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(RESEARCH ARTICLE)

Comparison of neuro-developmental status in preterm neonates with and without family based interventions

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Abstract

Objective: Preterm neonates are at risk of neuro-developmental delay. Proper contribution of parents may influence on their neurocognitive development. We aimed to compare neurodevelopmental status in preterm infants less than 1 year with and without parents based intervention.

Methods: A randomized controlled trial study (IRCT; IRCT201705079568N17) was done at NICU of Vali e asr Hospital (Tehran-Iran) in 2010-2011. During this period, parents of preterm neonates were trained to do some simple instructions for their children like performing gentle skin massage, hydrotherapy (water game), and use of mental targeted games. Control group composed of preterm infants whose parents refused regular visits, receiving consultation and training. They only received routine care and visits. Neurodevelopment status of children were evaluated based on WHO Milestones Chart, ASQ at enrollment time and a year later, then recorded data were compared between 2 groups.

Results: Forty five children in the control group and 48 in the intervention group were compared. The results showed that that after one year intervention, improvement of motor (P value=0.03), sensory (P value=0.005), and language abilities (p<0.002) among children in the intervention group were significantly more notable compared to the controls.

Conclusions: Appropriate parent based intervention may improve neurological development in preterm neonates.

Keywords: Outcome; Preterm Birth; Family; Intervention

1. Introduction

Preterm birth defines as delivery before 37-0/7 weeks of gestation and fifteen million preterm neonates are born annually worldwide. The last 6 weeks of gestation is a critical period for fetal brain to complete formation of gyral and sulcal structures increase its weight and cortical volume and develop of cerebellum. Several studies have shown the correlation between preterm delivery and neurodevelopmental disabilities. In addition to brain immaturity, preterm neonates are more susceptible to jaundice and neurotoxicity of hyperbilirubinemia when compared with term neonates [1, 2, 3]. As a result preterm neonates are prone to long-term neurologic sequelae including a wide spectrum of the major and minor disabilities like mental retardation, motor dysfunction, sensory impairments (visual and hearing

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impairment), language disorders, learning disabilities, attention deficit-hyperactivity disorder (ADHD), coordination disorders, behavioral problems, and social-emotional difficulties [4,5].

Today with advanced technology and medical treatment, survival of preterm infants has been increased and there is a growing concern for their growth and neurodevelopmental outcomes. Some post natal factors and relations may exacerbate or relieve the potentially adverse impact of preterm birth [6]. A systematic review study has indicated positive influences of the variety of early intervention programs (starting within the first 12 months of life) on psychomotor outcomes for preterm infants. The programs were family, social and environmental based interventions like parent-infant relationship, physiotherapy, stimulation programe and implementation of environmental programs [7]. Another systematic review study showed that intervention programs began post hospital discharge could prevent motor and cognitive impairments in preterm infants by improving developmental quotient and intelligence quotient ($P < 0.0001$) [8]. Considering the role of family, results of a meta-analysis revealed that early family based interventions could significantly increase the development of both cognitive and motor domains of preterm infants [9]. Other study has also indicated that paternal-infant skin-to-skin contact could affect on neurodevelopmental outcomes in preterm infants [10]. On the other hand, a randomized controlled trial study demonstrated that the benefits of post discharge intervention on developmental status of preterm infants were restricted to short-term gains in cognitive outcome. The authors showed that early intervention had no influence on motor function at infancy period or school age [11].

There are several evidences that show neurobehavioral problems related prematurity that extend into infancy, school age and adolescence [12, 13]. In the present study, we assessed the effectiveness of a 12 month, family-based intervention program on preterm infants' neurodevelopmental status. Stimulating hearing sense of infants by whispering, singing and music, stimulating eye sight by using some colorful papers and toys, skin stimulation by gentle, symmetric skin massage and water game were some performed interventions. It was supposed that final results may provide some suggestions for improving the long term morbidity of preterm birth.

2. Material and methods

A randomized controlled trial study was done at NICU of Vali e asr Hospital; an academic hospital in the capital city of Tehran in 2010-2011. Population study was preterm neonates (<35 weeks of gestation) who hospitalized at NICU. Inclusion criteria were preterm birth and NICU hospitalization. Congenital anomaly of neonates or no responses by parents were also considered as exclusion criteria. All participants gave written consent and accepted in time attending for receiving routine visits or any interventions.

Demographic data, prenatal and OB history including prenatal and neonatal complications, gestational age (based on LMP and ultrasound measures), mode of delivery, Apgar score, duration of NICU hospitalization and gender extracted and recorded. Anthropometric data like neonates' weight, length, and head circumference were determined at birth and time of discharge from hospital by standard anthropometric techniques and equipment based on standardized protocol [12].

Preterm newborns were divided into 2 groups;

Intervention group included preterm infants who were visited every 2 months for regular health check-ups and their parents received some training. Control group composed of preterm children whose parents refused regular visits and receiving consultation. We knew that it was not ethic to deprive some infants unless their parents would not like to participate in the study. Sampling was not random and blind; both groups were selected according to age, sex and social status.

Neurodevelopment status including cognition status, fine and gross motor function, speech and language ability, problem solving and social development were evaluated based on WHO Milestones Chart, Age & Stage Questionnaire (ASQ) by an expert specialist in 2 visits; enrollment time and a year later. ASQ questionnaire composed of 6 questions for each domain with score 0-6. ASQ questionnaire has been translated to Persian and validated for Iranian children by Child Bureau of Iran Health Ministry. Conclusions were stated as normal or abnormal according to cut off point for each domain written in the guide line.

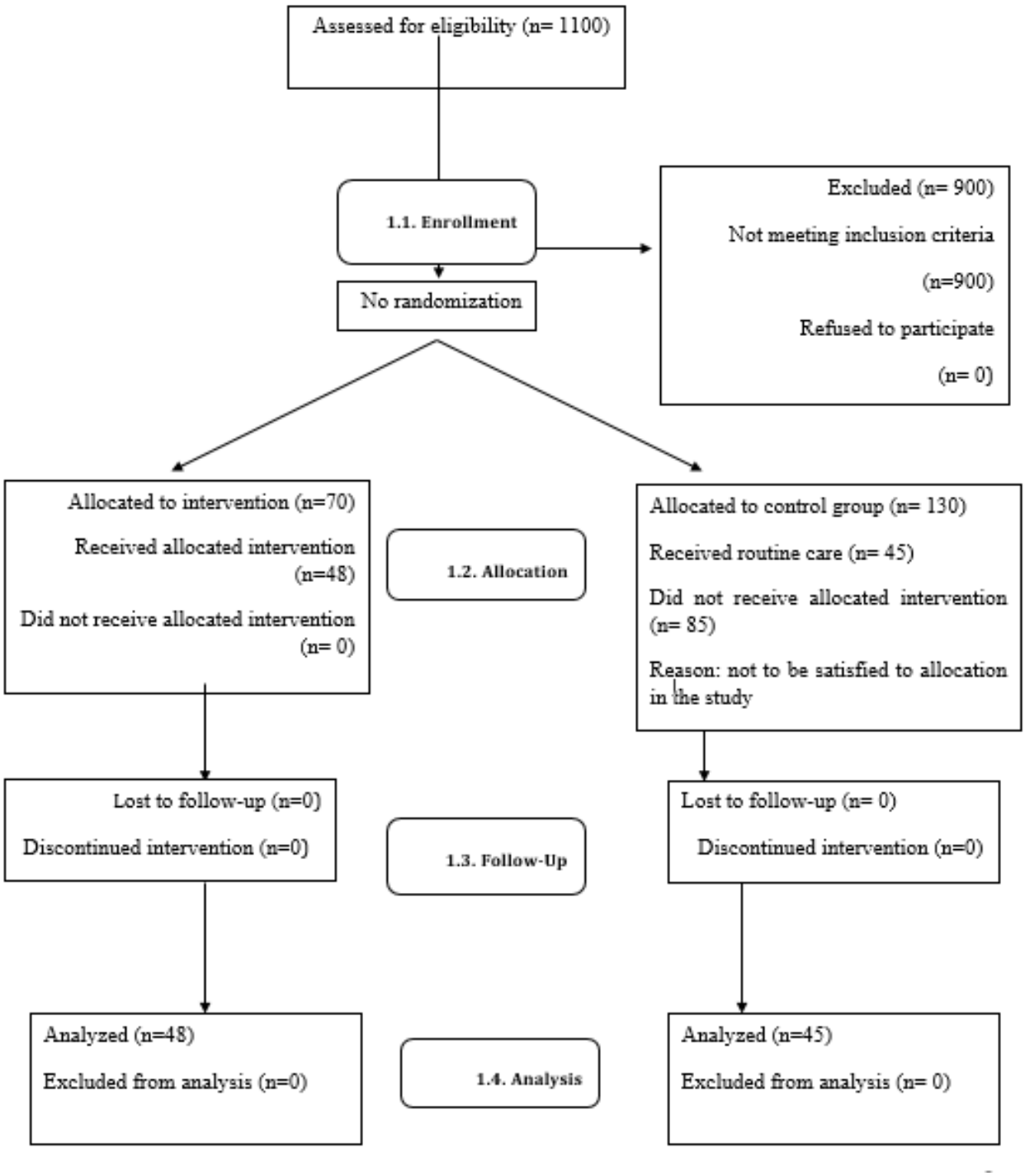

Figure 1 Consort flow chart of participants in the study

2.1. Intervention

A study nurse called the parents of intervention group and invited them to attend pediatrics clinic for reevaluation every 2 months in regard with growth and neurodevelopmental status and receiving some training. Parents were trained for simple instructions like performing some practice to improve their infant's senses, sensory and motor skills. Mothers were asked to stimulate hearing sense of their infants by whispering, singing and music. By using some colorful papers, tissue and toys, eye sight were stimulated. Gentle, symmetric skin massage and skin stimulation 3 times daily, 45 minutes daily Kangaroo Mother Care, 5 minutes daily hydrotherapy (water game) and use of mental targeted games 10 minute, 2 times daily were also trained to mothers during one year investigator-led study. Mothers also received some training packages composed of books, music and game CDs in each session.

Children in the control group were evaluated clinically and examined for physical and psychomotor development just at enrollment time and a year later.

Statistical analysis was done with spss v.18 software. Frequency and mean±standard deviation were considered for analysis of quantitative and qualitative variables. Chi square and T test were applied for comparison of demographic variables and outcome of 2 groups. Significance level was considered 95 % (P< 0.05). With the proposed sample size of 50, the study had a power of 75% and an alpha error of 0.05

2.2. Ethical considerations

Participants were assured about confidentiality of the personal information. No extra cost was imposed on subjects and they also had their right to discontinue the study course whenever they wished. Ethics approval for the study was obtained from the institutional review board of Tehran University of Medical Sciences according to Helsinki declaration (Registration number: 91-1097). Registration ID for this study in the Iranian Registry of Clinical Trials was obtained (IRCT; IRCT201705079568N17).

3. Results and discussion

Forty five children in the control group and 48 children in the intervention group were registered. With regard to demographic characteristics, there were no significant differences between two groups except from 5th minute apgar score (p value=0.03) (table 1).

Table 1 Demographic characteristics of intervention and control groups

Variables	Control group	Intervention group	P value
Gestational age	32.3±2.1	32.1±1.9	0.7
First minute apgar score	7.4±2	6.7±2	0.1
5th minute apgar score	9.4±1.06	8.6±1.8	0.03
Birth weight (gr)	1792.1±652.6	1709.3±562.9	0.5
Head circumference (Cm)	29.5±2.8	29.4±2.4	0.8
Type of deliveryC/S	91.1	89.6	0.8
GDM (%)	24.4	10.4	0.07
Pregnancy induced HTN (%)	40	35.5	0.6
Icter (%)	71.1	56.6	0.13
RDS (%)	64.4	72.9	0.3
NEC (%)	0	1	0.33
Sepsis (%)	20	8.3	0.1
Asphyxia (%)	8.9	12.5	0.5
Blood exchange (%)	0	8.3	0.06

Although motor dysfunction (sever and moderate delays) was significantly more frequent among children in the experimental group in compare to control group before initiation of intervention, after intervention no significant differences were notable between groups (p=0.73). Sensory delay was observed much frequently in the experimental group before intervention (p<0.001); however after intervention the frequency of abnormal sensory function was significantly more frequent in the control group (p=0.02). Language and social dysfunctions were significantly more common among children in the experimental group before intervention (p<0.001) while these disorders were more common among children in the counterpart group after intervention (p<0.001). Details are shown in tables 2-4.

Table 2 Motor functions status before and after intervention in the control and intervention groups

Motor functions status before intervention			
Motor function s	**Control group**	**Intervention group**	**P value**
Severe delay	28 (62.2)	46 (95.8)	<0.001
Moderate delay	1 (2.2)	2 (4.2)	
Normal	16 (35.6)	0	
Motor functions status after 12 months			
Motor function s	**Control group**	**Intervention group**	**P value**
Severe delay	8 (17.8)	11 (22.9)	0.73
Moderate delay	14 (31.1)	12 (25)	
Normal	23 (51.1)	25 (52.1)	

Table 3 Sensory functions status before and after intervention in the control and intervention groups

Sensory functions status before intervention			
Motor function	**Control group**	**Intervention group**	**P value**
Severe delay	28 (62.2)	44 (91.7)	<0.001
Moderate delay	1 (2.2)	4 (8.3)	
Normal	16 (35.6)	0	
Sensory functions status after 12 months			
Motor function	**Control group**	**Intervention group**	**P value**
Severe delay	9 (20)	7 (14.6)	0.02
Moderate delay	18 (40)	9 (18.8)	
Normal	18 (40)	32 (66.7)	

Table 4 Language and social functions status before and after intervention in the control and intervention groups

Language and social functions status before intervention			
motor function s	**Control group**	**Intervention group**	**P value**
Severe delay	27 (60)	43 (89.6)	<0.001
Moderate delay	1 (2.2)	3 (6.3)	
Normal	17 (37.8)	2 (4.2)	
Language and social functions status after 12 months			
motor function s	**Control group**	**Intervention group**	**P value**
Severe delay	6 (13.3)	5 (10.4)	<0.001
Moderate delay	21 (46.7)	5 (10.4)	
Normal	18 (40)	38 (79.2)	

We also assessed 2 groups' improvement trend (getting better, getting worse and no change) of each domain after 12 months. Results showed that all motor function, sensory function, language and social function of children in the intervention group got improved significantly in compare to these abilities of children in the control group. Improvement of each domain was more frequent and deterioration of these abilities was less common among children in the intervention group compared to controls 12 months later ($p<0.001$). Details are shown in tables 5.

Table 5 Trends of improvement of neurodevelopmental status after 12 months in the control and intervention groups

Groups	**Motor functions status N (%)**	**Sensory functions status N (%)**	**Language and social functions N (%)**
Control group			
Getting Improved	21 (46.7)	21 (46.7)	24 (53.3)
Getting worse	2 (4.4)	4 (8.9)	5 (11.1)
No change	22 (48.9)	20 (44.4)	16 (35.6)
Intervention group			
Getting Improved	38 (79.2)	37 (77.1)	41 (85.4)
Getting worse	0	4 (8.3)	0
No change	10 (20.8)	7 (14.6)	7 (14.6)
P value	0.03	0.005	0.002

Several studies have shown increased number of survivors of preterm birth; however preterm infants are high risk group of motor, cognitive and sensory impairments [6, 7, 8, 14]. As few reports assessed the influence of different types of intervention on growth & neurocognitive outcomes, this study is a survey of 12 months of neurodevelopmental progress in preterm infants who received a family based intervention.

Based on the results, motor function after one year intervention among preterm infants in the experimental group significantly improved compared to the controls. It is supposed that diseases and illnesses may deprive infants from some environmental stimulus exposures and communications. In such situations parents' engagement in the treatment process and supportive care would be beneficial. Other studies also confirmed the positive role of such programs; Oswalt revealed that daily massage as a quick, easy, and inexpensive intervention can influence on growth of complicated infants [15]. Hughes et al. by a Systematic Review and Meta-analysis indicated the positive influences of interventions up to 24 months on motor skills for preterm infants [16].Pickler et al. also reported that preterm infants who involved some care based on their neurobehavioral capabilities showed better motor system organization, improved autonomic regulation and Bailey motor scores [17]. Zhang et al. have shown that early familial intervention after NICU discharge (4 days weekly; 30 minutes daily) and follow-up visits in first year of life improved neurodevelopmental outcome significantly based on scores of physical development index (PDI) [18]. On the other hand a systematic review by Schulzke et al. showed some different findings; some investigations suggests that physical activity programs not only improve weight gain but also promote bone mineralization in preterm infants and others pointed to harm or long-term adverse effects of routine use of physical activity programs in preterm infants. However results may depend on age at birth, time of initiation of programs and type of physical activity [19].

Based on the results, although sensory delay, Language and social dysfunctions were observed much frequently in the experimental group before intervention, after intervention these abnormalities were significantly less common in comparison to the controls. It seems that involvement of infants in mental practice, exercise and games could enhance sensory, verbal, communicative and social abilities. In accordance to our results, Kang et al. have shown the positive correlation between training of mothers and improved social interaction of preterm infants [20]. Our findings were also confirmed by Pickler et al. They showed that such interventions for preterm infants significantly improved attention scores during their infancy [17]. Zhang et al. have shown that family based intervention and follow-up visits in first year of life improved scores of mental development index [18]. Perez also found a statistical relationship between a 15

minute daily massage therapy and improvement of hearing, speech and general quotient scores (Griffiths Scales) in complicated infants (p<.05) [21].

In the present study we used combination of Gesell and ASQ Questionnaire for evaluations of neuromotor function of preterm infants. Heineman et al. also indicated that in medical evaluations of high-risk infants, the use of multiple tools is the best. The combination of observation of milestones (with moderate predictive validity and good reliability) and assessment of quality of motor patterns (best predictive validity for major and minor developmental motor dysfunction for infants under the age of 4 months) were reported as valuable predictors in medical evaluations of high-risk infants [22].

4. Conclusion

Present results showed that the frequency of neurodevelopmental abnormalities in different domains significantly declined after 12 months of family involvement in the intervention.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that there is no conflict of interests.

Statement of ethical approval

Ethics approval for the study was obtained from the institutional review board of Tehran University of Medical Sciences according to Helsinki declaration (Registration number: 91-1097).

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Author's contribution

Dr. Sh. and D. carried out the design and coordinated the study, participated in most of the experiments. Dr K. and Z. coordinated and carried out all the experiments, Analysis of data and participated in manuscript preparation. Dr. F. provided assistance for all experiments and prepared the manuscript. All authors have read and approved the content of the manuscript.

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