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Effect of ultra-early intervention of NDT therapy on nerve and motor development in infants at high risk of cerebral palsy

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Abstract

Introduction: *The aim of the study was to investigate the effect of ultra-early intervention of nerve and motor development in infants at high risk of cerebral palsy.*
Material and methods: *One hundred and twenty cases of infants born in The Affiliated Hospital of Harbin Medical University from January 2017 to January 2019 and diagnosed with high risk of cerebral palsy were included in the observation group. In addition, 120 cases of infants at high risk of cerebral palsy (three to five months old) who were admitted to this hospital during the same period were included in the control group, and 120 healthy infants born in the same hospital were included in the healthy group. Intervention was performed on the observation group after diagnosis (within seven days of birth), mainly using neurodevelopmental therapy (NDT). Children in the control group underwent intervention after diagnosis (at three to five months old) using the same measures. The healthy group underwent no intervention. Changes in various indicators were compared among the observation group, healthy group, and control group.*
Results: *At baseline and at three months, the developmental quotient (DQ) at all functional areas, total DQ, and GESELL development scale (GDS) scores were significantly lower in the observation and control groups than in the healthy group ($p < 0.05$). At six months, 12 months, 18 months, and 24 months, the DQ at all functional areas, total DQ, and GDS (adaptability, gross motor, fine motor, language, personal social interaction) scores in the observation and control groups were significantly lower than those in the healthy group ($p < 0.05$). However, the observation group scores were significantly higher than the control group scores ($p < 0.05$). In the observation group, the normalisation rate was higher than in the control group, and the incidence rate of cerebral palsy and full developmental delay was lower than in the control group ($p < 0.05$).*
Conclusions: *Ultra-early diagnosis and NDT intervention can significantly accelerate the motor development of infants at high risk of cerebral palsy. The earlier, the better. Ultra-early intervention can promote the normalisation of infants at high risk of cerebral palsy and significantly reduce the risk of progression to cerebral palsy.*

Key words: *paediatric cerebral palsy, non-progressive neurological disorder, rehabilitation.*

Introduction

Paediatric cerebral palsy (CP) is a non-progressive neurological disorder, and it is one of the most common causes of disability in children [8]. Children often develop changes in muscle tone, muscle weakness, and coordination disorder [13], mainly manifested as postural abnormalities, cognitive impairment, and perceptual disorders [1]. Neurodevelopmental disorders form a heterogeneous group of disorders. The disorders

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are characterised by widespread alterations in the brain structure, with widespread deviancies found in the brain's grey and white matter [5, 12]. The brains of children with CP virtually always exhibit lesions of the white matter of the sensorimotor areas, often comprising the periventricular white matter [14]. The average age at diagnosis of cerebral palsy is two years or later [10]. In China, about 50% of patients fail to meet the diagnostic criteria before 18 months of age, and some children with mild symptoms were not diagnosed until preschool age, missing the period of the most effective intervention [9]. Early and accurate diagnosis of cerebral palsy can be made through standardised evaluation tools, greatly improving the prognosis of children with cerebral palsy [6, 21, 23]. At present, super-early intervention of high-risk children with cerebral palsy has attracted widespread interest. It is generally believed that the early intervention is necessary and effective [2, 16]. However, in China, this concept has rarely been applied in clinical practice. This study explores the impact of the application of early diagnosis and intervention on symptom improvement and prognosis in children with cerebral palsy, providing a basis for guiding clinical work.

Material and methods

Study subjects

In this study, 120 infants with high risk of cerebral palsy born and diagnosed in The Affiliated Hospital of Harbin Medical University from January 2017 to January 2019 were included as the observation group, 120 patients with high risk of cerebral palsy in the same period admitted to the same hospital as the control group, and 120 healthy infants born in the same hospital in the same period as the healthy group.

Inclusion and exclusion criteria

Inclusion and exclusion criteria for the observation group and the control group

Inclusion criteria: 1) Meeting the diagnostic criteria for infants at high risk of cerebral palsy [23]: (i) Motor dysfunction, including decreased motor quality, nervous system abnormalities, motor milestone delay, and some atypical performance; (ii) Cranial imaging abnormalities, including periventricular leukomalacia, haemorrhagic infarction, cortical and deep grey matter lesions; (iii) History of high risk of cerebral palsy. Before pregnancy: stillbirth, abortion, assisted reproduction and so on. Pregnancy: genetic diseases, birth defects, multiple births. Postpartum high-risk factors: ischemic and hypoxic encephalopathy, intracranial haemorrhage, jaundice and so on; (iv) Abnormal evaluation results of standardised evaluation tools, including qualitative general movements assessment (GMs) and GESELL development scale (GDS). Among these, criterion (i) is a prerequisite, with the presence of any two among (ii), (iii) and (iv) giving grounds for diagnosis; 2) First diagnosis, not having previously received rehabilitation treatment related to cerebral palsy; 3) The infants in the observation group were within seven days of birth, and those in the control group were six months of age or fewer; 4) The guardians had normal reading and communication skills and were able to complete various interventions.

Exclusion criteria: 1) With severe epilepsy; 2) With trisomy 21 syndrome; 3) With serious diseases of other organs; 4) With metachromatic leukodystrophy; 5) With other diseases causing muscle tone changes.

Inclusion and exclusion criteria for the healthy group

Inclusion criteria: 1) Without other systemic diseases; 2) GMs and GDS score results were normal.

Exclusion criteria: 1) Infants have high-risk factors of cerebral palsy. Before pregnancy: stillbirth, abortion, assisted reproduction. Pregnancy: genetic diseases, birth defects, multiple births. Postpartum high-risk factors: ischemic and hypoxic encephalopathy, intracranial haemorrhage, jaundice and so on; 2) History of motor dysfunction and high risk of cerebral palsy.

G-Power software was used to calculate the sample size. The statistical method (*F* tests) was selected in G-Power software, and then the classification (fixed effects, omnibus one-way) was selected. The parameter was set to 0.05, the inspection efficiency to 0.8, and the number of groups to three. Data from our team's pre-experiment were added, including the number of groups, variance within the group, the average number of each group, and the sample size of each group. The calculated effect size f was 0.28, and the total sample size was 360 cases, with 120 cases in each group.

All the guardians of the children in this study signed the informed consent forms, and the study was approved by the hospital ethics committee.

Intervention methods

In the observation group, after diagnosis (within seven days of birth), we provided basic health and disease-related education to the parents, including information about the disease and knowledge of daily feeding and care. We further provided psychological guidance and follow-up supervision for the parents. The internationally recognised neurodevelopmental therapy (NDT) intervention [17] was used, consisting chiefly of three components:

1. Exercise training: the therapist is goal-oriented and works with the neonatal guardian to make a family exercise plan. The plan is developed based on specific activities of the infants in the family. The plan is designed step by step, and all tasks allow the infant to complete at least some elements. Having set an exercise target, the infant is able to achieve the goal as his/her exercise ability increases. Subsequently, the difficulty level of the task is increased or the environment altered, so the infant continues to face challenges to exercise ability. In the process of implementing the training plan, the therapist should pay attention to the degree of completion and quality of infant movements, making corrections and offering guidance twice weekly. To ensure neonatal safety, therapists and parents only provide manual assistance if necessary. Manual assistance is immediately reduced or ceased once the task is performed independently. The exercise plan includes standing, grasping, stretching, and other movements.

2. Parental education: the therapist fully explains the concept and important principles of NDT therapy to the parents, so that the parents can understand the focus of NDT therapy. The therapist asks the parents to make maximal use of infant waking time and natural learning opportunities. The therapist trains the parents to identify the normal trajectory of neonatal motor movements and to guide neonatal progress, and encourages timely feedback to facilitate guidance from the therapist.

3. Creating a diverse environment: whenever possible, traditional neonatal equipment (e.g. highchairs, toys) are used to build different practice areas. Toys that match the required exercise task and physical training are selected. The parents are encouraged to establish exercise-rich play environments to facilitate neonatal voluntary exercise, exploration, and task success.

Observation method

The observation group took the day of diagnosis as baseline, and the healthy group took postnatal day seven as baseline. Changes in various indicators among the three groups were compared at three, six, 12, 18, and 24 months of age. GDS was used to evaluate the DQ in each functional area, including adaptability, gross motor, fine movement, language and personal socialisation, and total DQ. DQ = developmental age/actual age 100; the higher the score, the better the development. Comparing the proportion of children achieving normalisation, progressing to cerebral palsy and developmental development in the observation group and control group at follow-up to 24 months. Judgment criteria for normalisation: the DQ in each functional area and total DQ ≥ 70 points; increases in muscle strength and tone and cessation of abnormal posture. Precise diagnostic criteria for cerebral palsy are referred to the literature [18]; those infants who did not achieve normalisation or meet the precise diagnostic criteria for cerebral palsy were judged to have comprehensive developmental delay.

Statistical analysis method

Data were analysed using the SPSS20.0 statistical software. Measurement data are represented by mean ±SD, and count data are expressed by percentage. Repeated measure analysis of variance (ANOVA) was used to comparing data from the same set across different time periods. Multi-group comparisons were performed by one-way ANOVA; comparisons between groups, by the least significant difference *t*-test (LSD-*t*) method; and comparisons across count data, by the 2-test. $P < 0.05$ was considered as a statistically significant difference.

Results

Imaging results and basic information

There were 68 males and 52 females in the observation group, aged 0~7 days (4.2 ±1.0). Imaging examinations of this group showed 82 cases of intraventricular leukomalacia, 15 cases of intracranial haemorrhage,

Table I. Imaging findings and basic information of two groups of infants (*N* = 120)

Variable	The observation group, *n* (%)	The control group, *n* (%)	*P*
Ventricles paraleukomalacia	82 (68.33)	78 (65.00)	0.58
Intracranial haemorrhage	15 (12.50)	20 (16.67)	0.36
One side of brain parenchyma injury	9 (7.50)	14 (11.67)	0.27
Cerebral cortex malformation	8 (6.67)	6 (5.00)	0.58
Thalamic and basal nucleus lesions	6 (5.00)	2 (1.66)	0.15
Male	68 (56.67)	72 (60.00)	0.60
Female	52 (43.33)	48 (40.00)	0.60
Age (months)	0~7 (4.2 ±1.0)	3~5 (4.6 ±1.2)	–

nine cases of one side of cerebral parenchyma injury, eight cases of cerebral cortical malformation, and six cases of thalamic and basal nucleus lesions. In the control group, 72 males and 48 females were included, ranging from 3-5 months (4.6 ±1.2) of age. Imaging examinations of this group showed 78 cases of intraventricular leukomalacia, 20 cases of intracranial haemorrhage, 14 cases of one side of cerebral parenchy-

Table II. Comparison of functional areas and total DQ values among three groups of infants

Months of age	Group	*N*	Adaptability	Gross motor	Fine movement	Language	Personal social interaction	Total DQ
Baseline	The healthy group	120	86.21 ±15.42	87.45 ±14.26	89.03 ±16.16	86.15 ±17.43	89.37 ±12.48	89.56 ±14.14
	The observation group	120	54.05 ±13.21	45.49 ±14.83	51.67 ±13.97	58.63 ±14.66	58.51 ±17.13	53.67 ±14.46
	p		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
3 months old	The healthy group	120	88.32 ±14.34	88.25 ±13.73	90.22 ±16.47	88.34 ±15.22	91.07 ±13.57	90.76 ±14.14
	The observation group	120	56.44 ±16.47	47.53 ±15.23	53.81 ±12.78	61.02 ±13.53	59.95 ±16.45	55.95 ±14.85
	p		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
6 months old	The healthy group	120	90.12 ±15.65	91.05 ±14.62	91.92 ±17.56	89.74 ±13.97	92.67 ±16.38	91.36 ±15.05
	The control group	120	59.86 ±17.6	49.93 ±17.41	57.91 ±18.48	65.05 ±17.99	64.72 ±16.75	58.89 ±14.9
	The observation group	120	60.89 ±16.87	55.33 ±18.24	59.22 ±16.05	67.64 ±15.2	67.4 ±17.69	60.5 ±13.03
	p		0.042	0.015	0.043	0.035	0.026	0.036
12 months old	The healthy group	120	93.21 ±13.76	92.12 ±16.83	94.26 ±14.97	91.34 ±16.14	93.71 ±13.76	91.45 ±14.61
	The control group	120	65.88 ±17.57	55.58 ±18.02	65.42 ±19.18	68.35 ±18.39	70.33 ±17.19	64 ±15.28
	The observation group	120	69.29 ±17.18	58.6 ±18.5	68.96 ±17.57	69.16 ±14.93	73.98 ±17.61	68.4 ±13.55
	p		0.049	0.003	0.058	0.041	0.037	0.018
18 months old	The healthy group	120	97.52 ±15.72	95.43 ±13.48	96.45 ±14.69	94.84 ±16.31	96.51 ±13.57	95.15 ±14.35
	The control group	120	74.67 ±18.49	63.02 ±17.74	72.26 ±20.3	80.88 ±21.19	80.72 ±19.75	74.71 ±16.81
	The observation group	120	76.8 ±17.31	67.53 ±18.27	76.67 ±17.04	86.53 ±14.9	84.69 ±17.29	78.04 ±13.06
	p		0.046	0.025	0.038	0.028	0.035	0.047
24 months old	The healthy group	120	101.12 ±13.65	98.65 ±16.28	99.83 ±15.49	97.34 ±15.63	99.46 ±14.27	98.65 ±15.15
	The control group	120	82.95 ±19.57	75.19 ±17.74	84 ±20.89	91.19 ±21.12	87.72 ±21.27	83.61 ±17.62
	The observation group	120	89.27 ±12.5	81.24 ±14.6	90.42 ±18.93	95.29 ±17.63	94 ±17.98	85.44 ±14.55
	p		0.036	0.024	0.045	0.048	0.026	0.013

Table III. Outcome of children in two groups [cases (%)]

Group	*N*	Normalisation, *n* (%)	Cerebral palsy, *n* (%)	Comprehensive developmental delay, *n* (%)	χ^2	*P*
The control group	120	56 (46.70)	37 (30.83)	27 (22.50)	8.407	0.015
The observation group	120	77 (64.17)	29 (24.17)	14 (11.67)		

ma injury, six cases of cerebral cortical malformation, and two cases of thalamic and basal nucleus lesions. There was no significant difference in gender composition and imaging distribution between two groups ($p > 0.05$) (Table I).

Comparison of DQ value in each functional area and total DQ value among the three groups

As the infants' age increased, the DQ value in each functional area and total DQ value increased gradually across the three groups, which was statistically significant (all $p < 0.01$). At baseline and at three months of age, the DQ value in each functional area and total DQ value in the observation group were significantly lower than those in the healthy group, and the differences were statistically significant ($p < 0.01$). At six, 12, 18, and 24 months old, DQ value in each functional area and total DQ value were significantly different among the three groups ($p < 0.01$). Pairwise comparisons showed that DQ value in each functional area and total DQ value were significantly lower in the observation and control groups than in the healthy group, and that these values were significantly higher in the observation group than in the control group. The differences were statistically significant ($p < 0.05$) (Table II).

Comparison of the prognosis of the children in the two groups

Compared with the control group, the normalisation rate in the observation group was higher, and the incidence of cerebral palsy and comprehensive developmental delay was lower. The differences were statistically significant ($p < 0.05$) (Table III).

Discussion

Studies have shown that infants with cystic periventricular leukomalacia have an ~85% chance of being diagnosed with cerebral palsy, while infants with a term stroke have a chance of about 30% [8]. This indicates that infants at high risk of cerebral palsy have a high risk of developmental impairment, and that early intervention is essential. In early childhood, when brain plasticity is at its peak, many of these infants respond well to intervention [11], which can maximize developmental trajectory changes up to adulthood [7]. However, in most clinical settings, the average age of diagnosis of cerebral palsy is two years or later [10]. Thus, many children do not receive ultra-early intervention. Even where early diagnosis is possible, early intervention remains a significant challenge for many parents. Parental lack of understanding of the disease and interventions has led to suboptimal effects of early interventions. Children under three years of age are at the most consequential stages of brain development. The earlier the intervention, the better the clinical effect [3]. Therefore, clinicians must endeavour to diagnose children who show clinical characteristics of cerebral palsy, and who are at high risk of cerebral palsy, before the age of one. If early adverse factors negatively impact the infant's brain, these negative consequences can most effectively be averted in early life [6]. Clinical intervention and rehabilitation treatment should be started as soon as possible to promote the infant's neurological development of the baby. Providing a stimulating environment can produce positive results for sports [15]. Enriching the environment and engaging in family rehabilitation is the basis for ensuring the comprehensive clinical efficacy of high-risk children with cerebral palsy [25]. In addition to visual, auditory and sensory stimulation, family rehabilitation posture management can also improve the neural development of high-risk children with cerebral palsy. Furthermore, engaging with common household items can positively impact rates of abnormal posture and secondary injury in high-risk children with cerebral palsy [25]. For example, children's small quilts and bedsheets can be used for flexion position training, including supervising good limb positioning (including the correction of the postures of restraining the reverse angle bow, restraining the adduction of thumbs, supine, sitting and even standing positions) and guiding the children to grasp, actively extend their hands, and perform other daily activities.

In this study, the therapist team joined the parents to develop a plan and trained the parents to supervise and guide their infants' neonatal training, which improved the quality of ultra-early intervention. Studies have shown that NDT therapy is effective in improving trunk control, balance, and gross motor function [19].

It is also reported that gross motor function improves when NDT dosage is increased [4,24]. NDT affects postural control and balance in patients with cerebral palsy, leading to improved functional motor levels and functional independence [22].

In this study, targeted intervention with NDT was conducted immediately after diagnosis (within seven days of birth) in the observation group. This was compared with the control group, which underwent intervention after diagnosis (at three to five months old); and with the healthy group, which underwent no intervention. The results showed that the scores of DQ value in each functional area, total DQ value, and GESELL development scale (adaptability, gross motor, fine movement, language, and personal social interaction) all increased gradually as the infants' monthly age increased. NDT therapy led to improvements in the scores in neonatal adaptability, gross motor, fine movement, language, and personal social interaction in both the observation group and the control group. The observation group had higher scores than the control group, indicating that early active motor intervention is more beneficial to the development of the motor system and nerves in the infant brain, and promotes normal growth and development of muscle and bone. This study emphasises the establishment of diverse environments so that infants can be trained in a variety of settings. Through existing toys, infants can conduct exercise training, thus developing their cognitive ability, self-learning ability, gross and fine motor skills under the premise of good compliance.

In these efforts, parental education and guidance is essential. Parents' active participation and mastery of the key points of NDT operation leads to significant improvement in the quality of neonatal exercise training. Family-centred intervention is the most important component of various types of therapy for children, those with cerebral palsy and those at high risk. Therefore, targeted guidance and training for parents, which can enable parents to acquire the knowledge and skills to correctly guide children to complete various training programmes, is crucial [20]. Through the participation of the therapist team, this study educated and trained parents, designed training plans, and provided timely guidance and supervision. These efforts improved the effectiveness of early intervention of children with cerebral palsy and at high risk of cerebral palsy and demonstrate that the ultra-early intervention has great significance for children at high risk of cerebral palsy. Ultra-early diagnosis and intervention can significantly accelerate the motor development process of infants at high risk of cerebral palsy, and significantly reduce the risk of progression to cerebral palsy in infants at high risk of cerebral palsy.

There are some limitations. First, the family-centred rehabilitation place set by the research team still needs improvements, including effective utilisation of indoor facilities and single scene. Second, the guidance to parents is not sufficiently personalised. Finally, no additional support was provided to parents with low educational levels.

Conclusions

Ultra-early diagnosis and NDT therapy intervention can significantly accelerate the motor development process of high-risk children with cerebral palsy. The earlier the intervention is conducted, the better the effect. Ultra-early intervention can promote the normalisation of children at high risk of cerebral palsy and significantly reduce their risk of progression to cerebral palsy.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Harbin Children's Hospital Affiliated to Harbin Medical University.

Written informed consent was obtained from all parents/legal guardians.

Disclosure

The authors report no conflict of interest.

References

1. Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, Jacobsson B, Damiano D; Executive Committee for the Definition of Cerebral Palsy. Proposed definition and classification of cerebral palsy, April 2005. Dev Med Child Neurol 2005; 47: 571-576.
2. Byrne R, Noritz G, Maitre NL; NCH Early Developmental Group. implementation of early diagnosis and intervention guidelines for cerebral palsy in a high-risk infant follow-up clinic. Pediatr Neurol 2017; 76: 66-71.
3. Coq JO, Delcour M, Massicotte VS, Baud O, Barbe MF. Prenatal ischemia deteriorates white matter, brain organization, and function: implications for prematurity and cerebral palsy. Dev Med Child Neurol 2016; 58 Suppl 4: 7-11.
4. Evans-Rogers DL, Sweeney JK, Holden-Huchton P, Mullens PA. Short-term, intensive neurodevelopmental treatment program experiences of parents and their children with disabilities. Pediatr Phys Ther 2015; 27: 61-71.
5. Franki I, Mailleux L, Emsell L, Peedima ML, Fehrenbach A, Feys H, Ortibus E. The relationship between neuroimaging and motor outcome in children with cerebral palsy: A systematic review. Part A: Structural imaging. Res Dev Disabil 2020; 100: 103606.
6. Hadders-Algra M, Boxum AG, Hielkema T, Hamer EG. Effect of early intervention in infants at very high risk of cerebral palsy: a systematic review. Dev Med Child Neurol 2017; 59: 246-258.
7. Heckman JJ. Schools, skills, and synapses. Econ Inq 2008; 46: 289.

8. Hielkema T, Hadders-Algra M. Motor and cognitive outcome after specific early lesions of the brain – a systematic review. Dev Med Child Neurol 2016; 58 Suppl 4: 46-52.
9. Huang TT, Wang F, Hu WH, Zhou YP, Xing W, Wu YH, Zhou Z. Individualized prediction of high risk of cerebral palsy in children with periventricular leukomalacia. Chinese J Pract Nervous Dis 2019; 22: 1773-1779.
10. Hubermann L, Boychuck Z, Shevell M, Majnemer A. Age at referral of children for initial diagnosis of cerebral palsy and rehabilitation: Current practices. J Child Neurol 2016; 31: 364-369.
11. Johnston MV, Ishida A, Ishida WN, Matsushita HB, Nishimura A, Tsuji M. Plasticity and injury in the developing brain. Brain Dev 2009; 31: 1-10.
12. Key A, Thornton-Wells, TA. Brain-based methods in the study of developmental disabilities: examples from event-related potentials and magnetic resonance imaging research. In: Burack JA and others (Eds.). The Oxford Handbook of Intellectual Disability and Development, Oxford Library of Psychology 2011 (online edn, Oxford Academic, 18 Sept. 2012): 149-164.
13. Lorente-Hurtado I. La parálisis cerebral. Actualización del concepto, diagnóstico y tratamiento. Pediatr Integral 2007; 11: 687-698.
14. Mailleux L, Franki I, Emsell L, Peedima ML, Fehrenbach A, Feys H, Ortibus E. The relationship between neuroimaging and motor outcome in children with cerebral palsy: A systematic review. Part B: Diffusion imaging and tractography. Res Dev Disabil 2020; 97: 103569.
15. Morgan C, Darrah J, Gordon AM, Harbourne R, Spittle A, Johnson R, Fetters L. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. Dev Med Child Neurol 2016; 58: 900-909.
16. Morgan C, Fetters L, Adde L, Badawi N, Bancale A, Boyd RN, Chorna O, Cioni G, Damiano DL, Darrah J, de Vries LS, Dusing S, Einspieler C, Eliasson AC, Ferriero D, Fehlings D, Forssberg H, Gordon AM, Greaves S, Guzzetta A, Hadders-Algra M, Harbourne R, Karlsson P, Krumlinde-Sundholm L, Latal B, Loughran-Fowlds A, Mak C, Maitre N, McIntyre S, Mei C, Morgan A, Kakooza-Mwesige A, Romeo DM, Sanchez K, Spittle A, Shepherd R, Thornton M, Valentine J, Ward R, Whittingham K, Zamany A, Novak I. Early intervention for children aged 0 to 2 years with or at high risk of cerebral palsy: International clinical practice guideline based on systematic reviews. JAMA Pediatr 2021; 175: 846-858.
17. Morgan C, Novak I, Dale RC, Badawi N. Optimising motor learning in infants at high risk of cerebral palsy: a pilot study. BMC Pediatr 2015; 15: 30.
18. Novak I, Morgan C, Adde L, Blackman J, Boyd RN, Brunstrom-Hernandez J, Cioni G, Damiano D, Darrah J, Eliasson AC, de Vries LS, Einspieler C, Fahey M, Fehlings D, Ferriero DM, Fetters L, Fiori S, Forssberg H, Gordon AM, Greaves S, Guzzetta A, Hadders-Algra M, Harbourne R, Kakooza-Mwesige A, Karlsson P, Krumlinde-Sundholm L, Latal B, Loughran-Fowlds A, Maitre N, McIntyre S, Noritz G, Pennington L, Romeo DM, Shepherd R, Spittle AJ, Thornton M, Valentine J, Walker K, White R, Badawi N. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. JAMA Pediatr 2017; 171: 897-907.
19. Sah AK, Balaji GK, Agrahara S. Effects of task-oriented activities based on neurodevelopmental therapy principles on trunk control, balance, and gross motor function in children with spastic diplegic cerebral palsy: A single-blinded randomized clinical trial. J Pediatr Neurosci 2019; 14: 120-126.
20. Shore BJ, Martinkevich P, Riazi M, Baird E, Encisa C, Willoughby K, Narayanan UG; CHOP Investigative Team. Reliability of radiographic assessments of the hip in cerebral palsy. J Pediatr Orthop 2019; 39: e536-e541.
21. Spittle AJ, Morgan C, Olsen JE, Novak I, Cheong JLY. Early diagnosis and treatment of cerebral palsy in children with a history of preterm birth. Clin Perinatol 2018; 45: 409-420.
22. Tekin F, Kavlak E, Cavlak U, Altug F. Effectiveness of neurodevelopmental treatment (Bobath concept) on postural control and balance in cerebral palsied children. J Back Musculoskelet Rehabil 2018; 31: 397-403.
23. The CP Tool Kit Parent Leadership Committee. Early identification and early neurorehabilitation in cerebral palsy: 2014 summit report. Available at: https://cpnowfoundation.org/wp/wp-content/uploads/2015/11/CP-ToolKit.pdf. Accessed: July 1, 2017.
24. Tsorlakis N, Evaggelinou C, Grouios G, Tsorbatzoudis C. Effect of intensive neurodevelopmental treatment in gross motor function of children with cerebral palsy. Dev Med Child Neurol 2004; 46: 740-745.
25. Vanderveen JA, Bassler D, Robertson CM, Kirpalani H. Early interventions involving parents to improve neurodevelopmental outcomes of premature infants: a meta-analysis. J Perinatol 2009; 29: 343-351.