THE EFFECT OF MODIFIED SUPPORTING PLAY, EXPLORATION AND EARLY DEVELOPMENT INTERVENTION ON MOTOR PERFORMANCE IN BHUTANESE PRETERM INFANTS- RANDOMIZED CONTROLLED TRIAL

Investigators and institutions

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Abstract

Advancement of medical services has improved the survival of preterm infants but they are at high risk of neurodevelopmental impairments. There is growing evidence suggesting that early intervention is more effective in improving developmental outcomes in preterm infants but developmental services are limited and usually started very late in developing countries. Knowledge regarding effect of physical therapy intervention from resource limited settings is sparse and physical therapy has come under criticism for not evaluating and providing evidence-based interventions in infants born preterm. Objective of this study is to investigate the efficacy of customized physical therapy intervention on motor performance in preterm infants by conducting a randomized controlled trial where infants born preterm will be randomized into intervention and standard care group. 28 preterm infants shall be recruited for the study and followed up till 3 months of corrected age. Test for infant motor performance (TIMP) and Rapid neurodevelopmental assessment (RNDA) will be administered at baseline, 1 month, 2 months and 3 months of corrected age. The physical therapy intervention which includes supporting play exploration and early development intervention (SPEEDI) adapted for Bhutanese culture and setting will be provided post discharge from the hospital. A two-way mixed model ANOVA will be performed to investigate the motor performance and neurodevelopment of preterm infants and the significance level will be set at p-value <0.05. This study will be reported as the effectiveness of physical therapy intervention on motor performance in preterm infant.

KEY WORDS: PRETERM, NEURODEVELOPMENTAL IMPAIRMENTS, MOTOR PERFORMANCE, TEST FOR INFANT MOTOR PERFORMANCE, RAPID NEURODEVELOPMENTAL IMPAIRMENT, PHYSICAL THERAPY INTERVENTION, SPEEDI

1.1 Introduction

Globally around 15 million infants are born premature (<37 weeks gestation) annually which accounts to more than 1 in 10 live births and it's a leading cause of neonatal mortality and morbidity(1, 2). Most common complications of preterm birth are respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis, sepsis, periventricular leukomalacia, seizures, intraventricular hemorrhage, feeding difficulties, hypoxic ischemic encephalopathy, and visual and hearing problems(3-6). However, advances in neonatal intensive care has improved the survival of sick and vulnerable newborns, particularly infants born preterm but the rate of disability has relatively remained constant, with up to 50% of these infants later exhibiting developmental disabilities such as motor, cognitive or behavioral impairments(4, 6-11).These developmental disabilities are complex, diverse and impact multiple domains which restricts participation in home, at school and in community which ultimately affect the overall quality of life of the child and the family(12).

The effects of premature birth are not only experienced by the infants but also by the parents. The parents commonly experience helplessness, fear, loss and inadequacy(13, 14). Over the course of hospitalization parents feel increased stress, anxiety and depression(15, 16). Some parents also demonstrate symptoms of post-traumatic stress disorder(17). The emotional stress on parents of the infants born preterm can lead to disruptive interactive pattern with their infants which may have long term adverse effect on attachment pattern, affective state regulation, social interaction and overall developmental outcomes on the infant(18). Therefore, families of infants born preterm often experience immense psychological stress and financial burden due to prolonged stay and the infant requiring repeated admission in the hospital which further leads to significant cost to health system(19-21).

The preterm period is very crucial period in terms of high risk for injury to the brain as well as sensitive time frame for motor development (22). According to the dynamic system theory, motor development is believed to be a feedback process based on interaction among

different subsystems in the child, the environment and the task. Studies have established that motor and cognitive development go hand in hand such that delay in one domain can contribute to delay in another domain(23, 24). Typically developing infants uses movement to communicate and learn about the object by interacting physically with the environment allowing the development of other developmental domains besides motor, especially cognition which is usually impaired in children born preterm(25, 26). Postural control is the pre-requisite for development of motor skills which is usually impaired in infant born preterm which is later associated with motor impairments persisting throughout childhood(27, 28).

As infant's brain is highly plastic, interventions which focusses on enhancement of parent-child interaction, adaptation of environment to promote motor, social or cognitive development and parent education to promote developmental skill in the infant has been found effective (29-32). Numerous studies also focuses on interventions which involves active participation from the infants as it leads to structural and functional changes in the brain infant born preterm to promote neuroplasticity and as it is more likely to have maximum impact on the motor development of infant born preterm(33, 34). Since preterm period is considered sensitive time frame for motor development, intervention focused on motor skills might be beneficial for motor development in infants born preterm.

With the advancement of medical services the survival of preterm infants has improved but the developmental services to these vulnerable population continues to be "wait and watch" approach and they miss out on the critical period to start early intervention (35). There is growing evidence suggesting that early intervention is more effective in improving developmental outcomes in preterm infants compared to interventions which are started later in life(36-40). But most of these published studies on early interventions are laborious, time consuming and resource intensive limiting its use on a large scale particularly in some medical resource limited settings and are applicable in high income countries. Since there is a growing emphasis on evidence-based practice, physical therapy has come under criticism for not evaluating and providing evidence based interventions in infants born preterm (41) and as there is limited study on the effect of early physical therapy intervention (38), there is a need to study the effect of physical therapy intervention provided in a resource limited medical settings to improve the developmental outcome in infant born preterm.

With the launch of Every Newborn Action Plan at the sixty-seventh World Health Assembly in 2014, the focus of care has shifted from mere survival of newborns to thriving well especially among vulnerable small and sick newborns. The Nurturing Care Framework for Early Childhood Development, launched by WHO, UNICEF and the World Bank Group,

demonstrates that focusing on early childhood development is one of the wisest investments a country can make to boost economic growth. Therefore, there is a need of efficacious early intervention with clear evidence to optimize outcomes in preterm infants so that the preterm infants and families benefit in the long run.

At Jigme Dorji Wangchuck National Referral Hospital (JDWNRH), Thimphu Bhutan the prevalence of preterm birth was 6.4% (64 per 1000 live birth)(42). This study will be conducted at JDWNRH which is a tertiary care hospital with NICU facility. The participants for the study will be low risk preterm infants since these group of infants are followed up periodically to monitor for developmental outcome, the follow up starts only when the child attends 3 months of corrected age and they miss out on the critical period to start intervention. In Bhutan, due to a shortage of pediatric physical therapists (PT), this group of infants does not receive proper attention and if the parents are taught how to provide a home programme, it helps in empowering the parents and reducing the burden and stress of bringing the child for therapy at the clinic regularly. This will also help the limited number of PTs in the country to provide better care and support to the high-risk preterm infants.

Most of the early intervention programs are resource intensive and requires a multi-disciplinary team. In a setting where there is limited human resources, customized physical therapy intervention will empower parents to provide intervention to their infant within the natural environment of their home with no extra resources required. Involving parents as primary practitioners will help them to understand and respond more knowledgably to their infant's behaviour, which can promote optimal development. Therefore, the long-term outcome of this study is to provide appropriate physical therapy intervention to infants born preterm post discharge from the neonatal unit so that it can improve the motor development and prevent the neurodevelopmental impairments. The findings from this study will help in providing appropriate physical therapy intervention which involves parent, therapist and infant interactions to enhance the motor development of infants born preterm.

1.2 Conceptual framework

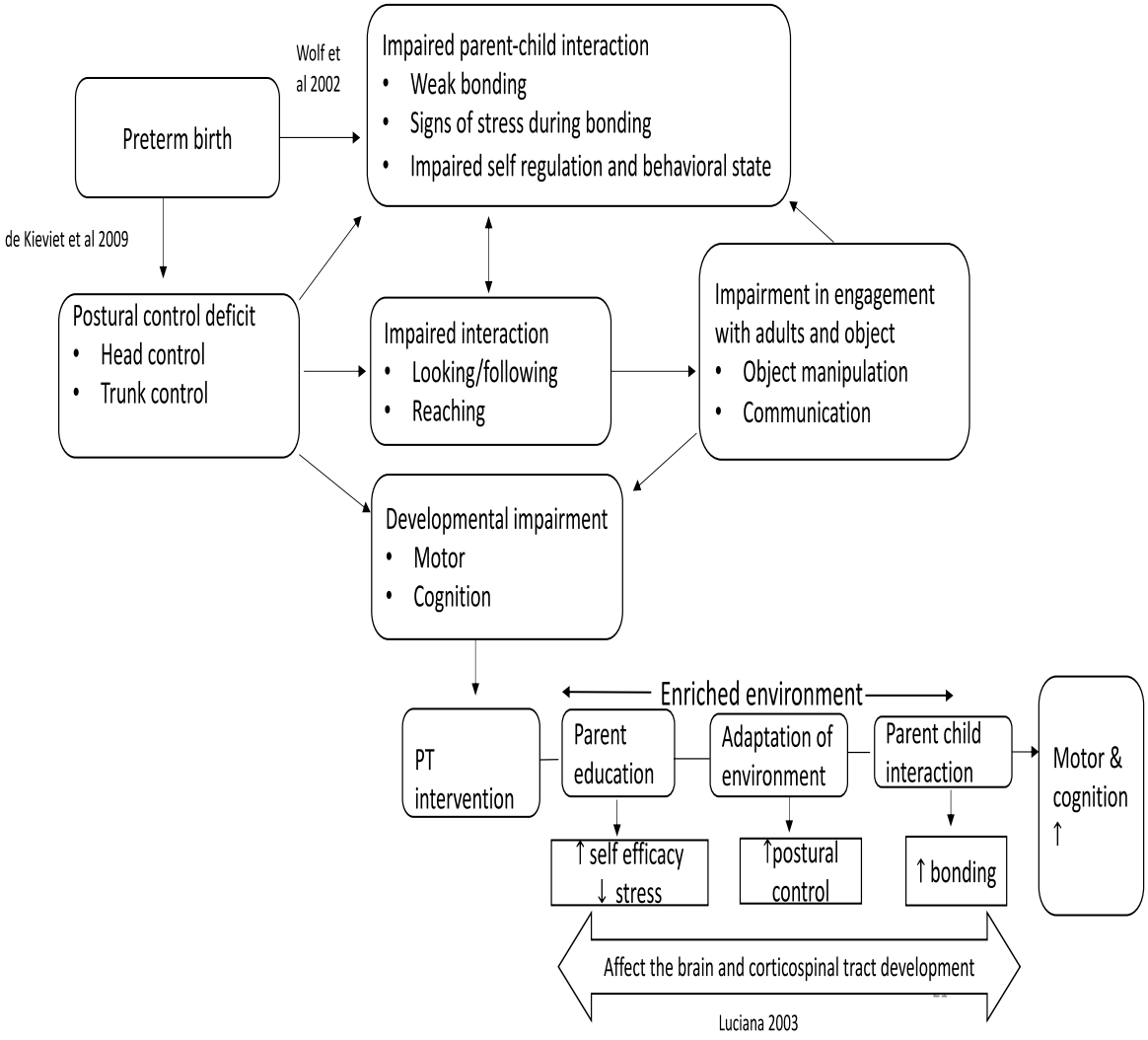

Figure 1: Conceptual framework

1.3 Objectives

To investigate the effect of modified supporting play, exploration and early development (SPEEDI) on neuromotor performance in infants born preterm when the intervention is provided by the parents post discharge from Neonate Intensive Care Unit (NICU) compared to infants born preterm receiving standard care at 3 months of corrected age

1.3.1 Specific objective

1. To compare the difference in motor performance between infants born preterm receiving modified supporting play, exploration and early development intervention (SPEEDI) and standard care at baseline, 1 month, 2 months and 3 months of corrected age.
2. To compare the difference in neurodevelopment between infants born preterm receiving modified supporting play, exploration and early development (SPEEDI) and standard care at baseline, 1 month, 2 months and 3 months of corrected age
3. To compare the compliance of parents with infants born preterm receiving modified supporting play, exploration and early development intervention (SPEEDI) and standard care.

1.4 Study design

The proposed study will be single-center, prospective, double-blinded randomized controlled trial (RCT) to study the effect of physical therapy intervention on motor performance of infant born preterm.

1.4.1 Study setting

All data collection will be performed at Pediatric Physiotherapy Unit, Jigme Dorji Wangchuck National Referral Hospital (JDWNRH), Thimphu Bhutan.

1.4.2 Participants

During the study period infants born preterm (<37 weeks) at Neonatal Intensive Care Unit (NICU) of Jigme Dorji Wangchuck National Referral Hospital (JDWNRH), Thimphu Bhutan meeting the following inclusion and exclusion criteria shall be recruited for the study.

1.4.3 Inclusion criteria

- Infants who are born <37 weeks' gestation
- Medically stable and off ventilator on discharge from NICU
- Parents who consent to come for follow up.

1.4.4 Exclusion criteria

Infants will be excluded from the study if they have

- Cortical blindness or retinopathy of prematurity causing blindness
- Musculoskeletal/congenital abnormalities
- Brain injuries including intraventricular hemorrhage (grade 3 and above), hypoxic ischemic encephalopathy and hydrocephalus
- Genetic syndrome
- Infants undergone major surgery
- Family who do not consent
- Parent with physical and psychological problems
- Infants with medical devices such as NG tube and gastrostomy

1.4.5 Sample size

Sample size calculation will be based on the study by Dusing et al(43). According to the study they found a significant difference in motor performance of infants born preterm who received physical therapist delivered intervention compared to the usual care group. The effect size from the study was Cohen's d of 1.29 for TIMP z- score. Using this data, the total sample size of 22 was obtained using G power program version3.1. However, with 20% drop out rate a total of 28 infants born preterm would be required with 14 in each group.

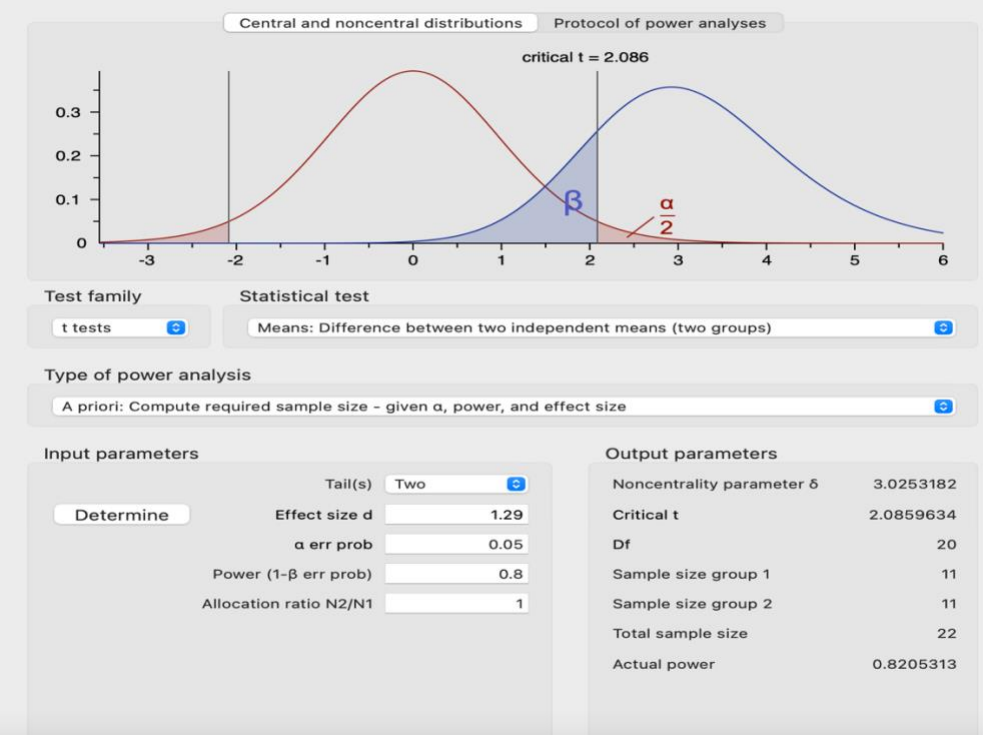

Figure 2: G power

1.4.6 Variables

Independent variable

1. Groups: Intervention group and standard care group
2. Time: At baseline, 1, 2 and 3 months of corrected age

Dependent variable

1. Motor performance
2. Neurodevelopment
3. Compliance

1.4.7 Data Collection

The study will be conducted after seeking ethical approval from Institutional Review Board (IRB), Khesar Gyalpo University of Medical Sciences of Bhutan (KGUMBS). The data will be collected at pediatric physiotherapy unit, JDWNRH. Preterm infants referred for high risk follow up clinic at Pediatric Physiotherapy Unit that evaluates neurodevelopmental outcome will be recruited. Oral and written information will be given to parents of the preterm babies fulfilling the inclusion criteria. Parents will be informed regarding the objectives, procedures, risk and benefits of the study. Informed consent will be taken from the parents prior to the study by the principal investigator. Strategies to achieve adequate participant enrolment to reach target sample size will be, establish a link between

the research team and mother and father of each of the subjects included, regardless of the group allocated since randomization.

Randomization will be performed by blindly drawing the slip from the container which will have equal numbers of same size and shape slips and will be performed by the research assistant who will not be responsible for any intervention nor outcome assessment. After randomization the infants in the control group will receive standard care and the infants in the intervention group will receive modified SPEEDI. The principal researcher will provide the modified SPEEDI. The research assistants shall be physical therapist or physical therapy assistants and occupational therapist who has over 2 years of experience in working with pediatric population and will be blinded to the group allocation since they will assess the outcome. These research assistants will be trained to use the measurement tools by the principal researcher. As the study participants are preterm infants, caution will be taken to avoid thermal stress to these infants by keeping the data collection room in pediatric physiotherapy unit warm. During the study process if there are amendments to the study protocol, the information shall be communicated with the IRB and the co-investigators of the study.

1.4.8 Measurement

Prior to the assessment of motor performance and neurodevelopment, demographic details such as gestational age, length of stay in the hospital and medical diagnosis will be recorded. The measurement will be taken at 40 weeks of post menstrual age, 1 month, 2 months and 3 months of corrected age by the research assistants who will be blinded to group assignment.

1.4.8.1 Motor performance

Motor performance will be assessed using The Test of Infant Motor Performance (TIMP) version 5.1, administered when the child is awake (Brazelton state 3,4 or 5). The infant should wear minimal clothing as possible. Testing will be performed on a firm surface with no distractions. No more than 3 trials will be allowed for each elicited item. If the infant gets fussy and irritable during the process of assessment, breaks can be taken in between the assessment and if the parents are not comfortable with the procedure the parents will have every right to withdraw and discontinue their infant's participation from the study. However, if the parent consents to continue the assessment, items that remain during the first session shall be

completed in second session within 24 hours so that it assessor does not have to redo the whole assessment again.

The Test of Infant Motor Performance (TIMP) was developed to assess functional motor performance in infants from 34 weeks postmenstrual age (PMA) through 4 months corrected age. The TIMP is a 42- item assessment with 13 dichotomous items scored based on observation of spontaneous movement and 29 elicited items with 4 to 7-point rating scales based on handling of the infant in a variety of positions in space. The test takes 20-35 min to administer and score with variation based on age and tolerance of the infant and the experience of the tester. It has been described as one of the best tools to discriminate between age-appropriate and delayed motor performance in preterm and term infants, and to predict later motor development. The TIMP is a valid and reliable tool developed to detect typical and atypical performance in preterm infants and evaluate the effect of an intervention on the infant motor performance(44-46). The assessment tool has been also used in multiple clinical trials to evaluate the effectiveness of therapy intervention.

1.4.8.2. Neurodevelopment

Neurodevelopment will be assessed using the Rapid Neurodevelopmental Assessment (RNDA), administered when the child is awake and there should be no distraction and prompting allowed from parents while performing the assessment. While administering the assessment the response elicited from the infant will be recorded.

The Rapid Neurodevelopmental Assessment (RNDA) tool is a reliable and valid developmental assessment tool for use by multidisciplinary professionals in developing country to assess the neurodevelopmental status of children from 0-24 months(47). The tool has been a useful to identify neurodevelopmental impairment (NDI) in resource limited settings where there is lack of trained professionals to identify children with neurodevelopmental impairments. It assesses developmental domains such as primitive reflexes (0 to <1 month), gross motor, fine motor, vision, hearing, speech, cognition, behavior and seizures. It helps to identify impairments in these developmental domains and categorizes into three degrees of impairments which are mild, moderate and severe impairment.

1.4.8.3. Compliance

Parent compliance will be measured by the ability of the parent to correctly demonstrate the home program activity when they come for the follow up visit. In addition, parental compliance will be measured by quantifying the amount of time spent with the infant

performing the intervention at home, number of intervention sessions attended, the number of enrolment and outcome assessment at the end of the study.

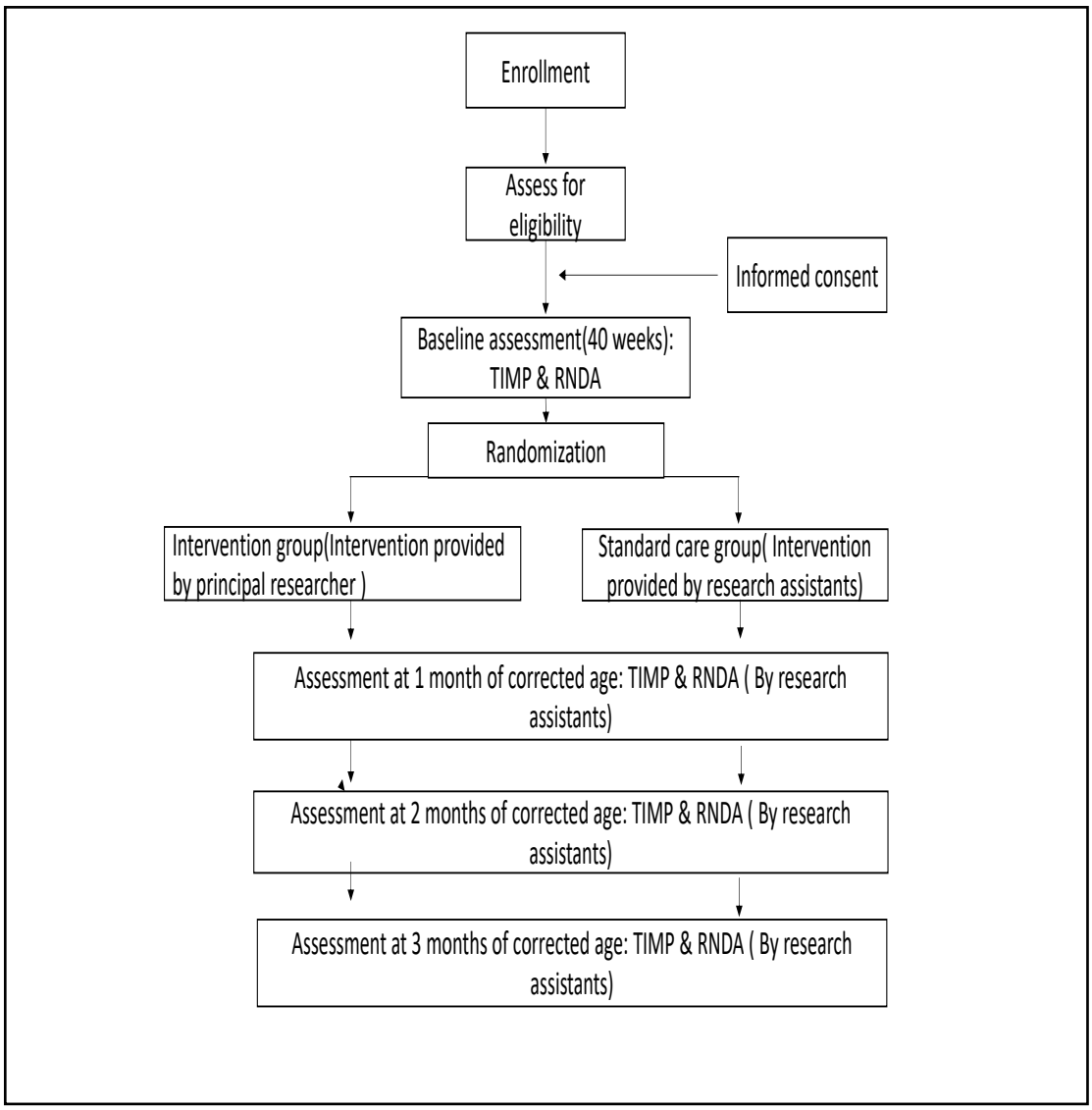

Figure 3: Procedure

1.4.8.4 Intervention

Intervention group

The intervention that will be used for this study will be adapted and modified for the Bhutanese cultural context, from supporting play exploration and early development intervention (SPEEDI) (43). The intervention is designed to improve the developmental outcome of preterm infants who are at risk of developmental disabilities. SPEEDI uses the combined therapist and parent delivered intervention to increase opportunities for developmentally appropriate social, cognitive and motor play without excessive parental and financial burden. SPEEDI blends the synactive theory of development and action perception theory to enhance developmental outcomes in high risk infants. The original version of SPEEDI consist of two phases where first phase is the intervention provided to the infants during the stay in NICU and phase two provided post discharge from NICU. For this study the infants will receive the interventions adapted from SPEEDI both as an outpatient based.

The Phase I of the original version of SPEEDI consist of parent therapist collaborative sessions to understand infant cues, readiness for interaction, developmental support and stressors, ideas to promote interaction and development and watching the videos which is provided during the stay in NICU. However, this phase I intervention will be provided post discharge from the NICU at 40 weeks. The main objective of making parents watch these videos would be to help parents interact with their infant and perform the activities at home since most of the parents would be anxious and not know how to interact with their infant. The Phase II from the original version consisted of home visit to provide the intervention post discharge from NICU. It consists of therapist guiding the parents to perform play-based activities at home with their infants and these activities can be performed as a part of daily activities with their infants especially during feeding, bathing and changing diapers. There are 5 main activities which the parents must perform with their infant at home. The activities are broken down into three stages that become progressively challenging over time. For this study purpose the phase II intervention will be provided at the hospital where the parent will need to bring their infant to the hospital and the 5 main activities will be broken down into two stages. During the monthly visit the principal researcher will assess and decide the infant's ability to progress the activity from stage 1(easy) to Stage 2(hard). If the infant is found to be not ready to progress to the next stage, they will continue with the same activity. The primary caretaker will be given activity booklet which will contain pictures, simple text and log to record daily

activities. To perform the play- based activities the primary caretaker will be asked to use toy within their natural home environment since the intervention does not require any specific or sophisticated toys.

Intervention	40 weeks	1 month	2 months
Activities	• Watching videos to understand cue-based interaction with the infant. • Introduce the activities that the parent can complete at home to promote midline and tracking of toys and faces	• Watching people and toy • Tummy time • Holding head up • Kicking • Toy play	• Watching people and toy • Tummy time • Holding head up • Kicking • Toy play
Duration	20 mins/day	20 mins/day	20 mins/day
Frequency	5 days /week	5 days /week	5 days /week

Figure 4: Intervention Program

Activity	Stage 1	Stage 2
Activity1 – Looking at people and toys (4 minutes)	• Looking at people with support in supine • In side lying and swaddled	• Tracking of caregiver in supine.
Activity 2- Tummy time (4 minutes)	• Tummy time on the caregiver's chest	• Tummy time on the floor
Activity 3- Holding head up (4 minutes)	• Head control with help from caregiver. • Head control by swaddling the baby.	• Head control with less support from caregiver, unswaddled.
Activity 4- Kicking (4 minutes)	• Kicking with swaddle to support to support the arms.	• Kicking with arms and legs free to move with slight support under the hips.
Activity 5- Toy play (4 minutes)	• With use of external support to bring hands and legs in middle.	• Toy play without external support and variety of position such as supine and side lying.

Figure 5: Activity Description

The intervention will be provided as an outpatient based at JDWNRH by the principal researcher. It will require the parents to come to the hospital every month for the assessments and interventions. The parents will be called every week to ensure that they have no problem with the activities until the infant is 3 months of corrected age. The principal researcher will review and assess if the parents are performing the intervention correctly with the infant during the monthly visit. The parents in the intervention group will be advised not to share the activities and any information related to the intervention to other parents of preterm infants whom they might know.

They will be given appointment for assessment at different day or time and the information regarding the enrollment will be kept confidential.

Standard care group

Standard care group will include education regarding early development which is present in the mother and child handbook and which is currently practiced. The standard care group will also be required to visit the clinic monthly and assessment will be performed monthly until the infant is 3 months of corrected age. During the monthly visit parents will be asked to report the amount of time spend with their infant performing the activity.

1.4.9 Data Analysis

The researcher assistant who performed the randomization will register all neonatal data, discharge variables and the follow-up data, during the appointments. Motor performance of the infant will be assessed using TIMP at 40 weeks, 1 month,2 months and 3 months of corrected age and neurodevelopment will be assessed using RNDA. Scores of TIMP items and items from RNDA will be transformed from categorical scale to a continuous scale. The Rasch Unidimensional Measurement Model (RUMM) will be used for this process. The number of sessions and amount of time spent performing the intervention will be recorded and analyzed. All the variables will have double data entry.

1.4.10 Statistical Analysis

Statistical analysis will be performed using Statistical Package for Social Sciences (IBM SPSS statistics for windows, version 28). Shapiro Wilk test will be used to test for normality of data. Descriptive statistics will be used to analyze patient's demographic data. To investigate the effect of physical therapist intervention on motor performance two-way mixed ANOVA will be performed. To investigate the effect of physical therapy intervention on neurodevelopment two-way mixed ANOVA will be performed. The level of significance will be set at a p-value < 0.05.

1.4.11 Data confidentiality

All research data and personal information will be under responsibility of the researchers in order to protect confidentiality before, during and after the trial. Confidentiality of data will be maintained by storing the filled proforma in a lockable cabinet and the electronic data file in a password protected computer accessible only to the

investigators. Dataset will be maintained securely for at least five years after completion of study.

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Declaration of interest

The author and co-authors involved in the study declare no conflict of interests.

References

1. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reprod Health. 2013;10 Suppl 1(Suppl 1):S2.
2. Chawanpaiboon S, Vogel JP, Moller A-B, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. The Lancet Global Health. 2019;7(1):e37-e46.
3. Platt MJ. Outcomes in preterm infants. Public Health. 2014;128(5):399-403.
4. Ramenghi LA. Late preterm babies and the risk of neurological damage. Acta Biomed. 2015;86 Suppl 1:36-40.
5. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, Opmeer BC, van Kaam AH, van Wassenaer AG, et al. A systematic review of severe morbidity in infants born late preterm. Am J Obstet Gynecol. 2011;205(4):374.e1-9.
6. Blencowe H, Lawn JE, Vazquez T, Fielder A, Gilbert C. Preterm-associated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. Pediatr Res. 2013;74 Suppl 1(Suppl 1):35-49.
7. Milner KM, Neal EF, Roberts G, Steer AC, Duke T. Long-term neurodevelopmental outcome in high-risk newborns in resource-limited settings: a systematic review of the literature. Paediatr Int Child Health. 2015;35(3):227-42.
8. Pascal A, Govaert P, Oostra A, Naulaers G, Ortibus E, Van den Broeck C. Neurodevelopmental outcome in very preterm and very-low-birthweight infants born over the past decade: a meta-analytic review. Dev Med Child Neurol. 2018;60(4):342-55.
9. Spittle A, Orton J, Anderson PJ, Boyd R, Doyle LW. Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. Cochrane Database Syst Rev. 2015(11):Cd005495.
10. Hee Chung E, Chou J, Brown KA. Neurodevelopmental outcomes of preterm infants: a recent literature review. Transl Pediatr. 2020;9(Suppl 1):S3-s8.
11. Manuck TA, Rice MM, Bailit JL, Grobman WA, Reddy UM, Wapner RJ, et al. Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort. Am J Obstet Gynecol. 2016;215(1):103.e1-.e14.
12. McCormick MC, Litt JS, Smith VC, Zupancic JA. Prematurity: an overview and public health implications. Annu Rev Public Health. 2011;32:367-79.
13. Fernández Medina IM, Granero-Molina J, Fernández-Sola C, Hernández-Padilla JM, Camacho Ávila M, López Rodríguez MDM. Bonding in neonatal intensive care units: Experiences of extremely preterm infants' mothers. Women Birth. 2018;31(4):325-30.
14. Roque ATF, Lasiuk GC, Radünz V, Hegadoren K. Scoping Review of the Mental Health of Parents of Infants in the NICU. J Obstet Gynecol Neonatal Nurs. 2017;46(4):576-87.
15. Pace CC, Spittle AJ, Molesworth CM, Lee KJ, Northam EA, Cheong JL, et al. Evolution of Depression and Anxiety Symptoms in Parents of Very Preterm Infants During the Newborn Period. JAMA Pediatr. 2016;170(9):863-70.
16. Howe TH, Sheu CF, Wang TN, Hsu YW. Parenting stress in families with very low birth weight preterm infants in early infancy. Res Dev Disabil. 2014;35(7):1748-56.
17. Schecter R, Pham T, Hua A, Spinazzola R, Sonnenklar J, Li D, et al. Prevalence and Longevity of PTSD Symptoms Among Parents of NICU Infants Analyzed Across Gestational Age Categories. Clin Pediatr (Phila). 2020;59(2):163-9.

18. Anderson C, Cacola P. Implications of Preterm Birth for Maternal Mental Health and Infant Development. MCN Am J Matern Child Nurs. 2017;42(2):108-14.
19. Johnston KM, Gooch K, Korol E, Vo P, Eyawo O, Bradt P, et al. The economic burden of prematurity in Canada. BMC Pediatr. 2014;14:93.
20. Korvenranta E, Lehtonen L, Rautava L, Häkkinen U, Andersson S, Gissler M, et al. Impact of very preterm birth on health care costs at five years of age. Pediatrics. 2010;125(5):e1109-14.
21. Singer LT, Salvator A, Guo S, Collin M, Lilien L, Baley J. Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant. Jama. 1999;281(9):799-805.
22. Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet Neurol. 2009;8(1):110-24.
23. Marlow N, Hennessy EM, Bracewell MA, Wolke D. Motor and executive function at 6 years of age after extremely preterm birth. Pediatrics. 2007;120(4):793-804.
24. Korkman M, Mikkola K, Ritari N, Tommiska V, Salokorpi T, Haataja L, et al. Neurocognitive test profiles of extremely low birth weight five-year-old children differ according to neuromotor status. Dev Neuropsychol. 2008;33(5):637-55.
25. Soska KC, Adolph KE, Johnson SP. Systems in development: motor skill acquisition facilitates three-dimensional object completion. Dev Psychol. 2010;46(1):129-38.
26. Oudgenoeg-Paz O, Mulder H, Jongmans MJ, van der Ham IJM, Van der Stigchel S. The link between motor and cognitive development in children born preterm and/or with low birth weight: A review of current evidence. Neurosci Biobehav Rev. 2017;80:382-93.
27. Fallang B, Hadders-Algra M. Postural behavior in children born preterm. Neural Plast. 2005;12(2-3):175-82; discussion 263-72.
28. Fallang B, Øien I, Hellem E, Saugstad OD, Hadders-Algra M. Quality of reaching and postural control in young preterm infants is related to neuromotor outcome at 6 years. Pediatr Res. 2005;58(2):347-53.
29. Dusing SC, Burnsed JC, Brown SE, Harper AD, Hendricks-Munoz KD, Stevenson RD, et al. Efficacy of Supporting Play Exploration and Early Development Intervention in the First Months of Life for Infants Born Very Preterm: 3-Arm Randomized Clinical Trial Protocol. Phys Ther. 2020;100(8):1343-52.
30. Ustad T, Evensen KA, Campbell SK, Girolami GL, Helbostad J, Jørgensen L, et al. Early Parent-Administered Physical Therapy for Preterm Infants: A Randomized Controlled Trial. Pediatrics. 2016;138(2).
31. Lekskulchai R, Cole J. Effect of a developmental program on motor performance in infants born preterm. Aust J Physiother. 2001;47(3):169-76.
32. Fan J, Wang J, Zhang X, He R, He S, Yang M, et al. A home-based, post-discharge early intervention program promotes motor development and physical growth in the early preterm infants: a prospective, randomized controlled trial. BMC Pediatr. 2021;21(1):162.
33. Kolb B, Mychasiuk R, Williams P, Gibb R. Brain plasticity and recovery from early cortical injury. Dev Med Child Neurol. 2011;53 Suppl 4:4-8.
34. Luciana M. Cognitive development in children born preterm: implications for theories of brain plasticity following early injury. Dev Psychopathol. 2003;15(4):1017-47.
35. Orton J, Spittle A, Doyle L, Anderson P, Boyd R. Do early intervention programmes improve cognitive and motor outcomes for preterm infants after discharge? A systematic review. Dev Med Child Neurol. 2009;51(11):851-9.
36. Johnston MV. Plasticity in the developing brain: implications for rehabilitation. Dev Disabil Res Rev. 2009;15(2):94-101.

37. Benzies KM, Magill-Evans JE, Hayden KA, Ballantyne M. Key components of early intervention programs for preterm infants and their parents: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2013;13 Suppl 1:S10.
38. Blauw-Hospers CH, Hadders-Algra M. A systematic review of the effects of early intervention on motor development. Dev Med Child Neurol. 2005;47(6):421-32.
39. Pelc K, Gajewska A. Early intervention and environmental factors: optimizing the development of infants born preterm. Dev Med Child Neurol. 2018;60(1):7.
40. Puthussery S, Chutiyami M, Tseng PC, Kilby L, Kapadia J. Effectiveness of early intervention programs for parents of preterm infants: a meta-review of systematic reviews. BMC Pediatr. 2018;18(1):223.
41. Bax M. Does 'therapy' have a future? Dev Med Child Neurol. 2001;43(1):3.
42. Pradhan D, Nishizawa Y, Chhetri HP. Prevalence and Outcome of Preterm Births in the National Referral Hospital in Bhutan: An Observational Study. J Trop Pediatr. 2020;66(2):163-70.
43. Dusing SC, Brown SE, Van Drew CM, Thacker LR, Hendricks-Muñoz KD. Supporting Play Exploration and Early Development Intervention From NICU to Home: A Feasibility Study. Pediatr Phys Ther. 2015;27(3):267-74.
44. Campbell SK, Zawacki L, Rankin KM, Yoder JC, Shapiro N, Li Z, et al. Concurrent validity of the TIMP and the Bayley III scales at 6 weeks corrected age. Pediatr Phys Ther. 2013;25(4):395-401.
45. Peyton C, Schreiber MD, Msall ME. The Test of Infant Motor Performance at 3 months predicts language, cognitive, and motor outcomes in infants born preterm at 2 years of age. Dev Med Child Neurol. 2018;60(12):1239-43.
46. Campbell SK. Functional movement assessment with the Test of Infant Motor Performance. J Perinatol. 2021;41(10):2385-94.
47. Khan NZ, Muslima H, Begum D, Shilpi AB, Akhter S, Bilkis K, et al. Validation of rapid neurodevelopmental assessment instrument for under-two-year-old children in Bangladesh. Pediatrics. 2010;125(4):e755-62.

ANNEXURE I

Part I: Information Sheet

Topic: The Effect of Modified Supporting Play, Exploration and Early Development Intervention on Motor Performance in Bhutanese Preterm Infants- Randomized Controlled Trial

Principal Investigator: Karma Lhaki
Address: Department of Physiotherapy, Jigme Dorji Wangchuck National Referral Hospital, Thimphu
Contact number: +97517606492 Email:klhaki@jdwnrh.gov.bt

Please take some time to read this information sheet. We are trying to compare the effect of customized physical therapy interventions provided by parents and standard care at 3 months of corrected age on motor performance in preterm infant's post discharge from Neonate Intensive Care Unit (NICU).

This study has been approved by the Institutional Review Board (IBR), KGUMSB, Bhutan, and will be conducted according to ethical guidelines and principles of the International Declaration of Helsinki, as well as Institutional Review Board (IBR), Bhutan.

What is this study about?

This research attempt to compare the effect of two types of interventions in preterm children post discharge from the NICU. One intervention is modified supporting play, exploration and early development intervention provided by parents. Another intervention is standard care which is normally practiced after your infant is discharged from the hospital. Your participation in the study is purely voluntary and you may refuse to participate or withdraw from the study, at any time, without any repercussions.

Why have you been invited?

Because your child was born pre-term and was admitted in NICU at JDWNRH.

What will be your responsibilities?

As a parent/legal guardian who has consented to this study, you will be required to bring your child to pediatric physiotherapy unit, JDWNRH monthly till 3 months of corrected age and you will be required to perform the intervention which will be taught to by your therapist.

Will you benefit from this research?

The intervention is designed to improve the developmental outcome of preterm infants who are at risk of developmental disabilities. The study findings may assist in planning appropriate policy and intervention for these vulnerable population of preterm infants.

Are there any risks for you child in getting involved in this study?

There are no invasive procedures involved during the assessment and while providing intervention. Both the assessment and intervention are delivered via play-based approach. Therefore, there is no risk involved.

Will your child experience any discomfort for being part of this study?

During the assessment we might ask you to remove the thick clothes, socks and mittens of your baby which might cause some discomfort but we will take extra care to avoid any discomforts to your baby.

Who will have access to the results of this study?

The information you provide is totally confidential and will not be disclosed to anyone. It will only be used for research purposes. Your name, address, and other personal information will be removed from the instrument, and only a code will be used to connect your name and your answers without identifying you. You may be contacted by the research team again only if it is necessary to complete the information on the study.

Where can participants get results of the study should they wish to have them?

You will get the details of the study results from the principal investigator and the Ministry of Health, Bhutan.

Do you have any questions about the research?

When you have read or listened to this information, the researcher will discuss it with you further and will answer any questions you may have. If you would like to know more about this study at any stage or have any queries about the study, please feel free to contact:

Karma Lhaki
Department of Physiotherapy, Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan
Mobile: +97517606492 Email: klhaki@jdwnrh.gov.bt

If you have any complaints regarding this study, you may contact Chairperson of the Institutional Review Board (IRB), Khesar Gyalpo University of Medical Sciences of Bhutan, Thimphu, Bhutan at the following address:

Institutional Review Board (IRB)
Khesar Gyalpo University of Medical Sciences of Bhutan
Thimphu, Bhutan
Contact no: 02-338005 Ext# 2146 Email: irbkgumsb@gmail.com

Part II: Informed Consent form

Section A: If the selected participant is a minor (less than 18 years of age)

The parent or the legal guardian of the participants need to provide the informed consent. I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to allow my child to participate in this study.

Name of Parent or legal guardian

_____

Signature of Parent or legal guardian

_____

Date _____(Day/month/year)

SECTION B:
Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the person understood it. I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Name of researcher /person taking the consent

_____

Signature of enumerator /person taking the consent

_____

Date _____ (Day/month/year)

Section C:

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness

_____

Signature of witness

_____

Date _____ (Day/month/year)