, 6, 7]. The developmental changes of the brain hamper prediction of cerebral palsy at early age [8].

Aim

The purpose of this study was to assess the developmental evaluation of preterm infants during early childhood and predict of disability. The aim was realized through searching answers to the following hypotheses:

(1) There is significant relationship between standard EEG, premature age for disability prognosis

(2) There is significant relationship between results of developmental scale KID-RCDI-2000, premature age for disability prognosis.

Material and methods

Study design

Observational cohort study included two stages: a prospective study on young children who were born prematurely during early childhood and retrospective division into groups depending on the functional deficit leads to disability (Figure 1).

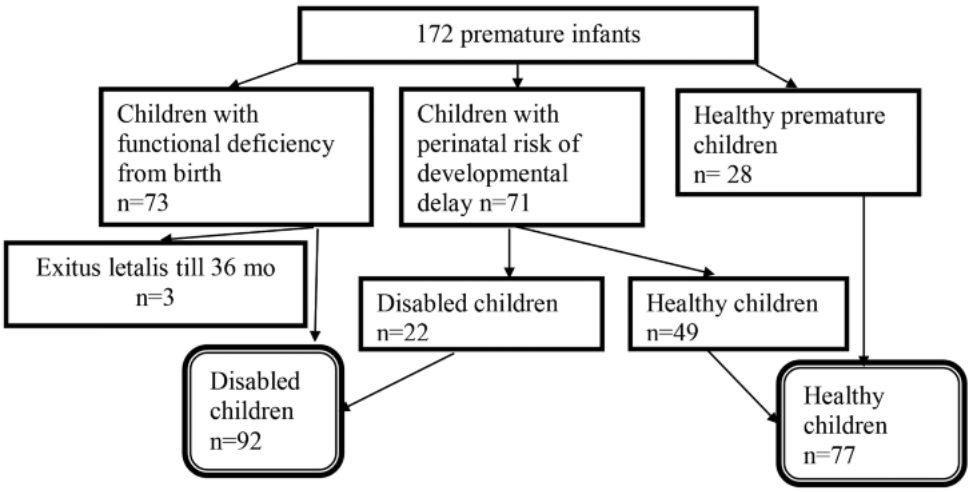

Fig.1. Scheme of prospective observation

Participants

The criteria for study inclusion in: 1) 172 children who were born prematurely in the Kharkiv region in the period 2012-2015; 2)gestational age of 22 weeks to 37 weeks incomplete; under the age of 36 months; informed consent of the parents.

Exclusion criteria were 1) surgery; 2) hereditary diseases; 3) congenital malformations; 4) coma in the early neonatal period; 5) the refusal of parents to participate in the study; 6)"loss" of research during the observation period due to changes in habitat.

The characteristics of the participants are presented in Table 1.

Table 1

Participants characteristics (N = 172)

Characteristics	N (%)
Sex	
Male	81 (47)
Gestational age	
34-37 weeks	28 (16.2)
32-34 weeks	41 (23.8)
28-32 weeks	81 (47)
22-27 weeks	22 (12.7)
Ponderal Index (PI)	
PI* < 2.32	76 (44.1)
Mechanical Ventilation (MV)	
Invasive MV over than 7 days	86 (50)
Bronchopulmanary displasia	249 (13.9)
Intravenricular hemorrhage III - IV degree by Papile LA, et al. [9]	41 (23.8)
Periventricukar leukomlacia	53 (30.8)
Disability	
Severe ophtalmopathy	18 (10.4)
Cerebral palsy	38 (22)
Cerebral palsy, ophtalmopathy, defness	18 (10.4)

For testing of the hypotheses the following methods were used:

(1) Estimation of body weight (kg) and growth (cm). In order to determine whether the growth and development of body weight for gestational age children who were born with different gestational age determined Ponderal Index* = (weight, g * 100) / (height3, cm) [10].

(2) Analysis of the main domains (cognitive, motor, speech and language, social-emotional, adaptive) measured on a scale KID-RCDI-2000, developed by H. Ayrton (USA) in the Russian version [11]. Questionnaire determined the behavior of children by 216 points in the following areas: social (40 points); self (40 points); gross motor skills (30 points); fine motor skills (30 points); expressive language (41 points); impressive language (40 points). Within each domain order of questions was accidental. The level of development was determined by the recommended technique points " age normal score", "age limit slight delay", "age limit delay", are presented in tables and on the linear scale of development by which each domain defined line of the child's age, category "normal development", "slight delay", "delay".

(3) To assess the functional status of brain on EEG (DXKC.941319.001-02P electroencephalogram (Ukraine, 2012)) by the standard method. Power and coherence spectra estimated in the range of delta (0.5-3 IIz), theta (4-8 IIz), alpha (8-13 IIz) and beta (13-30 Hz) rhythm. The time constant was 0.3 sec, write speed standard - 30 mm / sec [12].

(4) Used an corrected age (CA) in young children born premature [13].

Data analysis

For statistical analysis using statistical software packages "Excel for Windows", "Statistica 7.0. for Windows", "SPSS 16.0 for Windows". Multivariate statistical analysis of multiple stepwise regression removing insignificant variables from the regression model was performed of multiple stepwise regression removing insignificant variables from the regression model and calculating the coefficient of concordance for each equation. As a binary dependent variable (y) was selected out of early childhood: positive in case of disability (y = 1), negative (y = 0) in its absence. To predict the probability calculated referring the child to a particular group. The 38 clinical, anamnestic and instrumental characteristics were attracted. Statistical significance of the results (the likelihood that the baby will be classified on the basis of which is evaluated to a specific group supervision) estimated by Wald statistics, which represents the ratio of the square corresponding coefficient to its standard error.

Results

The result of the first step regression analysis was a group of factors (predictors) that are most associated with the development of disability (Table 2).

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Table 2

Results of the first step of multiple logistic regression

Predictors (Constant - 0, 811) df = 1	Code	β	p
Gestational age <32 weeks	c 2	3,722	0,054
Body weight <1500 g	c 3	0,656	0,418
Ponderal Index <2.3	c 4	22,498	0,095
Apgar Score, 5 min <7	c 5	11,545	0,001
Mechanical Ventilation	c 6	11,627	0,001
Retinopathy	c 7	2,275	0,131
Bronchopulmonary displasia	c 8	9,973	0,002
Periventricular leukomalacia	c 9	7,334	0,007
δ - rhythm	c 10	48,682	0,000
θ - rhythm	c 11	43,189	0,000
α - rhythm	c 12	5,102	0,024
β – rhythm	c 13	0,073	0,788
Diffuse EEG changes	c 14	16,761	0,000
Local slowing rate of EEG	c15	18,918	0,000
Motor developmental delay	c 16	13,826	0,000
Delay of weight gain in CA 2 months	c 17	3,370	0,066
Delay of growth in CA 12 months	c 18	0,471	0,493
Delay weight gain in CA 24 months	c19	2,530	0,112
Delay growth in CA 24 months	c 20	3,998	0,046
Delay growth in CA 24 months	c 21	1,391	0,237
% delta - rate over 28	c 22	0,142	0,706
% alfa - rhythm least 22	c 23	4,898	0,027
Slight lagging of cognitive development	c 24	10,087	0,001
Delay of cognitive development	c 25	30,962	0,000
Delay of large motor skills	c 26	10,087	0,001
Slight lagging of fine motor development	c 27	11,596	0,001
Delay of fine motor development	c 28	14,045	0,000
Slight lagging of expressive language development	c 29	11,596	0,001
Delay of expressive language development	c 30	10,830	0,001
Slight lagging of impressive language development	c 31	4,898	0,027
Delay of impressive language development	c 32	3,792	0,052
Slight lagging of socio-emotional development	c 33	4,898	0,027
Delay of socio-emotional development	c 34	9,367	0,002
Slight lagging of adaptive development	c 35	30,962	0,000
Delay of adaptive development	c 36	7,334	0,007
Deafness	c 37	2,351	0,125
Violations of vision	c 38	9,973	0,002

The analysis found that the proportion predictors did not demonstrate power relations and degree value, sufficient to take account of significant factors in the development of disability. Predictors of sufficient power relations led to the next, the second step of a logistic regression model, to the achievement of a high percentage of concordance. The 23 steps of removing each predictor were completed; the three final equations were built:

Z (Disability) – 200.759+ (52.056 * Availability BPD) + (-5.558 * theta – rhythm on standard EEG) + (32.657 * Delay of gross motor skills in CA 12 months) (1)

(This equation provided the concordance rate - 97%, $\chi 2 = 99.76$, (N = 171) (p <0,001));

and / or

Z (Disability) = -239.758 + (14,235 * delta-rhythm on standard EEG) + (-9.533 * delta-rhythm on standard EEG) + (136.601 * Slight lagging of gross motor skills at 12 months corrected age) (2)

(This equation provided the concordance rate - 98%, $\chi 2 = 108,5$, (N = 169) (p <0,001))

and / or

Z (Disability) = - 3.414 − (3.274 * Delay of gross motor skills in 12 months corrected age) − (2.879 * Slight lagging of fine motor skills development in 12 months corrected age) − (4.263 * Delay of adaptive developmental in 12 months corrected age) (3)

(This equation provided the concordance rate - 84%, $\chi 2 = 64,2$, (N = 69) (p <0,001)).

Predictive model (1) has shown that the most statistically selected among disparate and 38 characters for calculation of the probability of disability at an early age is one clinical indication (presence BPD), instrumental sign of (theta - rhythm on EEG) and symptoms assessment using the of development scale.

If the child does not has BPD (model (2)) and

slight lagging of gross motor development, for predicting disability in the logistic model should involve two standard EEG parameter (theta and delta-rhythm on EEG).

Both these equations demonstrate the use of standard EEG for predicting shortages of functions at an early age. Lack of perinatal data flow equations underscores the difficulty in predicting the outputs of premature infants in the neonatal period.

The last (3) model included data of children without lesions of central nervous system Equation (3) demonstrated that predicting disability and only possible when using the scale of KID-RCDI-2000 at the corrected age of 12 months. We consider this equation valuable for its use by primary care doctors where is impossible to perform a standard EEG.

Discussion

About 17% of children aged from birth to 18 years old have a developmental disability in the general pediatric population, but just only 30% of children are diagnosed in preschool age [14]. A particular risk for developmental disorders are premature infants, as a further careful monitoring after discharge from obstetric hospitals and their skilled training can reduce these risks [15]. Very premature babies have an increased incidence of cerebral palsy, 75% of which occurs in children with bilateral cystic periventricular leucomalacia. Even 4% of children with gestation age less than 32 weeks with the absence of neurosonographic changes are developing cerebral palsy [16].

Predictors of disability and cerebral palsy in premature infants are considered due to central nervous system injury and using neuroimaging methods (neurosonography and magnetic resonance imaging). Equally important the using of the multiple tools, such as neurological, motor exams, neurophysiological assessments in neonatal period [17, 18, 19]. But cerebral palsy may develops without evidence of organic damage to the central nervous system, because such a reputable organization as the Council on Children With Disabilities, to improve the early identification of children with retarded development and behavioral problems recommends that all infants and young children were examined for retention areas development. At a minimum, evaluation of using standardized screening tools should be made of all children aged 9 months, 18 months, 24 (or 30) months [20].

Our original study had shown an attempt to develop prediction improves by there were using non-invasive methods - standard EEG and scale development. This technological product that allows in terms of care young children who were born prematurely, predict its course and functional deficit are able to make of doctor's focuses on the child development for the purposes of

1) Early diagnosis of developmental disorders;

2) Timely guidance of children in rehabilitation programs and early intervention;

3) Planning follow-up observations for premature children after discharge from obstetric hospitals;

4) Create individual plans for health surveillance;

5) Counseling and parental involvement in children's development.

Conclusion

The tool for predicting the development delay and disability in children born prematurely was established by multiple logistic regression. The basis predictors are clinical, instrumental (standard EEG), and developmental scale results. This allows of a practicing doctor to focus on the development of the child and to apply of children with developmental delays to early intervention or rehabilitative services.

Contributors

The all authors designed the study, performed the statistical analyses and wrote the manuscript. The first and second authors were involved in data collection of the study. All authors contributed to and have approved the final manuscript.

Conflict of interest. None declared.

References

1. Baumann N, Bartmann P, Wolke D. Health-Related Quality of Life Into Adulthood After Very Preterm Birth. Pediatrics. 2016;137(4):e20153148. doi: 10.1542/peds.2015-3148.

2. Saigal S. Quality of life of former premature infants during adolescence and beyond. Early Hum Dev. 2013;89(4):209-13. doi: 10.1016/j.earlhumdev.2013.01.012.

3. Saigal S. Functional outcomes of very premature infants into adulthood. Semin Fetal Neonatal Med. 2014;19(2):125-30. doi: 10.1016/j.siny.2013.11.001.

4. Verrips E, Vogels T, Saigal S, Wolke D, Meyer R, Hoult L, et al. Health-related quality of life for extremely low birth weight adolescents in Canada, Germany, and the Netherlands. Pediatrics. 2008;122(3):556-61.

5. A World Bank Group Flagship Report. World Development Report 2015. Mind, Society, and Behavior [Internet]. Washington; 2015. Chapter 5, Early childhood development. [cited 2018 Feb 3]; p.98-109. Available from: http://www.worldbank.org/content/dam/Worldbank/Publications/WDR/WDR%202015/WDR-2015-Full-Report.pdf.

6. Christensen DL, Schieve LA, Devine O, Drews-Botsch C. Socioeconomic status, child enrichment factors, and cognitive performance among preschool-age children: results from the Follow-Up of Growth and Development Experiences study. Res Dev Disabil. 2014;35(7):1789-801.

7. Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waiswa P, et al. Every Newborn: progress, priorities, and potential beyond survival. Lancet. 2014;384(9938):189-205. doi: 10.1016/S0140-6736(14)60496-7.

8. Hadders-Algra M. Early Diagnosis and Early Intervention in Cerebral Palsy. Front Neurol. 2014;5:185. doi: 10.3389/fneur.2014.00185.

9. Papile LA, et al. Intraventricular hemorrhage in very low birth weight infants: associated risk factors and outcome in the neonatal period. J Pediatr. 1978;92:529.

10. Polin MD, Richard A, Spitzer MD, Alan R. Fetal & neonatal secrets. 2nd ed. Elsevier: Mosby Philadelphia; 2007. 499 p.

11. Program KID RCDI for assessment of child development. The e-resource available at: http://www.eii.ru/informacionnyj_centr/voprosnik_kid_i_rcdi/

12. Luders H, Noachtar S, editors. Atlas and Classification of Electro encephalo graphy. Philadelphia: WB Saunders; 2000. 203p.

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13. *Engle WA. Age Terminology During the Perinatal Period. Pediatrics. 2004;114(5):1362-4.*
14. Centers for Disease Control and Prevention. Developmental Screening. Available from: http://www.cdc.gov/ncbddd/child/devtool.htm
15. Stark AR, Adamkin DH, Batton DG, Bell EF, Bhutani VK, Denson SE, et al. Hospital discharge of the high-risk neonate. Pediatrics. 2008;122(5):1119-26. doi: 10.1542/peds.2008-2174.
16. Ancel PY, Livinec F, Larroque B, Marret S, Arnaud C, Pierrat V, et al. Cerebral palsy among very preterm children in relation to gestational age and neonatal ultrasound abnormalities: the EPIPAGE cohort study. Pediatrics. 2006;117(3):828-35.
17. Constantinou JC, Adamson-Macedo EN, Mirmiran M, Fleisher BE. Movement, imaging and neurobehavioral assessment as predictors of cerebral palsy in preterm infants. J Perinatol. 2007, 27(4):225-9 doi: 10.1038/sj.jp.7211664.
18. Leijser LM, Vein AA, Liauw L, Strauss T, Veen S, Wezel-Meijler GV. Prediction of short-term neurological outcome in full-term neonates with hypoxic-ischaemic encephalopathy based on combined use of electroencephalogram and neuro-imaging. Neuropediatrics. 2007;38(5):219-71. doi: 10.1055/s-2007-992815.
19. Skiöld B, Eriksson C, Eliasson AC, Adén U, Vollmer B. General movements and magnetic resonance imaging in the prediction of neuromotor outcome in children born extremely preterm. Early Hum Dev. 2013;89(7):467-72. doi: 10.1016/j.earlhumdev.2013.03.014.
20. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. Pediatrics. 2006;118:1808-9. doi: 10.1542/peds.2006-1231

ПРЕДИКТОРЫ ИНВАЛИДНОСТИ У НЕДОНОШЕННЫХ ДЕТЕЙ В РАННЕМ ВОЗРАСТЕ

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Резюме. Практическому врачу невозможно дать четкие рекомендации по траектории дальнейшего развития недоношенного ребенка. Несмотря на богатый накопленный опыт рисков нарушения развития у недоношенных детей, поиск его предикторов продолжается.

Цель исследования заключалась в анализе оценки развития недоношенных детей в раннем возрасте и прогнозировании инвалидности.

Материалы и методы. Были обработаны данные 172 детей. Изучены перинатальный период, электроэнцефалографические модели и оценка развития KID-RCDI-2000. Для определения предикторов инвалидности у детей был использован многомерный статистический логистический регрессионный анализ.

Результаты. Прогностическими факторами инвалидности (из 38 клинических и инструментальных характеристик) были следующие: бронхолегочная дисплазия, такие электроэнцефалографические паттерны, как дельта-и тета-ритм, задержка развития по шкале развития до 12-месячного скорректированного возраста.

Вывод. Инструмент прогнозирования задержки развития и инвалидности у детей, рожденных преждевременно, был установлен несколькими логистическими регрессиями. Основными предикторами являются клинические, инструментальные (стандартная ЭЭГ) показатели и показатели шкалы развития. Это позволяет практикующему врачу сосредоточиться на развитии ребенка и применять у детей с задержками развития раннего вмешательства или реабилитационные услуги.

Ключевые слова: недоношенные новорожденные; инвалидность; предикторы; раннее детство.

ПРЕДИКТОРИ ІНВАЛІДНОСТІ У НЕДОНОШЕНИХ ДІТЕЙ У РАННЬОМУ ВІЦІ

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Summary. Практичному лікарю неможливо дати чіткі рекомендації щодо траєкторії подальшого розвитку недоношеної дитини. Незважаючи на багатий накопичений досвід ризиків порушення розвитку у недоношених дітей, пошук його предикторів триває.

Мета полягала в аналізі оцінки розвитку недоношених немовлят у ранньому дитинстві та прогнозуванні інвалідності.

Матеріали та методи. Дані про 172 дітей були оброблені. Вивчено перинатальний анамнез, електроенцефалографічні показники та результати оцінки розвитку KID-RCDI-2000. Для визначення предикторів інвалідності у маленьких дітей був використаний багатомірний статистичний логістичний регресійний аналіз.

Результати. Прогностичні чинники інвалідності (з 38 клінічних та інструментальних характеристик) включали бронхолегеневу дисплазію, патерни електроенцефалографії такі, як дельта-тета-ритм, а також, затримку розвитку у період до 12-місячного віку.

Висновок. Інструмент прогнозування затримки розвитку та інвалідності у дітей, народжених передчасно, був встановлений кількома логістичними регресіями. Основними предикторами є клінічні, інструментальні (стандартні ЕЕГ) та результати розвитку шкали. Це дозволяє практикуючому лікареві зосередити увагу на розвитку дитини та застосуванні у дітей з затримками розвитку раннього втручання або реабілітаційних послуг.

Ключові слова: недоношена дитина; інвалідність; пре диктори; раннє дитинство.

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