Developmental care and very preterm infants : neonatal, neurological, growth and developmental outcomes

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CHAPTER 4

The Influence of Basic Developmental Care on Growth, Neurological, Cognitive and Psychomotor Development at 1 and 2 years of age in Very Preterm Infants

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Abstract

Objective: Randomized controlled trial investigating the effect of basic elements of developmental care (DC) on growth and neurodevelopment in infants born < 32 weeks.

Study design: Infants were randomized within 48 hours of birth to DC group or standard care (C) group. Outcome measures at 1 and 2 years corrected age (CA) were growth, standardized neurological exams and mental (MDI) and psychomotor (PDI) development (Dutch version of the Bayley Scales of Infant Development II). Outcome parameters were compared with the t-test, Mann-Whitney test or Chi-square test where appropriate. Linear regression was used to evaluate the influence of the duration of the intervention on 1 and 2 year outcomes.

Results: 192 infants were recruited (DC=98; C=94). Thirteen infants (DC=7, C=6) were excluded because they were admitted less than or died within the first 5 days. In total, 179 infants met inclusion criteria. In-hospital mortality was 12/91 (13.2%) in DC group and 8/88 (9.1%) in C group. 147 children (DC= 74, C= 73) at 1 year and 142 children (DC=72, C=70) at 2 years were assessed. No significant difference in growth, neurological outcomes or MDI was found. A positive trend in PDI at 1 year (p=0.05) did not continue once the children reached 2 years. When neurological and developmental scores were combined, the C group showed more definitely abnormal scores than the DC group at both ages, but this did not reach the level of significance.

Conclusions: Basic developmental care has a positive effect on psychomotor development at 1 CA, but this improvement does not continue at 2 years CA in infants born < 32 weeks. No significant difference in neurological and mental development or growth was found.

Introduction

The care and survival rate of preterm born infants has in recent years continued to improve [1-4]. Even as survival rates are improving, the risk of developmental disabilities remains high and increases as the gestational age at birth decreases [1,5-7]. The technological advances are improving the survival rates of preterm infants, but the question remains how these vulnerable infants can best be supported during their stay in the neonatal intensive care unit (NICU) in order to positively influence their developmental outcomes. Since the 1980's, programs have been created to support the infant's development in the NICU while at the same time providing the necessary medical and nursing interventions. Many of these programs are based on developmental care, with the most comprehensive being the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) developed by Als, an individual approach in which caregiving is based on the infant's behavior [8,9]. The first studies of the effectiveness of the NIDCAP developmental care program in the 1980's and 1990's showed promising results, however the sample size of the studies was small [10-14]. Follow-up studies published to date up to preschool age have been scarce and the results are conflicting[10,15-18]. In a recent Cochrane review of developmental care the need for larger trials, more follow-up and studying the effects of different aspects of developmental care was emphasized [19].

The aim of this randomized controlled trial (RCT) was to explore the effectiveness of the implementation of basic Developmental Care on growth, mental and psychomotor development and neurological outcome at 1 and 2 years CA of preterm infants born < 32 weeks gestational age. We hypothesized that by reducing stress and promoting physiological stability through the use of incubator covers and nesting, the stability provided to the infants during their NICU hospitalization would positively affect their later growth and development.

Patients and Methods

The study was carried out from April 2000 to June 2004 at a tertiary NICU at 2 locations in the Netherlands: Leiden University Medical Center in Leiden and Juliana Children's Hospital in The Hague. Inclusion criteria were: infants born with a gestational age < 32 (31+6) weeks. Exclusion criteria included: infants with major congenital anomalies, infants needing major surgery and infants of drug-addicted mothers. After parental informed consent was obtained by the resident or staff member on call, infants were randomized within 48 hours of birth to the Developmental care (DC) group or the Control (C) group using sealed envelopes made

in groups of 6 using a computer generated randomization allocation. According to protocol, infants in both groups who were admitted for less than 5 days were excluded from follow-up because the duration of the basic developmental care intervention was hypothesized not to be long enough to obtain an effect. A power analysis performed before the study showed that a sample size of 140 infants was needed to show a significant difference (p level < .05) with a power of 80%, based on the expected difference of half a standard deviation (7.5) on the developmental test scores at 1 and 2 years corrected age (CA).

The intervention included the reduction of light and sound through the use of standardized incubator covers and supporting motor development and physiological stability by positioning the infant in ways that encourage flexion and containment through the use of standardized nests and positioning aids. Infants in the control group received standard care, which at that time consisted of no covers or nesting[20]. The Ethical committees of both locations approved the study.

Measures

Infant characteristics (gestational age, birth weight, gender, small for gestational age, inborn, Apgar scores, CRIB score) and parental characteristics (age, ethnicity, educational level) were collected to compare groups (Tables 1 and 2). Inborn infants were infants born in the participating tertiary neonatal center. Severity of illness was analyzed using the CRIB (Clinical Risk Index for Babies) score which assesses initial neonatal risk. Scores are given for birth weight, gestational age, maximum and minimum fraction of inspired oxygen and maximum base excess during the first 12 hours, and the presence of congenital malformation [21].

Follow-Up

Children were assessed at 1 and 2 years of corrected age for prematurity (CA) for growth and neurodevelopment by neonatologists experienced in developmental assessments and blinded to the group assignment of the child. A standardized neurological exam according to Touwen [22,23] at one year CA and Hempel [24] at two years CA was administered and classified as definitely abnormal (DA) when there was definite neurological dysfunction such as cerebral palsy; mildly abnormal (MA) in the presence of mild deviations in muscle tone regulation, reflexes, fine or gross motor performance or cranial nerve function; or normal (N).

Weight was measured on a pediatric digital scale, length was measured from crown to heel on a standard measurement board and head circumference was measured around the largest area of the head, occipital-frontal circumference (OFC), using a non-stretch tape measure.

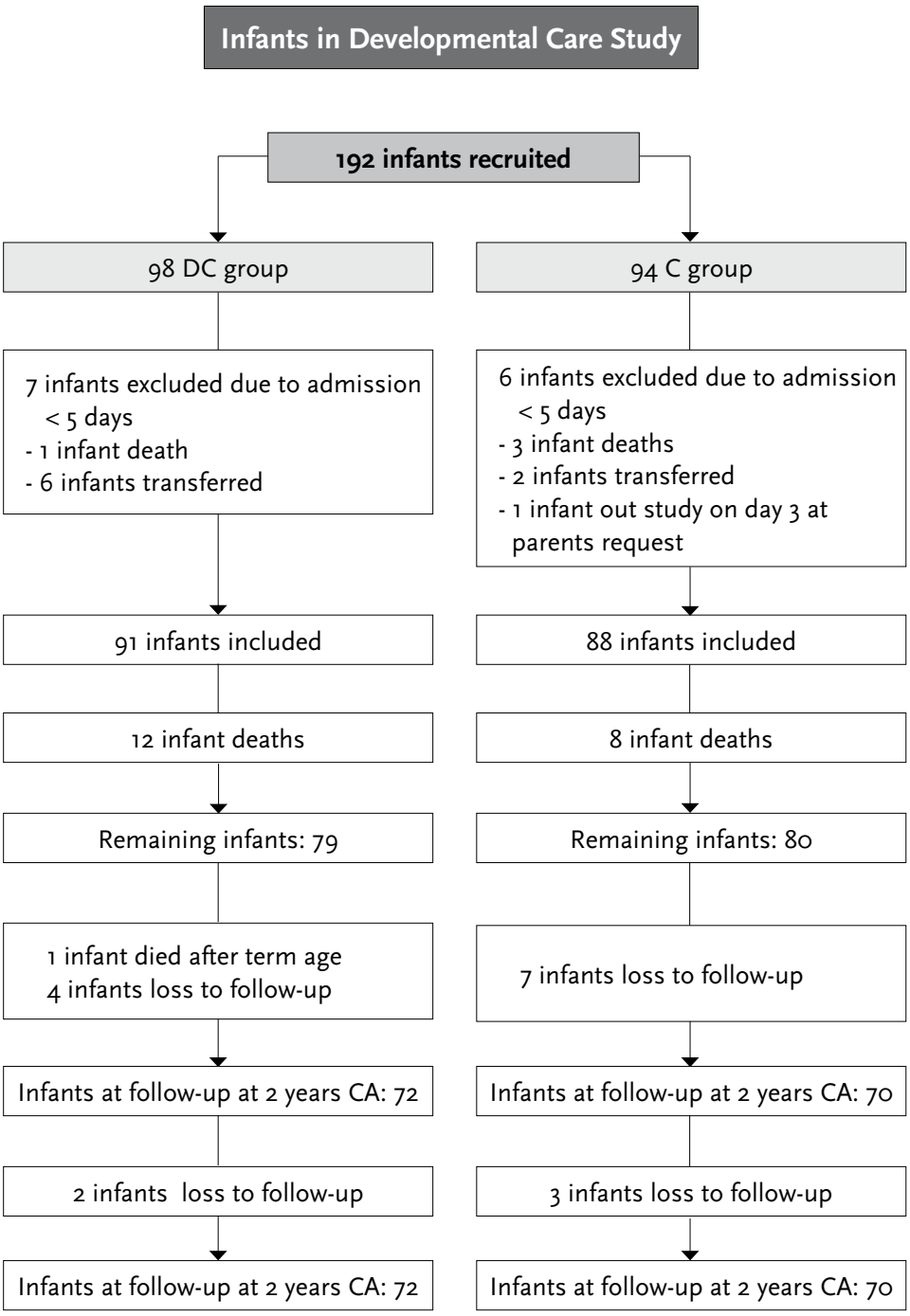
In addition, children were assessed at 1 and 2 years CA by psychology interns supervised by a clinical psychologist, who were blinded as to whether the child was in the DC or C group. Mental and psychomotor development was assessed using the Dutch version of the Bayley Scales of Infant Development II (BSID-II)[25,26]. The mean score of the mental developmental index (MDI) and the psychomotor developmental index (PDI) is 100, with 1 standard deviation (SD) of 15 points. An MDI or PDI ≥ 85 (≥ – 1 SD) is considered normal, an MDI or PDI between 70 and 84 (–2 to –1 SD) is considered mildly delayed and Index scores ≤ 69 (< – 2 SD) severely delayed. The Dutch norms, which had become available during our research, were used. To obtain a single outcome measure, neurological outcome, PDI and MDI were combined. When at least 1 of these 3 outcome measures was DA, children were considered DA, and when at least 1 outcome was MA, children were considered MA.

Statistical Analysis

Data was analyzed using SPSS 12.0 for Windows. The infant and parent characteristics were compared with the Chi-square test, the Chi-square test for trend or the two-sample t-test, where appropriate. Outcome parameters were compared between the two treatment groups with the t-test, Mann-Whitney test or Chi-square test where appropriate. P-values < 0.05 were considered significant. Linear regression was used to evaluate the influence of the duration of the intervention on 1 and 2 year outcomes by testing if there was an interaction effect between the intervention duration and the 2 treatment groups.

Results

In total 192 infants were recruited for the study; 98 in the DC group and 94 in the C group. Thirteen infants (DC=7, C=6) were excluded according to protocol because they were admitted less than 5 days or died within the first 5 days. One of the six infants in the C group was taken out of the study on day 3 at parents' request. This left a total of 179 infants that met inclusion criteria. Of the 179 included infants, 12/91 (13.2%) in the DC group and 8/88 (9.1%) in the C group died during hospitalization, with the main cause of death being cerebral or pulmonary complications. Two infants in each group died of NEC. There was no significant difference in the in-hospital mortality rate between the DC and C group (p=0.40). This left a remaining 159 infants (DC=79, C=80) for follow-up. At the 1 year assessment, there were 4 infants lost to follow-up in the DC group and 7 infants in the C group because they were either transferred to hospitals out of the health region or parents did not want


Infants in Developmental Care Study
192 infants recruited
98 DC group
94 C group
7 infants excluded due to admission < 5 days
- 1 infant death
- 6 infants transferred
6 infants excluded due to admission < 5 days
- 3 infant deaths
- 2 infants transferred
- 1 infant out study on day 3 at parents request
91 infants included
88 infants included
12 infant deaths
8 infant deaths
Remaining infants: 79
Remaining infants: 80
1 infant died after term age
4 infants loss to follow-up
7 infants loss to follow-up
Infants at follow-up at 2 years CA: 72
Infants at follow-up at 2 years CA: 70
2 infants loss to follow-up
3 infants loss to follow-up
Infants at follow-up at 2 years CA: 72
Infants at follow-up at 2 years CA: 70

to come back for follow-up. In addition, one infant in the DC group died between term age and 1 year. Between the 1 and 2 year assessment 2 children in the DC group and 3 children in the C group were lost to follow-up due to parents moving or not wanting to continue with the follow-up. The baseline data from the lost to follow-up infants was comparable to the infants that were assessed at follow-up (data not shown). There were 147 children: DC=74/79 (93.7%), C= 73/80 (91.3%) at 1 year corrected age and 142 children: DC=72/79 (91.1%), C=70/80 (87.5) at 2 years corrected age that were seen at the follow-up clinic of the total 159 surviving infants. The mortality rate and loss to follow up are shown in Figure 1.

There was no significant difference in infant characteristics between the DC and C groups assessed at 1 year or 2 years (Table 1). Parent characteristics (age, ethnicity and educational level) were similar in both groups with no significant differences found and are shown in Table 2.

Table 1. Infant medical background variables of children seen at 1 and 2 year follow-up

	DC n (%)	**C n (%)**	**DC n (%)**	**C n (%)**
	1 year		**2 years**	
Birth Characteristics	n=74	n=73	n=72	n=70
Gestational age mean in wks (sd) range	29.5 (1.6) 25.9-31.9	29.1 (1.9) 25.0-31.9	29.5 (1.6) 25.9-31.9	29.1 (1.9) 25.0-31.9
Birthweight mean in g, (sd) range	1248.4 (338.1) (585-2155)	1238.5 (337.2) (640-2080)	1266.3 (329.6) (585-2155)	1236.6 (338.5) (640-2080)
Male gender	39/74 (52.7)	46/73 (63.0)	38/72 (52.8)	44/70 (62.9)
SGA* SGA P < 10 and P ≥ 3 SGA P < 3	 8/74 (10.8) 6/74 (8.1)	 6/73 (8.2) 4/73 (5.5)	 8/72 (11.1) 4/72 (5.6)	 5/70 (7.1) 4/70 (5.7)
Inborn	46/74 (62.2)	46/72 (63.9)	45/72 (62.5)	44/70 (63.8)
Apgar scores at 5 minutes median (range)	n= 74 9.0 (2-10)	n= 72† 8.0 (5-10)	n= 72 9.0 (2-10)	n= 69† 8.0 (5-10)
CRIB Score mean (sd)* range	3.2 (2.9) 0-13	3.7 (2.9) 0-11	3.0 (2.7) 0-10	3.8 (3.0) 0-11

Data shown is n (%), unless otherwise indicated
Comparisons were done using chi-square test or t-tests where appropriate
* SGA: small for gestational age, P: percentile, CRIB: Clinical Risk Index for Babies
† Correct n is shown in table if there are missing values

Table 2. Parental demographic background variables

	DC n (%)	C n (%)	DC n (%)	C n (%)
	1 year follow-up		2 year follow-up	
Maternal age	n=74	n=73	n=72	n=73
mean in years (sd)	31.3 (5.1)	31.4 (4.9)	32.5 (5.1)	31.4 (4.9)
Paternal age	n=70	n=69	n=67	n=69
mean in years (sd)	34.3 (5.3)	35.0 (5.7)	35.0 (5.2)	35.0 (5.7)
Mother Caucasian	48/74 (64.9)	53/73 (72.6)	48/74 (64.9)	53/73 (72.6)
Father Caucasian	52/74 (70.3)	56/73 (76.7)	52/74 (70.3)	56/73 (76.7)
Education level mother*				
low	34/74 (46.0)	23/72 (32.0)	32/71 (45.1)	23/72 (32.0)
intermediate	24/74 (32.4)	33/72 (45.8)	23/71 (32.4)	33/72 (45.8)
high	16/74 (21.6)	16/72 (22.2)	16/71 (22.5)	16/72 (22.2)
Education level father*				
low	26/74 (35.2)	19/71 (26.8)	26/71 (36.6)	19/71 (26.8)
intermediate	30/74 (40.5)	29/71 (40.8)	28/71 (39.4)	29/71 (40.8)
high	18/74 (24.3)	23/71 (32.4)	17/71 (23.9)	23/71 (32.4)

Data shown is n (%), unless otherwise indicated
Comparisons were done using chi-square test (for linear trend) or t-tests where appropriate
* Low = vocational training, intermediate = high school, high = college/university

Growth

One child from the C group was not measured at 1 year of age. At 2 years of age one child from the DC group and one child from the C group were not measured. There was no significant difference found between the DC and C group in growth (weight in grams, height and head circumference in centimeters) at 1 or 2 years CA. When we calculated the standard deviation scores (SDS) using the Dutch growth charts, the DC group showed significantly better SDS for length than the C group and the weight (p=0.08) and head circumference (p=0.06) SDS showed a trend in favor of the DC group. There were however more infants in the C group (11.3 %) than in the DC group (4.4 %) that required postnatal corticosteroids (p=0.08), the usual dosage being 0.20 mg/kg/day in 2 doses with tapering of the dosage over a period of 16 days. As this may influence growth we corrected for use of postnatal steroids and then found no significant difference in growth SDS between the 2 groups (Table 3).

Developmental outcomes

At one year of age 145 children (DC=73, C=72) of the 147 children seen at follow-up were tested with the Bayley Scales-II-NL and at 2 years of age 140 (DC=70, C=70) of the 142 children seen at follow-up were tested. There were 3 children (DC=1, C=2) who were 13 or 14 months CA at the 1 year developmental follow-up and 8 children (DC=4, C=4) tested that were 26-27 months CA at the 2 year developmental follow-up, but their index scores were based on the norms for that age so we included them in the analysis. There was no significant difference in the mean age of all children assessed at the 1 and 2 year follow-up.

There were 2 children who did not have a developmental test due to illness or because they were uncooperative. At one year CA, the children in the DC group showed a trend of improvement (p=0.05) in the psychomotor developmental index (PDI) as compared to the C group but no significant difference (p=0.56) in their mental developmental index (MDI). At 2 years CA, this difference was no longer evident as both the MDI and PDI scores were comparable. While the PDI classifications at 12 and 24 months had a higher percentage of children in the C group with severe delays, this difference was not significant (p=0.27; p=0.20) (Table 4).

Neurological outcomes

There were 147 (DC=74, C=73) children who were assessed with a neurological exam at 1 year CA and 140 (DC=71, C=69) children at 2 years CA. Two children (DC=1, C=1) were not able to be tested at 2 years CA because they were uncooperative. There was no significant difference found between the DC and C group in neuromotor development at 1 year and 2 years CA. Although there were twice as many children in the C group with definitely abnormal scores at 1 year and more than 3 times as many C children at 2 years of age, the difference was not significant (Table 5).

Combining neurological development, MDI and PDI scores in a Total Outcome Score

When we combined the developmental and neurological score, the percentage of C group children that were definitely delayed at both 1 and 2 years compared to the DC group was much higher (1 year: DC=12.2%, C=23.3%; 2 year: DC=5.6%, C=18.3%), however the difference did not reach the level of significance (Table 5).

We then carried out a linear regression analysis to see if the number of days infants received the DC intervention influenced the neurological outcomes at 1 and 2 years according to Touwen and Hempel by testing if there was an interaction effect between the intervention duration and the two treatment groups. There was no

Table 3. Growth outcomes at 1 and 2 years CA

	1 year			2 years			
Growth outcomes	**DC**	**C**	***p* value**	**DC**	**C**	***p* value**	***p* value** [§]
Weight	n=74	n=72		n=72	n=69		0.18
mean in kg, sd	9.31 (1.38)	9.11 (1.28)	0.37	11.9 (1.5)	11.5 (1.4)	0.10	
SDS[‡] (mean, sd)	-0.72 (1.27)	-0.94 (1.28)	0.31	-0.69 (1.12)	-1.03 (1.1)	0.08	
Head circumference	n=72[†]	n=71		n=71	n=68		0.10
mean in cm, sd	46.4 (1.7)	46.2 (1.7)	0.42	48.6 (1.7)	48.2 (1.7)	0.14	
SDS [‡] (mean, sd)	-0.15 (1.10)	-0.38 (1.11)	0.21	-0.06 (1.03)	-0.41 (1.09)	0.06	
Length	n=74	n=70		n=72	n=69		0.10
mean in cm, sd	74.7 (3.7)	74.1 (3.6)	0.36	87.3 (3.6)	86.0 (4.0)	0.06	
SDS[‡] (mean, sd)	-0.54 (1.27)	-0.77 (1.31)	0.29	-0.36 (1.06)	-0.75 (1.24)	0.04*	

Comparisons were done using t-tests;
* *p* value significance = < 0.05
[†] Correct n is shown in table if there are missing values
[‡] SDS (standard deviation scores) according to Fredriks et al [33]
[§] *p* value after correction for postnatal steroid use

Table 4. Mental and psychomotor development at 1 and 2 years corrected age (CA)

	DC Mean (sd or %)	C n (sd or %)		DC Mean (sd or %)	C n (sd or %)	
	1 year CA			2 years CA		
	n=73	n=72	*p* value*	n=70	n=70	*p* value*
Age at test in months mean (sd) range	 12.14 (0.34) 11.2-13.2	 12.14 (0.40) 11.4-12.1	0.99	 24.3 (0.68) 23.2-26.4	 24.1 (0.47) 23.5-27.4	0.12
MDI mean (sd) range	102.3 (15.1) (57-138)	101.2 (15.7) (55-132)	0.66	100.9 (14.9) (55-130)	102.3 (16.2) (56-132)	0.58
PDI mean (sd) range	99.2 (17.0) (55-135)	93.7 (16.1) (55-124)	0.05	96.0 (14.6) (55-121)	92.3 (17.0) (55-145)	0.18
MDI classification scores† ≥ 85 70-84 ≤ 69	 64 (87.7) 7 (9.6) 2 (2.7)	 62 (86.1) 7 (9.7) 3 (4.2)	0.69	 61 (87.1) 7 (10.0) 2 (2.9)	 60 (85.7) 9 (12.9) 1 (1.4)	1.00
PDI classification scores† ≥ 85 70-84 ≤ 69	 62 (84.9) 6 (8.2) 5 (6.8)	 56 (77.8) 8 (11.1) 8 (11.1)	0.27	 54 (77.1) 13 (18.6) 3 (4.3)	 48 (68.6) 16 (22.9) 6 (8.6)	0.20

Comparisons were done using chi-square test (for linear trend) or t-tests where appropriate

* p value significance = < 0.05

† ≥ 85= normal or above normal, 70-84=mildly delayed, ≤ 69=significantly delayed

Table 5. Neurological outcomes and combined score of neurological outcomes, MDI and PDI at 1 and 2 years corrected age (CA)

	1 year CA				**2 years CA**		
	DC n (%)	**C n (%)**			**DC n (%)**	**C n (%)**	
	Neurological Outcome*				Neurological Outcome*		
	n=74	n=73	*p* value		n=71	n=69	*p* value
- N†	56 (75.7)	52 (71.2)	0.25	- N	50 (70.4)	46 (66.7)	0.18
- MA	13 (17.5)	10 (13.7)		- MA	17 (24.0)	11 (15.9)	
- DA	5 (6.8)	11 (15.1)		- DA	4 (5.6)	12 (17.4)	
	Combined neurological score MDI and PDI				Combined neurological score MDI and PDI‡		
	n=74	n=73			n=72	n=71	
- N†	48 (64.8)	45 (61.6)	0.26	- N	38 (52.8)	37 (52.1)	0.25
	17 (23.0)	11 (15.1)		- MA	30 (41.7)	21 (29.6)	
- MA	9 (12.2)	17 (23.3)		- DA	4 (5.6)	13 (18.3)	
- DA							

Comparisons were done using chi-square test (for linear trend) where appropriate

* neurological exam according to Touwen at 1 year and Hempel at 2 years

† N=normal, MA=mildly abnormal, DA=definitely abnormal (MDI/PDI scores ≥ 85 = N, 70-84=MA, ≤69=DA)

‡ one DC group child's en 2 C group children's combined scores were derived from the PDI and MDI

significant effect on the neurological outcome at 1 year (p=0.79) or 2 years (p=0.67) or on the combined neurological and developmental scores at 1 year (p=0.86) and 2 years (p=0.60) found.

Discussion

This randomized controlled trial showed that basic developmental care (incubator covers and positioning aids) for infants born < 32 weeks gestational age has a positive effect on psychomotor development at 1 CA, but this improvement does not continue at 2 years CA and no significant effect on MDI at 1 and 2 years CA. There may be some positive influence on neurological outcomes at 1 and 2 years as there were more DA scores in the C group than in de DC group; however the effect was not statistically significant.

There were also some differences seen between the neuromotor and the developmental scores. While the percentages of children scoring severely delayed on the PDI were comparable with scores of definitely abnormal on the Touwen exam at 1 year of age, there were twice as many children in the C group who scored 'definitely abnormal' in the Hempel neuromotor exam than children that scored 'severely delayed' in the PDI of the Bayley exam at 2 years of age. One explanation for this discrepancy is that the Touwen and Hempel measure qualitative minor neuromotor dysfunction whereas the BSID-II PDI measures motor skills and identifies motor delays and gives a quantitative score. We therefore combined the scores into a single 'mildly abnormal' or 'definitely abnormal' score in order to get a clearer picture of the outcomes. We observed more children in the C group with scores of definitely abnormal; however the difference was not significant. There appeared to be a shift to mildly abnormal in the DC group as both groups had comparable percentages of normal scores.

In addition, we looked at the amount of days infants had received developmental care when hospitalized to see if that positively influenced neurological and developmental outcomes at 1 and 2 years, but found no interaction effect.

To get a better picture of the growth outcomes, we corrected growth for CA by using standard deviation scores (SDS), which did show a significant improvement in length at 2 years in the DC group and a trend in improved head circumference growth at 2 years. However once SDS was corrected for postnatal steroid use, these differences were no longer apparent.

To date, there has been no large RCT examining growth and neurodevelopmental outcome of a basic developmental care program. Therefore comparison to other studies is not possible. Most of the studies examined the more intensive individualized NIDCAP developmental care program and had smaller sample sizes and mixed results [15-17,19]. Most outcomes of developmental care studies have focused on short term morbidity and growth or neurodevelopment up to 9-12 months[11,15,17] with only one study that followed the infants' development to 3 years which showed no significant difference in development between the two groups[16]. There were no

studies reported in the Cochrane meta-analysis examining the effect of basic developmental care programs such as ours on neurodevelopment[19].

We have tried with this study to answer some of the questions posed concerning developmental care and follow-up to 2 years of age. The percentage of lost to follow-up was low and the assessors were blinded to the treatment group the children participated in and the neurological outcomes were obtained using a standardized neurological examination.

Our conclusion is that a less intensive, cost-saving form of developmental care has a positive effect on psychomotor development at 1 year of age but no significant effect on neurodevelopment of preterm infants at 2 years of age. Perhaps a more intensive, individualized developmental care program such as the NIDCAP program based on a larger sample size than previous studies will show improved outcomes.

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