Randomized Trial of a Parenting Intervention for Very Preterm Infants: Outcome at 2 Years

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Objectives To determine the efficacy of a neonatal parenting intervention for improving development in very preterm infants.

Study design A cluster-randomized, controlled trial with a cross-over design and washout period was conducted in 6 neonatal centers. Two hundred thirty-three babies <32 weeks' gestation were recruited (intervention = 112; control = 121). Intervention families received weekly Parent Baby Interaction Programme (PBIP) sessions during neonatal intensive care unit admission and up to 6 weeks after discharge. Control families received standard care. All 195 infants remaining in the study at 24 months' corrected age were assessed by psychologists blinded to group allocation.

Results There was no significant difference in Mental Development Index (−0.9 points; 95% CI, −5.0, 3.2) or Psychomotor Development Index (2.5; −3.3, 8.4) scores between the intervention and control groups and no significant effect of intervention on Mental Development Index or Psychomotor Development Index scores for subgroups dichotomized by gestational age (<28 weeks/≥28 weeks), parity (1st/other child) or mother's cohabiting status (supported/unsupported).

Conclusions There was no effect of PBIP on infant development at 2 years' corrected age. Parenting interventions may be better delivered after discharge or targeted for preterm infants with high biological and social risk. *(J Pediatr 2009;155:488-94)*.

Preterm birth places a child at high risk for neuropsychological impairments, learning difficulties, and behavior problems later in life.[1,2] Although preterm interruption to the developing brain and associated perinatal insults can account for much of the impairment observed,[3,4] the developmental vulnerability conferred by preterm birth may be mediated by environmental experience.[5,6] Hence, developmental care practices are often implemented by clinical staff to minimize the adverse impact of the neonatal intensive care unit (NICU) environment.[7] Early maternal factors also may moderate outcomes for these children. The psychological stress associated with preterm birth[8-10] adversely affects attachment, maternal sensitivity to baby's cues, and mother-infant interaction,[8,9] factors that are predictive of infant development and long term outcome.[11,13-16] Therefore, interventions designed to enhance the parent-infant relationship may have positive effects on infant cognitive outcomes.

Results regarding the efficacy of early parenting interventions for preterm infants are conflicting and inconclusive, however.[10] Although some trials report modest beneficial effects of intervention on cognitive development,[11,12] others have failed to detect an effect[13] or have shown benefits only after adjustment for confounders.[21,22] A recent meta-analysis found a significant effect of early parenting programs on cognitive outcomes in infancy and early childhood, with some evidence of a greater effect for interventions that were focused on facilitation of the parent-infant relationship.[10]

We conducted a randomized, controlled trial of a neonatal parenting intervention for very preterm infants and have previously reported that this did not improve maternal outcomes at three months corrected age.[14] We have subsequently followed up this cohort to determine whether there are longer-term effects of intervention on infant outcomes. We hypothesized that the Parent Baby Interaction Programme (PBIP) would improve cognitive development at 2 years' corrected age in very preterm infants.

BSID-II	Bayley Scales of Infant Development, 2nd Edition
IMD	Index of Multiple Deprivation
MDI	Mental Development Index
NICU	Neonatal intensive care unit
PDI	Psychomotor Development Index
PBIP	Parent Baby Interaction Programme
PSI	Parenting Stress Index
RN	Research nurse

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Methods

The study design (ISRCTN56341521) has been described in detail previously.[14] Briefly, a cluster-randomized, controlled trial with a cross-over design was conducted in 6 neonatal centers (incorporating 7 NICUs) in 2 regions of the United Kingdom (3 each in the South West and Trent regions). Approval was obtained from the South West multi-center ethics committee and the local research ethics committees at each center. Within regions, 2 centers were paired on the basis of deprivation indices, and the third center from each region formed the final pair. As a measure of deprivation, an Index of Multiple Deprivation (IMD)[15] score was assigned for each family that is derived from data on deprivation at the small area level in 7 domains including income, employment, and crime. Scores for England range from 0.59 (least deprived) to 86.36 (most deprived), with a median of 17.02. Recruitment was conducted in 2 phases. For the first phase, 1 center from each pair was randomized by the toss of a coin to the intervention with the other center randomized to control. During this phase participants were recruited for 6 months in the Trent region and 7 months in the South West to achieve target recruitment. After a 3-month washout period implemented to eliminate contamination of the control group, each center crossed over to the opposite treatment condition. During this second phase, participants were recruited for 7 months in Trent and 6 months in the South West.

Babies born at <32 weeks' gestational age in participating centers were recruited. Babies with illness incompatible with life and families resident outside the study catchment area were excluded. Recruitment was conducted by 7 research nurses (RNs) who obtained written informed consent from parents as soon as possible after birth. Given the study design, neither RNs nor parents were blinded to group allocation before recruitment. Babies were followed up at discharge and at 3-months'[14] and 24 months' corrected age. At 24 months' corrected age, 1 of 2 psychologists who were blinded to treatment group allocation contacted parents to schedule a home visit during which a standardised developmental test was administered. One week after the home visit, parents were sent a letter detailing the child's test results.

Intervention

The PBIP[16] provides structured parental support during the neonatal period to facilitate attachment, enhance parent-infant interaction, sensitize parents to their baby's cues, facilitate parents' confidence in identifying and meeting their baby's needs, and to educate parents in developmental care principles. It is delivered through a framework of activities in 4 areas comprising discursive (eg, infant development), tactile (eg, handling), verbal (eg, talking to the baby), and observational (eg, identifying behavioral states and baby's cues) sessions.

For this study, the mother was the primary recipient of the intervention. The intervention was delivered by RNs trained in PBIP before study commencement. Regular meetings were held with the clinical trial manager (C.I.) to ensure skills maintenance throughout the intervention period. PBIP activities were designed to be delivered in weekly 1-hour sessions beginning from the first weeks after birth up to a maximum of 6 postdischarge sessions. The intervention was directed only to parents. Regular NICU nursing staff were neither recipients of the intervention nor trained in PBIP principles and continued to deliver standard care throughout the study periods at their center. This was required to enable the cross-over design to be implemented in which standard care alone was provided by NICU staff during the control period. Families in the control group received standard care.

Measures

Developmental outcome at 24 months' corrected age was assessed using the Bayley Scales of Infant Development 2nd Edition (BSID-II).[17] This is a norm-referenced test that yields standardised scores (mean, 100; SD, 15; range, 50 to 150) for cognitive (Mental Development Index; MDI) and motor development (Psychomotor Development Index; PDI). MDI scores were the primary outcome measure for this study, and PDI scores were a secondary outcome measure.

Children who could not be assessed because of severe disability and those whose index scores fell below test limits were assigned a nominal index score of 49 (1 point below the basal test score) for quantifying severely delayed outcome.[18] Psychologists were formally trained in test administration before study commencement and achieved excellent inter-rater reliability (MDI, 97% item-by-item agreement; PDI, 94% agreement) in 11 randomly selected assessments scored simultaneously by both examiners throughout the period of data collection. Index scores were used to classify developmental delay using conventional SD-banded cutoffs (mild, −1 to −2 SD; moderate, −2 to −3 SD; severe, < − 3 SD). RNs collected clinical and demographic information from mothers' and babies' medical notes and through parental interviews during NICU admission.

Statistical Analyses

The predefined trial primary outcomes were the Parenting Stress Index (PSI)[19] at 3 months' corrected age and the BSID-II MDI at 24 months' corrected age. Results for the PSI have been reported previously.[14] In power calculations, a sample size of 172 would have 90% chance of detecting a 0.5 SD difference in PSI scores at $P < .05$. The target sample size was increased to 250 to allow for possible clustering.[14]

Data were double-entered, verified, and analyzed using Stata and SPlus. A prespecified 2-stage analysis method was developed for the study and is described in detail elsewhere.[20] A brief outline of these analyses follows. In the first stage, differences (d) in mean outcome between the 2 periods of recruitment were calculated for each cluster. In the second stage, t tests were used to compare the mean of d between clusters that received the experimental intervention in Phase 1 versus Phase 2. To allow for differences in sample sizes,