



The Stockholm Neonatal Family-Centered Care Study: Effects on salivary cortisol in infants and their mothers

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ABSTRACT

Background: Parental involvement in the care of preterm infants in neonatal intensive care units (NICUs) is common, but little is known about the effect on stress responses in mothers and infants.

Aims: The aim of this study is to evaluate the effect of family-centered care on salivary cortisol reactivity in mothers and preterm infants and the correlation between the mothers' and the preterm infants' salivary cortisol levels.

Methods: This study is part of a randomized controlled trial conducted at two level-II NICUs, including Family Care (FC), where parents were able to stay 24 h/day from admission to discharge, and Standard Care (SC). To investigate the cortisol response, saliva was collected from 289 preterm infants and their mothers before and after a diaper change at the time of discharge.

Results: No significant differences were found between the two groups in salivary cortisol reactivity, either in mothers or in infants. The results revealed a correlation between preterm infants' and their mothers' baseline and response cortisol in the FC group: $r = 0.31$ ($p = 0.001$) and $r = 0.24$ ($p = 0.01$), respectively. Such correlation was not observed in the SC group: $r = 0.14$ ($p = 0.14$) and $r = 0.18$ ($p = 0.07$), respectively.

Conclusions: Family-centered care had no effect on salivary cortisol reactivity during diaper change. However, sharing the same environment may increase the concordance between preterm infants' and their mothers' salivary cortisol levels.

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1. Introduction

The preterm infant requiring neonatal intensive care is often separated from the mother. The mother and the infant stay at different wards, in different environments making parental caregiving more difficult [1,2]. It is well known that mothers of preterm infants are experiencing more stress compared to mothers of healthy full-term infants and that the separation from the infant is one major stressor [3,4]. Animal studies have shown that rodent pups separated from the dam for 3 h per day in the neonatal period become more sensitized to stressors compared to pups separated for shorter periods or not at all [5,6]. Repeated maternal separations have also caused increased levels of the stress hormone cortisol in rhesus monkey offsprings [7,8]. Infants in a Neonatal Intensive Care Unit (NICU) are

exposed to several stressful and painful procedures every day [9]. However, both in animal and in human infant studies, quality of maternal caregiving behavior, such as high sensitivity and responsiveness to the infant's signals, has been found to buffer the infant's response to stressors, resulting in a lower rise in cortisol [10–14]. Providing facilities for parents to stay in the NICU, sharing the same environment round the clock might be an important intervention to satisfy the infant's need for parental responsiveness, stimulation and proximity and consequently lower the cortisol reactivity in response to stressful interventions [6]. Family-centered care places the needs of the infant in the context of the family [15]. Since information-sharing, participation, and collaboration are cornerstones of this model, parental presence might be an important condition for the application [16]. Parental presence from admission to discharge has previously proven to decrease the total length of hospital stay with 5.3 days and decrease the risk of moderate-to-severe bronchopulmonary dysplasia [17].

Infants are born with a functioning stress response system allowing them to react to changes in the external and internal environment [18–20]. The fetal hypothalamic–pituitary–adrenal axis (HPA axis), resulting in cortisol release functions from at least the beginning of the second trimester [21]. Measurement of cortisol in saliva instead

Abbreviations: Clinical Risk Index for Babies, CRIB; Family Care, FC; Gestational Age, GA; General Linear Model, GLM; Hypothalamus Pituitary Adrenal, HPA; Neonatal Intensive Care Unit, NICU; Standard Care, SC.

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of plasma is valuable and feasible when studying stress reactivity early in life [22]. Handling such as in a diaper change has frequently been used as a stressor in studying stress in infants younger than three months since handling does not involve additional pain [23–28]. Although cortisol has been measured frequently to study the stress response in full-term infants [29], studies of salivary cortisol reactivity in preterm infants admitted to a NICU are more rare and usually involves fewer participants. Salivary cortisol reactivity in preterm infants has previously been studied in relation to heel lance [30–35], massage [36], skin-to-skin care or holding [36–38], screening for retinopathy of prematurity [39], and diaper change [40]. Methodological issues as obtaining optimal sample volumes of saliva without using saliva stimulants is one reason explaining the small number of studies of preterm infants in NICU [31,34,41–43]. However, a method to collect saliva and analyze cortisol in small volumes was published some years ago making studies of salivary cortisol in preterm infants feasible [44,45].

It has been suggested that genetic as well as environmental factors can affect the concordance between the mother's and infant's cortisol values [38,46–49]. A correlation in cortisol levels has been described between three-month-old infants and their parents [50] and also between six-month-old infants and their mothers, but not their fathers possibly because the infants spent most of their time in the same environment as their mothers, who were the primary caregivers [49]. A correlation in cortisol levels has also been found for twins sharing the same environment [51,52] but not for twins living in different environments [53]. The concordance between mothers' and preterm infants' cortisol values has not been studied.

The aims of the present study were to evaluate (i) the effect of family-centered care on salivary cortisol reactivity in mothers and infants and (ii) the correlation between mothers' and infants' salivary cortisol during a diaper change.

2. Patients and methods

2.1. Design

This study is part of a randomized controlled trial comparing outcomes of family-centered care in two level-II NICUs in Stockholm: Sachs' Children's Hospital and Karolinska University Hospital Danderyd. Each NICU had two wards, one family-centered and one with standard care. Recruitment to the study took place between September 2006 and March 2008. The infants were allocated to Family Care (FC) or Standard Care (SC) on admission to the respective NICU by a staff nurse (Fig. 1). Allocation was by sealed, opaque, and consecutively numbered envelopes. The study design has been described in detail previously [17]. The study was approved by the Ethical Regional Board in Stockholm, (D# 2006/532-31/3, 2008/1392-32).

2.2. Family-centered wards

The family-centered wards had 13 and 10 infant beds, respectively. There were separate rooms for each family, including beds for both parents and infant, a private bathroom, and equipment for supplementary oxygen and telemetric wireless monitoring. At least one of the parents was expected to stay round the clock from admission until discharge. Each family-centered ward had a four-bed intensive care room, with staff continuously present. Infants in the intensive care rooms moved to the family rooms as soon as they reached a stable state – usually around 32–33 weeks postmenstrual age.

2.3. Standard-care wards

The standard care wards had 15 and 14 infant beds, respectively, with one four-bed intensive care room in each ward and intermediate care rooms with two to four beds. These wards had a couple of rooms for parents; however, opportunities to stay overnight were limited to

a few days prior to discharge. Parents were not asked to record their presence at the ward since this may evoke stress and senses of guilt for those who cannot manage to stay as much as they would like to. In general, mothers remained with the infants on the ward during daytime, while fathers made shorter visits.

2.4. Inclusion criteria

Inclusion criteria were preterm birth (<37 weeks), no diagnosis of major congenital malformation at admission, and requiring in-hospital care in a level-II NICU.

2.5. Participants

Of 652 eligible infants, a total of 366 infants (322 families) were randomized to FC or SC [17]. After randomization, 18 families declined to participate, seven families in FC and 11 in SC (Fig. 1). Eight families in FC and 15 in SC (8 and 17 infants, respectively) were never approached for consent. The reasons in FC were requiring level-III care ($n=2$), maternal medical reasons ($n=1$), moving to a hospital closer to home ($n=1$), discharge to the maternity ward ($n=3$), and language difficulties ($n=1$). The reasons in SC were requiring level-III care ($n=4$), heart surgery ($n=1$, +1 twin), transfer to specialized care due to liver disease ($n=1$), discharge to the maternity ward ($n=4$, +1 twin), and language difficulties ($n=5$).

In total, 289 infants were included in the analysis: 152 (91%) in FC and 137 (89%) in SC.

Six families in SC did not receive the allocated intervention (Fig. 1). The reasons for this crossover were admission to the wrong ward by mistake after a stay at a level-III NICU ($n=1$), medical indication to improve infant stability by creating a quieter environment ($n=1$), and to enhance mother–infant contact ($n=4$). All these decisions were made by the attending neonatologist.

2.6. Characteristics

There were no significant differences in gender, mode of delivery, Clinical Risk Index for Babies (CRIB) score [54], gestational age (GA) at birth, or number of infants receiving breast-milk respectively formula between the two groups of infants (Table 1). All mothers with threatening premature labor before 33 weeks of gestation are given steroids (Betamethasone) in Sweden. Five infants were treated with steroid inhalation at the time of saliva sampling, four in SC and one in FC. There were no significant differences in age, marital status, primipara, or twin mothers between the two groups of mothers. There was a significant difference in ethnicity between the groups (Table 1).

2.7. Salivary cortisol

To investigate the cortisol reactivity, saliva was collected before (baseline) and 30 min after (response) a diaper change performed by the mother [55]. The mother–infant dyad was approached the same day or the day before hospital discharge. Saliva was collected from mothers and infants using cotton buds, as described previously [44,45]. Because of components that can disturb the salivary cortisol analysis, saliva was collected one hour after food intake. After collection the saliva was centrifuged, frozen at -20°C , and stored at -70°C . A radioimmunoassay for cortisol was used to analyze cortisol concentrations in saliva (Orion Diagnostica, Turku, Finland) [44]. Samples were run in duplicate, and all samples from each individual were run in the same assay. Intra-assay coefficients of variation were 12% at 2.0 nmol/L and 6% at 10.0 nmol/L.

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