

This thesis describes the effect of the Infant Behavioral Assessment and Intervention Program (IBAIP) on the developmental and behavioral outcome of very low birth weight (VLBW) infants (< 32 weeks and/or < 1500 gram) at 6 and 24 months of corrected age and evaluates the clinimetric properties of the Infant Behavioral Assessment (IBA).

Introduction

Chapter 1 provides an introduction that describes the incidence of preterm birth and its associated risks, the motivation for this study, and the basic principles of the used early intervention program.

Because of an increasing incidence of preterm births and a remarkably decreased mortality rate more and younger VLBW infants are discharged home after neonatal intensive care. Despite advances in perinatal care VLBW infants are at increased risk for neurodevelopmental disabilities. Recent studies report a shift from severe disabilities, such as cerebral palsy, to multiple mild problems in different developmental domains. About 50% of VLBW infants have various mild disabilities, such as language disorders, learning disabilities, motor coordination problems, behavioral and/or social–emotional difficulties. In early adulthood, VLBW children may experience health and participation problems; 3 times as many 19 year old Dutch VLBW children were neither employed nor in school compared with the general Dutch population and many experience difficulties establishing social contacts.

Increasing evidence shows that these multiple mild disorders found in VLBW children are already apparent in early infancy. From a functional perspective they may be seen as problems to self-regulate. These self-regulatory efforts or competencies are modulatory mechanisms that infants use to approach information and respond in an adaptive fashion, to cope with sensory input, or to protect themselves from too much stimulation. Self-regulatory competence is seen as basic to social and cognitive development and its development relies heavily on the child's relationship with caregivers or parents. Parental sensitivity and responsiveness positively influences the infant's early experiences, supports self-regulatory competence, and may even compensate for the infant's perinatal problems. Therefore, the importance of early preventive support for VLBW infants and their parents, who undergo additional stress, has been widely recognized.

However, children who experience mild problems, and those with both biological and social risk factors, appear to receive least health services during critical periods in their development. Moreover, despite growing evidence of the important role of environmental factors on child development, there is a lack of effective post-discharge early intervention programs. New directions in early assessment and intervention recommend the use of multidimensional and functional assessments to early identify problem areas in the infant's functioning and participation as well as a more integrated intervention approach. This recent knowledge and the positive short term effects of the hospital-based Newborn Individualized Care and Assessment Program (NIDCAP) inspired us to introduce the IBAIP, in order to support very low birth weight infants and their parents after discharge from hospital. The IBAIP, based on the same theory as NIDCAP (the "Synactive Theory" by H.AIs) is designed for infants at risk and can be used until approximately 8 months of age. The IBAIP aims to support the infant's self-regulatory competence as well as the infant's developmental functions in an integrative way, via responsive and positive parent-infant interactions. Assessment tool of the IBAIP intervention is the IBA. The IBA evaluates physiologic, motor, state, and attention / interactive characteristics, in order to investigate the infant's efforts and/or competence to approach information, to self-regulate and the infant's expressions of stress, thus enabling individual developmental support.

A multi-centre randomized effect-study on the IBAIP in a VLBW infant population was started as evidence based services are needed to assist parents to support their infant's resilience after discharge from hospital.

Pilot studies

Chapter 2 and 3 describe 2 pilot studies that were performed on the IBA and the IBAIP, respectively, between 1999 and 2002.

Chapter 2 describes the first pilot study in which we explored the ability of the IBA to discriminate between term and preterm behavior. We described the neurobehavioral and developmental profile of 20 low-risk VLBW infants at term, 3 and 6 months corrected age, and compared their profile with 10 healthy term infants. At term age the measurements consisted of the Neonatal Behavioral Assessment Scale (NBAS) and the IBA. At 3 and 6 months corrected age the infants were assessed with the IBA and the 3 scales of the Bayley Scales of Infant Development II (BSID-II). The results of the IBA showed that both very

preterm and term infants demonstrated more approach and less stress behavior over time. However, VLBW infants, even when at low risk, showed significantly less approach and more stress compared to term infants, thus expressing more problems with self-regulation in early life. The developmental outcomes were also lower in very preterm than in term infants, as was shown in the mental and motor scale of the BSID-II. We concluded that the IBA was able to detect considerable differences between (low risk) preterm and term infants and changes in the infants' neurobehavioral performance over time, indicating that the IBA might be a valuable instrument in discriminating differences in self-regulation in early infancy.

Chapter 3 describes the second pilot study in which we explored the feasibility of the corresponding early intervention program of the IBA, the IBAIP, in a group of 20 low risk VLBW infants. The infants received 6 to 8 IBAIP interventions at home, from discharge until 6 months corrected age, by a pediatric physical therapist that was specially trained in the IBAIP. At the age of 6 months the infants' neurobehavioral organization and development were compared with the 20 VLBW infants from the first pilot study, who served as historical controls. The results from this study showed that at 6 months, intervention infants demonstrated less stress and more approach behaviors (indicating more subsystem stability, information processing behavior and engagement in interactions) on the IBA compared with the historical control group. In addition, we found that the intervention infants scored significantly higher on the mental, motor and behavioral scale of the BSID-II, and that there was an increasing divergence on all outcomes between the 2 groups over time.

We concluded that these results warranted further evaluation of the IBAIP in a randomized controlled trial. In addition, we planned to evaluate this intervention program not only on infant outcomes, but also on parental well-being and parent-infant interaction, with long-term follow-up.

Chapter 3 also contains a Letter to Editor, which is a reaction on an article by Dr. H.Als that showed enhanced brain function and structure as well as improved developmental outcomes due to NIDCAP, in a group of low-risk VLBW infants at the corrected age of 9 months. In our letter we confirmed her experiences in our similar group of VLBW infants after post-discharge intervention with the IBAIP. Both NIDCAP and IBAIP seem to improve outcomes on the Behavior Rating Scale (BRS) of the BSID-II. Motor quality on the BRS, however, proved to be more improved of after NIDCAP than after IBAIP intervention.

The multi-centre randomized controlled trial

In 2004 we started a multi-centre randomized controlled trial to determine both the effect of the IBAIP on the VLBW infants' developmental and behavioral outcome, and on the parent's wellbeing and parent-infant interaction. Two level III hospitals and all 5 city hospitals participated in this study.

Recruitment took place between January 2004 and April 2006. A total of 315 VLBW infants whose parents lived in Amsterdam were eligible for the study. Infants with severe congenital abnormalities, infants born of mothers with a documented history of illicit drug use or severe physical or mental illness, infants from non-Dutch speaking families for whom an interpreter could not be arranged, and infants participating in other trials were excluded. Ultimately 176 infants participated. Baseline assessment and randomization took place between 35-38 weeks postmenstrual age (PMA); 86 infants were assigned to the intervention group and 90 infants to the control group. Infants and parents of the intervention group received 1 intervention session before discharge and 6 to 8 home interventions up to the corrected age of 6 months. Interventions were carried out by 6 pediatric physical therapists specially trained in the IBAIP. Control infants received standard care and, if required, additional pediatric physical therapy by a non-IBAIP trained physical therapist. The implementation of the IBAIP by pediatric physical therapists resulted in a comprehensive intervention model in which "prevention" and "treatment" overlapped to a large extent, supporting the parents, the evolving infant-parent relationship and the infant's emerging functions.

At 6 and 24 months corrected age the mental, motor and behavioral scales of the Dutch version of the BSID-II were used to assess developmental and behavioral outcomes. At baseline and 6 months corrected age neurobehavioral competence was assessed with the IBA. At 24 months corrected age the Child Behavioral Checklist 1½-5 (CBCL) was used to score the child's behavioral performance as rated by the parents. Neurological examinations at 6 and 24 months were conducted as described by Touwen. At both ages the motor and/or mental scales of the BSID-II were the primary outcome measures. At 6 months, secondary outcomes were the IBA, the behavioral scale of the BSID-II and neurologic outcome measures. At 24 months secondary outcomes were the behavioral scale of the BSID-II, the CBCL and neurologic outcome measures.

Chapter 4 describes the effect of the IBAIP on developmental and (neuro) behavioral outcomes in VLBW infants at 6 months corrected age, directly after the termination of the intervention. At 6 months all 86 intervention infants and 83 out of 90 control infants were available for follow-up. Despite randomization,

more infants in the intervention group were < 28 weeks gestational age (GA). In addition, the infants in the intervention group had more septic episodes and were longer oxygen-dependent compared to the control group.

After adjustment for baseline characteristics, intervention effects of 7.2 points on the mental and 6.4 points on the motor scale favored the intervention infants. Intervention infants also showed significantly higher scores on the behavioral scale of the BSID-II compared with control infants. Moreover, the outcomes on the IBA showed more approach and less stress over time. No interactions between intervention and perinatal characteristics of the infant or maternal socio-demographic factors were found to reveal which infants or parents profited most from the intervention.

We concluded that the IBAIP improved the mental, motor, and behavioral outcomes of VLBW infants at 6 months corrected age and hypothesized that enhanced self-regulatory competence may provide a strong foundation for the infants' next developmental steps.

Chapter 5 describes the effect of the IBAIP on developmental and behavioral outcomes in VLBW infants at 24 months corrected age. At that age 97% of the intervention infants and 89% of the control infants were available for follow-up. Intervention and control infants differed in some perinatal characteristics, e.g. more infants in the intervention group were < 28 weeks GA, they were longer oxygen dependent and there were more boys in the intervention group, compared to the control group.

After adjustment for baseline differences and maternal education, an intervention effect of 6.4 points on the motor scale of the BSID-II favored the intervention infants. Groups did not differ on the mental scale, the behavioral scale of the BSID-II, or on the CBCL. A significant interaction between intervention and infants with bronchopulmonary dysplasia (BPD, oxygen dependence \geq 36 weeks) and infants with combined biological and social risk factors (a combination of low maternal education and abnormal cranial ultrasound and/or BPD) was found, indicating that these groups profited most from the intervention. Post-hoc subgroup analyses showed improved motor as well as improved mental outcomes in these 2 high risk intervention subgroups.

Apart from the outcomes described above, significantly less intervention infants received paramedical services (pediatric physical therapy, occupational therapy and/or speech therapy) between 6 and 24 months and they were more compliant for follow-up, which underlines the positive effects of the intervention. We concluded that the IBAIP shows sustained motor improvement in VLBW infants until 2 years corrected age.

Clinimetric properties of the IBA

The data from the trial described above were subsequently used to evaluate the clinimetric properties of a standardized version of the IBA.

Chapter 6 presents the outcomes of our study on the inter-observer reliability, sensitivity and responsiveness of the IBA. Inter-rater reliability was based on 40 videos scored by 2 independent observers. Sensitivity was evaluated by investigating if the IBA was able to discriminate between neurobehavioral outcomes of subgroups of infants with or without developmental risk factors, like $GA \leq 28$ weeks, $O2 \geq 28$ days, and severe abnormal cranial ultra sound at 35-38 weeks PMA. IBA responsiveness was investigated over the period 0 to 6 months in the total group and in 2 subgroups of infants with $O2 \geq 28$ days.

Inter-observer agreement was moderate (in approach) to good (in self-regulation and stress) and observers achieved an item-by-item agreement of 93% for the total assessment. The IBA proved to be sensitive for differences in neurobehavior in infants with or without $GA \leq 28$ weeks and in infants with or without $O2 \geq 28$ days. These outcomes were comparable with those found with hands-on neonatal neurobehavioral assessments at the same age. The IBA discriminated infants with severe abnormal cranial ultrasound findings only in state approach. Large Effect Sizes over time were found in the total group and in the 2 subgroups of infants with $O2 \geq 28$ days. The IBA revealed the largest neurobehavioral changes in intervention infants with $O2 \geq 28$ days, which is in agreement with the improved developmental outcomes of these infants in our trial. Neurobehavioral changes were least large in control infants with $O2 \geq 28$ days, which is consistent with the strong negative impact of long-term oxygen dependency on developmental outcome in our RCT.

This study indicated that the IBA is a reliable, sensitive and responsive tool to detect subtle neurobehavioral changes in infants from 0 until 8 months developmental age. Complementary use of the IBA to neurological and functional developmental measures provides a more comprehensive picture of the infant's development, including the infant's participation in interactions and well-being. Additional valuation of the IBA in different infant populations and at different ages is warranted.

General discussion

Chapter 7 provides a general discussion of the results, the strengths and limitations of the study, followed by recommendations and conclusions.

The Infant Behavioral Assessment and Intervention Program effectively assists parents to support the resilience of their very preterm infants, as the program improves the infant's mental and motor development, behavior and self-regulatory competence at 6 months and the child's motor outcome at 24 month corrected age. Future research is needed to determine whether this early intervention program indeed improves the resilience of the most vulnerable infants and their parents, such as infants with bronchopulmonary dysplasia and infants with combined biological and social risk factors. Studies evaluating the effect of the IBAIP until early school-age are underway. Apart from long-term follow-up, we also need to focus on the development and evaluation of age-appropriate interventions to support very preterm infants and their parents in a continuous preventive chain.

The IBA proves to be a valid instrument to guide and evaluate neurobehavioral organization and participation in very preterm infants. Additional research is required to validate the IBA in other infant populations and different ages.

Grants for implementation of the IBAIP have been obtained, in order to disseminate evidence based preventive support for very preterm infants and their parents after discharge from hospital. Complementary support for the parents' well-being needs further study, in order to determine if such an extension improves the effectiveness of the program.